**OMNIBUS SOLICITATION OF THE
NATIONAL INSTITUTES OF HEALTH,
CENTERS FOR DISEASE CONTROL AND PREVENTION,
FOOD AND DRUG ADMINISTRATION, AND
ADMINISTRATION FOR CHILDREN AND FAMILIES FOR**

SMALL BUSINESS INNOVATION RESEARCH (SBIR)

AND

SMALL BUSINESS TECHNOLOGY TRANSFER (STTR)

GRANT APPLICATIONS

NIH, CDC, FDA, and ACF Program Descriptions and Research Topics

SUBMISSION DATES

APRIL 5, AUGUST 5, AND DECEMBER 5, 2011

**(MAY 7, SEPTEMBER 7, 2011 AND JANUARY 7, 2012
FOR AIDS/AIDS-RELATED RESEARCH)**

National Institutes of Health (SBIR and STTR)

Centers for Disease Control and Prevention (SBIR)

Food and Drug Administration (SBIR)

Administration for Children and Families (SBIR)

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Funding Opportunity Announcements, Application Instructions, and Appendices are contained in separate files. Follow the links below to view these documents.

FUNDING OPPORTUNITY ANNOUNCEMENTS

REMINDER: ALL APPLICATIONS MUST BE SUBMITTED IN RESPONSE TO A FUNDING OPPORTUNITY ANNOUNCEMENT THROUGH GRANTS.GOV

SMALL BUSINESS INNOVATION RESEARCH PROGRAM PARENT ANNOUNCEMENT (SBIR [R43/R44]) HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-11-096.HTML

SMALL BUSINESS TECHNOLOGY TRANSFER PROGRAM PARENT ANNOUNCEMENT (STTR [R41/R42]) HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-11-097.HTML

ADDITIONAL SPECIAL ANNOUNCEMENTS FOR SMALL BUSINESS RESEARCH OPPORTUNITIES HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIR_ANNOUNCEMENTS.HTM

APPLICATION INSTRUCTIONS

SF424 (R&R) APPLICATION INSTRUCTIONS AND ELECTRONIC SUBMISSION INFORMATION (HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/424/INDEX.HTM)

APPENDICES

STTR MODEL AGREEMENT (MS WORD)

EXTRAMURAL INVENTION REPORTING COMPLIANCE RESPONSIBILTIES (HTTPS://S-EDISON.INFO.NIH.GOV/IEDISON/TIMELINE.JSP)

PROGRAM DESCRIPTIONS AND RESEARCH GRANT TOPICS

The research topics shown in this solicitation represent program areas that may be of interest to applicant small business concerns in the development of projects that have potential for commercialization. Small business concerns are encouraged to submit SBIR/STTR grant applications in these areas.

APPLICABLE TO NIH ONLY: SBIR and STTR grant applications will be accepted and considered in any area within the mission of the awarding components (i.e., Institutes and Centers (ICs)) identified in this solicitation.

Applicants are strongly encouraged to subscribe to the NIH Guide for Grants and Contracts LISTSERV (http://grants.nih.gov/grants/guide/listserv.htm) or query program administrators periodically via email to learn of new or emerging scientific interests of the NIH, CDC, FDA, and ACF awarding components.

You may also subscribe to the SBIR-STTR LISTSERV list to get timely information about the NIH SBIR/STTR Programs (http://grants.nih.gov/grants/funding/listserv.htm).

Additional information on each of the awarding components (ICs) and their research interests is available electronically on the home pages shown throughout the "Research Topics" section of the solicitation.

The Fogarty International Center, which provides support only for conferences, postdoctoral fellowships for research in the United States and abroad, and senior scientist exchanges between the United States and other countries, does not participate in the SBIR/STTR program.

NATIONAL INSTITUTES OF HEALTH (NIH)

NIH is the steward of medical and behavioral research for the Nation. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.

The goals of the agency are as follows:

1. foster fundamental creative discoveries, innovative research strategies, and their applications as a basis to advance significantly the Nation's capacity to protect and improve health;
2. develop, maintain, and renew scientific human and physical resources that will assure the Nation's capability to prevent disease;
3. expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research; and
4. exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

In realizing these goals, the NIH provides leadership and direction to programs designed to improve the health of the Nation by conducting and supporting research:

- in the causes, diagnosis, prevention, and cure of human diseases;
- in the processes of human growth and development;
- in the biological effects of environmental contaminants;
- in the understanding of mental, addictive and physical disorders; and
- in directing programs for the collection, dissemination, and exchange of information in medicine and health, including the development and support of medical libraries and the training of medical librarians and other health information specialists.

In addition, the NIH sponsors training of research personnel; career development of new and established scientists; construction and renovation of research facilities and provision of other research resources.

To carry out these responsibilities, the NIH is organized into awarding components (Institutes/Centers). Those components that have an extramural element, that is, provide funds for research and research training activities in organizations external to the NIH, are shown below. The NIH makes every effort to finance worthy applications, including the co-funding of such applications by one or more awarding components having relevance in the projects.

Funding levels for projects are determined through the combined interaction among peer review, grants management, program, budget, and other Institute and/or Centers (IC) staff. These levels are based on allowable costs that are consistent with the principles of sound cost management and in consideration of IC priorities, constraints on the growth of average grant costs, and the availability of funds.

TRANS-NIH RESEARCH PROGRAMS

Phase IIB Competing Renewal Awards

Some NIH Institutes/Centers (ICs) offer Phase II SBIR/STTR awardees the opportunity to apply for Phase IIB Competing Renewal awards. These are available for those projects that require extraordinary time and effort in the R&D phase and may or may not require FDA approval for the development of such projects, including drugs, devices, vaccines, therapeutics, and medical implants related to the mission of the IC. Some ICs have announced this opportunity through the NIH Guide for Grants and Contracts (see link below), and some are using this Omnibus SBIR/STTR Grant Solicitation. Only those small business concerns who have been awarded a Phase II are eligible to apply for a Phase IIB Competing Renewal award. Prospective applicants are strongly encouraged to contact NIH staff prior to submission. Additional requirements and instructions (e.g., submission of a letter of intent) are available in the specific IC research topics section and in the specific IC Program Funding Opportunity Announcements (http://grants.nih.gov/grants/funding/sbir_announcements.htm). The following NIH ICs will accept applications for Phase IIB Competing Renewal awards: **NIA, NIAAA, NIAID** (SBIR only)**, NICHD** (SBIR only and only Competing Renewals of NICHD-supported Phase II awards)**, NIDA, NIDCD, NIDDK** (only Competing Renewals of NIDDK-supported Phase II awards**), NEI** (SBIR only and only Competing Renewals of NEI-supported Phase II awards**), NIGMS** (SBIR only), **NHLBI** (SBIR only and only Competing Renewals of NHLBI-supported Phase II awards), **NIMH** (SBIR only), **NINDS,** and **NCRR** (SBIR only). NCI offers Phase IIB opportunities that focus on the commercialization of SBIR-developed technologies. Contact the NCI SBIR Development Center at 301-594-7709, NCISBIR@mail.nih.gov for additional information.

Research Supplements to Promote Diversity in Health-Related Research

(See Funding Opportunity Announcement at http://grants.nih.gov/grants/guide/pa-files/PA-08-190.html.)

The NIH recognizes a unique and compelling need to promote diversity in the biomedical, behavioral, clinical and social sciences research workforce. The NIH expects efforts to diversify the workforce to lead to the recruitment of the most talented researchers from all groups; to improve the quality of the educational and training environment; to balance and broaden the perspective in setting research priorities; to improve the ability to recruit subjects from diverse backgrounds into clinical research protocols; and to improve the Nation's capacity to address and eliminate health disparities.

The NIH notifies Principal Investigators holding specific types of NIH research grants (including SBIR and STTR awards) that funds are available for administrative supplements to improve diversity by supporting and recruiting students, postdoctorates, and eligible investigators from groups that have been shown to be underrepresented in the biomedical, behavioral, clinical, and social sciences research workforce. Although the administrative supplements supported under this program provide funding for less than one

percent of all individuals involved in NIH supported research, the NIH has found these awards to be an effective means of encouraging institutions to recruit from currently underrepresented groups. Administrative supplements must support work within the scope of the original project.

All NIH awarding components and the National Institute for Occupational Safety and Health at the CDC participate in this program. Candidates eligible for support under this supplement program include individuals at various career levels who come from groups that have been shown to be underrepresented in science. Such candidates include individuals from underrepresented racial and ethnic groups, individuals with disabilities, and individuals from disadvantaged backgrounds. Detailed eligibility criteria are described in the full announcement.

An application for a supplement may be submitted at any time. In making requests, the grantee institution, on behalf of the Principal Investigator of the parent grant and in cooperation with the candidate **must submit the application for supplemental funds directly to the awarding component that supports the parent grant. The application must not be submitted through grants.gov or to the NIH Center for Scientific Review.**

Requests for administrative supplements can be submitted to the NIH Program Official listed in the contacts section of the FOA PA-08-190 at any time. Administrative supplements normally end with the competitive cycle of the parent grant

TECHNICAL ASSISTANCE PROGRAMS
Available to NIH SBIR Awardees
(Note that STTR Awardees are not eligible for these programs)

One of the goals of the Small Business Innovation Research (SBIR) program is to "increase private sector commercialization of innovations developed through Federal SBIR R&D." To help NIH SBIR awardees move their products into the marketplace, NIH has developed several assistance programs that provide technical and/or commercialization assistance specific to the individual needs of NIH SBIR awardees.

Additional information about these programs is available at http://grants.nih.gov/grants/funding/tap.htm. Questions may be addressed to the NIH SBIR Office at sbir@od.nih.gov or 301-435-0921.

Niche Assessment Program
(For NIH SBIR Phase I awardees)

The Niche Assessment program focuses on obtaining the necessary information for strategizing and making deals. Often, a research scientist does not have the entrepreneurial skills to assess whether there are other applications or market niches for their SBIR-developed technology. As a result, they may underestimate its true market value. This program assesses the market opportunities, needs and concerns of end-users and helps to discover new markets for possible entry for the SBIR-developed technology. With the assistance of the participant, a contractor helps identify niches and potential partners. The contractor performs the due diligence and provides an in-depth report that assesses such items as the potential end-users needs, the competing technologies and products, the competitive advantage, the market size and share that the participant might expect, etc. Targets (end users) are contacted to ensure they are viable leads and their contact information is included in the report for possible follow-up. Participants may find this report helpful in preparing the requisite Commercialization Plan for a Phase II application. For detailed information about the Niche Assessment Program, see http://grants.nih.gov/grants/funding/nap.htm.

Participation in this program is limited to NIH SBIR Phase I awardees (grants and contracts) and participants need only commit a few hours to inform and make the contractor fully conversant on their technology and the niche they would like to have investigated. There is no cost to the NIH SBIR awardee to participate in this program.

Commercialization Assistance Program (CAP)
(For NIH SBIR Phase II awardees)

The Commercialization Assistance Program (CAP) assists small companies with getting their SBIR-developed technologies more rapidly into the marketplace. It provides assistance with developing and implementing an appropriate business strategy aimed at commercializing the products or services that have resulted from NIH-supported SBIR awards.

CAP includes two distinctive tracks that offer customized assistance to meet the specific needs of both early stage and seasoned companies: (1) Commercialization Training Track (CTT), and (2) Accelerated Commercialization Track (ACT). CTT is aimed at assisting participants with evaluating their commercialization options based on their specific technologies and to develop a solid market-entry plan covering an 18-month period. It also assists in the development of market-appropriate tools to accomplish these objectives.

The ACT track assists those companies that may have successfully commercialized products and/or services, generated revenue, established partnerships and/or otherwise achieved a level of market development that is sustainable over a definitive period. However, they may be lacking in a specific, applicable issue (such as a solid regulatory plan, a license-focused IP strategy or a term sheet for investors), whose resolution is key to their continued growth.

Participation in CAP is limited to NIH SBIR Phase II awardees (grants and contracts) from the previous six years. Applications to participate are typically accepted in early summer. Participation is free to the NIH SBIR awardee; however, participants are responsible for travel and lodging expenses associated with attending workshops and partnering investment events. Detailed information is available at http://grants.nih.gov/grants/funding/cap/index.htm.

NIH, CDC, FDA, AND ACF AWARDING COMPONENT CONTACT INFORMATION

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute on Aging http://www.nia.nih.gov	Dr. Michael-David A.R.R. Kerns Phone: 301-402-7713 Fax: 301-402-2945 Email: Michael-David.Kerns@nih.gov	Ms. Linda Whipp Phone: 301-496-1472 Fax: 301-402-3672 Email: Linda.Whipp@nih.gov
National Institute on Alcohol Abuse and Alcoholism http://www.niaaa.nih.gov	Dr. Q. Max Guo Phone: 301-443-0639 Fax: 301-594-0673 Email: Max.Guo@nih.gov	Ms. Judy Fox Phone: 301-443-4704 Fax: 301-443-3891 Email: Judy.Fox@nih.gov
National Institute of Allergy and Infectious Diseases http://www.niaid.nih.gov	Dr. Gregory Milman Phone: 301-496-8666 Fax: 301-402-0369 Email: Gregory.Milman@nih.gov	Mr. Michael Wright Phone: 301-451-2688 Fax: 301-493-0597 Email: mawright@mail.nih.gov
National Institute of Arthritis and Musculoskeletal and Skin Diseases http://www.niams.nih.gov/	Dr. Xibin Wang Phone: 301-451-3884 Fax: 301-480-1284 Email: wangx1@mail.nih.gov	Ms. Sheila Simmons Phone: 301-594-9812 Fax: 301-480-5450 Email: simmonss@mail.nih.gov Mr. Erik (Timothy) Edgerton Phone: 301-594-3968 Fax: 301-480-5450 Email: edgertont@mail.nih.gov
National Institute of Biomedical Imaging and Bioengineering http://www.nibib.nih.gov/	Mr. Todd Merchak Phone: 301-496-8592 Fax: 301-480-1614 Email: merchakt@mail.nih.gov	Ms. Florence Turska Phone: 301-496-9314 Fax: 301-480-4974 Email: turskaf@mail.nih.gov
National Cancer Institute http://sbir.cancer.gov	Mr. Michael Weingarten Phone: 301-594-7709 Fax: 301-480-4082 Email: ncisbir@mail.nih.gov	Mr. Allen Lo Phone: 301-496-8796 Fax: 301-496-8601 Email: loa2@mail.nih.gov
Eunice Kennedy Shriver National Institute of Child Health and Human Development http://www.nichd.nih.gov	Louis A. Quatrano, Ph.D. Phone: 301-402-4221 Fax: 301-402-0832 Email: Louis.Quatrano@nih.gov	Mr. Ted Williams Phone: 301- 435-6996 Fax: 301- 451-5510 Email: williate@mail.nih.gov
National Institute on Drug Abuse http://www.nida.nih.gov	Elena Koustova, Ph.D., MBA Phone: 301-496-8768 Email: koustovae@nida.nih.gov	Ms. Diana Haikalis, M.B.A. Phone: 301-443-6710 Fax: 301-594-6849 Email: dhaikali@nida.nih.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute on Deafness and Other Communication Disorders http://www.nidcd.nih.gov	Dr. Roger L. Miller Phone: 301-402-3458 Fax: 301-402-6251 Email: Roger.Miller@nih.gov	Mr. Christopher P. Myers Phone: 301-435-0713 Fax: 301-402-1758 Email: Christopher.Myers@nih.gov
National Institute of Dental and Craniofacial Research http://www.nidcr.nih.gov	Dr. R. Dwayne Lunsford Phone: 301-594-2421 Fax: 301-480-8319 Email: lunsfordr@mail.nih.gov	Ms. Mary Greenwood Phone: 301-594-4808 Fax: 301-480-3562 Email: mary.daley@nih.gov
National Institute of Diabetes and Digestive and Kidney Diseases http://www.niddk.nih.gov	Ms. Christine Densmore Phone: 301-402-8714 Fax: 301-480-8300 Email: densmorec@niddk.nih.gov	Mr. Gene McGeehan Phone: 301-594-0417 Fax: 301-594-9523 Email: mcgeehane@niddk.nih.gov
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National Heart, Lung, and Blood Institute http://www.nhlbi.nih.gov	Ms. Susan Pucie Phone: 301-435-0079 Fax: 301-480-0867 Email: Susan.Pucie@nih.gov	Mr. Robert Vinson Phone: 301-435-0166 Fax: 301-451-5462 Email: Robert.Vinson@nih.gov Mr. David Ruane Phone: 301-435-0150 Fax: 301-451-5462 Email: ruaned@nhlbi.nih.gov
National Human Genome Research Institute http://www.genome.gov	Dr. Bettie J. Graham Phone: 301-496-7531 Fax: 301-480-2770 Email: Bettie_graham@nih.gov	Ms. Cheryl Chick Phone: 301-435-7858 Fax: 301-402-1951 Email: ChickC@mail.nih.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
National Institute of Mental Health http://www.nimh.nih.gov	Dr. Michael F. Huerta Phone: 301-443-3563 Fax: 301-443-1731 Email: mhuert1@mail.nih.gov	Ms. Rebecca Claycamp Phone: 301-443-2811 Fax: 301-443-6885 Email: rclaycam@mail.nih.gov
National Institute on Minority Health and Health Disparities http://www.ncmhd.nih.gov	Mr. Vincent A. Thomas, Jr. MSW, MPA Phone: 301-402-2516 Fax: 301-480-4049 Email: thomasvi@mail.nih.gov	Ms. Priscilla Grant, J.D., C.R.A. Phone: 301-594-8412 Fax: 301-480-4049 Email: Priscilla.Grant@nih.gov
National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov	Ms. Stephanie Fertig Phone: 301-496-1447 Fax: 301-480-1080 Email: fertigs@ninds.nih.gov	Ms. Tijuanna Decoster Phone: 301-496-9231 Fax: 301-402-4370 Email: decostert@mail.nih.gov
National Institute of Nursing Research http://www.nih.gov/ninr	Dr. Paul A. Cotton Phone: 301-402-6423 Fax: 301-480-8260 Email: Paul.Cotton@nih.gov	Mr. Brian Albertini Phone: 301-594-6869 Fax: 301-402-4502 Email: albertib2@mail.nih.gov
National Center for Research Resources http://www.ncrr.nih.gov	Dr. Mary Ann Wu Phone: 301-435-0787 Fax: 301-480-3659 Email: maryann.wu@nih.gov	Ms. Leslie Le Phone: 301-435-0856 Fax: 301-480-3777 Email: LeLeslie@mail.nih.gov
National Center for Complementary and Alternative Medicine http://www.nccam.nih.gov/	Dr. Craig Hopp Phone: 301-496-5825 Fax: 301-480-1587 Email: hoppdc@mail.nih.gov	Mr. George Tucker, MBA Phone: 301-594-8853 Fax: 301-480-1552 Email: George.Tucker@nih.gov
National Library of Medicine http://www.nlm.nih.gov	Dr. Jane Ye Phone: 301-594-4882 Fax: 301-402-2952 Email: yej@mail.nih.gov	Mr. Dwight Mowery Phone: 301-496-4221 Fax: 301-402-0421 Email: moweryd@mail.nih.gov

AWARDING COMPONENT	PROGRAM CONTACT	GRANTS MGMT. CONTACT
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Food and Drug Administration (FDA) http://www.fda.gov	Ms. Kimberly Pendleton Phone: 301-827-9363 Fax: 301-827-7101 Email: kimberly.pendleton@fda.hhs.gov	Ms. Gladys Melendez-Bohler Phone: 301-827-7168 Fax: 301-827-7101 Email: Gladys.Melendez-Bohler@fda.hhs.gov
Administration for Children and Families http://www.acf.hhs.gov	Anne F. Bergan Phone: 202-260-8515 Fax: 202-205-3598 E-mail: abergan@acf.hhs.gov	Edeltraud Fernandez Phone: 202-401-2346 Fax: 202-205-3598 E-mail: efernandez@acf.hhs.gov

NATIONAL INSTITUTE ON AGING (NIA)

The NIA SBIR-STTR Programs support biomedical, behavioral, and social research and research training on the aging process as well as on the diseases and other special problems and needs of older people. It supports SBIR and STTR grant research under four established divisions: Behavioral and Social Research, Aging Biology, Geriatrics and Clinical Gerontology, and Neuroscience.

Examples of research topics within the mission of the NIA that may be of interest to small businesses are shown below. These listings illustrate the range of areas that are of interest to the NIA and are not intended to be exhaustive.

For additional information about areas of interest to the NIA, please visit our home page at http://www.nia.nih.gov.

Phase IIB Competing Renewal Awards

NIA accepts Phase IIB Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue the process of developing products, primarily for pharmaceutical compounds and medical devices, requiring regulatory approval by the Food & Drug Administration (FDA). NIA will accept applications for up to two (2) years and up to $750,000 per year in total costs. The Phase IIB Competing Renewal award is intended to allow small businesses the opportunity to advance research to a stage where interest in and investment by third parties would be more likely.

Prospective Phase IIB Competing Renewal applicants are strongly encouraged to submit a letter of intent to Dr. Kerns that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Anticipated Budget
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX, if relevant)

Although a letter of intent is not binding and does not enter into the review of a subsequent application, it allows NIA staff to estimate the potential review workload, plan the review, and consider budget implications. It is anticipated that only a small number of NIA SBIR/STTR Phase II awards would be eligible for a Phase IIB Competing Renewal award.

The following examples would make appropriate topics for Phase IIB Competing Renewal projects. These are meant only as indications of potential Phase IIB Competing Renewal projects and are not exclusive of other appropriate activities. Research and development efforts can be focused, for example, on medications to treat, delay the progression of or prevent age-related cognitive decline, mild cognitive impairment (MCI), Alzheimer's disease, and other dementias of aging.

1. Studies for preclinical discovery and development of drugs, natural products, or other types of compounds, including pharmacology and toxicology studies, beyond those conducted under the initial SBIR Phase I and Phase II grants. The studies conducted under the previous grants should be sufficient to provide a sound rationale for continued development of the compound, drug or natural product.
2. Completion of studies as required by the FDA for an IND application.
3. Human clinical trials/studies to determine a drug's, natural product's, or other type of compound's safety profile, metabolism, and/or efficacy.

For questions relating to Phase IIB Competing Renewal applications, please contact:

Dr. Michael-David ("M-D") A.R.R. Kerns
301-402-7713, Fax: 301-402-2945
Email: kernsmd@mail.nih.gov

Division of Behavioral and Social Research (DBSR)

Basic and translational social and behavioral research on aging processes and the place of older people in society. The division focuses on how people change with age, on the interrelations between older people and social institutions (e.g., the family, health-care systems), and on the societal impact of the changing age-composition of the population. Special emphasis areas are (1) Health Disparities; (2) Aging Minds; (3) Increasing Health Expectancy; (4) Health, Work, and Retirement; (5) Interventions and Behavior Change; (6) Genetics, Behavior, and the Social Environment; and (7) the Burden of Illness and the Efficiency of Health Systems.

In the past, DBSR has supported development of training videos for programs or interventions and development of medication reminder devices through the SBIR-STTR grant mechanism. DBSR currently has minimal interest in development of new training videos (especially for programs or interventions that have not been subjected to rigorous evaluation) or in the development of medication-reminder devices (without clear demonstration that a new & previously unidentified market of public-health importance would be served).

A. Social, behavioral, environmental and or/technical interventions on the individual, institutional, family, community or national level intended to maintain older adult independence or functioning, increase well-being and prevent disease and/or disability.

    1. Interventions to address cognitive aging;
    2. Interventions directed at self-management of chronic diseases among the elderly, including behavioral change and applications to enhance compliance;
    3. Interventions to enhance social function or to improve physical and psychological well-being in midlife and older age;
    4. The development of evidence-based, risk-reduction programs (also referred to as health promotion, health management, demand management, and disease-prevention programs) that are applicable to older U.S. workers.

B. The development of software to improve financial decision making among older people. The software should include projected retirement earnings and expenditures on long term care and out of pocket medical expenditures.

C. The development of practical applications using innovative technologies (e.g. hand-held, internet, telemedicine GPS, robotics, social networking and communications technologies) to support and improve quality of life, well-being, and the ability of older adults to live independently and safely at home..

D. Interventions or programs for issues impacting caregivers of the elderly and older individuals needing long-term care

    1. Development of strategies for care providers (both professionals and families) to deal with burdens associated with chronic disabling illness or disease (including Alzheimer's disease);
    2. Programs or interventions that address/decrease the trauma and difficulty of elders, their families, and care providers faced with end of life decisions and events that surround the end of life.

E. New sampling and data collection methodologies for use in large population-based household surveys and behavioral interventions of relevance to aging. These include:

1. Experience sampling and new devices for real-time collection of data;
2. Performance based measures for cognitive or physical functioning as well as new instruments for cognitive testing, sleep quality, assessment of basic decision-making domains, or assessments of social behaviors;
3. Improvements to blood spot technology for biological data collection (this includes the development of multiple and reliable assays for limited blood spot specimens).

F. Survey Development/Archiving/Database support.

1. Development of new databases and database support infrastructure to satisfy data and research needs in aging as well as the development of innovative data archives to make current statistical and epidemiological data more accessible and policy relevant;
2. Development of data extraction web tools for public use databases;
3. Development of innovative methods and software to provide improved access to complex longitudinal studies or surveys that cannot be placed in open data archives because of issues relating to confidentiality;
4. Development of innovative methods and software to facilitate analysis of personal data linked to geocoded data, biological, cognitive or genetic measures, with improved protection for confidentiality of respondents;
5. Development of data infrastructure and tools for assessing the economic impact of federally-funded research.

G. Forecasting and Software for analyzing of healthcare claims.

1. Development of models that will lead to improved forecasting of national, state and county level estimates of the demand for aging-related services; and improved prediction of the costs and effects of public health interventions, changes in health-care financing and insurance, social security, pension coverage or changes in the retirement age. Both domestic and international projections are of interest;
2. Development of software which will provide insight on key factors that contributes to growth of medical expenditures through analysis of claims data.

Dr. Partha Bhattacharyya
301-496-3138, Fax: 301-402-0051
Email: bhattacharyyap@nia.nih.gov

Division of Aging Biology (DAB)

DAB sponsors research on the physiological, molecular, and cellular causes and consequences of aging processes. DAB also has responsibility for maintaining existing resources and developing new resources for aging research, such as populations of well-characterized animals and specific cell lines including, for example, human fetal lung fibroblasts.

DAB areas of research that may be of interest to small businesses include, but are not limited to:

A. Effects of metabolism on the aging process, e.g., how metabolic regulation influences longevity, and the development of anti-oxidant interventions to reduce oxidative stress in vivo.

Dr. David Finkelstein
301-496-6402, Fax: 301-402-0010
Email: df18s@nih.gov

B. Development of minimally-perturbing techniques for collecting blood from mice, rats, and other animals several times a day in sufficient quantities for measurement of hormone levels and other circulating factors in young and old animals, or development of non-invasive research and test methods for use in animals.

Dr. Nancy Nadon
301-496-6402, Fax: 301-402-0010
Email: nn37a@nih.gov

C. Development of molecular probes such as antibodies, DNA sequences and expression vectors useful in studying aging, senescence, and longevity both in vivo and in vitro.

Dr. Rebecca Fuldner
301-496-6402, Fax: 301-402-0010
Email: Fuldnerr@mail.nih.gov

D. Instruments and/or methodology to monitor dynamic progression of ovarian follicles from primordial through antral stages in humans and other mammals with sufficient sensitivity to obtain an accurate profile during the perimenopausal period when relatively small numbers of follicles are present.

Dr. Felipe Sierra
301-496-6402, Fax: 301-402-0010
Email: sierraf@mail.nih.gov

E. Development of new animal models, including transgenic animals, for studying aging processes, as well as development of new biological model systems for research on aging to replace or reduce vertebrate animal use in research. These models may include better in vitro systems, improved cell culture methods, mathematical models, and computer simulations.

Dr. Mahadev Murthy
301-496-6402, Fax: 301-402-0010
Email: murthy@mail.nih.gov

F. Development of interventions to slow down the degenerative processes associated with aging. These would include techniques with commercial potential to: (1) manipulate the control of cell proliferation or programmed cell death, (2) reduce the level of damage to nucleic acids, proteins and lipids and the macromolecular complexes formed from these molecules, (3) improve the damage surveillance and repair potential of cells, (4) improve the immune response to foreign molecules or reduce the response to self, and (5) reverse age-related changes in hormone production and function.

Dr. Nancy Nadon
301-496-6402, Fax: 301-402-0010
Email: nn37a@nih.gov

G. Development of treatments for wound healing in the aged. These would include devices, processes, and pharmacological agents with the potential to (1) promote would healing in aged tissues such as skin, muscle, cartilage, and bone, or (2) reduce scar formation without compromising effective healing. Wounds produced by accidental damage or resulting from surgery would be appropriate for consideration.

Dr. John Williams
301-496-6402, Fax: 301-402-0010
Email: williamsj6@mail.nih.gov

H. Development of appropriate animal and human culture model systems to explore underlying molecular and cellular mechanisms of prostate growth in middle-aged and older subjects.

I. Development of appropriate animal model systems to explore underlying molecular and cellular systems of female reproductive aging processes as well as the development of pathophysiologic processes associated with the human menopause, including bone loss, cardiovascular pathology, hot flashes, and excessive uterine bleeding.

Dr. Rebecca Fuldner
301-496-6402, Fax: 301-402-0010
Email: fuldnerr@mail.nih.gov

or

Dr. Felipe Sierra
301-496-6402, Fax: 301-402-0010
Email: sierraf@mail.nih.gov

J. Development of cell-based therapies or other treatments to repair myocardial or vascular tissues after ischemia. The work should include consideration of age-related effects on the therapy or treatment.

Dr. Ronald Kohanski
301-496-6402, Fax: 301-402-0010
Email: kohanskir@mail.nih.gov

Division of Neuroscience (DN)

DN supports research on age-related changes in the brain or nervous system in the context of other age-related physiological or homeostatic regulator changes (e.g., endocrine, dietary, sleep and circadian rhythms, immune, disease states); degenerative processes or pathological changes in the aging brain in the context of understanding normal age-related changes; and the sensory, motor, perceptual and cognitive processes and changes that occur with aging as related to their underlying biological mechanisms.

An important component of DN is the support of studies on Mild Cognitive Impairment (MCI), Alzheimer's disease (AD), and other dementias of aging such as Frontotemporal Dementia, Lewy Body Dementia, and Vascular Dementia.

Areas that may be of interest to small businesses include, but are not limited to:

A. Development of sensitive, specific and standardized tests for diagnostic screening of cognitive decline and dementia; for example, the development of novel neuropsychological, biochemical and neuroimaging methods for the early detection of cognitive decline and MCI and the early diagnosis of AD.

Dr. John Hsiao
301-496-9350; Fax: 301-496-1494
Email: jhsiao@mail.nih.gov

or

Dr. Nina Silverberg (neuropsychological detection methods)
Email: silverbergn@mail.nih.gov

B. Discovery, development, and/or evaluation of drugs, biological or natural products, including central-nervous-system delivery systems, to enhance cognitive functioning in normal aging and to treat the cognitive deterioration and/or behavioral symptoms associated with MCI, AD, and other dementias of aging as well as to slow and/or reverse the course of the disease or to prevent it entirely.

Dr. Neil Buckholtz (MCI, AD, & other dementias of aging)
301-496-9350, Fax: 301-496-1494
Email: nb12s@nih.gov

and

Dr. Suzana Petanceska (MCI, AD, & other dementias of aging)
301-496-9350; Fax: 301-496-1494
Email: petanceskas@nia.nih.gov

and

Dr. Molly Wagster (Cognitive functioning in normal aging)
301-496-9350; Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

The development of practical applications using innovative technologies (e.g. hand-held, internet, telemedicine GPS, robotics, social networking and communications technologies) to support and improve quality of life, well-being, and the ability of people with MCI, AD or other dementias of aging to live independently and safely at home for an extended period of time. Examples include systems and devices to: evaluate, monitor and improve or adapt to changes in cognition; improve health service delivery; support independent living and the conduct of everyday tasks at home; provide information to health care providers and family members with which to evaluate the need for intervention; and promote communication and interaction between individuals living in the community or in institutional settings and their health care providers, friends and family members.

Dr. Nina Silverberg
Email: silverbergn@mail.nih.gov

C. Testing in clinical trials of drug, nutritional, behavioral, cognitive or other types of interventions to enhance cognitive functioning in normal aging and to treat cognitive deterioration and/or behavioral symptoms associated with MCI, AD, and other dementias of aging as well as to slow and/or reverse the course of disease or to prevent the onset of disease.

Dr. Laurie Ryan (MCI, AD, & other dementias of aging)
301-496-9350; Fax: 301-496-1494
Email: ryanl@mail.nih.gov

and

Dr. Molly Wagster (Cognitive functioning in normal aging)
301-496-9350; Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

D. Devices or intervention strategies that may prolong functional independence when there are dysfunctions of the central nervous system.

E. Behavioral, environmental, pharmacological, & nutritional interventions to prevent and/or remediate brain biochemical and/or neurophysiological changes caused by normal aging and neurodegenerative diseases, including age-related sensory dysfunction (e.g., pain, hearing loss, speech communication disorders, olfaction loss, & vision loss), motor dysfunctions (including Parkinson's disease & other age-related psychomotor disorders) or age-related decrements in balance & postural control, gait performance, and mobility.

F. Biosensors and prosthetic devices, technologies, and related software development to aid in the assessment, diagnosis, and remediation of age-related cognitive decline or sensory dysfunction (including pain), motor dysfunction (including Parkinson's disease and other motor disorders of

aging), or age-related changes in balance, postural control, and gait. Novel markers of normal age-dependent cognitive decline or sensory and/or motor system changes at the molecular cellular, circuitry, physiological or behavioral level in humans or relevant animal models.

Dr. Wen G. Chen
301-496-9350, Fax: 301-496-1494
Email: chenw@mail.nih.gov

or

Dr. Molly Wagster
301-496-9350, Fax: 301-496-1494
Email: wagsterm@mail.nih.gov

G. New technologies to screen for the presence of sleep disorders in older persons, to aid in the diagnosis of these disorders, and to enable their remediation.

H. Minimally invasive technologies to detect prion diseases early in the course of the disease process in older adults, as well as effective treatment strategies to slow, halt or prevent these diseases.

Dr. Miroslaw Mackiewicz
301-496-9350, Fax: 301-496-1494
Email: mackiewiczm2@mail.nih.gov

I. Improved instrumentation, imaging technology, related devices, and software packages for use in visualizing neural activity during cognitive or sensory behavior in older adults. Also of interest would be new technologies to combine neural imaging and behavioral assessment in awake animals.

Dr. Molly Wagster
301-496-9350, Fax: (301)496-1494
Email: wagsterm@mail.nih.gov

J. Development of technology and analysis tools to examine cellular patterns of gene and protein expression in the normal and diseased aging nervous system, including the identification of aberrant gene products expressed in the aging brain. Development of molecular imaging technology for the in vitro and in vivo analysis of gene and protein function in the normal aging brain and in the diseased aging nervous system.

K. Development of technology, including non-invasive methods and novel probes, to monitor and manipulate the plasticity of neural circuits in the adult and aged nervous system. Development of novel markers of neural stem cell function (proliferation, migration, and differentiation) as well as methods to assess the integration and function of stem cells in the nervous system.

Dr. Brad Wise (Normal brain aging)
301-496-9350, Fax: 301-496-1494
Email: bw86y@nih.gov

and

Dr. Lawrence Refolo (Alzheimer's disease & other dementias of aging)
301-496-9350, Fax: 301-496-1494
Email: refolol@mail.nih.gov

Division of Geriatrics and Clinical Gerontology (DGCG)

DGCG supports clinical and translational research on health and disease in the aged and research on aging over the human life span and its relationships to health outcomes. Translational research is of interest for developing and testing the effectiveness of interventions known to be efficacious for everyday

clinical practice and health decision making. Research on Geriatrics focuses primarily on health issues regarding the aged, and deals with research on disease and disability in older persons, including both specific conditions and issues related to multiple morbidity. Clinical Gerontology Research focuses primarily on clinically related issues regarding aging, and deals with research on aging changes over the life span. A major focus is on the determinants of rates of progression of age-related changes that affect disease risk, particularly those affecting risk for multiple age-related conditions.

Areas of interest include but are not limited to:

A. Development of vaccines and other agents for preventing and treating infections in older persons, including development of new vaccines or preventive interventions, and new methods using currently available vaccines or preventive medications.

B. Development of clinical decision support tools that helps physicians caring for patients with multiple chronic conditions to prioritize the interventions that are most beneficial and relevant within the context of these patients' lives.

C. Devices and/or techniques for preventing or treating urinary incontinence.

D. Development of improved post-surgical treatments/technologies promoting wound healing and reduced scar formation.

Dr. Marcel Salive
301-496-6761, Fax: 301-402-1784
Email: saliveme@nia.nih.gov

E. Refinements in techniques for the measurement of age-related changes in hormone levels, status or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function). The objective is to enhance sensitivity and achieve greater economy in the assay cost.

F. Effects of menopause on woman's aging and subsequent health. Effects of age-related changes in endocrine status in men on subsequent aging, morbidity and mortality.

   1. Refinements in techniques for the measurement of age-related changes in hormone levels or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function).

   2 Development and testing of alternative strategies (to conventional estrogen/ progestin therapy) for the management of short-term menopausal symptoms and for the reduction in risks of cardiovascular disease, osteoporosis, and other menopause-related conditions, disorders and diseases. Development and testing of new tissue-specific modulators of estrogen/ androgen receptor activity in men and in women for the prevention or treatment of age-related diseases.

   3. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy of treatment or enhanced risk or progression of adverse effects/events.

   4. Determine drug interactions, i.e., potential alterations in pharmacokinetics and pharmacodynamic properties of drugs taken concomitantly with postmenopausal hormones.

G. Osteoporosis. Development, testing, and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy, response to treatment or enhanced risk or progression of adverse effects/events.

   Development and validation of non-invasive methods of examining bone quality (density, architecture, and strength of bone).

Dr. Sherry Sherman
301-435-3048, Fax: 301-402-1784
Email: ss80t@nih.gov

H. Improved instrumentation and imaging techniques for measuring body composition and properties such as muscle function in older persons.

I. Development of techniques/devices (e.g., non-invasive, portable) for improved monitoring of caloric intake and/or energy expenditure in epidemiological studies.

Dr. Chhanda Dutta
301-435-3048, Fax: 301-402-1784
Email: cd23z@nih.gov

J. Measuring ambulation and assessing factors contributing to problems in and/or related to ambulation and mobility in general

   1. Development of improved instrumentation for biomechanical assessment of ambulation and falls.

   2. Development of improved instrumentation to assess balance, sway, gait, and postural control to identify stable and unstable patterns of movement during activities of daily living

   3. Development of improved quantitative methods of assessing postural perturbations relevant to activities of daily living.

K. Development of improved, lightweight, and absorbent materials or other interventions to prevent, protect against and minimize injuries suffered from falls.

L. Development of assistive technologies to enable and support older persons to live independently and safely at home

   1. Development of devices/assistive technologies addressing complications of limited mobility among older persons.

M. Development of technologies to assist in the improvement of physical function and mobility in older persons prior to (prehabilitation) or following (rehabilitation) elective/planned surgery.

N. Research on better ways to prevent injuries and deaths associated with the use of currently-available bed rails in populations of older patients. Such research would include work on their identification and testing of improved designs of bed systems for use in homes, skilled nursing facilities, and hospitals.

Dr. Lyndon Joseph
301-496-6761; Fax: 301-402-1784
Email: Lyndon.Joseph@nih.hhs.gov

O. Development of devices and techniques for screening substantial numbers of individuals for particular alleles at loci of relevance to human genetic studies of aging.

P. Development and validation of imaging and sensor technologies to improve measures of physiologic changes with age.

Ms. Winifred Rossi, M.A.
301-496-3836, Fax: 301-402-1784
Email: wr33a@nih.gov

Q. Development and validation of improved approaches for evaluation, monitoring or treatment of diastolic dysfunction in older adults.

R. Development and validation of improved techniques for hemodynamic monitoring of older adults in emergency and/or critical care settings.

S. Development and validation of instruments or methods to evaluate fatiguability—the level of fatigue related to the intensity, duration, and/or frequency of activity (in contrast to measures of fatigue), particularly in adults with or at-risk of developing age-related conditions or diseases leading to physical disability.

T. Development and validation of innovative approaches to pain control that consider age-related physiologic changes such as gastrointestinal absorption, cutaneous integrity, and musculoskeletal structure and function.

U. Development and evaluation of treatment approaches to age-related diseases or conditions based on modulation of the thyroid hormone axis.

V. Interventions and methods for screening, diagnosis, and treatment of cancer in older persons.

W. Development of methods to accurately determine the renal glomerular filtration rate (GFR) in older persons and patients with chronic kidney disease. The new methods should justify the effects of age-related changes in muscle mass, levels of serum creatinine, renal blood flow and renal concentrating ability.

X. Identification of novel biomarkers of acute kidney injury and chronic kidney disease in older persons. Such research would include identification of biomarkers and evaluation of their clinical utility for early diagnosis, prediction of the course of progression of diseases and/or monitoring the effects of treatment.

Y. Development and validation of new technology such as non-invasive methods to examine blood-flow velocity in arteries, individual coronary arteries, renal arteries, and cerebral arteries.

Dr. Basil A. Eldadah
301-496-6771; Fax: 301-402-1784
Email: eldadahb@nia.nih.gov

For additional information on research topics and administrative questions, contact:

Dr. Michael-David ("M-D") A.R.R. Kerns
Health Scientist Administrator
National Institute on Aging
Gateway Building, Suite 2C218
7201 Wisconsin Ave., MSC 9205
Bethesda, MD 20892-9205
301-402-7713, Fax: 301-402-2945
Email: michael-david.kerns@nih.hhs.gov

For budget management questions, contact:

Ms. Linda Whipp
Grants Management Officer
National Institute on Aging
Gateway Building, Room 2N212
7201 Wisconsin Ave., MSC 9205
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NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

NIAAA supports research on the causes, prevention, control, and treatment of the major health problems associated with alcohol use. Through its extramural research programs, NIAAA funds a wide range of basic and applied research to develop new and/or improved technologies and approaches for increasing the effectiveness of diagnosis, treatment, and prevention. NIAAA also is concerned with strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

For additional information about areas of interest to the NIAAA, you are invited to visit our home page at http://www.niaaa.nih.gov.

Phase IIB Competing Renewal Awards

NIAAA will accept SBIR/STTR Phase IIB Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA, FCC). Such products include, but are not limited to, medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

Please contact Dr. Max Guo (contact information provided below) before beginning the process of putting an application together. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIAAA SBIR/STTR Phase II awards will be eligible for a Phase IIB Competing Renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase IIB Competing Renewal projects.

These examples are meant for illustrative purposes and are not exclusive of other appropriate activities:

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants. Some in vivo or in vitro studies would be expected to have been carried out in Phase I or the initial Phase II grant.

- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application

- Development and clinical evaluation of new alcohol-sensitive biomarkers

- Assessment of devices with regard to performance standards related to the FDA approval process

- Safety and effectiveness studies of novel medical devices

- Biocompatibility studies of surface materials of putative medical implants
- Evaluation of novel imaging approaches for diagnostic purposes
- Clinical studies in support of New Drug Application approval by the FDA
- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA

Direct your questions about scientific/research issues to:

Q. Max Guo, Ph.D.
Phone: 301-443-0639
Email: Max.Guo@nih.gov

Pharmaceutical Development for Alcoholism Treatment

The topic focuses on applied and, where appropriate, clinical research on pharmacologic agents for use in the treatment or medical management of alcoholism, disorders resulting from alcoholism, the improvement and refinement of drugs currently available for therapeutic purposes, or drugs suitable for use in basic research studies on alcohol addiction. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of agents to attenuate drinking behavior, e.g., drugs to curb craving

B. Development of aversive agents such as disulfiram that can attenuate drinking behavior

C. Development of agents to treat acute alcohol withdrawal

D. Development of drugs that are capable of improving or reversing alcohol-induced cognitive impairments

E. Development of agents to induce sobriety in intoxicated individuals (i.e., amethystic agents)

F. Development of agents to treat associated psychiatric disorders and/or drug abuse, and to diminish drinking

G. Development of improved methods of drug delivery for the treatment of alcoholism. The systems developed must be capable of maintaining therapeutic drug levels for extended periods of time to alleviate compliance problems.

H. Development of drugs for the treatment of alcoholic hepatitis, cirrhosis, pancreatitis, cardiomyopathy, or other alcohol-induced tissue damage

I. Research on the pharmacodynamics and pharmacokinetics of concurrent ethanol and other drug use.

For clinical questions, contact:

Joanne B. Fertig, Ph.D.
301-443-0635
Email: Joanne.Fertig@nih.gov

For pre-clinical questions, contact:

Mark Egli, Ph.D. (Neuroscience and behavior)
301-594-6382
Email: Mark.Egli@nih.gov

Svetlana Radaeva, Ph.D. (Organ damage)
301-433-1189

Email: sr252a@nih.gov

Diagnostic Assessment of Alcohol Use Disorders and Comorbidity

Innovative self-report and biochemical approaches to the early identification of alcohol use problems and diagnosis of alcohol use disorders and comorbidity are needed. The research design should include measurements of reliability and validity in appropriate population samples. Areas that may be of interest to small businesses include, but are not limited to:

A. Development or adaptation of diagnostic instruments measuring alcohol use disorders and related comorbid conditions in general population and treated samples, including youth, the elderly, pregnant women, ethnic minorities, the handicapped, and persons with low-level reading skills).

B. Development and testing of computer algorithms necessary to derive diagnoses of alcohol use disorders and associated comorbidity.

C. Development of innovative methods for diagnostic assessment in clinical settings. Development and testing of detailed audio, visual, or printed training modules to accompany diagnostic instruments.

Cherry Lowman, Ph.D.
301-443-0637
Email: Cherry.Lowman@nih.gov

Treatment of Alcoholism

A. Development and evaluation of innovative therapeutic approaches across the continuum of alcoholism care.

B. Development and validation of tools to aid in the clinical management of patients, including selection of appropriate interventions, process evaluation, assessment of outcome, aftercare, and patient tracking, in various treatment settings.

Cherry Lowman, Ph.D.
301-443-0637
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Alcohol Biosensors and Data Analysis Systems

It is anticipated that innovative and improved alcohol sensors would be useful in a variety of situations including, but not limited to, clinical monitoring, forensics and human or animal research. Specific sensor characteristics would complement their intended use. This applies to characteristics such as sampling frequency, degree of accuracy, data storage capacity and data transmission frequency.

Depending on their intended purpose and use, alcohol sensors may be augmented with additional information such as other physiological measurements or geospatial determinations. Devices need to be compatible with human comfort, and devices to be worn for weeks or months may present particular challenges. Since alcohol readings are likely to be baseline most of the time, these sensing devices generally require ways to monitor contact and readiness to record. Moreover, where necessary, measurement fidelity should be robust to subject's activities including active efforts at tampering.

The mode of data storage will need to conform to power limitations and strategies for data transmission which may require telemetry.

In addition to alcohol monitoring and data transmission this program also includes the opportunity to develop appropriate data analysis systems. Examples include: estimating blood alcohol concentrations, reconstructing patterns of alcohol consumption, and monitoring large numbers of devices to identify significant, but infrequent, events while minimizing false positives.

R. Thomas Gentry, Ph.D.
301-443-6009
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Promoting Adherence to Medical, Pharmacologic, and Behavioral Treatments for Alcohol Use Disorders

Several recent reports and literature reviews point to the continuing need for improving adherence to therapeutic regimens. Adherence rates vary considerably across diseases and treatments, measuring instruments, and populations, with rates ranging from 30% to 60% in many instances. The reasons for non-adherence are multifaceted. Health-care providers, organizational systems, and patient factors all play a role in adherence to therapeutic regimens. Thus, to understand and eventually improve adherence, conceptual frameworks and interventions need to take into account institutional, system, situational, interpersonal, and personal factors as well as the characteristics of the illness or condition and of the treatment regimen. While extensive research exists and successful techniques have been identified, greater efforts are needed to develop and implement programs based upon these findings. Applications are sought to develop:

A. Programs to implement effective interventions and to evaluate their implementation.

B. Professional education courses or web-based training modules on interventions and to monitor their effectiveness.

In both cases, the emphasis is on how to encourage health practitioners to utilize interventions that will improve their patients' adherence to medical, pharmacologic, and behavioral regimens for alcohol abuse and dependence.

Margaret E. Mattson, Ph.D.
301-443-0638
Email: Margaret.Mattson@nih.gov

Prevention

This area of interest focuses on the development and evaluation of innovative prevention and intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Applicants are strongly encouraged to consult with research methodologists and statisticians to ensure that state-of-the-art approaches to design, analysis, and interpretation of studies under this topic are used. Areas that may be of interest to small businesses include, but are not limited to:

A. Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Special emphasis should be placed on the needs of high-risk groups, ethnic and minority populations, youth, children of alcoholics, women, the handicapped, and the elderly. Examples of such materials include school-based curricula, interactive videos, computer-based multimedia programs, training manuals for teachers or parents, and community-based programs.

B. Development and evaluation of educational materials designed to intervene with the elderly around specific age-related risks for alcohol problems. Particular attention should be given to age-related reductions in alcohol tolerance, interactions between alcohol and prescription and over-the-counter medications, possible exacerbation of some medical conditions common among the elderly, potential biomedical and behavioral consequences of excessive alcohol use, and the role of alcohol in falls, fires, burns, pedestrian and traffic injuries, and other unintentional injuries.

C. Development and evaluation of statistical analysis programs tailored to the design and analysis of alcohol prevention-relevant research. Programs could focus on a variety of areas including: imputation of missing data under varying design assumptions; simulation of distributions of outcomes based on varying mixtures of sample populations; application of chronic or infectious disease models to targeted communities; and models of the potential effect of various policy-based interventions, such as increased taxation or reduction of outlet density by license revocation and control.

Robert C. Freeman, Ph.D.
301-443-8820
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Health Services Research on Alcohol-Related Problems

Research projects are sought that will expand knowledge and improve delivery of alcohol treatment and prevention services. The research objectives include, but are not limited to, the effects of organizational structures and financing mechanisms on the availability, accessibility, utilization, delivery, content, quality, outcomes, and costs of alcohol treatment services. Objectives also include studying the effectiveness and cost-effectiveness of alcohol prevention services in reducing the demand for health care services and improving the methodological tools useful for conducting health services research. Areas that may be of interest to small businesses include, but are not limited to:

A. Development and assessment of protocols to assist in the identification, recruitment, and selection of treatment personnel to enhance the matching of staff to program needs.

B. Development and assessment of computer software or other protocols to assist in the management of treatment delivery. Software should be useful for assessment, diagnosis, patient placement criteria, monitoring of services received, tracking patient progress, and billing.

C. Development and assessment of software to assist clinicians in scoring and assessment of score norms for commonly used assessment instruments. These packages should include protocols for guiding client feedback in a clinic or office-based setting.

D. Development and assessment of software or other protocols to assist treatment programs and service agencies in measuring, assessing, or otherwise documenting clinically relevant performance indicators or improvements in quality of service provision.

E. Development and assessment of protocols to facilitate the selection, implementation, adoption, and maintenance of evidence-based services consistent with target population need, staffing and program resources, and expected outcomes. These protocols should be flexible enough to work across a variety of settings and modalities.

F. Development and assessment of software or other protocols to facilitate the incorporation of screening and identification tools into routine usage in primary care, emergency, obstetric, mental health, and other health care settings. Research projects should facilitate both the provisions of brief interventions, medical management, effective referral to specialized alcohol treatment, and follow-up.

G. Development and assessment of software or other protocols for monitoring service costs of alcohol treatment services including core, ancillary, out-sourced services. These tools should provide a user-friendly system of monitoring costs that could be implemented without additional accounting expertise by the staff at a typical treatment setting. At the same time, such tools should be defensible as measures of the true opportunity costs of providing alcohol treatment services. Such software might be bundled with billing software.

Robert Huebner, Ph.D.
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Fetal Alcohol Spectrum Disorder (FASD) and Alcohol-Related Birth Defects

FASD is the collective term for the broad array of documented adverse effects resulting from in utero alcohol exposure. The most serious of these is fetal alcohol syndrome (FAS), a devastating developmental disorder characterized by craniofacial abnormalities, growth retardation, and nervous system impairments that may include mental retardation. Other diagnostic categories include partial FAS, alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD). Children and adults with FASD may exhibit multiple cognitive, behavioral, and emotional deficits that impair daily functioning in many domains. The NIAAA supports research leading to improved diagnosis and assessment of impairment and disability, as well as the development of tools to enhance academic and daily living skills. Areas that may be of interest to small businesses include, but are not limited to:

A. Development and assessment of diagnostic and/or screening methods that can be used prenatally to identify fetuses affected by ethanol.

B. Development and validation of biomarkers that can be used to verify prenatal alcohol exposure in neonates.

C. Development and validation of assessment methods to provide more accurate clinical diagnosis of FASD at all life stages.

D. Development and testing of skill-building, therapeutic, and education program products that enhance the social, cognitive, adaptive and motor abilities of individuals with FASD.

E. Development of neurobehavioral tools or instruments to assess responsiveness of individuals with FASD to medications and/or cognitive/behavioral therapies.

F. Development of accurate measures of the responsiveness of children affected by prenatal exposure to alcohol to stress and predictors of vulnerability to alcohol-drinking or other psychopathology during adolescence and adulthood.

G. Development and evaluation of educational and training programs designed to enhance the skills of non-professional caregivers in dealing with the problems associated with FAS.

H. Development and validation of innovative approaches to prevent harmful drinking during pregnancy.

For basic research questions, contact:

Dale Hereld, MD, Ph.D.
301-443-0912
Email: Dale.Hereld@nih.gov

William C. Dunty, Ph.D.
301-443-7351
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For prevention research questions, contact:

Marcia Scott, Ph.D.
301-402-6328
Email: Marcia.Scott@nih.gov

Alcohol Use and HIV, HBV, or HCV Infection

Alcohol use, including hazardous drinking, by persons infected with HIV, HBV, and HCV, is quite common in the United States. Alcohol consumption is widely acknowledged as a co-factor in the sexual transmission, susceptibility to infection, and progression of the infectious diseases. However, detailed relationships between alcohol use and viral infections, diseases progression, antiretroviral therapy and adverse outcomes, notably in liver disease progression, are less recognized or understood. Recent

research indicates that inflammatory pathways predominate in alcoholic hepatitis whereas adaptive immunity plays a primary role in viral hepatitis, offering multiple targets for novel preventive and therapeutic interventions. Comprehensive studies to improve understanding of the factors underlying alcohol and viral etiologies in liver disease and the impact of antiretroviral drugs on liver disease progression are needed. A better understanding of alcohol's effects on liver disease in patients with HIV/HBV/HCV infection may improve diagnosis and treatment outcomes. NIAAA supports research leading to improved diagnosis and treatment of alcohol-induced disorders in people infected with HIV, HBV, or HCV.

Areas that may be of interest to small businesses include, but are not limited to:

A. New preventive and therapeutic approaches designed to protect the liver from alcohol and antiretroviral drug-induced liver injury in patients infected with HIV, HBV, or HCV.

B. Development of therapies aimed at molecular targets that play a role in the development of alcoholic and viral liver diseases.

C. Develop and evaluate drugs that mitigate the effects of oxidative stress on mitochondrial function thereby preventing liver disease progression.

D. Development of biomarkers for individuals who are most prone to alcohol-induced damage in those patients infected with HIV, HBV, or HCV.

For HBV/HCV and basic research questions on HIV, contact:

H. Joe Wang, Ph.D.
301-451-0747
Email: He.Wang@nih.gov

For clinical or epidemiological questions on HIV, contact:

Kendall J. Bryant, Ph.D.
301-402-9389
Email: Kendall.Bryant@nih.gov

Research Tools

The NIAAA supports the development of new or improved tools to enhance the ability to conduct alcohol-related laboratory studies on humans and animals and to more effectively analyze data from large databases. Examples include transgenic animal models, cell lines, new ligands for neuroimaging, and simulators of alcohol impairment. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of novel animal models, including transgenic animals, possessing specific traits of significance for the study of alcoholism, or for the study of specific pathologic disease states which arise from excessive alcohol consumption.

B. Development of a hepatocyte cell line capable of maintaining viability and metabolic functions in culture systems for an indefinite period.

C. Development of new methods of ethanol administration to animals that produce precise dose control or that closely mimic types of alcohol exposure occurring in humans, including, but not limited to, binge drinking, acute consumption, moderate consumption and chronic consumption.

D. Development of specialized cell culture chambers to provide controlled administration of ethanol to in vitro cell systems.

E. Development of ligands which will enhance the potential usefulness of PET and SPECT imaging technologies for the study of the etiology of alcoholism and related brain pathology.

F. Development of genetic, epigenetic, genomic, proteomic, metabolomic, lipidomic, glycomic or other systems-wide methods for assessment, prognosis, diagnosis or treatment of alcohol-induced disorders.

G. Development of computational, statistical or bioinformatics tools to organize and manage high throughput data obtained by genomic, functional genomic or other 'omic strategies.

H. Development of databases, methods for integration of databases, or data analysis systems for alcohol research.

Kathy Jung, Ph.D.
301-443-8744
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Development of Biomolecular Signatures of Alcohol Exposure and Alcohol-induced Tissue Injury

Acute and chronic alcohol consumption leads to health-related complications and ultimately to significant societal costs. Quantitative and qualitative markers of high-risk drinking behavior and alcohol-induced tissue damage would greatly improve medical efforts to recognize and treat alcohol-related disorders. Traditional biomarkers currently in clinical use lack specificity, sensitivity, and accuracy, and fail to provide long-term information. Biomarkers of sufficient reliability, sensitivity and specificity are likely to be comprised of a panel of physiological parameters, rather than a single molecular entity. Thus, NIAAA seeks to support the discovery and development of pattern-based molecular fingerprints or signatures of alcohol consumption and of alcohol-induced tissue injury. High throughput approaches using genomics, epigenomics, transcriptomics, proteomics, metabolomics, lipomics, or glycomics are encouraged. Biomarker signatures may be composed of multiple genes, RNAs, microRNAs, proteins, or metabolites, or combinations thereof. Furthermore, alterations in lipid, lipoprotein, or glycoprotein profiles may reflect the metabolic effects of alcohol exposure and may be considered as potentially predictive. Biomarker signatures that address multiple aspects of alcohol consumption and alcohol damage are needed. These include, but are not limited to:

A. Biomarkers of long-term alcohol consumption. A biomarker panel reflecting the cumulative intake of alcohol over a period of months or more would be of great diagnostic use, both in terms of recognizing problem drinking and in terms of the potential for organ damage.

B. Biomarkers that distinguish between binge, acute, moderate and chronic drinking. Each of these modes of alcohol intake has different physiological effects. The ability to distinguish dose and timing of drinking would enhance clinicians' ability to design appropriate treatment and intervention protocols.

C. Biomarkers of compliance after withdrawal. Biomarker signatures in this class would be comprised of metabolic products that decrease rapidly upon abstinence, in contrast to the characteristics of biomarkers that reflect cumulative alcohol. The ability to detect relapse accurately will support successful behavioral interventions.

D. Biomarker signatures of alcohol-induced organ damage. The damage due to alcohol consumption is likely to be organ-specific, with signatures reflecting alcohol-induced damage likely to be different for heart damage, liver damage, encephalopathy, a dysregulated immune system, or other alcohol target.

E. Biomarker signatures of familial risk factors for alcoholism. Early identification of subjects predisposed to alcoholism will allow for early intervention, and allow the subject to make informed decisions.

Kathy Jung, Ph.D.
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Clinical Testing of Biochemical Markers

The development of effective biochemical markers represents a powerful means for early diagnosis and treatment of alcohol dependent/abuse patients and for the identification of individuals who have a predisposition for alcoholism. There are two different types of biochemical markers: trait markers and state markers.

Trait biomarkers have the ability to detect inborn characteristics of individuals who are vulnerable for alcoholism. This type of marker would be invaluable for screening of high-risk individuals (e.g., children of alcoholics) and targeting them with preventive or early treatment interventions. In addition, trait markers might assist practitioners in identifying subpopulations of alcoholics who may need different treatment strategies. An ideal trait marker should have several features. First, it should display validity in detecting people susceptible to alcoholism, particularly before the onset of alcoholism or during periods of stable abstinence. Second, it should be easily and reliably measured. Third, it should be specific for alcoholism only and not affected by other medical or psychiatric disorders or drugs. Since alcoholism is a complex disease, it is likely that more than one type of gene and protein exist as trait marker.

State markers or markers of alcohol consumption serve several important purposes. First, they can assist physicians in diagnosing individuals with chronic drinking problems, particularly patients who deny excessive drinking. Moreover, they may also identify individuals in early stages of heavy drinking, thus avoiding the long-term medical, psychological, and social consequences of chronic alcoholism. Second, state biomarkers can aid in the diagnosis and treatment of other diseases (liver diseases, pancreatitis, and cardiovascular diseases) that were, at least, caused by excessive drinking. Third, they are useful in alcohol treatment and prevention programs. Since the goal of many of programs is abstinence, monitoring relapse is important in gauging success. Last, state biomarkers are important in clinical alcohol trials. Although self-reports have become more sophisticated and valid (e.g., Timeline Followback), they still rely on accurate reporting. These new and reliable biomarkers could then be used to confirm the self-report. Several biomarkers with certain limitations are currently in use including carbohydrate-deficient transferrin (CDT), gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and mean corpuscular volume (MCV). New state markers need to be developed that incorporate the following attributes: validity, reliability, stability, cost, practicability, acceptability, and transportability.

Areas that may be of interest to small businesses include, but are not limited to:

A. Develop and evaluate clinically alcohol-sensitive biomarkers to identify individuals who are predisposed to alcoholism; determine relapse; measure levels of drinking; and determine alcohol-induced tissue damage.

B. Identify genes, and proteins that are expressed during the development of alcohol dependence for biomarker development.

C. Develop methodologies for high throughput identification of alcohol metabolites and other signaling molecules that are expressed during alcohol intake.

D. Use knowledge of genetic and molecular mechanisms underlying alcohol-induced organ damage (including alcohol-related liver, pancreas, heart disease and FAS) to develop new biomarkers of tissue and cell damage.

E. Evaluate clinically innovative alcohol-sensitive biomarkers (trait, relapse, organ damage) for sensitivity and specificity.

Raye Z. Litten, Ph.D.
301-443-0636
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Stem Cell Research for Alcohol-induced Disorders

Stem cells are master cells in the body and they have the remarkable potential to develop into many different cell types. Stem cells may become a renewable source of replacement cells to treat alcohol related diseases. They can also be used to study disease processes, and to develop new and more effective drugs.

Recent research progress on stem cells has offered great opportunities to study conditions and diseases related to alcohol abuse and alcoholism. Stem cells can come from embryos or adult tissues. They are generally categorized into 1) Embryonic stem cells; 2) Induced pluripotent stem cells (iPS cells); and 3) Adult stem cells. The NIAAA supports SBIR/STTR research using any of these 3 types of stem cell, which can lead to improved understanding of alcohol related diseases and conditions, and better treatment.

Areas that may be of interest to small businesses include, but are not limited to:

A. Generate and disseminate induced pluripotent stem cells (iPS) from mature human cells to resemble diverse individual variations regarding alcohol metabolism. Use these genetic variant models to study alcohol dependence and pharmacotherapy development. Examples of these genetic variations include Alcohol Dehydrogenase (ADH), Aldehyde Dehydrogenase (ALDH), cytochrome P450 isozyme CYP2E1, and Glutathione S transferase (GST).

B. Generate and disseminate disease-specific iPS cell lines for studies on the biology and signaling pathways that contribute to the alcohol-related disease pathology.

C. Study the potential of using patient-specific iPS cells for cell replacement therapies to treat alcohol-caused tissue damages.

Peter Gao, M.D.
301-443-6106
Email: Peter.Gao@nih.gov

Real-time Detection of Neurochemical Changes in Response to Alcohol Drinking

Many pharmacological mechanisms of ethanol action in the brain are mediated by time-dependent neurochemical events in multiple brain regions. Despite great progress in identifying ethanol's neurochemical actions, we do not fully know how neurochemicals change in real time following ethanol administration and drinking (acute and chronic). Multidimensional measurement of neurochemical change (i.e., concentration, time, region) are needed to reveal kinetics underlying alcohol effects to guide future medication development and promote mechanistic understanding of alcohol drinking.

With this SBIR/STTR grant solicitation, NIAAA seeks development of biosensors enabling monitoring of regional neurochemical changes in the brains of rats and/or mice in real time as they drink alcohol. Recent studies report the plausibility of using microsensors coupled with wireless detection methods to instantaneously monitor multiple neurochemical changes in animals. NIAAA seeks development of microsensors with sufficient resolution to provide neuroanatomical regional specificity. In addition to brain ethanol concentration, neurochemicals of interest include, but are not limited to, glutamate, dopamine, GABA, acetylcholine, and signaling molecules. Work under this solicitation should be directed toward the development of commercial strategies for the real-time measurement of extracellular neurochemical and brain ethanol concentrations in behaving animals.

Changhai Cui, Ph.D.
301-443-1678
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Mark Egli, Ph.D.
301-594-6382

Email: Mark.Egli@nih.gov

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Q. Max Guo, Ph.D.
National Institute on Alcohol Abuse and Alcoholism
5635 Fishers Lane, Room 2037
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For Federal Express delivery, use:
Rockville, MD 20852-1705
Phone: 301-443-0639
Email: Max.Guo@nih.gov

For administrative and business management questions, contact:

Ms. Judy Fox
Grants Management Officer
National Institute on Alcohol Abuse and Alcoholism
Phone: 301-443-4704, Fax: 301-443-3891
Email: Judy.Fox@nih.gov

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

The NIAID's Division of AIDS, Division of Allergy, Immunology, and Transplantation, and Division of Microbiology and Infectious Diseases fund SBIR/STTR grants on topics related to their mission and activities as described below. Questions on specific research areas may be addressed to the NIAID Program Officials listed below. General questions on the NIAID SBIR and STTR programs and on administrative and business management may be addressed to contacts listed for the NIAID section. When possible, *applicants are encouraged to use email* for communication.

For information about NIAID's Small Business Programs, please visit http://funding.niaid.nih.gov/researchfunding/sb/pages/default.aspx.

Limited Amount of Award (Total not Annual)

For budgetary or programmatic reasons, NIAID may decrease the requested length of an award or the requested amount of an award. Applicants considering requesting a Phase I grant greater than $300,000 total cost or a Phase II grant greater than $2 million total cost are strongly encouraged to contact Gregory Milman (below) before submitting an application.

Phase IIB SBIR Competing Renewal Awards

The NIAID will accept Phase IIB SBIR Competing Renewal grant applications to continue the process of developing products that require approval of a regulatory agency (e.g., FDA). Projects that are particularly encouraged include those in the NIAID Small Business High Priority Areas of Interest (http://funding.niaid.nih.gov/researchfunding/sb/pages/sbirareas.aspx). NIAID will not accept Phase IIB STTR Competing Renewal applications.

NIAID will accept Phase IIB SBIR Competing Renewal applications for a project period of up to three years and a budget not to exceed a total cost of $1 million per year (including direct cost, F&A, and fee/profit) provided the time period and amount are well justified.

The total amount of all consultant costs and contractual costs normally may not exceed 50% of the total costs requested for initial SBIR Phase II applications. NIAID SBIR Phase IIB Competing Renewal grant applications may exceed this guideline, however, when well justified and when those costs are necessary to support preclinical studies and related expenses. Examples of well founded reasons for exceeding this guideline include, but are not limited to, subcontracts for safety, toxicity, or efficacy testing in animals, and subcontracts to assure compliance with Good Manufacturing Practices expectations of the FDA.

Human clinical trials may not be a component of proposed SBIR or STTR research. See Notice of NIAID Policy on investigator initiated clinical trials at http://grants.nih.gov/grants/guide/notice-files/NOT-AI-10-024.html. Small business applicants are encouraged to contact Gregory Milman (below) to discuss NIAID funding for human clinical trials.

NIAID does NOT request a letter of intent for Phase IIB Competing Renewal Applications. However, prior to submission, applicants are strongly encouraged to contact:

Gregory Milman, Ph.D.
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room 2130, MSC-7610
6700-B Rockledge Drive
Bethesda, MD 20892-7610 (US Mail)
Rockville, MD 20817-7610 (Delivery Services)
Telephone 301-496-8666
Fax: 301-402-0369
Email: gm16s@nih.gov

Division of AIDS

The Division of AIDS (DAIDS) supports research on the pathogenesis, natural history, and transmission of HIV and HIV disease, and promotes progress in its detection, treatment, and prevention.

Director: Dr. Carl Dieffenbach
301-496-0545
Email: cd17u@nih.gov

BASIC SCIENCES PROGRAM

Supports basic and applied research on the causes, diagnosis, treatment and prevention of HIV and AIDS.

Director: Dr. Susan Plaeger
301-402-9444
Email: splaeger@niaid.nih.gov

A. ***Epidemiology Branch.*** Population-based research and modeling studies of HIV transmission and associated biological and behavioral factors. Also, the treated and natural history of HIV, including research on immunology, virology, therapy and other issues surrounding care, and other co-morbidities, their interactions and impact on clinical outcome.

Contact: Joana Roe
301-435-3759
Email: jr108r@nih.gov

B. ***Pathogenesis Branch.*** Molecular and cellular biology, virology, and immunology of virus-host interactions and mechanisms of immunopathogenesis and HIV transmission. Identification and

characterization of host and viral factors that impact viral transmission, host restriction, pathogenesis and latency. Characterization of potential targets for discovery or design of novel therapeutic strategies. Innovative approaches for monitoring or studying viral infection, pathogenesis and latency.

Contact: Dr. Karl Salzwedel
301-496-5332
Email: salzwedelkd@niaid.nih.gov

C. ***Targeted Interventions Branch.*** Research areas: (1) targeted therapeutics emphasizing under-explored viral and cellular targets; (2) innovative therapeutic strategies including immune-based and gene-based therapies and therapeutic vaccines; (3) translational research for effective therapeutics spanning preclinical discovery through IND-enabling studies; (4) animal models for evaluating new therapeutic entities, regimens, and strategies; and (5) therapeutic approaches using nanotechnology.

Contact: Dr. Roger Miller
301-496-6430
Email: rm42i@nih.gov

VACCINE RESEARCH PROGRAM

Supports the development of vaccines to prevent AIDS.

Director: Dr. Margaret (Peggy) Johnston
301-402-0846
Email: pj7p@nih.gov

A. ***Vaccine Clinical Research and Development Branch.*** Research areas: (1) coordination of phase I, II, and III domestic and international clinical trials of candidate AIDS vaccines; (2) coordination of the characterization of immune responses in HIV-infected and uninfected immunized volunteers, using micro and macro assays; and (3) coordination of studies to identify, validate, and standardize immunologic and virologic markers for monitoring response of participants in vaccine clinical trials.

Contact: Dr. Jim Lane
301-451-2758
Email: laneji@mail.nih.gov

B. ***Preclinical Research and Development Branch.*** Support of applied preclinical development of candidate AIDS vaccines, delivery methods and novel vaccine vectors, and adjuvants for the prevention of AIDS; promotion and evaluation of safety and efficacy of the prevention modalities, especially novel vaccine concepts identified in preclinical models including trials in non-human primates; genetic and immunologic variation; and mucosal immunity in SIV, HIV, and SHIV models.

Contact: Dr. Yen Li
301-496-3816
Email: yli@niaid.nih.gov

C. ***Vaccine Discovery Branch.*** Research on: 1) identification of optimal antigens for HIV vaccine design (e.g., epitope mapping, epitope dominance, etc.); 2) identification of cellular components or novel antigens created by env-host interactions as vaccine targets; 3) development of innovative small animal models and in vitro systems to assess immune responses to vaccines; and 4) novel innate and mucosal immune pathways, adjuvants and immunomodulators to improve vaccine responses.

Contact: Dr. Geetha Bansal
301-496-5042

Email: gbansal@niaid.nih.gov

THERAPEUTICS RESEARCH PROGRAM

Develops and oversees research and development of therapies for HIV disease, including complications, co-infections, co-morbidities and cancers, in adults, infants, children, and adolescents.

Acting Director: Dr. Carla Pettinelli
301-402-5582
Email: pettinelli@niaid.nih.gov

A. ***Drug Development and Clinical Sciences Branch.*** Discovery and preclinical development of experimental therapies for HIV, TB and other infectious diseases; maintenance of a database of potential anti-HIV and anti-opportunistic infection compounds; immunologic, virologic, and pharmacologic research related to the design and conduct of clinical trials.

Chief: Dr. Mike Ussery
301-402-0134
Email: mussery@niaid.nih.gov

B. ***HIV Research Branch.*** Clinical research of strategies to treat adult primary HIV infection and complications; strategies to augment HIV immune responses and general host immunity.

Contact: Daniella Livnat
301-435-3775
Email: dlivnat@niaid.nih.gov

C. ***Complications & Co-Infections Research Branch.*** Preclinical and clinical research to develop new or improved therapies for the treatment and prophylaxis of Pneumocystis carinii pneumonia, Mycobacterium avium disease, and cryptococcosis. Evaluation of diagnostics of or agents for treatment or prevention of hepatitis B or hepatitis C secondary to HIV infection in adults.

Contact : Dr. Chris Lambros
301-435-3769
Email: clambros@niaid.nih.gov

D. ***International Maternal, Adolescent and Pediatric Medicine Branch.*** HIV therapies in children and adolescents. Strategies to reduce transmission from mother to infant or fetus.

Chief: Dr. Ed Handelsman
301-402-3221
Email: handelsmane@niaid.nih.gov

E. ***Prevention Sciences Program.*** Conduct basic research on mechanisms of HIV transmission supportive of new biomedical strategies for interrupting transmission. Conduct of domestic and international phase I, II, and III clinical trials to evaluate HIV/AIDS prevention strategies, including microbicides, chemoprophylactic agents, and other biomedical and behavioral risk reduction interventions.

Acting Director: Sheryl Zwerski, MSN, CRNP
301-402-4032
Email: szwerski@niaid.nih.gov

F. ***Microbicide Research Branch.*** Basic research on mechanisms of HIV transmission leading to new biomedical strategies for interrupting transmission. Translational research on microbicides, spanning discovery and preclinical through pilot human clinical research. Pilot clinical studies of the performance of microbicide vehicles with regard to coverage of and persistence on mucosal

surfaces, potential biomarkers of safety, behavioral acceptability, and new technology to evaluate safety.

Dr. Roberta Black
Chief Topical Microbicide Research Branch
301-496-8199
Email: rblack@niaid.nih.gov

Division of Allergy, Immunology, and Transplantation

The Division of Allergy, Immunology, and Transplantation (DAIT) supports studies of the immune system in health and the cause, pathogenesis, diagnosis, prevention, and treatment of disease caused by immune dysfunction.

Director: Daniel Rotrosen, M.D.
301-496-1886
Email: drotrosen@niaid.nih.gov

A. ***Asthma, Allergy, and Inflammation Branch.*** Asthma, atopic dermatitis, hypersensitivity reactions, rhinitis, sepsis, sinusitis, urticaria, basic studies of asthma and allergy mechanisms, new therapies to prevent or treat asthma and allergic diseases, food allergies, epidemiology and prevention, phagocyte biology, eosinophilic gastroenteritis, and mechanisms of host defense. Methodologies to design, manage, and analyze clinical and epidemiologic research of the etiology, prevention, and treatment of asthma, allergy, and inflammatory diseases.

Chief: Dr. Matthew Fenton
301-451-0144
Email: fentonm@niaid.nih.gov

B. ***Basic Immunology Branch.*** Origin, maturation, and interactions of immune cells, immune cell receptors, ligands, cytokine biology, molecular basis of activation, antigen recognition, immune tolerance, immune response regulation, hematopoiesis and stem cell biology, enhancement of vaccine effectiveness in neonates and adults, and basic immunology of vaccines and immunotherapeutics as medical countermeasures for biodefense.

Chief: Dr. Helen Quill
301-496-7551, Fax: 301-480-2381
Email: hquill@niaid.nih.gov

C. ***Clinical Immunology Branch.*** Preclinical and clinical research to develop and improve therapies for the treatment of autoimmune diseases, primary immune deficiencies (not HIV), basic research of disease mechanisms, and biomarkers, immunotherapy of disease processes, disorders mediated by lymphocyte products, and mucosal immunity.

Chief: Dr. James McNamara
301-451-3121, Fax: 301-480-1450
Email: jmcnamara@niaid.nih.gov

D. ***Transplantation Immunobiology Branch.*** Acute and chronic graft rejection, allogeneic and xenogeneic transplantation, development of immunomodulatory agents to prevent and treat graft rejection, genomics of the alloimmune response, hematopoietic stem cell transplantation, major histocompatibility complex, minor histocompatibility antigens, infectious and malignant complications of immunosuppression in transplantation, and technologies for MHC typing.

Chief: Dr. Nancy Bridges
301-496-5598
Email: nbridges@niaid.nih.gov

E. ***Radiation Countermeasures Program.*** Radioprotectants, mitigators and therapeutics for acute radiation syndrome or the delayed effects of acute radiation exposure; radionuclide-specific therapies, including chelating agents, blocking agents, and other novel decorporation agents; improved methods of radiation biodosimetry and bioassay for radionuclide contamination; biomarkers of organ-specific radiation injury; therapeutics for radiation combined injury; therapeutics for radiation-induced immunosenescence.

Chief: Dr. Richard Hatchett
301-451-3109
Email: hatchettr@niaid.nih.gov

Division of Microbiology and Infectious Diseases

The Division of Microbiology and Infectious Diseases (DMID) supports research to better understand, treat, and ultimately prevent infectious diseases caused by virtually all infectious agents, except HIV. DMID supports a broad spectrum of research from basic molecular structure, microbial physiology and pathogenesis, to the development of new and improved vaccines and therapeutics. DMID also supports medical diagnostics research, which is defined as research to improve the quality of patient assessment and care that would result in the implementation of appropriate therapeutic or preventive measures. DMID does not support research directed at decontamination or the development of environmentally oriented detectors, whose primary purpose is the identification of specific agents in the environment. Note that some of the organisms and toxins listed below are considered NIAID priority pathogens or toxins for biodefense and emerging infectious disease research.

Director: Dr. Carole Heilman
301-496-1884
Email: ch25v@nih.gov

A. ***Bacteriology and Mycology Branch.*** The branch oversees research on medical mycology, hospital infections (including Acinetobacter, Klebsiella, Serratia, Legionella, Pseudomonas, Aeromonas, Enterobacter, Proteus, non-enteric E. coli, actinomycetes and others), staphylococci, enterococci, bacterial zoonoses (plague, anthrax, tularemia, glanders, melioidosis, Lyme disease, rickettsial diseases, anaplasmosis, ehrlichiosis and Q fever), and leptospirosis. Research is encouraged in the following general areas: (1) product vaccines, adjuvants, therapeutics and diagnostics (including target identification and characterization, device or apparatus development, novel delivery, and preclinical evaluation); (2) products to combat antibacterial and antifungal drug resistance; (3) applied proteomics and genomics; (4) host-pathogen interactions, including pathogenesis and host response; (5) genetics, molecular, and cell biology; (6) microbial structure and function; and (7) vector-pathogen interactions or disease transmission to humans via arthropod vectors. Research in the following areas is of particular interest to the branch, but research on all of the above is welcome:

- Vaccines, therapeutics, and medical diagnostics for hospital infections
- Adjunctive therapies to combat antimicrobial resistance
- Diagnostics for aspergillosis
- Novel approaches for the diagnosis of Lyme disease

Contact: Dr. Alec Ritchie
301-402-8643, Fax: 301-402-2508
Email: aritchie@niaid.nih.gov

B. ***Enteric and Hepatic Diseases Branch.*** Special emphasis areas include vaccines against hepatitis C virus; antimicrobials and antivirals that focus on novel targets such as host-pathogen interactions

to combat the development of resistance; vaccines and therapies for botulinum neurotoxins, especially therapies that that target toxins once they enter cells; therapies and diagnostics for *Clostridium difficile* that include recurrent disease issues; development of a simple, rapid point-of-care diagnostic tool for the simultaneous identification of multiple diarrheal pathogens that includes their antibiotic resistance profiles; pediatric vaccines to prevent the major worldwide causes of diarrhea; more stable vaccines and improved formulation methods; and novel therapeutics for chronic hepatitis B and C.

Research areas of the Branch include the following organisms and diseases: astrovirus, *Bacteroides spp.*, *Campylobacter spp.*, enteric *Clostridia spp.* including botulinum neurotoxins, commensals and normal flora, pathogenic *Escherichia coli*, gastroduodenal disease, gastroenteritis, *Helicobacter spp.*, *Listeria spp.*, Noroviruses including Norwalk, ricin toxin, rotaviruses, *Salmonella* serovars, *Shigella spp.*, Staphylococcus enterotoxin B, *Vibrio spp.* enteric *Yersinia spp.*, hepatitis viruses A, B, C, D, and E, as well as cholera, diarrhea, enterotoxins, gastroenteritis, gastroduodenal disease and ulcers, and Guillain-Barre syndrome.

Program Contact: Dr. Marian Wachtel
301-451-3754, Fax: 301-402-1456
Email: wachtelm@niaid.nih.gov

C. ***Parasitology and International Programs Branch.*** Research areas: (1) protozoan infections, including amebiasis, cryptosporidiosis, cyclosporiasis, giardiasis, leishmaniasis, malaria, trypanosomiasis, toxoplasmosis; helminth infections, including cysticercosis, echinococcosis, lymphatic filariasis, schistosomiasis, onchocerciasis, others (e.g., roundworms, tapeworms, and flukes); invertebrate vectors/ectoparasites, black flies, sandflies, tsetse flies, mosquitoes, ticks, snails, mites; (2) parasite biology (genetics, genomics, physiology, molecular biology, and biochemistry); (3) protective immunity, immunopathogenesis, evasion of host responses; (4) clinical, epidemiologic, and natural history studies of parasitic diseases; (5) research and development of vaccines, drugs, immunotherapeutics, and medical diagnostics, and (6) vector biology and management; mechanisms of pathogen transmission.

Chief: Dr. Lee Hall
301-496-2544, Fax: 301-402-0659
Email: lhall@niaid.nih.gov

D. ***Respiratory Diseases Branch.*** Research areas: (1) viral respiratory diseases, including those caused by: human coronaviruses (including SARS), influenza viruses, and paramyxoviruses (including parainfluenza viruses and respiratory syncytial virus); (2) bacterial respiratory infections, including those caused by *Moraxella catarrhalis* (chronic obstructive pulmonary disease), *Pseudomonas aeruginosa* and *Burkholderia cepacia* (associated with cystic fibrosis), *Corynebacterium diphtheriae* (diphtheria), groups A and B streptococci, *Haemophilus influenzae*, *Neisseria meningitidis*, *Bordetella pertussis* (pertussis), *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Klebsiella pneumoniae* and community acquired pneumonia; (3) acute otitis media; (4) mycobacterial diseases, including those caused by: *M. tuberculosis* (tuberculosis), extensively- and multi-drug resistant *M. tuberculosis*, *M. leprae* (leprosy), and *M. ulcerans* (Buruli ulcer) and other non-tuberculous mycobacterial diseases. Areas of emphasis include: development of new antibiotics with novel mechanisms of action, improved therapeutics for viral and bacterial respiratory diseases including immunotherapeutics, new or improved vaccines (with and without adjuvants), improved and more rapid multiplex point-of-care diagnostic tests or other screening tools that can detect infection prior to active disease and identify drug resistance.

Contact: Dr. Gail Jacobs
301-496-5305, Fax: 301-496-8030
Email: ggjacobs@niaid.nih.gov

E. ***Sexually Transmitted Infections Branch.*** Areas of emphasis include the development of medical diagnostics including better and more rapid multiplex point of care tests and other screening or novel delivery systems for diagnostic tools, topical microbicides, vaccines and drugs for sexually transmitted infections (STIs) and other reproductive tract syndromes, such as bacterial vaginosis; molecular immunology; vaginal ecology and immunology; epidemiologic and behavioral research including strategies to reduce transmission of STIs; genomics and proteomics of sexually transmitted pathogens; adolescents and STIs; STIs and medically underserved populations and minority groups; STIs and infertility and adverse outcomes of pregnancy; role of STIs in HIV transmission; role of HIV in altering the natural history of STIs; and other sequellae of STIs.

Contact: Elizabeth Rogers
301-451-3742, Fax: 301-480-3617
Email: erogers@niaid.nih.gov

F. ***Virology Branch.*** Areas of emphasis for SBIR/STTR applications include:1) vaccine development; 2) viral vectors; 3) structure and function of viruses and viral proteins as targets for therapeutic interventions or diagnostics; 4) the development and validations of assays for disease diagnosis and to measure response to therapy; 5) the development and preclinical testing of immunotherapeutic and antiviral drugs for acute and chronic viral illnesses; 6) approaches to identify antiviral targets and agents; 7) chemical design and synthesis of novel antiviral agents; 8) preclinical antiviral evaluations including *in vitro* screening and prophylactic or therapeutic antiviral evaluations of human viral infections in animal models; 9) the development of rapid medical diagnostic systems.

The Virology Branch focuses on the following: acute viral infections (including Nipah and Hendra viruses), arthropod-borne and rodent-borne viral diseases (including Dengue, West Nile, Japanese encephalitis, Chikungunya, yellow fever, hantavirus, etc.), viral hemorrhagic fevers (Ebola, Lassa fever, etc.), measles, polio, coxsackie virus, enterovirus 71 and other enteroviruses, poxviruses, rabies, and rubella. The Virology Branch also focuses on the following persistent viral diseases and viruses: adenoviruses, BK virus, bornaviruses, coronaviruses, herpesviruses, human T-lymphotrophic virus, JC virus, human papillomaviruses, parvoviruses, and prion diseases. Applications targeting the development of therapies, immunotherapies, vaccines and diagnostics for any of these infections are sought. The Virology Branch does not support applications covering environmental detection and decontamination.

Contact: Dr. Ramya Natarajan
301-594-1586, Fax: 301-402-0659
Email: ramya.natarajan@nih.gov

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Dr. Gregory Milman
National Institute of Allergy and Infectious Diseases
301-496-8666, Fax: 301-402-0369
Email: gmilman@niaid.nih.gov

For administrative and business management questions, contact:

Mr. Michael Wright
Grants Management Specialist
National Institute of Allergy and Infectious Diseases
301-451-2688, Fax: 301-493-0597
Email: mawright@mail.nih.gov

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)

The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases, the training of basic and clinical scientists to carry out this research, and the dissemination of information on research progress in these diseases.

For additional information about areas of interest to the NIAMS, please visit NIAMS Long Range Plan at http://www.niams.nih.gov/About_Us/Mission_and_Purpose/long_range.asp.

Arthritis and Musculoskeletal and Skin Diseases

A. ***Division of Skin and Rheumatic Diseases.*** This division promotes and supports: basic and clinical studies of the skin in normal and disease states; and research leading to prevention, diagnosis and cure of rheumatic and related diseases. In the area of Skin Diseases, the division has a wide range of skin diseases under study with NIAMS support, to include keratinizing disorders such as psoriasis and ichthyosis, atopic dermatitis and other chronic inflammatory skin disorders, the vesiculobullous diseases such as epidermolysis bullosa and pemphigus, acne, and vitiligo. In the area of Rheumatic Diseases, the division supports basic, epidemiologic, and clinical research on etiology, pathogenesis, course, interventions, and outcomes in rheumatic and related diseases.

   This is not an inclusive list of all research topics covered by the Division of Skin and Rheumatic Diseases. To learn more, please visit the Division page at http://www.niams.nih.gov/Funding/Funding_Opportunities/Supported_Scientific_Areas/Skin_Rheumatic_Diseases/default.asp.

B. ***Division of Musculoskeletal Diseases.*** The musculoskeletal system is comprised of the skeleton, which provides mechanical support and determines shape; the muscles, which power movement; and connective tissues such as tendon and ligament, which hold the other components together. The cartilage surfaces of joints and the intervertebral discs of the spine allow for movement and flexibility.

   The Division of Musculoskeletal Diseases of the NIAMS supports research aimed at improving the diagnosis, treatment, and prevention of diseases and injuries of the musculoskeletal system and its component tissues. Key public health problems addressed by this research include osteoporosis, osteoarthritis, and muscular dystrophy. Research is conducted at every level, from fundamental biology to clinical intervention.

   This is not an inclusive list of all research topics covered by the Division of Musculoskeletal Diseases. To learn more, please visit the Division page at http://www.niams.nih.gov/Funding/Funding_Opportunities/Supported_Scientific_Areas/Musculoskeletal_Diseases/default.asp.

For general SBIR/STTR program information, contact:

Dr. Xibin Wang, NIAMS SBIR/STTR Coordinator
301-451-3884, Fax: 301-480-1284
Email: wangx1@mail.nih.gov

For administrative and business management questions, contact:

Ms. Sheila Simmons
301-594-9812, Fax: 301-480-5450
Email: simmonss@mail.nih.gov

Mr. Erik (Timothy) Edgerton

301-594-3968, Fax: 301-480-5450
Email: edgertont@mail.nih.gov

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING (NIBIB)

The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) is to improve health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the physical and engineering sciences with the life sciences to advance basic research and medical care. This is achieved through: research and development of new biomedical imaging and bioengineering techniques and devices to fundamentally improve the detection, treatment, and prevention of disease; enhancing existing imaging and bioengineering modalities; supporting related research in the physical and mathematical sciences; encouraging research and development in multidisciplinary areas; supporting studies to assess the effectiveness and outcomes of new biologics, materials, processes, devices, and procedures; developing technologies for early disease detection and assessment of health status; and developing advanced imaging and engineering techniques for conducting biomedical research at multiple scales. More specifically, the mission of the NIBIB includes the following research areas:

A. ***Biomaterials.*** Development of new or novel biomaterials that can be used for a broad spectrum of biomedical applications such as implantable devices; drug and gene delivery; tissue engineering; imaging agents; and biosensors and actuators. Research that is supported includes the design, synthesis, characterization, processing and manufacturing of these materials as well as the design and development of devices constructed of these materials and their clinical performance.

B. ***Biomechanics and Rehabilitation Engineering.*** Research on biomechanics which can be applied to a broad range of applications including implants, prosthetics, clinical gait and posture biomechanics, traumatic injury, repair processes, rehabilitation, sports and exercise, as well as technology development in other NIBIB interest areas applied towards biomechanics. Rehabilitation engineering research that is supported includes theoretical models and algorithms for understanding neural, motor, and robotic control strategies; quantitative analysis algorithms for predicting therapeutic outcomes; and early stage development of neuroprosthesis technology, virtual rehabilitation, and robotics rehabilitation.

C. ***Biomedical Informatics.*** Development of new technologies to collect, store, retrieve, and integrate quantitative data; large-scale data-driven knowledge base and database methods that support data mining, statistical analysis, systems biology and modeling efforts; and improvement of computer science methods to protect confidentiality of patient data.

D. ***Drug and Gene Delivery Systems and Devices.*** Development of new and improved technologies for the controlled and targeted release of therapeutic agents. Areas of emphasis include: the development of new delivery vehicles such as nanoparticles and micellar systems; energy-assisted delivery using ultrasound, electroporation, etc.; and the integration of biosensing with controlled dosage delivery using BioMEMS and other emerging technologies.

E. ***Image-Guided Interventions.*** Research on use of images for guidance, navigation and orientation in minimally invasive procedures to reach specified targets. Examples include image-guided interventions for minimally invasive therapies such as surgery and radiation treatment, for biopsies, and for the delivery of drugs, genes and therapeutic devices.

F. ***Image Processing, Visual Perception, and Display.*** Study, invention, and implementation of structures and algorithms to improve communication, understanding, and management of information related to biomedical images. Research that is supported includes software and hardware for image reconstruction, analysis, display and perception, visualization, and computer-aided interpretation.

G. ***Imaging Agents and Molecular Probes.*** Development and application of novel imaging agents and probes for clinical or pre-clinical applications. Examples of supported research include the development and application of quantum dots, nanoparticles, nanoshells, microbubbles, and radio-labelled contrast materials, and smart imaging agents that are bio-activatible or activated by other chemical, physical, or biological means.

H. ***Magnetic, Biomagnetic and Bioelectric Devices.*** Development of magnetic, biomagnetic and bioelectric devices, e.g., EEG, MEG, etc. Examples include (but are not restricted to) novel detectors, increased sensitivity and spatial resolution, improved reconstruction algorithms, multiplexing with other imaging techniques, etc.

I. ***Magnetic Resonance Imaging and Spectroscopy.*** Development of MR imaging and MR spectroscopic imaging, for both animal and human research, and potential clinical applications. Examples include (but are not restricted to) fast imaging, high field imaging, design of novel RF and gradient coils, novel pulse sequences, design of novel contrast mechanisms, imaging informatics, in vivo EPR imaging, molecular imaging, etc. The emphasis should be on technological development rather than detailed applications to specific diseases or organs.

J. ***Mathematical Modeling, Simulation and Analysis.*** Development of mathematical models and computational algorithms with potential clinical or biomedical applications, including multi-scale modeling, modeling at or above the cellular level, and modeling at subcellular level, including those developed to support technology development in other program areas related to the NIBIB mission. Research that is funded includes studies that focus on the development of algorithms, mathematical models, simulations and analysis of complex biological, physiological, and biomechanical systems and use genomics and proteomics.

K. ***Medical Devices and Implant Science.*** Design, development, evaluation and validation of medical devices and implants. This includes exploratory research on next generation concepts for diagnostic and therapeutic devices; development of tools for assessing host-implant interactions; studies to prevent adverse events; development of predictive models and methods to assess the useful life of devices; explant analysis; improved in vitro and animal models for device testing and validation.

L. ***Micro- and Nano-Systems, Platform Technologies.*** Development of BioMEMS, microfluidics and nanoscale technologies, including micro-total analysis systems, arrays, and biochips, for detection and quantitation of clinically relevant analytes in complex matrices. Application areas include biomedical research, clinical laboratory diagnostics, biodefense, high-throughput screening, drug delivery, tissue engineering, and implantable devices, among others.

M. ***Nanotechnology.*** Research and development of new enabling technologies for the fabrication and use of nanoscale components and systems in diagnostic and therapeutic applications. Examples include: development of new nanoscale patterning and manipulation systems; new approaches to the sensing and quantification of biologically important molecules using nanoscale specific properties; studies relating to the safety and commercialization of nanotechnology-enabled biomedical products.

N. ***Nuclear Medicine.*** Research and development of technologies that create images out of the gamma-ray or positron (and resulting photon) emissions from radioactive agents that are injected, inhaled, or ingested into the body and then concentrate in specific biological compartments. Two particularly active areas are the wedding of positron emission tomography (PET) and single photon emission computed tomography (SPECT) to CT and/or to MRI, and the design of higher resolution, lower cost PET and SPECT devices for the study of molecular probes in small animals. Other topics of interest include the development of better radiopharmaceuticals, crystal scintillators, and collimators, and novel approaches to dual-isotope imaging and to dosimetry.

O. ***Optical Imaging and Spectroscopy.*** Development and application of optical imaging, microscopy, and spectroscopy techniques; and development and application of optical imaging contrasts. Examples of research areas include fluorescence imaging, bioluminescence imaging, OCT, SHG, IR imaging, diffuse optical tomography, optical microscopy and spectroscopy, confocal microscopy,

multiphoton microscopy, flow cytometry, development of innovative light sources and fiber optic imaging devices.

P. ***Sensors.*** Development of sensor technologies for the detection and quantitation of clinically relevant analytes in complex matrices. Application areas include (among others) biomedical research, clinical laboratory diagnostics, and biodefense, covering in vitro diagnostics, noninvasive monitoring, and implantable devices. Technologies encompassed include novel signal transduction approaches, materials for molecular recognition, biocompatibility, signal processing, fabrication technologies, actuators, and power sources.

Q. ***Structural Biology.*** Development of structural biology techniques, including (but not restricted to) solid state NMR, EPR, synchrotron radiation, etc. The emphasis is on technological development, rather than applications to specific structural biology problems.

R. ***Surgical Tools and Techniques.*** Research and development of new medical technologies to improve the outcomes of surgical interventions. Examples of relevant technologies include: minimally invasive surgeries, energy-based interventions such as RF ablation, robotically assisted surgical systems, integration of imaging and interventional modalities, image guided interventions and telehealth.

S. ***Telehealth.*** Development of software and hardware for telehealth studies that have broad applications as well as early stage development of telehealth technologies that may have specific focus areas. Research that is supported includes methods to address usability and implementation issues in remote settings, and methods to develop technology for standardizing and incorporating state of the art security protocols for verifying user identities and preserving patient confidentiality across remote access.

T. ***Tissue Engineering and Regenerative Medicine.*** Development of enabling technologies including real-time, non-invasive tools for assessing the function of engineered tissues; real-time assays that monitor the interaction of cells and their environment at the molecular and organelle level; predictive computational models for engineering function 3D tissues; high-throughput assays and instruments to reduce the cost, time, and complexity of tissue engineering; novel bioreactor techniques for expanding stem cells and growing tissues and organs on a large scale; and strategies for preserving, sterilizing, packaging, and transporting living-tissue products. The program also supports applications of rational engineering design principles to functional engineered tissues; the development of novel biomaterials for use as tissue scaffolds that mimic the extracellular matrix and support multiple cell types in defined spatial orientation; and engineering approaches to study how biomaterials interact with cells and guide cell growth, differentiation, and migration.

U. ***Ultrasound.*** Improvement of technologies for diagnostic, interventional and therapeutic uses of ultrasound. The diagnostic ultrasound program includes, but is not limited to the design, development and construction of transducers, transducer arrays, and transducer materials, innovative image acquisition and display methods, innovative signal processing methods and devices, and optoacoustic and thermoacoustic technology. It also includes the development of image-enhancement devices and methods, such as contrast agents, image and data presentation and mapping methods, such as functional imaging and image fusion. The interventional ultrasound program includes the use of ultrasound for therapeutic use, or as an adjunct for enhancement of non-ultrasound therapy applications. Examples include, but are not limited to, high-intensity focused ultrasound (HIFU) as a non-invasive or minimally invasive interventional surgical or therapy tool, and as an adjunct interventional tool. It also includes the use of ultrasound contrast agents for therapy and for targeted drug delivery, and the use of ultrasound for image-guided surgery, biopsy, and other interventions.

V. ***X-ray, Electron, and Ion Beam.*** Enhancement of computed tomography (CT), computed radiography (CR), digital radiography (DR), digital fluoroscopy (DF), and related modalities. Research areas of support include the development of: flat panel detector arrays and other detector systems; flat-panel CT; CT reconstruction algorithms for the cone-beam geometry of multi-slice CT;

approaches to radiation dose reduction, especially with CT; and novel x-ray applications, such as those utilizing scattered radiation, tissue-induced x-ray phase shifts, etc.

For additional information on research topics, contact:

Mr. Todd Merchak
National Institute of Biomedical Imaging and Bioengineering
301-496-8592, Fax: 301-480-1614
Email: merchakt@mail.nih.gov

For administrative and business management questions, contact:

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National Institute of Biomedical Imaging and Bioengineering
301-496-9314, Fax: 301-480-4974
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NATIONAL CANCER INSTITUTE (NCI)

The goal of the NCI is to eliminate the suffering and death due to cancer. The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs are NCI's engine of innovation for developing and commercializing novel technologies and products to prevent, diagnose, and treat cancer. NCI's SBIR and STTR Programs offer funding in nanotechnology, anti-cancer agents, biomarkers, proteomics, diagnostics, imaging technologies, pharmacodynamics, and many more areas of interest to the NCI.

NCI's SBIR and STTR programs focus on research, development and delivery and are critical to achieving the institute's goals. Research opportunities cited below are not all inclusive; those listed are "open-ended" to encourage submission of innovative projects that fit NCI's mission. For additional information, access the NCI SBIR homepage: http://sbir.cancer.gov/. In addition, please see the contact list at the end of the NCI section to identify the Program Director within the NCI SBIR Development Center who specializes in your technology area.

Phase IIB SBIR Competing Renewal Awards

NCI offers Phase IIB opportunities that focus on the commercialization of SBIR-developed technologies. Contact the NCI SBIR Development Center at 301-594-7709, NCISBIR@mail.nih.gov for additional information.

Center to Reduce Cancer Health Disparities

Established in March 2001, CRCHD is the cornerstone of the Institute's efforts to reduce the unequal burden of cancer in our society. A central goal of the Center is to translate research discoveries into policies and/or services aimed at reducing cancer-related health disparities in racial, ethnic, elderly and medically underserved communities. To learn more about the Center, please visit our website: http://crchd.cancer.gov.

The Center is interested in the following SBIR/STTR applications:

A. ***Communication.*** Training tools to help health professionals deal with issues concerning health literacy and cultural competency.

B. ***Health Care and Epidemiology.*** Computer software and hardware for hand-held data input and analysis devices; databases and other tools to study patterns of cancer care in underserved communities.

C. ***New Technology.*** Instrumentation to facilitate early detection and screening, including telemedicine and remote medical imaging, and bioengineering technology (including nanotechnology) applied to cancer detection and diagnosis in underserved communities.

D. ***Geographic Information Systems.*** Simple, low-cost mapping software to overlay cancer patterns with socioeconomic data, health system infrastructure, healthcare, personal behaviors, ethnicity, risk factors, and consumer profiling among underserved communities.

E. ***Human Genomics.*** Tools and technology for health care providers using cancer research developments from genomics, pharmaco-genetics and proteonomics for underserved populations.

Division of Cancer Biology

The Division of Cancer Biology (DCB) plans and directs, coordinates, and evaluates a grant- and contract-supported program of extramural basic research on cancer cell biology and cancer immunology, and cancer etiology, including the effects of biological, chemical and physical agents, in the promotion of cancer; maintains surveillance over developments in its program and assesses the national need for research in cancer biology, immunology and etiology; evaluates mechanisms of biological, chemical and physical carcinogenesis and subsequent tumor growth and progression to metastasis; tests for carcinogenic potential of environmental agents; and serves as the focal point for the Federal Government on the synthesis of epidemiological and experimental data concerning biological agents relating to cancer. For additional information, please visit our home page at http://www.nci.nih.gov/dcb/dcbhom.htm.

A. ***Cancer Cell Biology.*** The Cancer Cell Biology Branch (CCBB) seeks to understand the biological basis of cancer at the cellular and molecular level. This research utilizes lower eukaryote and animal models, and animal and human tumor cells and tissues to analyze the mechanisms responsible for the growth and progression of cancer. Specific research and technologies supported by CCBB include but are not limited to the following:

1. Development of novel methods and tools to study key aspects of programmed cell death including its regulation and modulation.
2. Development of methods to identify and isolate tissue-specific stem cells.
3. Development of markers associated with specific cellular processes or differentiation.
4. Development of novel techniques, tools, and vectors to transfer functional genes, proteins, antibodies, etc. into intact cells or organisms.
5. New or improved technologies for the efficient microdissection of tumor tissue sections to isolate and preserve human cancer cells appropriate for research.
6. Generation of new inbred genetic animal models that transmit defective or altered cancer-related genes.
7. Development of novel technologies, methodologies, tools, or basic instrumentation to facilitate basic cancer research (research tools).
8. Development of methods and tools to study processes of protein trafficking, post-translational modification, and degradation.
9. Development of novel methods and tools for the analysis of intracellular organelles.
10. Development of novel methods and tools to determine intracellular gradient status.
11. Improved extraction methodologies and tools for tumor specimens for the subsequent analysis of DNA, RNA, and proteins.
12. Development of new or improved methods to isolate intact cellular regulatory complexes for functional studies.

13. Development of novel methods and tools to examine key cellular communication pathways.
14. Improved extraction methodologies and tools for tumor specimens for the subsequent analysis of DNA, RNA, and proteins.
15. Development of new or improved methods to isolate intact cellular regulatory complexes for functional studies.
16. Development of novel methods and tools to examine key cellular communication pathways.

B. ***Cancer Etiology.*** The Cancer Etiology Branch (CEB) supports research that seeks to determine the role of chemical, physical and biological agents as factors or cofactors in the etiology of human and animal cancer. The biological agents of primary interest are DNA viruses, RNA viruses, AIDS and AIDS-associated viruses, although the research may encompass all forms of life including bacteria and other microbial agents associated with cancer and use animal models of cancer and cancer vaccines. Chemical Carcinogenesis studies are concerned with cancers initiated or promoted by chemical or physical agents. A wide range of approaches are supported, including studies of the genetics of cell transformation, mutagenesis, tumor promotion and DNA damage, as well as studies of basic biochemistry and molecular biology of oncogenic and suspected oncogenic agents, viral oncogenes and associated tumor suppressor genes, pathogenesis and natural history studies, animal models, and preventive vaccine research. Mechanistic studies are encouraged in areas such as metabolism, toxicity and physiological distribution of carcinogens, genetics and regulation of enzymes, biochemical and molecular markers, and organ and cell culture systems and animal models. Also of interest are studies on cancer etiology by environmental chemicals, tobacco consumption and exposure, nutritional hazards, alcohol, asbestos, silica, and man-made fibers. CEB supports studies on endogenous exposure to steroid hormones and the generation of oxygen radicals during normal metabolism, studies on phytoestrogens and xenoestrogens and their impact on the metabolism of endogenous estrogens. In addition, CEB supports the development of analytical technologies to facilitate studies relating to carcinogenesis and mutagenesis. Specific research and technologies supported by CEB include but are not limited to the following:

1. Development of reagents, probes, and methodologies to evaluate the etiologic role of oncogenic viruses and other microbial agents (such as bacteria) in human cancer.
2. Development of novel in vitro culture techniques for oncogenic viruses or other microbial agents associated with or suspected of causing human cancer.
3. Development of sensitive, simplified diagnostic kits or reagents for the detection of oncogenic viruses or other microbial agents.
4. Development and characterization of animal models for studies of the mechanism of cancer induction by viruses or other microbial agents. The animals should faithfully mimic the human diseases associated with the virus or other microbial agent.
5. Development of methods (e.g., new-anti-microbial compounds, new vaccine approaches) to avert the induction of neoplasia in humans and animals by oncogenic viruses or bacteria.
6. Development of other novel technologies, methodologies or instrumentation to determine the role of biological agents, especially viruses, in the etiology of cancer.
7. Development and validation of methods for food treatment, preparation, or processing that will reduce or eliminate carcinogen/mutagen content.
8. Development of rapid analytical techniques for the qualitative and quantitative detection and screening of xenobiotics, chemical contaminants, and carcinogens/mutagens in human foods and biological and physiological specimens.
9. Development of in vitro and in vivo models for basic studies of carcinogenesis in specific organ systems, such as the pancreas, prostate, ovary, central nervous system, kidney, endometrium, stomach, and upper aerodigestive tract.

10. Development of methods for the production of carcinogens, anticarcinogens, metabolites, biomarkers of exposure, oxidative damage markers, and DNA adducts, both labeled and unlabeled, which are neither currently available commercially nor offered in the NCI Chemical Carcinogen Reference Standard Repository. The production of these compounds, in gram quantities, is desired for sale/distribution to the research community.
11. Development of methods for detection, separation, and quantitation of enantiomeric carcinogens, metabolites, adducts, and biomarkers of carcinogen exposure.
12. Development of monoclonal antibodies that are specific for different carcinogen-nucleoside adducts and demonstration of their usefulness in immunoassays. Of particular interest are antibodies to alpha-beta unsaturated carbonyl compounds (such as acrolein and crotonaldehyde) which can form exocyclic nucleoside adducts with DNA, and immunoassays for carcinogen/protein adducts as potential biomarkers of exposure.
13. Development of immunoassays using monoclonal antibodies that are specific for different polymorphs of Phase I and II carcinogen-metabolizing enzymes and repair enzymes. Included, but not limited to, are antibodies to the cytochrome P450 isozymes, glutathione S-transferases, and N-acetyl transferases.
14. Development of rapid, sensitive, and quantitative assays for the identification and measurement of androgens, estrogens, phytoestrogens, and xenoestrogens in complex biological matrices.
15. Development of rapid analytical techniques for the direct measurement of ligand-protein receptor interactions and determination of binding coefficients.
16. Development of analytical instrumentation for the detection and quantitation of extremely low levels of Tritium (3H) or 3H and Carbon-14 (14C) from biological samples. Of particular interest is the development of small-sized, accelerator-based mass spectrometry equipment capable of measuring down to, or below, contemporary background levels of 3H and 14C that would make this sensitive technique more widely available to research groups. The design and development of technologically improved and miniaturized individual components, including ion source, sample preparation (autosampling apparatus), accelerator, and mass spectrometric detectors, are also solicited.
17. Synthesis of selective suicide inhibitors of cytochrome P450 isoforms and selective arachidonic acid pathway inhibitors/ enhancers for basic biochemical studies and anticarcinogenic potential.
18. Development of invertebrate animal models (such as Drosophila, C. elegans, clam, and sea urchin) for the study of environmental chemicals and/or hormonal carcinogenesis.
19. Development of more efficient and reliable methods of preserving valuable animal model gene stocks by innovative in vitro techniques.
20. Development of a defined diet for support and maintenance of aquatic and marine fish models of cancer including but not limited to swordtail, zebrafish, medaka, mummichog, guppy, Fugu, and Damselfish.
21. Development of serum free tissue culture media for aquatic and marine fish models of cancer.

C. ***Cancer Immunology and Hematology.*** The Cancer Immunology and Hematology Branch (CIHB) supports a broad spectrum of basic research focused on the earliest stages of hematopoiesis and tracing the molecular events that lead to the development of all the functional elements of the immune system and, when errors occur, to the development of leukemias and lymphomas. Most research of interest falls into three major areas. The first is the immune response to tumors to include studies of all of the cells (T, B, NK, antigen-presenting, and other myeloid cells) and secreted molecules (antibodies and cytokines) of the immune system that can recognize and affect tumor growth. Emphasis is placed on the alteration in the mechanisms responsible for the failure of immune response to eradicate most tumors under normal conditions, and the development of strategies to circumvent these mechanisms. A second major area of interest examines the biology of

hematopoietic malignancies to describe the molecular biology reasons underlying the cell's failure to respond to normal growth controls and to develop novel approaches to prevention or therapy. The third distinct area supported is the basic biology of bone-marrow transplantation, including studies of host cell engraftment, graft-versus-host disease, and the basis of the graft-versus-leukemia effect. Specific research and technologies supported by CIHB include but are not limited to the following:

1. Development of improved or novel monoclonal antibody technologies including improvements of methodologies for fusion, production of novel cells as fusion partners, selection and assay of antibody producing clones, and production of new and improved monoclonal antibodies.
2. Synthesis, structure and function of antibodies capable of reacting with tumor cells, agents that induce tumors and agents used in the treatment of tumors.
3. Development of in vivo animal models systems that can be used to study the immune response to tumors and the mechanisms of immunotherapy.
4. Synthesis, structure and function of soluble factors that participate in, activate and/or regulate hematopoietic cell growth and the immune response to tumors, including interferons, other lymphokines and cytokines (interleukins), hematopoietic growth factors, helper factors, suppressor factors and cytotoxic factors.
5. Application of biochemical, molecular biological and immunological techniques for identifying tumor antigens that are good targets for the development of vaccine-type strategies of cancer immunotherapy.
6. Development of techniques to enhance the immune response to tumors, including modification of tumor cells and/or antitumor lymphocytes to facilitate cancer vaccine strategies.
7. Development of improved methodology for manipulating bone marrow inoculum to decrease the incidence of graft-versus-host disease without increasing the risk of graft failure or leukemic relapse.
8. Development of improved methodology for increasing the number of peripheral blood stem cells available for harvest for use in transplantation, including improved methods of identifying and removing residual leukemic cells in the autologous transplant setting.
9. Development of methods to identify and define human minor histocompatability antigens.
10. Development of novel culture systems to improve the expansion of lymphocytes and dendritic cells.
11. Development of the combination of cell culture and other research tools to better expand human hematopoietic stem cells.
12. Development of improved techniques for computational simulation/modeling of biological processes involved in immunologic defenses against tumor cells such as signal transduction, cell cycle progression, and intracellular translocation.
13. Development of other novel technologies, methodologies or instrumentation to facilitate basic research in either tumor immunology or cancer hematology.
14. Development of molecular, cellular or biochemical techniques to isolate and/or characterize tumor stem cells from hematologic malignancies.

D. ***DNA and Chromosome Aberrations.*** The DNA and Chromosome Aberrations Branch (DCAB) seeks to study the genome at the DNA and chromosome level, including discovery of genes at sites of chromosome breaks, deletions, and translocations; DNA repair; structure and mechanisms of chromosome alterations; epigenetic changes; radiation- and chemical-induced changes in DNA replication and other alterations; and analytical technologies. Specific research and technologies supported by DCAB include but are not limited to the following:

1. Development of new, improved technologies for characterization of chromosomal aberrations in cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for chromosome aberrations in cancer.
3. New or improved technologies to increase accuracy of karyotypic analyses of tumor specimens.
4. New or improved methods to mutate or replace genes at specific sites in intact cells.
5. Development of new, sensitive methods to assess the methylation status of genes.
6. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
7. Technologies for assaying for mammalian genes relevant to repair of damage induced by exposure of mammalian cells to ionizing and non-ionizing radiations, with special emphasis on human cells.
8. Methods/approaches to study the repair of DNA lesions induced by exposure of mammalian cells to ionizing radiations (both high- and low-LET).
9. Development and characterization of human cell lines with specific DNA-repair deficiencies.
10. Development of genetic constructs that utilize radiation-responsive regulatory genes to control the expression of targeted structural genes in mammalian cells.
11. Development of new methods/technologies to assay transcription factor binding sites across whole genomes.
12. Use of RNAi and siRNA in the development of novel methods and tools for the study of gene expression, gene silencing, gene regulation, and genome-wide screening in cells and tissues.
13. Development and integration of nanotechnology and microfluidics in the analysis of DNA and chromosomal aberrations and the identification, mapping, and cloning of cancer susceptibility and resistance genes.
14. Development of human tumor cDNA library banks to study gene expression in cancer.
15. Generation of new or improved animal models or non-mammalian models (e.g. flies, worms) as research tools to study human cancers.

E. ***Mouse Models of Human Cancers Consortium.*** The Mouse Models of Human Cancer Consortium is a program based in the Office of the Director, DCB. The Consortium has the important goal of providing mouse cancer model-related resources and infrastructure to the research community, in part through various outreach activities. The outreach requirement generates the need for innovative educational or informational materials that convey the content of Consortium meetings and symposia, or document hands-on workshops in which models or techniques that are pertinent to mouse modeling are demonstrated. The instructional materials may be CD-ROMs, videotapes, Web-based interactive programs, or other media.

F. ***Structural Biology and Molecular Applications.*** The Structural Biology and Molecular Applications Branch (SBMAB) focuses on structural and molecular studies to explore the processes of carcinogenesis and tumorigenesis. Areas of interest include structural biology, genomics, proteomics, molecular and cellular imaging, enzymology, bio-related and combinatorial chemistry, bioinformatics, systems biology and integrative biology as they apply to cancer biology. Interests also include modeling and theoretical approaches to cellular and molecular dimensions of cancer biology. Specific research and technologies supported by SBMAB include but are not limited to:

1. Development of new, improved, or high throughput technologies for whole genome scanning for gene identification.
2. Development of systems that will automate the technology of culturing or assaying single cells.

3. New or improved technologies for efficient microdissection of tumor tissue sections for the development of tissue arrays.
4. Improved extraction techniques for tumor specimens for subsequent DNA, RNA, and protein analyses.
5. Rapid methods to isolate intact complexes of regulatory proteins and to separate and identify the proteins for biophysical studies.
6. New or improved technologies for the preservation of small amounts of DNA/RNA/protein samples
7. Development of new techniques and vectors for transfer of genes, proteins, and antisense molecules into cells.
8. Generation of software and computer models for the prediction of macromolecular structure and function.
9. Development of bioinformatic tools for the study of cancer biology including facilitating genome data, gene "mining," cluster analysis, and data base management.
10. Development of novel gene technology (e.g., microarray, differential display technology) for measurement of differential gene expression levels and functional genomics studies.
11. Development of novel proteomic tools for the analysis of protein expression in cancer biology.
12. Computer-based methodologies to assist in the understanding of signal transduction and cancer biology.
13. Methodologies and techniques for the imaging of macromolecules in vitro and in vivo.
14. Development of other novel technologies, methodologies or instrumentation to facilitate basic research (research tools) in cancer biology.
15. Develop new approaches and technologies for the structural determination of large biomolecular complexes.
16. Development and integration of nanotechnology approaches and tools in basic cancer biology research.
17. Application and development of novel approaches for in vivo and in vitro modifications of protein expression in cells and tissues, e.g. RNAi, microRNA, other small molecules.
18. Mathematical and theoretical models for the understanding of cancer biology.
19. Development of new software and lab analysis tools that will improve the recording and collection of data and experimental protocols in order to facilitate cancer biology research.
20. Technology and software for elucidating molecular interactions and networks.
21. Develop new, improved or high-throughput technologies for analyzing epigenomic changes.
22. Improved software for the integration of heterogeneous data sources.
23. Development of new, improved or high-throughput technologies for understanding the cancer metabolome.

G. ***Tumor Biology and Metastasis.*** This branch supports research that seeks to understand the interactions of cancer cells with the tumor and/or host microenvironment in order to delineate the molecular mechanisms and signaling pathways of tumor angiogenesis and lymphangiogenesis, cell migration and invasion, tumor progression, and metastasis. This includes examination of cell-cell and cell-matrix interactions, and the roles played by cell growth factors and cytokines, adhesion molecules, cytoskeleton and the nuclear matrix, and matrix-degrading enzymes, as well as studies on the pathology and biology of solid tumors and tumor bearing animals, and the development of

technology to facilitate these studies. Emerging areas of emphasis are the microenvironment created by inflammation and the inflammatory signaling molecules in tumor initiation and progression and the role of somatic stem cells in determining tumor progression and metastatic behavior. Stem cell motility, positional information cues from surrounding tissue and adhesion properties together with issues of epithelial-mesenchymal transitions related to cancer progression are supported. Emphasis is also placed on the role of the extracellular matrix and tissue microenvironment during development and tissue morphogenesis, and on the role of glycoproteins in tumor growth, invasion, and metastasis. The branch also focuses on the function of steroid hormones, their receptors and coregulators during tumor growth and progression. Models utilized in these studies may include animal models, tumor tissues/cells, their components, or their products. The development of organotypic models that closely mimic in vivo models is encouraged. Specific research and technologies supported by TBMB include but are not limited to:

1. New technical strategies to identify and assess the function of components of the extracellular matrix.
2. Development of new in vitro cancer models to study the pathology and biology of solid tumors and tumor bearing animals.
3. New in vivo models of angiogenesis, lymphangiogenesis, cancer progression and metastasis.
4. Development of technologies to identify novel factors that modulate angiogenesis and lymphangiogenesis.
5. Identification of genes and/or enzymes associated with glycosylation in tumor cells.
6. Identification of novel coregulators of nuclear steroid receptor superfamily.
7. Development of improved techniques for computational simulation/modeling of biological processes involved in malignant transformation, persistence, or invasion, such as signal transduction, cell cycle progression, and intracellular translocation.
8. Development of new assays or methods to evaluate tumor cell invasiveness.
9. Development of new assays or methods to study molecules and pathways involved in cell-to-cell signaling or communication.
10. Development of appropriate new animal, cellular or organotypic models to study tumor stroma interactions, 3-D models that closely mimic *in-vivo* conditions.
11. Study roles of cytokines/growth factors released by host cells during inflammation, invasion, tumor progression and metastasis.

Division of Cancer Control and Population Sciences

The Division of Cancer Control and Population Sciences conducts basic and applied research in the behavioral, social, and population sciences, including epidemiology, biostatistics, and genetics that, independently or in combination with biomedical approaches, reduces cancer risk, incidence, morbidity, and mortality. Laboratory, clinical and population-based research, and health care are translated into cancer prevention, detection, treatment, and rehabilitation activities that cross the life span and the entire process of carcinogenesis, from primary behavioral prevention in youth, to screening, treatment, and survivorship. For additional information, please visit our home page at http://dccps.nci.nih.gov.

A. ***Epidemiology and Genetics.*** The Epidemiology and Genetics Research Program supports research in epidemiology, biometry, genetic epidemiology, molecular epidemiology, nutritional epidemiology, infectious epidemiology, environmental epidemiology, computing methodology, and multidisciplinary activities related to human cancers.

The topics of interest to the Epidemiology and Genetics Research Program (EGRP) are:

- **Tools for assessment of exposures and biomarkers:**
  - Development of methods for measuring biomarkers of human exposure or susceptibility, and of nutritional status, and methods for monitoring changes in biomarkers for use in cancer epidemiologic studies.
  - Development of new or improved devices for quantitative measurement of human exposure to environmental carcinogens for epidemiologic studies.
  - Development of methods to evaluate potential cancer clusters for epidemiologic studies.
- **Tools for cancer epidemiology studies:**
  - Development of tools to model cancer risks from environmental and occupational agents.
  - Development of software for electronic capture of risk factor data for cancer epidemiologic studies.
  - Build consumer-friendly risk prediction models from epidemiologic data.
  - Development of software for tracking biological specimens for cancer epidemiologic studies.
  - Development of software for electronic identification, screening, and recruitment of participants, especially minorities, into epidemiologic studies.
  - Development of Web-based data collection or applicable bioinformatics tools for cancer epidemiology.
  - Development of software or methods for rapid case ascertainment of cancers.
  - Development of geographic information systems with special visualization techniques for the simultaneous assessment of environmental exposures and health outcomes.
  - Development of tools using publicly available data to identify population-based controls for epidemiologic studies.
  - Development of software for analysis of DNA methylation biomarkers for early detection of prostate or breast cancers with use of specimens from biorepositories.
  - MicroRNA Profiling in Epidemiologic studies.
  - Detection of mitochondrial DNA alterations for Cancer Epidemiologic studies.

For more information on this program please go to http://epi.grants.cancer.gov.

B. ***Multimedia Technology and Health Communication in Cancer Control.*** Over the past few decades, advances in technology have played a key role in enhancing the quality of cancer care through improvements in the prevention, diagnosis, and treatment of cancer. A driving force fostering the utilization of media technology to develop cancer communication products and their dissemination is NCI's Multimedia Technology and Health Communication SBIR/STTR Program. The Program serves as an 'engine of innovation' translating cancer research into commercially viable products for primary care professionals, researchers, patients and their families, and the general public.

The objectives of this program are to (1) *fund* science-based, theory-driven, user-centered grants and contracts to translate cancer research into programs, interventions, systems, networks, or products needed by professionals or the public to reduce cancer risk or improve the quality of life of

cancer survivors; (2) *promote the use of* innovative media technology and/or communication approaches in cancer prevention and control applications used in medical and community settings; (3) *improve* communication behaviors of primary care professions, patients, and care-givers in cancer-related matters; (4) *promote* organizational infrastructures changes that promote the use of products developed in the program; (5) *promote* the development of system models; and (6) *expand* the methods for evaluating ehealth research and developed products.

Investigators interested in applying for grants in this SBIR program should access: http://cancercontrol.cancer.gov/hcirb/sbir/ for a list of topics that address current gaps in ehealth research and that are updated during the fiscal year. This site also provides important program requirements and other SBIR information.

Division of Cancer Treatment and Diagnosis

The Division of Cancer Treatment and Diagnosis funds research into the development of tools, methodologies and therapeutic agents that will better diagnose, assess, cure and effectively treat cancer. We support a spectrum of research projects from preclinical exploratory research and development through clinical trials.

A. ***Cancer Diagnosis.*** The Cancer Diagnosis Program (CDP) supports the development of technologies, reagents, instrumentation, and methodologies to improve cancer diagnosis or prognosis or to predict or assess response to therapy. This does not include technologies for imaging of patients. CDP also supports the adaptation or improvement of basic research technologies for use as clinical tools. Technologies supported by CDP may be designed to work with tissues, blood, serum, urine, or other biological fluids. Technologies supported by CDP include but are not limited to the following:

1. Technologies for comprehensive and/or high throughput analysis of molecular alterations at the level of DNA, RNA, or protein. Includes for example, mutation detection systems, gene expression arrays, systems for monitoring epigenetic changes (alternative splicing or methylation), high throughput proteomics (including post-translational modification and protein-protein interactions and methods for protein quantitation).
2. Micro-electro mechanical systems (MEMs) and other nanotechnologies for the analysis of DNA, RNA, or protein (e.g., micro-capillary systems, lab on a chip applications, micro-separation technologies).
3. Mass spectrometry for the analysis of nucleic acids or proteins.
4. Discovery and development of new or improved diagnostic markers or probes targeting changes in DNA, RNA, or proteins, including the generation of molecular diversity libraries by phage display and other combinatorial techniques, and affinity-based screening methods.
5. cDNA library technologies, including improved methods for generating high quality cDNA clones and libraries and methods for generating high quality cDNA from tissues (including archived specimens).
6. Resources for clinical research.
    a. Instruments, technologies or reagents for improved collection, preparation, and storage of human tissue specimens and biological fluids.
    b. Improved methods for isolation and storage of DNA, RNA, or proteins.
    c. Tissue and reagent standards: development of standard reagents such as representational DNA, RNA, and proteins and standard tissue preparations to improve the quality of or facilitate the validation of clinical laboratory assays.

d. Methodologies for directed micro-sampling of human tissue specimens, including for example, new or improved methodologies for tissue microarrays.

7. Tissue preservation: fixatives and embedding materials or stabilizers that preserves tissue integrity and cellular architecture and simultaneously allows molecular analysis of DNA, RNA, or proteins.

8. Bioinformatics.

   a. Methods for acquisition and analysis of data associated with molecular profiling and other comprehensive molecular analysis technologies, including for example, analysis of microarray images and data as well as methods to combine, store and analyze molecular data produced by different techniques (e.g., combined analysis of proteomics and gene expression data).

   b. Methods for collecting, categorizing or analyzing large data sets containing pathology data or histological images and associated clinical or experimental data, including for example, tumor marker measurements, tissue microarray data, and other relevant biological information.

   c. Software/algorithms to interpret and analyze clinical and pathology data including methods that relate data from clinical databases to external data sources. Includes for example, neural networks, artificial intelligence, data-mining, data-trend analysis, patient record encryption protocols, and automatic diagnostic coding using standard nomeclatures.

   d. Informatics tools to support tissue procurement and tissue banking activities.

9. Statistical methods and packages designed for data analysis including correlation of clinical and experimental data.

10. Automated Cytology.

    a. High resolution image analysis for use with specimens (e.g., blood, tissues, cells) and tissue microarrays.

    b. Instrumentation including microscopy and flow cytometry.

    c. CGH, FISH, immunohistochemical staining and other hybridization assays using probes with fluorescent or other novel tags.

    d. Methods for single cell isolation and sorting.

    e. Methods for single cell classification and analysis.

11. Instrumentation for the detection and diagnosis of tumors, including endoscopy and magnetic resonance spectroscopy (MRS).

12. Immunoassays using monoclonal, polyclonal, or modified antibodies. Affinity-based binding assays using libraries of aptamers including chemical ligands, small peptides or modified antibodies.

For additional information about areas of interest to the CDP Technology Development Branch, visit our home page at: http://cancerdiagnosis.nci.nih.gov.

B. ***Biochemistry and Pharmacology.*** Preclinical and Exploratory Investigational New Drug (IND) studies designed to improve cancer treatment. General areas of interest: Discovery of new drugs or drug combinations and treatment strategies, selective targeting, development of clinically relevant preclinical models, pharmaceutical development, ADME (absorption, distribution, metabolism and excretion) studies and toxicologic evaluations, understanding mechanisms of drug actions (responses to therapies), and preventing and overcoming drug resistance. Areas of current emphasis: Molecular targeted approaches, including application of safety and efficacy biomarkers to the discovery and development of drugs; application of advanced technologies, such as

nanotechnology and imaging technologies, to improved assays for quantitation of safety and efficacy biomarkers; approaches that reduce costs and increase speed of preclinical drug development; and approaches that will lead to "personalized medicine," including better predictions of drug response and adverse reactions, drug-drug interactions, and drug efficacy monitoring. For additional information, please visit our home page at http://dtp.nci.nih.gov and select "Grants/Contracts."

1. *Drug Discovery.*

    a. Design and synthesize novel compounds for evaluation as potential anticancer agents. Synthesize simpler analogs of complex antitumor structures that retain antitumor activity.

    b. Develop computer modeling and biophysical techniques such as x-ray crystallography and NMR spectroscopy.

    c. Design prodrugs of anticancer agents that are selectively activated in cancer cells.

    d. Discover new anticancer agents that exploit unique properties of tumors, that induce or modulate apoptosis, or that induce or modulate differentiation.

    e. Design and synthesize anticancer prodrugs, latent drugs, or modifiers of cancer drug metabolism or excretion.

    f. Develop ways to produce adequate quantities of promising natural products or natural product derivatives through total synthesis.

    g. Develop scale-up and manufacturing technology for the synthesis of materials with promising anticancer potential.

    h. Develop chemical libraries for anticancer drug screening programs. The generation of small molecular weight libraries (<700 MW, e.g., non-polymeric organic molecules, transition-state analogs, cyclic peptides, peptidomimetics) is encouraged.

    i. Develop and apply technologies in genetics, genomics, proteomics, glycomics, lipidomics, metabolomics, and systems biology to the discovery of potential drug targets associated with multiple pathways or networks. Design and optimize agents that block or activate targets/pathways that are likely to control, re-program, retard or kill cancer cells, especially cancer initiating cells (often called cancer stem cells).

2. *Drug Evaluation.*

    a. Develop and evaluate anti-metastatic and/or anti-angiogenesis agents or strategies, including combination therapies, in appropriate model systems.

    b. Develop and evaluate anticancer gene therapy in appropriate model systems. The development of new gene delivery approaches is encouraged.

    c. Develop novel or improved in vitro and in vivo test systems. There is a special need for new types of in vivo tumor models, such as orthotopic tumor models, models using transgenic or gene knockout animals, and models to evaluate agents that induce differentiation or apoptosis or that target cancer initiating cells (often called cancer stem cells).

    d. Develop strategies to detect, prevent, or overcome drug resistance.

    e. Develop novel treatment strategies such as extra corporeal treatment.

    f. Develop new assays based on molecular targets, especially those that may be amplified or altered in cancer cells. For example, develop assays for agents that interact with oncogenes, suppressor genes, signal transduction pathways, transcription factors, or promoters. Assays based on molecular targets that can be adapted for high volume screening of chemical libraries are especially encouraged as well as in vivo models, which can be used for "proof of concept" (i.e., validating selectivity of the agent for the target and confirming that modulation of the target results in antitumor activity).

g. Develop cost-effective and useful techniques to improve in vitro cell culture methodology, such as the development of automated systems, serum-free media, or carbon dioxide-free buffering systems to stabilize cell culture performance.

h. Identify and employ novel targets for antitumor drug discovery utilizing non-mammalian genetically defined organisms, such as fruit flies, worms, zebrafish and yeast.

i. Develop and apply technologies such as microarrays, proteomics or RNAi to improve the efficiency of drug discovery.

j. Develop cell lines that contain bioluminescent reporter genes, such as luciferase, that can be controlled by activating specific promoters.

3. *Pharmaceutical Development.*

a. Develop new methods to improve drug solubility for administration of promising antitumor compounds, such as water miscible nontoxic water solubility enhancing agents.

b. Develop bioavailable alternatives to the intravenous delivery of cytotoxic chemotherapy. For example, develop new excipients to enhance oral bioavailability of anticancer agents.

c. Develop biocompatible additives and excipients for highly concentrated proteins and peptide formulations to enhance bioavailability and stability suitable for subcutaneous delivery of agents.

d. Develop improved methods to reduce thrombophlebitis and other related side effects observed following intravenous injection of some anticancer drugs.

e. Develop new and innovative techniques for sterilization of parenteral dosage forms.

f. Develop in vitro and in vivo models to predict human oral bioavailability of anticancer drugs.

g. Develop practical delivery systems involving nanotechnology (dendrimers, nanoparticles, nanoshells, etc.) or other strategies to deliver anticancer drugs to specific target sites.

h. Develop new technology to manufacture liposomal and intravenous emulsions in an environmentally friendly manner and in accordance with OSHA standards.

i. Develop additives and/or processes to eliminate cold chain storage of biotherapeutic agents, especially vaccines.

4. *Toxicology and Pharmacology.*

a. Develop biochemical or molecular (genomic, proteomic, or metabolomic) response profiles of specific target organs (e.g., bone marrow, gastrointestinal tract, liver, kidney, heart, lung) to permit rapid identification of toxic effects resulting from anticancer drug administration.

b. Develop clinically relevant in vitro and/or in vivo tests for estimation and prediction of gastrointestinal toxicity, neurotoxicity (central and peripheral), cardiotoxicity, hepatotoxicity, nephrotoxicity and pulmonary toxicity.

c. Correlate in vivo and in vitro models for organ toxicity as described above in 4b. Validate for various anticancer drugs.

d. Develop drug metabolism (Phase I and Phase II) profiles for anticancer agents in human, mouse, rat and dog liver S-9, microsomes and slices.

e. Develop systems to identify toxic effects of drugs by characterizing reactions with biomolecules or receptors.

f. Develop in vitro tests to detect, qualify and quantify toxic effects of antineoplastic drugs. Develop techniques for determining individual variations in drug responses due to genetic polymorphisms or other factors. Develop pharmacodynamic endpoints and surrogate

endpoints using appropriate biomarkers to aid in the selection of doses and schedules and the monitoring of responses and toxicity.

g. Develop personal computer programs for pharmacokinetics models capable of predicting drug behavior in humans from preclinical pharmacokinetics data in mice, rats, dogs, and non-human primates.

h. Investigate and develop techniques for relating specific enzyme activities (both catabolic and anabolic) to body sizes of different species.

i. Investigate techniques that would allow parameters, e.g., Km and Vmax for enzymes, to be scaled from preclinical to clinical models.

j. Develop analytical strategies applicable to the quantitation of potent anticancer drugs in biological fluids at the pg/ml level, e.g., Bryostatin.

k. Develop non-invasive techniques to determine drug distribution in various animal models.

l. Evaluate interspecies transporter distribution and its impact on pharmacokinetic parameters, e.g., the impact of pharmacogenetic variation in biodistribution.

m. Determine optimal pharmacokinetic sampling schedules for use in dose titration/pharmacodynamic assessment by integrating information such as pre-clinical pharmacokinetic data, physico-chemical drug properties and mechanism of action.

n. Develop an in vitro/in situ system for high throughput drug screens for oral bioavailability.

o. Develop and deliver organ specific chemo-protective agents.

p. Develop and evaluate rapid, cost-effective methods, including biochemical, functional multiplexed, imaging, nanotechnology-based, and microfluidics-based assays, to quantitate surrogate endpoints for determination of doses, dosing schedules, safety, and efficacy of drugs.

q. Identify and develop biomarkers to evaluate drug activities and toxicities.

r. Develop assays in support of Exploratory Investigational New Drug Studies using biomarkers or other appropriate endpoints.

s. Develop, standardize, and validate cost-effective tools for obtaining comprehensive ADME and toxicology profiles that may better predict the performance of drugs in humans.

t. Develop and analytically validate assays or tools for measuring safety, efficacy, and dosing biomarkers.

5. *Animal Production and Genetics.*

a. Investigate alternatives to expensive barrier systems for exclusion of pathogens from rodent colonies, e.g., by use of micro-isolator cages, and evaluate their performance.

b. Develop and evaluate specialized shipping containers for pathogen-free animals.

6. *Natural Product Discoveries.* Note that execution of projects in most of these topic areas will require collaboration and signed agreements with countries where the source organism was originally collected.

a. Develop techniques for the study of non-culturable organisms in order to identify antitumor agents.

b. Develop techniques for the genetic and biochemical characterization and the manipulation of biosynthetic pathways to create leads. Use combinatorial biosynthesis to generate libraries of un-natural natural products as drug leads.

c. Use genetic techniques for the identification of microbial consortia, and for the identification and isolation of genes controlling the biosynthetic pathways producing potential antitumor agents.

d. Express biosynthetic pathways from microbes or microbial consortia that are known to produce antitumor agents, but in organisms amenable to standard fermentation techniques.

e. Investigate new biological methods, such as tissue culture, aquaculture, hydroponics, etc., for the production of natural products as potential anticancer agents.

f. Develop new systems of large-scale production using biotransformation, tissue or cell culture, biotechnology, modification of the chemical ecology of producing organisms, etc., in order to produce the large quantities of anticancer drugs needed for preclinical or clinical development.

g. Develop methods for the isolation, purification, identification, cultivation, and extraction of microorganisms from unusual marine or terrestrial habitats for antitumor screening. Examples are gliding bacteria, barophilic, endophytic, thermophilic, and tropical canopy organisms.

h. Investigate newer methods of isolation and purification, such as super-critical fluid extraction and chromatography, centrifugal countercurrent chromatography or affinity-based separations, in the isolation and purification of natural products with anticancer activity.

i. Develop simple immunoassays that can be used to monitor the levels of natural products of interest in simple extracts of the relevant raw material. These assays should be capable of being developed for use “in the field” and also in developing countries.

j. Develop analytical and biological methods for isolation, purification and validation of active constituents identified from alternative medicine and complementary studies; use of these purified constituents alone or in combination with conventional anticancer agents.

7. *Data Management Systems.*

a. Develop data support systems for chemical library programs.

b. Develop bioinformatics tools to accelerate the identification, functional understanding and validation of drug targets.

c. Develop bioinformatics tools to predict ADME and toxicology characteristics of drug candidates.

d. Develop “data mining” strategies such as neural networks.

e. Develop algorithms for determining optimal drug combinations and for prediction of optimal effectiveness of individual agents.

f. Develop bioinformatics tools to support a systems biology approach to drug discovery and development.

g. Develop bioinformatics tools to support genomic/proteomic and other "omics" profiling experiments in support of drug discovery and development.

C. ***Cancer and Nutrition.*** Research to improve the methodology of nutritional assessment in a cancer population. Innovative approaches to evaluate the contribution of nutritional status to response to cancer treatment.

1. Research to improve the methodology of nutritional assessment in a cancer population.

2. Develop means to evaluate the contribution of nutritional status to response to cancer treatment.

D. ***Clinical Treatment Research.*** Clinical research studies designed to improve cancer treatment. Emphasis is on clinical trials for the evaluation of new therapeutic agents, development of assay

systems to measure patient response to chemotherapy, development of prognostic assays, and development of methods of analysis and management of clinical trials data. Studies designed to improve human subject protections for patient access to clinical cancer trials.

1. *Evaluation of New Cancer Therapies.*

    a. Conduct clinical trials for the evaluation of new therapeutic agents or modalities of treatment employing drugs, biologics or surgery.

    b. Clinical trials using "unconventional therapies," including, but not limited to, behavioral and psychological approaches, dietary, herbal, pharmacologic and biologic treatments, and immuno-augmentative therapies.

    c. Development and evaluation of new clinical approaches using gene transfer or gene therapy technologies.

    d. Development and evaluation of new clinical approaches using tumor associated antigens or vaccines in order to enhance immunogenicity.

    e. Develop and characterize novel chemical compounds that may be useful anticancer agents, either alone or in combination with other modalities such as radiotherapy.

    f. Develop techniques to lessen the toxicity of existing anticancer treatments.

    g. Develop new techniques for the delivery of anticancer agents that will maximize therapeutic effects and minimize toxicity.

    h. Develop new surgical techniques or tools or improve existing techniques that are/may be utilized in cancer treatment.

    i. Characterize and produce clinical grade monoclonal antibodies to detect and treat malignancies.

2. *Development of Prognostic Assays to Monitor Patient Response to Therapies.*

    a. Develop assay systems to measure the response of human tumors to chemotherapy or biologics.

    b. Characterize drug resistance mechanisms and design methods to overcome clinical drug resistance.

    c. Develop assays for prognostic factors to identify patient subsets who may benefit from specific cancer treatment therapies.

    d. Development of assays to assess effects of agents on specific molecular targets in clinical studies.

    e. Develop new techniques for relating past preclinical information to past clinical results for prediction of future useful clinical agents from future preclinical data (both in vitro and in vivo).

3. *Clinical Trials Informatics.*

    a. Develop new tools and methodologies for the analysis of clinical trials results.

    b. Develop new informatics tools to facilitate clinical trials data entry from the bedside and coordination of data entry and transmission throughout the institution and to other collaborating institutions or organizations.

    c. Development of novel web-based approaches to clinical trials informatics for transmission of data to NCI or other organizations. Topics include point of treatment data capture and reporting, electronic protocols, OLAP (On-line Analytical Processing), support for the Common Toxicity Criteria, and drug accountability support.

d. Develop new interchange standards, based on technologies such as XML, for sharing data among heterogeneous systems. Specific applications areas include, Adverse Even Reporting, Case Report Forms.

e. Develop new tools for support of Common Data Elements.

f. Develop new approaches for interface with electronic medical records, with intent to streamline data reporting, registration, and toxicity reporting of Clinical Trial information.

E. ***Cancer Imaging Program.*** The mission of this program is to promote and support: Cancer-related basic, translational and clinical research in imaging sciences and technology, and integration and application of these imaging discoveries and developments to the understanding of cancer biology and to the clinical management of cancer and cancer risk.

Toward this effort, CIP 1) funds research in the development of tools, methodologies and imaging agents/probes that will better diagnose, assess, and effectively treat cancer, and 2) supports a spectrum of research projects from preclinical exploratory research and development through clinical trials. Areas of interest include but are not limited to:

1. Development of medical imaging systems for early cancer detection, screening, response to therapy and interventions including image-guided therapy.
2. Development of preclinical and clinical in vivo imaging systems, methods, imaging probes and contrast agents and related image reconstruction, image processing, image display and image-based information as required to detect, classify, monitor and guide therapeutics to cancer and precancerous conditions.
3. Development of methods to assess the value of imaging procedures for the above goals.
4. Development of systems and methods for improved production and distribution of radioactive materials for cancer imaging and/or treatment.
5. Development of systems, methods and their optimization for studying the adverse reactions/effects of image-guided and other diagnostic and therapeutic interventions.
6. Any other investigator-initiated research idea that is relevant to cancer biomedical imaging.
7. Development of systems, methods and their optimization to advance the role of imaging in assessment of response to therapy through increased application of quantitative anatomic, functional, and molecular imaging endpoints in clinical therapeutic trials and dissemination of these systems and methods with appropriate scientific communities.

F. ***Radiation Research.*** The Radiation Research Program (RRP) supports basic, developmental and applied research (including clinical) related to cancer treatment utilizing ionizing and non-ionizing radiations. Therapeutic modalities include photon therapy, particle therapy, photodynamic therapy (PDT), hyperthermia, radioimmunotherapy (RIT), systemic targeted radionuclide therapy (STaRT), and boron neutron capture therapy (BNCT). Radiation research encompasses a range of scientific disciplines including basic biology, chemistry, physics and clinical radiation oncology. Topics of interest include, but are not limited to, the following areas:

1. Development of devices for planning, measuring, and delivering radiation therapy or related therapies, including devices for patient positioning and quality assurance for the following: (a) ionizing radiation, particularly 3-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT); (b) PDT; (c) hyperthermia; (d) RIT; (e) STaRT; and (f) particle therapy.
2. Development of devices for dosimetry for (a) ionizing radiation; (b) PDT, particularly those capable of measuring light doses at depth in tissues; (c) thermometry for hyperthermia, particularly non-invasive thermometry; and (d) RIT.

Devices may include chemical, solid state, film, biological or ionization systems to detect or read out exposures. Accuracy, precision and linear response are essential over the range of doses and temperatures employed in the research laboratory and/or in the clinic, depending on their intended use. Devices for thermometry during hyperthermia treatment must give accurate readings with the heating device(s) with which they are to be used.

3. Development and evaluation of computer hardware and software for radiation therapy, such as computation algorithms, computer workstations, image guidance techniques, and informatics methods for treatment planning, delivery and outcomes analysis.
4. Development of novel drugs to increase the effectiveness of radiation therapy or related therapies: (a) chemical modifiers of radiation response, particularly small molecules directed at molecular targets involved in tumor radioresistance; (b) photosensitizers for PDT; (c) sensitizers for use with hyperthermia; and (d) prodrugs that are selectively activated within the tumor.
5. Development of drugs to prevent, reduce or reverse normal tissue response, especially the late effects that develop months or years after therapy.

   Compounds that are based on a rationale for achieving a therapeutic gain (an improved differential response between tumor and normal tissue) are of greatest interest. Enhancement of response must be achieved at radiation doses and treatment schedules employed clinically.
6. Development of predictive assays and monitors of response to radiotherapy, PDT, hyperthermia, STaRT, or RIT. Tools are needed to identify patients that would benefit from specific therapeutic approaches.

G. ***Biological Response Modifiers (BRM).*** Research on agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells with resultant therapeutic benefits. Both preclinical and clinical investigations are conducted on the utility of a wide variety of natural and synthetic agents and on biological manipulations of immunological and non-immunological host mediated, tumor-growth controlling mechanisms in cancer therapy.

Studies are encouraged which utilize in vitro assays and/or animal model systems to investigate mechanisms of BRMs. Examples of innovative research include but are not limited to:

1. Evaluation of molecular genetic approaches to discovery of new therapeutic agents, delivery of BRMs or development of gene therapy.
2. Development of improved techniques to synthesize, screen and develop new oligonucleotides including iRNA sequences for therapeutic purposes, such as signal modulation, anti-oncogene or anti-viral effects.
3. Improvement in cell-culturing techniques, e.g., by developing automated cell culture systems, specialized media, or improved methods to induce activation, proliferation or differentiation.
4. Development of new procedures or reagents for the modulation of the suppressor arm of the immune system in experimental models, directed towards successful immunotherapy.
5. Improvement of tumor-associated antigens or vaccines in an attempt to enhance immunogenicity.
6. Evaluating autoimmunity in the context of anti-tumor response *in vivo* to vaccines.
7. Development of novel in vitro assays for the primary screening of BRMs.
8. Application of observations describing shared receptors and mediators between the neuroendocrine and immune systems in studying immunobiology and immunotherapy of cancer.
9. Development and optimization of viral oncolytic agents.
10. Development of novel or improved methods for process development and manufacture of biotherapeutics, including but not limited to antibodies, recombinant proteins, peptides,

oligonucleotides, and products based on viral or bacterial vectors, per executive order (E.O. 13329) mandating federal agencies assist the private sector in manufacturing innovation efforts.

11. Development of innovative methods for monitoring the manufacturing process for biotherapeutics using in-line or on-line process analyzers to improve the efficiency of process controls and determination of production end-points (see Guidance for Industry, PAT-A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance, www.FDA.gov).
12. Development of methods to more efficiently assess factors related to the ultimate product quality, safety and efficacy of biologics.

Division of Cancer Prevention

The Division of Cancer Prevention (DCP) directs an extramural program of cancer prevention research including chemoprevention, nutritional science, genetic, epigenetic, infectious agents, and early detection including biomarker development and validation and biometry for the Institute. DCP also supports research training and career development in cancer prevention and early detection and coordinates community-based clinical research in cancer prevention and dissemination of cancer treatment practice through a consortium of community clinical centers. For additional information, please visit our home page at http://www.cancer.gov/prevention/index.html.

A. ***Prevention.*** Research studies to identify, evaluate, and implement techniques and approaches for the prevention, risk assessment, and early detection of cancer. Those studies capable of achieving these objectives with minimal risk and cost are preferred.

1. *Chemoprevention.* Studies in which naturally occurring or synthetic agents are identified, or further evaluated for efficacy or safety. Studies involving in vitro assays with cell transformation systems, in vivo assays involving animal models to evaluate agents against typical carcinogenic agents at specific sites, and studies involving clinical chemistry measurement of agents in sera or other biological fluids are of highest program relevance. Studies aimed at improving future research designs for chemopreventive trials; providing additional biological understanding, identification and evaluation of modulation of quantitative or qualitative biological endpoints, and/or markers for surveillance of compliance will also be considered. Examples of tests might include measurements of biochemical parameters, cytological screening techniques, in vitro studies of suppression of oncogene protein products, enhancement of tumor suppressor genes, in vitro toxicological studies, and synthesis of novel chemopreventive agents based on structure/activity relationships.
2. *Diet and Nutrition.* The Nutritional Science Research Group supports studies that aim to reduce the incidence of cancer through dietary modification, which may include additions, deletions, or substitutions of foods or dietary factors.

   Topics of interest include the development of:

   a) Animal models, including transgenic and knockout, to examine the cancer prevention effects of bioactive food components.

   b) Invertebrate models for the study of bioactive food component-gene interactions involved with cancer prevention.

   c) Novel technologies for measuring the effects of diet on differential gene expression, epigenetic events, proteomics, and associated metabolomic changes.

   d) New models/approaches for examining diet on cancer related processes; i.e., cell division, apoptosis, immunity, angiogenesis.

   e) Educational interactive software packages that focus on dietary exposures and cancer prevention.

f) Effective methods for assessing the content of bioactive food components in foods and dietary supplements.

g) Bioengineering tools for the study of bioenergetics and obesity.

h) New and/or improved diagnostic markers for assessing the nutritional status of individuals prior to developing a neoplasm.

i) Technologies for detecting and identifying carcinogenic and cancer protective compounds in foods.

j) Surrogate cells for predicting the response to bioactive food components in target tissue(s).

k) Methods for the isolation and preparation or synthesis of candidate nutrients in quantities suitable for preclinical and clinical screening.

l) Blends/combinations of bioactive food components for cancer prevention.

m) Novel technologies for assessing the effects of dietary components on the extracellular matrix and tissue microenvironment.

n) Methodologies to understand stem and progenitor cells with the microenvironment as determined by dietary components.

o) Approaches for identifying responders from non-responders of dietary prevention intervention strategies.

B. ***Community Oncology.*** Introduction, application, and evaluation of effective and practical cancer control intervention programs in community settings. Primary emphasis is on the integration and involvement of community physicians and allied health professionals in cancer control efforts and the promotion of linkages between community practitioners/hospitals and other regional resources for cancer control.

Objectives are to: (1) reduce the time between research advances in prevention, detection, and patient management and their application in community settings; and (2) expand extend the cancer care knowledge and applications bases; and (3) evaluate new detection and diagnostic methods for specificity, sensitivity, reliability, validity, safety, feasibility and cost when applied to defined or target populations. This may include screening research as well.

C. ***Rehabilitation and Continuing Care.*** Development and evaluation of rehabilitation or continuing care strategies which directly enhance functioning of patients with cancer or which contribute to understanding of factors impacting utilization of supportive services by cancer patients. Clinical applications include development and testing of interventions to enhance multidisciplinary approaches to cancer rehabilitation, and research on effective symptom management (e.g., cancer-related pain, fatigue, nausea, mucositis). Areas of general program interest include innovative approaches to measuring and enhancing quality of life of cancer patients; research to investigate and enhance clinical decision-making by both patients and physicians; and studies of the impact of individual preferences for health care outcomes and their impact on cancer prevention practices in persons without cancer and on treatment decisions in patients with cancer.

D. ***Early Detection and Screening.*** New diagnostic or screening methods for early detection of cancer, especially for asymptomatic patients. Detection methods can include any cancer site, although there is more interest in the common cancers, such as those of the lung and colon. Methods should be cost beneficial and applicable in a clinical setting.

1. Studies which identify and document new databases relevant to early cancer detection and propose using new and experimental analytical techniques.

2. Analyses of long-term, follow-up data from completed studies for potential new interpretations based on the passage of time.

3. Studies which propose to develop and evaluate new detection techniques and measures for sensitivity specificity, reliability, validity and safety.
4. Determinations of the cost/benefit or risk/benefit ratios of cancer screening and detection methods when applied in defined or target populations.
5. Currently, the most commonly used method to detect prostatic cancer is the digital rectal examination. Various devices and models would be necessary for the early detection of prostate cancers by physical examination. They would include, but not limited to the following disease states: (1) absence of disease (normal model); (2) benign prostatic hypertrophy; (3) prostatitis; (4) Stage B1 prostatic cancer (T2a); (5) Stage B2 prostatic cancer (T2b); and (6) Stage C prostatic cancer (T3z, T3b, and T4).
6. Development of products that aid the systematic collection and transport of specimens used for the early detection of cancer, including devices for the collection and transport of urine, serum, fecal material, exfoliated cells, and other potential materials.
7. Develop computer utility programs that can increase the clinical uses of existing programs commonly found in medical offices creating age-sex registries, predicting population risks, determining screening needs of patients, reminder systems, etc. Develop bioinformatics to study gene profiling.
8. Develop personal computer programs that can be used to determine population risks and the effect of interventions. These programs might also be adopted to the concept of Community Oriented Primary Care.
9. Use of ultrasonography with color flow imaging for the early detection of cancer. Research on the use of ultrasonography with color flow imaging (US-CFI) for the early detection of cancer of the ovary, breast and/or prostate. Emphasis should be given to the ability of the US-CFI to differentiate between malignant and benign disease at these sites. Criteria for the discrimination of malignant from benign disease would be developed as well as performance characteristics of this method, particularly for breast and prostate. Studies on symptomatic populations should yield sensitivity, specificity and positive predicative values when breast and prostate are the target sites. Studies on asymptomatic populations should yield sensitivity, specificity and positive predicative values when ovarian cancer is the target site.
10. As more women seek mammographic breast screening, the importance of efficient, high speed, “intelligent” mammographic systems capable of acquiring and storing large volumes of images and enhancing image interpretation will become more important. Technological developments of interest are:
    a. Develop digital mammographic systems for high volume applications with electronic archiving and image analysis capabilities.
    b. Develop artificial intelligence based interactive image analysis software to enhance mammographic sensitivity and specificity.

E. ***Cancer Biomarkers.*** The Cancer Biomarkers Research Group (CBRG) promotes research on the discovery, development, and validation of biomarkers for pre-cancer and early cancer detection and relevant technologies so that risk can be more accurately assessed and cancers can be detected at early stages of development. Early detection has the potential to reduce cancer morbidity and mortality. In cancer research, biomarkers refer to substances that are indicative of the presence of cancer in the body. Biomarkers include genes, RNAs, proteins, and metabolites. As the molecular changes that occur during tumor development can take place over a number of years, biomarkers can be potentially used to detect cancers early. Topics of interest include, but are not limited to, the following areas:

1. Discovery, development and/or validation of biomarkers (genomic, epigenomic, proteomic and metabolomic) for precancerous lesions, early cancer detection, and identification of risk.

2. Development of new biological, genetic, histochemical, immunologic, and molecular assay or analyses applied to early cancer detection, risk assessment, or susceptibility.
3. Development of new tools and technologies, including microfluidics and nanotechnologies, for analyzing biomarkers for early cancer detection and risk assessment.
4. In silico data analysis for the discovery and identification of cancer biomarkers.
5. Ancillary studies to discover biomarkers from ongoing prevention and treatment trials and any large studies.
6. Development of statistical and epidemiological approaches to biomarkers evaluation for early cancer detection and risk.

Other Research Topic(s) Within the Mission of the Institute

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For NCI-related SBIR Information, visit: http://www3.cancer.gov/admin/gab/index.htm.

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)

The NICHD conducts and supports research and research training on biological and behavioral aspects of human development. Primary program areas include: reproduction and population studies, pregnancy, perinatal biology, maternal and infant well-being, developmental and reproductive immunology, congenital defects, developmental biology, teratology, nutrition and growth, human learning and behavior, learning disabilities, cognitive and social development, mental retardation and developmental disabilities, pediatric, adolescent, and maternal AIDS and HIV, obstetric and pediatric pharmacology, and medical rehabilitation.

For additional information about areas of interest to the NICHD, please visit our home page at http://www.nichd.nih.gov.

Phase IIB Competing Renewal Awards

NICHD will accept Phase IIB SBIR Competing Renewal grant applications to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA, FCC). Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Applicants who received NICHD SBIR Phase I or Phase II support and who are currently Phase II awardees are eligible. Budgets for Phase IIB renewals should not exceed 3 million dollars total costs for three years. Depending on the research proposed the amounts may vary each year for the time requested.

You are strongly encouraged to contact Dr. Louis Quatrano (contact information provided below) before beginning the process of putting a Phase IIB Competing Renewal application together. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NICHD SBIR/STTR Phase II awards will be eligible for a Phase IIB Competing Renewal grant.

Examples of research that would be considered responsive to this announcement are listed below for illustrative purposes and are not exclusive of other appropriate activities. Preclinical studies, including

pharmacology and toxicology, and other clinical studies beyond those conducted under the initial Phase II (R42, R44) grants such as:

- innovative assistive devices and techniques to minimize residual disability and to impact on critical illness, physical behavior and cognitive development in childhood;
- novel assays, kits, and devices to monitor fertility;
- new and improved methods of fertility regulation, for men and for women, that are safe, effective, inexpensive, reversible, and acceptable;
- new tools to monitor the state of various organ systems during therapy in pregnancy or infancy; and,
- Evaluation of neuroimaging tools specific to brain development in pediatric populations or individuals with injuries.

Direct your questions about scientific/research issues to:

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Population Research

Research on topics in reproductive sciences, contraceptive development, and demographic and behavioral sciences. Examples of research topics that may be of interest to small businesses include, but are not limited to:

A. ***Reproductive Sciences.*** Research on the reproductive processes of men and women and of animals with similar reproductive systems related to developing safer and more effective means of regulating, preserving or achieving fertility. Particular areas of programmatic interest relative to small business initiatives include, but are not limited to:

- Development of reagents to facilitate study of reproductive and developmental processes.
- Development of improved methods of growing and differentiating stem cell lines in vitro, including feeder cell-free approaches.
- Development of novel assays, kits, and devices to monitor fertility and treat infertility and gynecological disorders.
- Use of genomics and proteomics to develop novel diagnostics and treatments for reproductive diseases and disorders.
- Development of high resolution technologies to provide invasive or noninvasive assessments of reproductive and developmental competence.
- Development of experimental animal models that would be useful for studying the physiology and pathophysiology of reproductive processes.
- Development of improved and novel technologies for the preservation of human gametes.
- Development of improved technologies for preimplantation genetic diagnosis.

- Development of improved technologies for the reprogramming of cells, including embryonic stem cells or adult cells, into eggs and sperm.

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B. ***Contraception and Reproductive Health Research.*** Emphasis is on developing new and improved methods of fertility regulation; developing new and improved treatments for disorders of the reproductive system including female pelvic floor disorders; and research on the benefits and risks of contraceptives and other drugs, devices, and surgical procedures as they affect reproductive health. Areas of interest include, but are not limited to:

- Developing new and improved methods of fertility regulation, for men and for women that are safe, effective, inexpensive, reversible, and acceptable. This includes, but is not limited to, synthesis and testing of novel chemical compounds.

- Developing new and improved treatments for disorders of the male and female reproductive system, including those used for hormone therapy and drugs, graft materials, and devices used for non-surgical and surgical treatment of pelvic organ prolapse, urinary incontinence, and other female pelvic floor disorders.

- Discovering and disseminating new knowledge about the medical benefits and risks of contraceptives and other drugs, devices, and surgical procedures affecting reproductive health. We will primarily support applied research projects such as epidemiologic studies or Phase III trials designed to detect clinically significant adverse effects, particularly those too rare to be determined through the FDA's premarketing approval process. Laboratory models will be used when human studies are not feasible or to explore mechanisms of action or supplement epidemiologic and clinical observations.

- Studies relating contraception or reproductive health to STDs such as HIV, including but not limited to development of new contraceptive products with microbicidal activity against STDs such as HIV; studies to define the relationships among contraceptive methods and HIV acquisition, transmission, or disease progression; and studies to clarify mechanism of interaction between contraceptives and other disease processes or conditions.

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C. ***Demographic and Behavioral Sciences.*** Research on the size, growth, and composition of populations and the impact of changes in population on the health and well-being of individuals, families, and the population itself. The program emphasizes not only factors affecting fertility, mortality, population movement and compositional change, but also demographic, social, and behavioral research on teenage childbearing, AIDS, single-parent families, fatherhood, racial and ethnic differentials in infant mortality and child health, migration, and the well-being of children. Applications are encouraged, but are not limited to these areas:

- Technological innovations/inventions to help collect biomarker data, especially technologies that can be used in large surveys.

- Creation of hardware/software to aide in the collection of accurate cause of death/health diagnosis for the purposes of statistical analysis in population based datasets.

- Innovative use/implementation in integrating geographical information systems, spatial network analysis, and/or simulation methods for demographic research.

- Innovative approaches to analyzing and disseminating large-scale data sets.
- Development of effective tools for prevention research and intervention programs related to STD/HIV, pregnancy, divorce, child health, at risk youth, and other health-related topics.
- Innovative approaches to teaching population studies and other behavioral and social sciences at the undergraduate and graduate level.
- Innovative approaches for research design, data collection techniques, measurement, and data analysis techniques in the social and behavioral sciences, with particular attention to methodology and measurement issues in studying diverse populations, sensitive behaviors, confidential behaviors; in issues related to the protection of research subjects; and in issues related to the archiving and disseminating complex datasets.

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Research for Mothers and Children

Research in three major program areas includes: learning disabilities; cognitive and social development; nutrition and growth; obstetric and pediatric pharmacology, and pediatric, adolescent, and maternal AIDS. Topics that may be of interest to small businesses include, but are not limited to, those identified below.

A. ***Child Development and Behavior.*** Research programs on psychological, social and emotional, psychobiological, and educational development from conception to maturity, specifically:

- Social and Affective Development, Child Maltreatment and Violence, including normative social, affective, and personality development and the impact of the physical and social environments on health and psychological development; investigations of socio-cultural, familial, individual, and biological influences on development; and child developmental processes in high-risk settings (e.g., in violent or abusive environments, or families experiencing stressors such as poverty, unemployment or parental depression).
- Developmental Cognitive Psychology, Behavioral Neuroscience, and Psychobiology, including linkages among developing brain, behavior, and genes; developmental pathways leading to normal and atypical brain development and behaviors and their underlying developmental mechanisms at the molecular, genetic, cellular and network levels; biological and behavioral indices of individual differences predictive of development at different points of development; neuroanatomical, neurofunctional, electrophysiological and neurochemical correlates of sensorimotor and cognitive abilities; tools to measure these; the effect of hormonal influences on behavioral development, including the development of gender-specific behaviors, the role of endocrines in social, emotional, and cognitive development, and the interaction of hormones and stress-related behaviors during development.
- Risk Prevention and Health Promotion: behavioral and developmental aspects of health risk behaviors and health promotion from infancy to young adulthood, including individual, interpersonal, and social factors; environmental and contextual factors; and interactions of genes and environment as they relate to health and health behaviors. Issues of risk behaviors, health literacy, adherence, pain, obesity, influence of electronic media, and influences of religiosity and spirituality are of interest.
- Reading, Writing, and Related Learning Disabilities: relative contributions of environmental, experiential, instructional, cognitive, linguistic, genetic, and neurobiological factors to the developmental reading process and to reading disabilities and writing, including the longitudinal

course of development and the interactions among these factors at different stages of reading development, in both mono- and bilingual individuals; use of technology to facilitate development of reading and/or writing skills, these technologies could include but are not limited to assistive technologies, interactive technologies for use by children, adolescent or adult struggling learners as well as technologies for instructors, parents and/or caregivers for use within or outside of the classroom context, as appropriate.

- Language and Bilingualism: language development and disorders and second language acquisition, including studies within a developmental context, that identify and explicate the cognitive, linguistic, social, cultural, socioenvironmental, geographic, environmental, instructional, and neurobiological factors affecting the development of language abilities.

- Early Learning and School Readiness: experiences children need from birth to age eight to prepare them to learn, read, and succeed in school; early interactions with adults and peers; early childhood education teaching methods and curricula; comprehensive early childhood interventions that support learning and development; use of technology in promoting school readiness skills in disadvantaged children from birth to age six, including interactive technologies for use by parents, child care providers, and teachers and technologies for direct use by children.

- Math and Science Cognition, Learning and Learning Disabilities: mathematical thinking and problem solving; scientific reasoning, learning, and discovery; studies that explore the genetic and neurobiological substrates of normal and atypical development in mathematics and science learning and cognition, as well as cognitive, linguistic, sociocultural, and instructional factors; individual differences that may moderate achievement; the delineation of skill sets needed to attain proficiency; development of effective instructional methods for typical development and interventions for learning disabilities.

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B. ***Endocrinology, Nutrition, and Growth.*** Research on the nutritional needs of pregnant women and their fetuses; aspects of nutrients related to reproduction, growth, and development; breast feeding and lactation; the immunology of breast milk; development of the gastrointestinal system; childhood obesity and the nutritional antecedents of adult disease; developmental endocrinology; mechanisms of hormone action during growth and development, and the impact of hormonally active agents in the environment on growth and development. Applications to advance the study of obstetric and pediatric pharmacology include: Research and tools to better characterize the impact of physiological and developmental changes on pharmacokinetics and pharmacodynamics; advancements in modeling which improve therapy during pregnancy, among premature infants, children and adolescents; research on tools to monitor the state of various organ systems during therapy in pregnancy or infancy; such as, cerebral monitors, placental function, etc.; models to characterize molecular, dosing or other modification to improve therapy.

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C. ***Pediatric, Adolescent, and Maternal AIDS.***

Domestic and international research on human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) in women of child-bearing age, pregnant women, mothers, fetuses, infants, children and adolescents. Specific areas of interest include but are not limited to epidemiology, clinical manifestations, pathogenesis, transmission, treatment and prevention of HIV

infection, including prevention of mother to child transmission, and HIV-related complications in these populations. Additional areas of interest include:

- New technologies relevant to resource-limited countries for:
  - diagnosis of HIV infection in infants;
  - diagnosis and treatment of HIV-related complications of HIV (e.g., diagnosis of tuberculosis in children);
  - simple and less technical assays to monitor CD4 cell percentage/count, HIV viral load, or other surrogate markers of disease progression in children.
- Drug formulations for antiretroviral drugs and/or drugs used to treat complications of HIV infection relevant to children (preferably not liquid preparations), particularly in resource-limited countries and including fixed dose drug formulations and innovative methodologies for development of solid formulations capable of being administered to young children (e.g., sustained release beads, etc).
- Simple, standardized tools to evaluate neurodevelopmental outcome in children in resource-limited settings.
- Topical microbicide agents to prevent sexual acquisition of HIV in women or in adolescents.
- New, non-invasive technologies to evaluate complications of antiretroviral drugs in HIV-infected infants, children, adolescents (e.g., mitochondrial toxicity) and pregnant women, their fetuses and children.

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Developmental Biology & Perinatal Medicine Research

Research in three major program areas includes: pregnancy and Perinatology; developmental biology, genetics and teratology; and mental retardation and developmental disabilities. Topics that may be of interest to small businesses include, but are not limited to, those identified below.

A. ***Pregnancy and Perinatology.*** The topic areas of research include the physiology of pregnancy and labor; high-risk pregnancies, including those with hypertensive disorders, diabetes or seizure disorders; fetal pathophysiology; premature labor and birth; diagnostic, monitoring, and therapeutic devices and instruments for newborn infants in the nursery and in Neonatal ICU setting; improving the existing products or developing new products that would improve the routine and extended care of the newborn infants; products and agents related to breastfeeding; hospital supplies specifically related to use in the care of newborn infants; nanotechnology and its application for the care of newborn infants; instruments and devices assessing and monitoring the nursery environment (noise, lighting, and odor); disorders of the newborn; sudden infant death syndrome; and biological and behavioral antecedents of low birth weight.

The following topic areas are of high priority:

- Non-invasive methods for assessing cardiovascular and pulmonary functions, including cardiac output, systemic blood pressure, airway resistance, pulmonary compliance, vital capacity and various lung volumes.
- Metabolic profile assessment using non-invasive or minimally invasive approaches. Particular area of expertise include measurement of glucose and lactate/pyruvate; assessing ketone body

measurements; free indirect bilirubin (uncongjugated, free indirect); major chemicals (Na^+ Ca^+ Cl^+ K^+ etc.) in the blood.

- Improved point of care methods to measure plasma glucose concentrations quickly and accurately.
- Devices, instruments, and tools to minimize bacterial colonization, reduce proclivity for thrombous formation; reduce health-care associated infection risks.
- Rapid methods for diagnosis of bacterial infections and inflammation.
- Non-invasive measures to assess brain energy utilization, especially glucose, oxygen, lactate, ketones, and other energy substrates.
- Innovative ideas to reduce stress for the staff, parents and infants in the NICU.

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B. ***Developmental Biology, Genetics, and Teratology.*** Biomedical research on the cellular, molecular, and genetic aspects of normal and aberrant embryonic and fetal development including early embryogenesis, limb formation, organ and limb regeneration, development of the nervous system, developmental immunology, and causative factors in teratogenesis. Areas of interest included but are not limited to:

- development and application of new animal model systems
- innovative and high throughput genomic and proteomic techniques
- systems biology approaches to advance the study of embryonic development and structural birth defects
- in vivo techniques for optical imaging and quantitative measurement of physical properties of cells/tissues
- innovative technologies for imaging of developmental processes and gene expression

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C. ***Intellectual and Developmental Disabilities.*** Biomedical, behavioral and biobehavioral research in neuroscience, genetics, biochemistry, molecular biology, and psychobiology aimed at identifying factors that cause abnormal brain maturation and function; identification of direct and indirect environmental factors (e.g., social, economic and cultural) that influence the occurrence of intellectual and developmental disabilities (IDD); and research leading to the prevention, amelioration, assessment and treatment of IDD, including approaches that involve expanded newborn screening and prenatal diagnosis.

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Medical Rehabilitation Research

This Center supports innovative research on the restoration, replacement, enhancement or adaptation of function for people with chronic physical disabilities. This includes rehabilitative approaches across etiologies and the lifespan, as well as the environmental and policy factors that promote full participation. We encourage studies that integrate biomedical, engineering and/or psychosocial approaches to develop practical and creative solutions to the daily functioning of people with disabilities and their families. The mission of the NCMRR is to increase the effectiveness of medical rehabilitation practices through research. Information about specific program areas within NCMRR can be found at: http://www.nichd.nih.gov/about/ncmrr/ncmrr.htm. Examples may include but are not limited to:

- Enabling technologies for restoration of function.
- Promoting behavioral adaptation to functional losses.
- Assessing the efficacy and outcomes of medical rehabilitation therapies and practices.
- Developing improved assistive technology.
- Promoting rehabilitative outcomes in pediatric critical care.
- Understanding whole body system responses to physical impairments and functional changes.
- Developing more precise methods to measure impairments, disabilities, and societal limitations.
- Training health professionals in the field of medical rehabilitation.
- Development of Home Centered Rehabilitation care systems.
- Promoting profession structured/directed self care and wellness.
- Development of tools to assist and facilitate families in their involvement in rehabilitation.

Investigators proposing budgets exceeding the guidelines are encouraged to contact program staff six weeks prior to submitting the application.

For additional information on research topics, contact:

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or

Louis A. Quatrano, Ph.D.
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Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Louis A. Quatrano, Ph.D.
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For administrative and business management questions, contact:

Mr. Ted Williams
Grants Management Specialist
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NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

The mission of the NIDA is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy. For additional information about areas of interest to the NIDA, please visit our home page at http://www.nida.nih.gov/.

Phase IIB Competing Renewal Awards

NIDA will accept SBIR/STTR Phase IIB Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue the process of developing products that require approval of a Federal regulatory agency. Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

Transitioning a new molecular entity from preclinical to the clinical phase of development, requires large-scale production of the new molecular entity and toxicity testing, activities which are both costly and time consuming. The cost and time constraints imposed by advanced stage development of a new molecular entity pose significant obstacles for small businesses. Although Phase I and Phase II SBIR support is sufficient for initial discovery efforts (e.g., compound synthesis and some in vitro and in vivo preclinical pharmacological testing), it is not adequate to support either the kind of developmental work needed for compliance with the FDA's requirement for an investigational new drug (IND), or for clinical trials.

This announcement adds another three years of support to SBCs for drug development by providing a second stage of Phase II SBIR funding through the mechanism of a Phase IIB SBIR Competing Renewal grant. It is recognized that an award of this type may not support the entire medications development timeline for any given drug. The Competing Renewal grant will however, allow small businesses to carry a medication from the preclinical to the clinical stage, which will aid in attracting interest and investment by third, parties, and provide an important resource for new pharmaceuticals for the treatment of substance abuse.

Please contact Kris Bough (contact information provided below) before beginning the process of putting an application together. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Phase IIB Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIDA SBIR/STTR Phase II awards will be eligible for a Phase IIB Competing Renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase IIB Competing Renewal projects. These are meant for illustrative purposes only and are not exclusive of other appropriate activities.

Research and development efforts can be focused on medications for the treatment of cocaine, methamphetamine, and other stimulant abuse, as well as towards opiate, cannabis, PCP and club drugs. The medications under development should be targeted towards attainment of abstinence, maintenance, and/or relapse prevention.

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the initial SBIR Phase I and Phase II grants. The studies conducted under the previous grants should be sufficient to provide a sound rationale for continued development of the entity or entities.
- Completion of studies as required by the FDA for an IND application.
- Human laboratory clinical trials to determine a medication's safety profile, metabolism, cardiovascular effects, interaction with drugs of abuse, etc.
- Clinical studies to assess the efficacy of the medication under development.

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Division of Basic Neuroscience and Behavioral Research (DBNBR)

DBNBR's basic neuroscience and behavioral research focuses on understanding the mechanisms, characteristics, and processes of drug abuse both in adult and developing organisms. Basic behavioral, cognitive, neurobiological, cellular, molecular, chemical, and genetics research aims at characterizing and understanding drug seeking, compulsive behavior, and addictive processes. These research areas necessarily include studies of normal processes. Using both animal and human studies, basic behavioral research focuses on behavioral and cognitive processes that may or do lead to drug initiation, and the behavioral and cognitive consequences of drug abuse. Neurobiology research focuses on the neural mechanisms and substrates underlying behavioral and cognitive processes and vulnerability factors associated with drug abuse, addiction, sensitization, tolerance, and relapse. DBNBR also supports basic chemistry and pharmacological studies focusing on structure/activity relationships, definition, and characterization of systems involved in drug actions, chemical synthesis of new ligands, pharmacokinetics, analytical methods, understanding basic mechanisms of drug action and drug testing. The focus of maternal and paternal drug use is to ascertain the consequences of drug exposure on brain development as well as on other physiological systems.

Computational and theoretical modeling of biological systems and behavioral processes, biomedical computing and/or information science and technology development is supported by DBNBR.

1. *Metabolomics in Drug Abuse Research.* Metabolomics is the study of all molecules of a cell or organism and their identification and quantification that helps to understand the cellular regulation, metabolic pathways and activity and response under normal and other conditions. This technique

thus could be used to develop metabolic profiling of normal or healthy subjects and subjects under the influence of substances of abuse or those undergoing drug rehabilitation programs.

NIDA is looking for applications on development of novel metabolomics technologies toward practical application in pathway and network investigation in biological systems particularly in understanding the mechanisms of drug addiction and discovering biomarkers for developing treatment for drug addiction.

Phase I application should demonstrate the feasibility of developing new metabolomics technology and phase II should focus on the application of this technology in drug abuse research.

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2. *Development of Alternate Drug Delivery Dosage Forms for Drugs Abuse Studies.* SBIR applications are solicited to design and develop alternate dosage forms for drugs that are not orally administered such as nicotine, marijuana, heroin, etc. Phase I should demonstrate the feasibility of the proposed innovation and Phase II, the development and testing of the innovation.

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3. *Discovery of New Chemical Probes.* SBIR applications are solicited to discover new chemical compounds as biological probes either by synthesis or isolation from natural resources in studying the mechanisms of action of drugs of abuse. Such substances could be new chemical compounds, drug products, or peptides. Currently there are several ligands available through the NIDA drug supply system such as SR 141716A, SR144528, CP 55,840, anandamide, epibatidine, Kaffiralin 1 and 2, etc. All probes for cannabinoids, neuropeptides, nicotinic acetylcholinergic receptors and related probes for drug abuse study are encouraged. In addition applications on biological screening of such new compounds as potential ligands for drug abuse research will also be considered.

   Phase I should demonstrate the feasibility of the proposed innovation and Phase II, the development, characterization, testing, and screening of innovation. It should also be demonstrated that the new or modified chemical compounds are suitable for drug abuse research.

Rao S. Rapaka, Ph.D.
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4. *Discovery and Study of Psychoactive Components of Botanicals.* NIDA is looking for applications to develop methods for the isolation, purification, identification and characterization of active and inactive ingredients of herbal plants (stimulants, hallucinogenic, analgesics, and/or narcotics) and evaluation of their biological properties. Such studies may include chemistry, toxicology, pharmacodynamics, pharmacokinetics and the mechanisms of action of active and inactive ingredients to understand their efficacy, usefulness, adverse effects and abuse potential.

   Phase I should demonstrate the feasibility of the proposed innovation and Phase II, the development, characterization, testing, and screening of innovation.

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5. *Virtual Reality for Treatment of Pain.* Virtual Reality (VR) exposure can reduce reported pain during wound care. Grant applications are sought to examine the utility of VR technologies in the treatment of various types of pain. Development of treatments for both acute and chronic pain is sought. These

treatments can be based in clinical settings or the patients' homes. Phase I testing should establish the feasibility of the use of this technology in the particular population to be tested. Phase I should also produce data that demonstrates that this methodology is effective for the particular type of pain being treated. Phase II should involve larger-scale testing (e.g., more subjects and treatment trials) examining various treatment parameters (e.g., timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in pain patients.

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6. *Virtual Reality for the Treatment of Drug Abuse.* Virtual Reality (VR) can be a useful clinical tool. In this particular study, VR exposure was used to allow patients to selectively not attend to an otherwise painful procedure. Drug abuse, like pain, is a problem that is strongly impacted by stimuli in the abuser's environment and psychological factors. Thus, it is reasonable to assume that VR may be useful in allowing individuals to ignore drugs cravings, withdrawal symptoms or environmental cues that promote drug abuse. Grant applications are sought to examine the utility of VR technologies in the treatment of various types of drug abuse. These treatments can be based in clinical settings or the patients' homes. These treatments can be developed to address drug withdrawal, drug craving or on-going drug related behaviors. The development of VR technologies to address abuse of all types of drugs (e.g., cocaine, marijuana, nicotine, alcohol, inhalants) is sought. Phase I testing should establish the feasibility of the use of this technology for the particular drug problem addressed (e.g., cocaine craving, opioid withdrawal) and should also produce data that demonstrates that this methodology is effective for the particular drug problem. Phase II should involve larger-scale testing (e.g., more subjects and treatment trials) examining various treatment parameters (e.g., timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

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7. *Development of a Virtual Reality Environment for Teaching about the Impact of Drug Abuse on the Brain.* Virtual reality (VR) is emerging as a technology with a multitude of uses within the medical sciences. In terms of the science of drug abuse, it is being developed as a treatment tool. The current solicitation seeks the development of a virtual reality environment that can be used in educational settings to teach about how drugs of abuse (both illicit and licit) affect the brain and behavior.

   The cost of portable hardware needed to present a VR environment is relatively inexpensive. If education programs like the one sought in this solicitation were available, it is likely that VR would be used as a teaching tool in many settings, including classrooms and museums.

   The particular program sought here is to present an interactive three-dimensional virtual brain that shows normal brain functions and, in contrast, brain function after exposure to drugs of abuse. This technology could illustrate the neurotoxic and long-term effects of drug abuse on the brain. This VR may include other features that are not described above, provided that it will be useful in educating individuals about the medical, behavioral and social effects of drug abuse.

   The phase I application should develop a beta version of the program. Further, the phase I application should include a preliminary demonstration of "usability," where it is shown that the types of people being educated with this program (e.g. teachers) can effectively operate this system without extensive training. Further, it should be demonstrated that the hardware is easily worn by subjects, and that the subjects can rapidly understand how to effectively interact in the VR environment.

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8. *Nanoscience-based Design of Therapies for Substance Abuse Treatment.* Nanoscience and nanotechnology, by manipulating matter at the atomic or molecular levels, are emerging research areas that have the potential to fundamentally transform the study of biological systems and lead to the development of new methods for detection, prevention, and treatment of substance abuse and related disease states. NIDA invites nanotechnology-based applications in the following areas:

    a. Methods to enhance the efficacy of FDA-approved compounds by reducing their size to the nanoscale range to alter absorption, distribution, metabolism, or excretion.

    b. Development of new compounds, through manipulation of matter at the atomic or molecular levels that could more readily pass the blood-brain-barrier or cell membranes.

    c. Development of nanoscale particles for controlled targeted delivery of therapeutics, genes, or antibodies.

    d. Methods to enhance existing imaging technologies using magnetic properties at the nanoscale.

    e. Application of nanostructures (e.g. noble metal nanoparticles, quantum dots, and nanolithographic structures that show promise for diagnostic development) for identification and analysis of genes, proteins, and other biological molecules implicated in the actions of drugs of abuse.

    Applications are invited from any of the above areas. Phase I should demonstrate convincingly the viability of the proposed innovation, whereas Phase II should carry out the development, characterization, testing, and screening of the innovation.

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9. *Functional Genomics Resources and Strategies.* In the post-genomic era, an explosion of gene discovery studies utilizing strategies such as genome-wide association scans, microarrays, and proteomics have identified a host of genes/gene variants associated with susceptibility to, or protection from, diseases of addiction. A critical next step is to validate these candidate genes/variants to determine which ones play an authentic functional role in mediating addiction. Functional validation could occur at many different phenotypic levels ranging from the molecular to the behavioral. Studies could investigate a few high priority genes/variants or could test several hundred genes/variants rapidly. The development of resources and strategies that would facilitate functional validation of genes/gene variants include (but are not limited to) the following areas:

    a. Gene/variant effects on subcellular localization, stability, or function of mRNAs/proteins relevant to drug addiction.

    b. The development of imaging and other strategies to identify gene/variant effects on neuronal or brain functions relevant to addiction.

    c. Strategies to identify gene/variant effects on behavior, such as response to addictive stimuli, stress, or changes in social situations.

    d. RNA interference-mediated depletion of candidate genes in cells or whole organisms to look for phenotypic alterations such as changes in synapse, dendritic spine, or cell morphology, gene expression, or behavioral responses to drugs of abuse.

    e. Strategies exploiting the growing collection of genetic mutants in candidate genes (particularly utilizing model organisms such as mouse, zebrafish, *Drosophila*, *C. elegans* or yeast) to functionally validate genes/variants.

f. Approaches enabling comparison of wild type protein function to the function of allelic variants using *in vivo* transgenes or *in vitro* biochemical assays, especially if these approaches reveal whether a variation increases or decreases gene function.

g. Systems-based approaches investigating whether a set of candidate genes is co-expressed in a particular brain region or cell type, physically interacts with one another, or functions together in a signal transduction cascade are also of great interest.

h. Approaches to ascribe drug abuse-related function to genes/variants in non-coding RNAs, microRNAs, gene regulatory elements, gene copy number, or other putative non-protein coding regions of the genome.

i. Methods of translating functional studies in model systems to validate gene/variant function in humans.

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10. *Genetic Studies.* The National Institute on Drug Abuse is interested in applications that would facilitate the identification of genetic loci that confer vulnerability to substance abuse and addiction. Areas of interest include but are not limited to:

    a. Collection and genotyping of human pedigrees and sib-pairs for vulnerability or resistance to drug abuse.

    b. Isolation and identification of mutant strains in genetic model systems such as Zebra fish, Drosophila, C. elegans, mice, and rats that are more vulnerable or resistant to drugs of abuse.

    c. Throughput screens for identifying genetic vulnerability to addiction in genetic model systems.

    d. Development of transgenic models for drug abuse using bacterial artificial or yeast artificial chromosomes.

    e. Development of software and databases for candidate genes for drug abuse.

    f. Identification and mapping of functional polymorphisms of candidate genes for drug abuse.

    g. Placement of candidate genes for drug abuse on biochips.

    h. Marker-assisted breeding of congenic mouse and rat strains for mapping quantitative trait loci associated with addiction and drug abuse.

    i. Vectors for gene transfer into neurons.

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11. *Effects of Drugs at the Cellular Level.* Development of new imaging techniques, reagents and related hardware and software for dynamic investigations of the effects of drugs of abuse on cellular activities and communications. For example, these techniques might include, but are not limited to, development and utilization of reagents for magnetic resonance microscopy and other MRI methods; development of methodologies applying functional MRI to drug abuse studies; the use of dyes, intrinsic signals, and other optical indicators for studying signal transduction mechanisms, the regulatory control of protein entities (such as phosphorylation), and neuronal excitatory and inhibitory pathways. Areas of interest may include but are not limited to:

    a. Studies using molecular biological techniques to scale-up protein production for investigations aimed at enhancing understanding of the structure, function and regulation of molecular entities involved in the cellular mechanisms through which abused drugs act.

b. Validated in vitro test systems can reduce the use of animals in screening new compounds that may be of potential benefit in treating drug abuse. Test systems are needed to evaluate activity at receptors or other sites of action, explore mechanism(s) of action, and assess potential toxicity.

c. With the recent success in molecular cloning of various drug abuse relevant receptors, enzymes, and other proteins, researchers will elucidate the molecular mechanism of action of these drugs. Studies to generate strains of transgenic animals carrying a gene of interest are solicited. Of special interest are knockout and tissue-specific knockout animals. These animals can be used to identify gene function, and to study the pharmacological, physiological, and behavioral role of a single gene.

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12. *Research Resources.* The National Institute on Drug Abuse is interested in applications that would generate the following resources for drug abuse research:

    a. Resources for the application of genetic engineering to dynamically monitor neuronal function.

    b. C57BL6 Mouse embryonic stem cells and spermatogonial stem cells.

    c. Turnkey technology for proteomics such as the development of protein and peptide chips to study drug effects on neuronal mechanisms.

    d. Antibodies, aptamers, ligands, etc. relevant to drug abuse research.

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13. *Computation, Modeling and Data Integration in Drug Abuse Research.*

    a. Development of software or other tools, which enable data integration, and the development of computational models related to addiction and other medical consequences of substance abuse, e.g. tools that enable the integration of proteomics, genomics, transcriptomics, metabolomics and other data into applications leading to systems understanding of drug effects upon biological systems, or developing innovative approaches for managing knowledge and integrating information from text, data, image, and other sources or files generated in addiction research.

    b. Tools, which enable multilevel and multiscale modeling of biological and behavioral systems relevant to substance abuse research, such as those relevant to evaluations of expected utility.

    c. Development of software tools and interactive technologies (such as applications of grid technologies and networked appliances) which enable the prevention, treatment and study of substance abuse as well as the evaluation of prevention and treatment strategies.

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Division of Epidemiology, Services and Prevention Research (DESPR)

A. ***Prevention Research Branch (PRB).*** The Prevention Research Branch (PRB) supports a program of research in drug abuse and drug related HIV prevention to (1) examine the efficacy and effectiveness of new and innovative theory-based prevention approaches for drug abuse, drug-related HIV/AIDS and other associated health risks, (2) determine the cognitive, social, emotional, biological and behavioral processes that account for effectiveness of approaches, (3) clarify factors

related to the effective and efficient provision of prevention services, and (4) develop and test methodologies appropriate for studying these complex aspects of prevention science.

Prevention Research. Rigorous scientific prevention research is encouraged to study novel approaches to substance abuse prevention for use at multiple levels of the social environment including: the family, schools, peer groups, community and faith-based organizations, the workplace, health care systems, etc. The purpose of this research is to determine the efficacy and effectiveness of novel program materials, training strategies, and technologies developed to prevent the onset and progression of drug abuse and drug-related HIV/AIDS infection. Materials and technologies may target a single risk-level or may take a comprehensive approach encompassing audiences at the universal, selective, and/or indicated levels. Universal interventions target the general population; selective target subgroups of the population with defined risk factors for substance abuse; indicated interventions target individuals who have detectable signs or symptoms foreshadowing drug abuse and addiction, but who have not met diagnostic criteria. NIDA encourages the development and testing of innovative prevention intervention technologies that are sensitive and relevant to cultural and gender differences.

1. Laboratory studies of the underlying mechanisms and effects of various prevention approaches such as persuasive communication (e.g., mass media and print media) as they are affected by and effect drug related cognition, emotion, motivation and behaviors.
2. Decomposition of prevention programs, practices and strategies to understand components that account for program effectiveness.
3. Research on features of prevention curricula, materials, implementation, approaches, training, technical assistance, and systems integration that contribute to positive outcomes.
4. Training modules and ongoing technical assistance for program implementers of research based substance abuse prevention programming strategies.
5. Prevention intervention dissemination technologies and mechanisms that integrate research with practice; specifically the transfer of drug abuse prevention information to decision-makers, funders, and practitioners.
6. Prevention services research on the organization, financing, management, delivery, and utilization of drug abuse prevention programs.
7. State-of-the-art and practical strategies for the integration of evidence-based prevention approaches into existing prevention service delivery systems.
8. Studies that develop and assess reliability and validity of developmentally appropriate self-report, physiological, and biochemical measures for use in prevention trials in a variety of settings and a variety of audiences.
9. Development of and testing of environmental change strategies for schools, neighborhoods, communities, etc. to use in reducing substance use initiation and/or progression.
10. Development of practical and affordable community tools for: needs and resource assessment, selection of appropriate evidence-based programs and strategies, high-quality implementation of identified programs and strategies, evaluation at community, organization and individual levels, and sustainability.
11. Drug abuse prevention methodological research on promising data collection, data storage, data dissemination, and reporting techniques.
12. Promoting wider and more effective (e.g. with enhanced fidelity) use of evidence-based prevention interventions for substance abuse and related HIV prevention, including interventions made available thru CDC and other federal agencies.
13. Studies applying technologies and strategies that have been developed for use in other disciplines in order to examine the utility of their application for drug abuse prevention, such as

virtual reality technologies being used for some clinical conditions (e.g. phobias, eating disorders), and serious video games are being used for some clinical conditions (e.g., cancer patients), but not for drug abuse prevention.

14. Development and testing of innovative drug abuse prevention intervention products, using discoveries from the basic biological (e.g. neurobiological), psychological (e.g. emotional, behavioral, cognitive, and developmental) and social (e.g. social learning, peer network, and communications) sciences.
15. Development and testing of adaptations for efficacious prevention research approaches to make these more appropriate for special populations including racial and ethnic minorities, non-English speaking populations, immigrant populations, rural and migrant populations, low literacy populations, or persons with disabilities.
16. Development of methods, state-of-the-art tools and systems for community coalition-building.
17. Development and testing of tools to measure intervention costs, cost effectiveness, and net economic benefits.
18. Development and testing of rapid assessment tools of sexual and drug use risk behaviors for use in health care and public health environments, including STI clinics and AIDS research centers.
19. Development and testing of tools to promote security and appropriate prescribing of scheduled prescription drugs. Technologies can be developed to assist medical professionals, schools, service providers and others in making prescribing decisions, educating patients and their caretakers, or dispensing and monitoring of medications.
20. Development of new technologies to support drug abuse prevention interventions with military personnel, veterans and their families. Tools can include adaptations of efficacious and effective drug abuse prevention interventions to maximize health care efficiencies and to address negative life stress resulting from sustained combat operations, a major contributor to both the onset and exacerbation of substance abuse and mental health problems.
21. Development of new technologies for delivery and implementation of efficacious drug abuse prevention interventions for rural and frontier communities.

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B. ***Epidemiology Research Branch (ERB).*** The ERB supports a research program on drug abuse epidemiology that includes (1) studies of trends and patterns of drug abuse and related conditions such as HIV/AIDS in the general population and among subpopulations, (2) studies of causal mechanisms leading to onset, escalation, maintenance, and cessation of drug abuse across stages of human development, (3) studies of person–environment interactions, (4) studies of behavioral and social consequences of drug abuse, (5) bio-epidemiologic studies including genetic epidemiology studies, (6) methodological studies to improve the design of epidemiologic studies and to develop innovative statistical approaches, including modeling techniques.

1. *Improvement of Reliability and Validity of Reporting of Sensitive Data.* The reliability and validity of self-report of drug use and related behaviors (e.g., HIV risk behavior) is a matter of great concern. Use of new technologies for real time data collection in ecological settings is of great interest because these technologies enable collection of drug consumption data in context. Studies to improve methodologies based on variations of standard survey protocols or computer-assisted self-interview (CASI) and personal interview (CAPI) are also encouraged.
2. *Instrument Development.* Easy-to-use assessment instruments are needed to enhance epidemiology research. Areas of interest include but are not limited to:

a. *Community Assessment.* The development of community diagnostic instruments for psychometrically sound assessment of community characteristics is essential to improve our understanding of how community factors affect drug abuse and ensuing behavioral and social consequences. Standardized assessments of community characteristics are needed to better understand the full impact of drug use and to develop targeted interventions to specific community needs.

b. *Assessment of Psychiatric Comorbidity in Community Settings.* Easy to use, reliable, and valid instruments are needed to assess psychiatric comorbidity in different populations of drug abusers, including adolescents and those in community drug abuse treatment settings.

c. *Assessment Instruments to Measure CNS Function Related to Drug Abuse.* The development of age-appropriate assessment instruments to measure behavioral and cognitive function over the course of development will contribute to our understanding of vulnerability to drug abuse and functional impairment due to drug use.

3. *Development of State-of-the-Art Mechanisms for Epidemiological Research.* The development of state-of-the-art mechanisms to facilitate the use of Geographical Information Systems (GIS) in community epidemiology studies (for example Community Epidemiology Work Groups) and other drug abuse research is if great interest. There is a need for enhanced software and hardware for GIS interfaces, database management, visualization, and innovative spatial analysis capabilities. The role of GIS in public health management and practice continues to evolve. Application of this technology is an important step towards better understanding drug abuse issues and their inherent complexities. The ability to evaluate geospatial information provides a unique perspective of public health issues such as emerging and shifting epidemics, the utilization of treatment services, and rapid assessment of the impact of incidents ranging from natural disasters to bioterrorism. When used alongside more traditional epidemiological techniques, GIS provides epidemiologists the ability to address new questions, refine, or enhance existing analyses.

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4. *Improving Measures of Addiction Risk.* Individual differences in risk for drug addiction are often expressed in degree rather than kind, that is, as gradations along an underlying continuum that stretches from unobservable variations in risk for addiction to extreme and fully debilitating addiction severity. Assessment instruments in use today for measuring drug addiction (i.e., compulsivity in seeking and using drugs despite harmful consequences) have proven reliability and validity, but are of limited use for evaluating individual differences in risk for drug addiction. Advances in computerized adaptive testing methods, computer-assisted technologies, and psychometrics, including item response theory, suggest that the capabilities now exist for the development of the next generation in addiction assessment. New assessment instruments are needed to detect meaningful variation between, within, and across individuals over time that is scalable along the dimension of risk for addiction; these instruments should allow for efficient assessment of the risk construct with minimal burden for administration, training, and cost to the researcher, clinician, research participant, or patient; and they should ultimately provide valid and reliable scores corresponding to established diagnostic criteria for substance use disorders.

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5. *Developing, Validating, Refining Tools for Ecologic Momentary Assessment.* Ecologic Momentary Assessment (EMA) includes the measurement of exposures and events in real time as they occur, and in the natural environment where they occur, such as the home,

neighborhood, or workplace. EMA tools include portable technologies for longitudinal data collection in the field, such as mobile phone electronic diaries and PDAs, geopositioning devices, motion sensors, biosensors, environmental sensors, and audiovisual devices. In addiction and behavioral research, new EMA tools may enhance the contextual and temporal resolution of exposures, and the biological or behavioral processes presumed to occur in response. Specific challenges to address in the implementation of EMA include optimizing the timing of measurement and data quality, establishing sensor validity and reliability in different populations, reducing intensely longitudinal data for statistical analysis, achieving user acceptability, and safeguarding user privacy. Studies are encouraged that address these and other challenges to improve the validity and acceptability of EMA tools.

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C. ***Services Research Branch (SRB).*** The SRB supports a program of research on the effectiveness of drug abuse treatment with a focus on the quality, cost, access to, and cost-effectiveness of care for drug abuse dependence disorders. Primary research foci include: (a) the effectiveness and cost-benefits and cost-effectiveness of drug abuse treatment, (b) factors affecting treatment access, utilization, and health and behavioral outcomes for defined populations, (c) the effects of organization, financing, and management of services on treatment outcomes, (d) drug abuse service delivery systems and models, such as continuity of care, stages of change, or service linkage and integration models, and (e) drug abuse treatment services for HIV seropositive patients and for those at risk of infection.

1. *Drug Abuse Treatment Economic Research.* This initiative will support research to design and develop data systems for financial management and economic analysis of treatment programs and larger systems in new healthcare settings and managed care networks. Managerial decision-making requires the implementation of sophisticated data systems to facilitate routine budgeting processes, allocation of resources, performance measurement, and pricing decisions. The focus is on the needs of managers within the organization and managers outside of the organization. Data system development must be based on standard cost behavior and profit analysis. Data systems must be designed with correct cost concepts (accounting and economic) in order to permit cost and pricing decisions to be developed for new treatment technologies and management of ongoing systems. In research settings, such an initiative is vital for the assessment of new technologies developed for transfer to practice.

2. *Determining the Costs of Implementing Evidence-Based Practices (EBPs) and Other Technologies in Drug Abuse Treatment.* Research shows that new technologies or evidence-based practices (EBPs) can improve drug treatment outcomes, and it has been asserted that large-scale drug abuse treatment improvement requires systematic implementation of proven practices, processes, and technologies. Often, however, new drug treatment approaches are not adopted or sustained in usual practice, even in programs that served as settings for research showing their effectiveness. This may be due in part to a poor understanding of the initial or ongoing costs entailed by new practices, processes, or technologies (hereafter referred to as technologies). Methods and tools need to be developed and tested to help drug abuse treatment service providers and payers arrive at realistic estimates of the costs of implementing and sustaining new technologies in usual practice settings. With regard to new technologies, implementing is defined as an ongoing process of selecting, adopting, and adapting these new technologies into ongoing treatment, particularly with consideration for the local setting, population and available resources. Sustaining is defined as an ongoing process of providing needed resources (such as staffing, training, and equipment), maintaining the quality of the new technology through evaluation, monitoring, and improvement, and determining its ongoing utility compared to alternatives. The tools and methodologies should be able to identify and estimate costs separately for implementing and for sustaining new technologies, and should consider

both clinical and administrative technology. At a minimum, domains in which costs should be estimated include assessment of programmatic need, appropriateness, and value; staffing qualifications (salary and competencies); training, support, equipment, and other infrastructure requirements; information / data requirements; quality monitoring and improvement; and evaluation of outcomes.

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3. *Personnel Selection Technology Research for Drug Abuse Treatment Clinics.* Research is showing that employee turnover is a substantial problem among substance abuse treatment services providers. Applications supporting innovative research that develops and validates generic staff selection systems which could be adopted and tailored for use by drug abuse treatment clinics are welcome. Like many small businesses, drug abuse treatment clinics have problems attracting and retaining qualified personnel. Also like many small businesses, treatment clinics have limited resources to apply to the recruiting, screening, and hiring of new and replacement personnel. Research has shown that the application of standardized screening and selection methods designed to maximize person-job fit can cost-effectively reduce staff turnover. Systematic methods such as background inventories, protocol-driven interviews, aptitude tests, and credit checks have demonstrated validity for improving person-job fit. Examples of possible projects might include development of easy-to-understand guidance about legal considerations in hiring practices, software that transform job task analysis into selection criteria, interview protocols to standardize applicant screening, tolls to help improve recruitment, and/or self-paced training for hiring officials or interview panels to improve screening reliability.
4. *Customer Retention Technology.* Premature disengagement from drug abuse treatment participation is a common problem and ranges from approximately 30 to 60% based upon the clinic and modality studied. Past research has very frequently attributed dropping out of treatment to participant characteristics (e.g., motivation, addiction severity, comorbidity) and/or environmental factors (e.g., social pressures, unemployment, homelessness). Seldom has the dropout problem been studied in the context of customer satisfaction. That is, there is little research looking at the causes of dropping out of treatment attributable to organizational factors (e.g., policies, practices, context) that influence participant withdrawal decisions. Needed are tools and systems for assessing and surveying drug abuse treatment program participant perceptions and satisfaction levels, summarizing and report participant assessments, interpreting results, and adjusting policies and practices to improve satisfaction and participant retention in treatment.
5. *Effective Management and Operation of Drug Abuse Treatment Services Delivery.* The bulk of drug abuse treatment is conducted in small clinical settings with therapeutic staffs of less than a dozen people. Small clinics lack resources to help improve efficiency and effectiveness in both business and therapeutic practices. Areas that may be of interest to small businesses include, but are not limited to:

    a. Computer-based leader/manager self assessment tools: On-line and other types of tools to help those supervising the delivery of drug abuse treatment services to gain insights about personal strengths and weaknesses, and to help guide them to improved leadership and management practices.

    b. Organizational change tools: Handbooks describing step-by-step way to introduce more efficient business practices such as quality management/monitoring, creating empowered work teams, formalized goal setting, improved customer relations, forming organization linkages, and adopting new fiscal and resource management techniques.

    c. Organizational change tools: Handbooks describing step-by-step ways to introduce more efficient or effective therapeutic practices such as, adding pharmacotherapy in a previously

drug-free clinic, adopting new medical/pharmacotherapy or behavioral interventions, and adopting new approaches to clinical collaboration and/or case management.

6. *Assessment Tools for Quantifying and Organizational Culture that Promotes and Sustains a Drug-Free Workforce.* Though drug-free workplace programs are ubiquitous in large businesses, small businesses often lack the staff and resources to create effective drug-free programs because they may involve in-house or contract experts to educate, train, monitor, and enforce policies and practices that will sustain a healthy workforce and a safe and healthy workplace. Though there are numerous model drug-free workplace policies and programs provided free by federal, state, and local governments as well as nongovernmental organizations, many fail to provide management with affordable or free, easy-to-use tools to assess the baseline of their organizations' culture for drug abuse intolerance, and to monitor progress in building a drug-free organizational culture. Research shows that individual employees and organizations vary in their support for a drug-free workplace. Surveys indicate that coworker tolerance for illicit drug use varies by the type of drug, the type of industry, and the work role of the respondents. A drug-free culture creates commonly-held attitudes, beliefs and practices among employees that are socially reinforced. Once established, the need for costly external incentives and other measures abates as coworkers socialize new incumbents and enforce behavior promoting abstinence. Tools and methodologies need to be developed to a) assess an organization's baseline culture for drug abuse intolerance both on and off the job, b) identify policies and practices that undermine a drug-free culture, c) enable the identification of programs, policies, and practices capable of helping the workforce develop/strengthen an organizational culture of intolerance for drug use, and d) estimate the impact on the organization's quality of work-life, job safety, individual and group performance and productivity, and the profitability of the organization itself. Included would be inexpensive and easy to use tools for monitoring workforce behavior change, and changes in the impact on the organization (as outlined in "d").

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7. *Web-Based Technologies: Transporting Services Research to Practice.* This initiative will support the development and testing of the effectiveness of web-based technologies that facilitate the translation of drug abuse prevention and treatment services research into practice. The ultimate goal is the delivery of efficacious, low-cost interventions to the greatest number of individuals in community settings. Delivery of evidence-based services in community settings often is hampered by lack of state-of-the-art information about the contents of efficacious interventions, the organizational structures and processes that make effective implementation possible, and available training and technical assistance. Applications may include, but are not limited to, the development and testing of new and innovative Internet-based systems that provide practitioners with (a) current information on evidence-based treatments with the greatest promise for defined populations of drug abusers; (b) assistance in translating clinical trials data into clinically useful information; (c) information and training on how to effectively organize, manage, and deliver evidence-based prevention and treatment services; (d) strategies for organizational change and capacity building; and (e) access to training and technical assistance on the adoption of new prevention and treatment interventions.

8. *New Technologies for Screening, Assessing, and Preventing Problem Drug Use and HIV, Matching Patients with Appropriate Treatment Services.* Increased understanding of the complexities of problem drug use and HIV risk behaviors has sparked growing interest in and increased need for new user-friendly technologies to assist in the screening, assessment, and prevention of drug abuse and HIV, and in the matching of patients with appropriate treatment services. New technologies, including CD-ROM, hand-held, Internet, videotape, videodisc, and other electronic means have great potential for helping treatment providers in specialty and non-

specialty care settings including primary care contexts to (a) screen for problem drug use and associated health problems and risk behaviors, including HIV, (b) assess the nature and degree of drug use and HIV risk behaviors, (c) embed items for screening or assessing problem drug use within existing clinical tools, (d) deliver appropriate prevention interventions, and (e) identify appropriate types and levels of treatment services for patients based on their individual treatment needs. These new technologies potentially can provide a more cost effective way of identifying problem drug use, HIV risk behaviors and infection, and associated health problems in a variety of health care settings, speeding the assessment and treatment process, and improving treatment placement decisions.

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9. *Reintegration of Criminal Offenders into the Community.* Many offenders enter the criminal justice system with drug abuse problems and related health issues. In addition to addressing these health care issues within the prison walls, treatment programs are increasingly called upon to help offenders successfully reintegrate into the community following incarceration. This often means helping offenders to manage their recovery through monitoring, linkage with continuing care services, development of social support networks, and education of friends and family members about the nature of drug abuse and the challenges facing the offender upon release from prison. It is estimated that over the next several years, more than 600,000 criminal justice offenders, many of whom have drug abuse problems, per year will be released to return to their communities. New technologies are needed to help treatment providers in the criminal justice system and in the community coordinate efforts to effectively (a) monitor offenders' recovery once they have been released into the community, (b) prevent relapse, (c) identify relapse early and efficiently re-engage released offenders in appropriate treatment, (d) link released offenders with continuing care services in the community, (e) develop social support networks for recently released offenders in recovery, and (e) educate offenders' family members so that they can more effectively support offenders in recovery once they have been released from prison.

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10. *Technologies to Support Quality Improvement in Addiction Treatment Systems.* New technologies to support quality improvement in community-based, addiction treatment provider systems are needed. Quality improvement methods, although well established in business and healthcare management, are underutilized in addiction treatment. Addiction treatment systems have limited resources for initiating, developing, implementing, and sustaining quality improvement practices. Most community-based provider systems have limited capacity to capture and integrate information about (a) the nature and extent of community needs and resources; (b) organizational and management processes to facilitate adoption, adaptation, implementation, and sustained use of science-based innovations; (c) implementation costs for new service innovations; (d) client satisfaction; and (e) quality of care. Centralized, automated and cost-efficient technological tools for these purposes could help provider systems improve the quality and efficiency of their treatment services, meet accreditation requirements, and reduce operating costs.

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11. *Electronic Drug Abuse Treatment Referral Systems for Physicians.* Research shows that primary care physicians often do not screen for drug abuse disorders. While this may be related to stigma attached to illicit drug use or to a lack of adequate health insurance, it may also be due

to the lack of an adequate referral system that primary care physicians can use for the patients they identify as having a potential drug problem. The lack of a referral system places a greater burden on the physician to secure treatment resources for the patient, and also places the physician at greater risk if no appropriate treatment can be found. A practical and usable electronic drug abuse treatment referral system needs to be developed and tested for use by physicians in primary care settings, including doctor's offices. To be effective and useful, the system needs to be targeted at local needs, for example by taking into account local private insurance coverage and the types of insurance accepted by local treatment providers. It should also include an actively-maintained database of local providers, with information on insurance carrier, geographic "catchment" area of treatment providers, types of substance disorders treated, types of co-occurring disorders (mental disorders, etc.) treated, gender, age, other pertinent treatment factors needed by primary care physicians to make appropriate referrals. The system should be designed to be reliable and efficient, allowing for appointment scheduling or other needed arrangements to ensure a successful referral. Feasibility and cost-efficiency should be carefully considered.

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Center for the Clinical Trials Network

The mission of the Clinical Trials Network (CTN) is to improve the quality of drug abuse treatment throughout the country using science as the vehicle. The CTN provides an enterprise in which the National Institute on Drug Abuse, treatment researchers, and community-based service providers cooperatively develop, validate, refine, and deliver new treatment options to patients in community-level clinical practice. This unique partnership between community treatment providers and academic research leaders aims to achieve the following objectives:

- Conducting studies of behavioral, pharmacological, and integrated behavioral and pharmacological treatment interventions of therapeutic effect in rigorous, multi-site clinical trials to determine effectiveness across a broad range of community-based treatment settings and diversified patient populations; and

- Ensuring the transfer of research results to physicians, clinicians, providers, and patients.

Materials and processes that facilitate clinical trials in community practice settings are particularly needed in this program. Areas of research include but are not limited to:

- Projects that would simplify, automate, standardize, or reduce the cost of administration of clinical research instruments used in CTN trials

- Projects that would reduce error rates in completing assessment or clinical instruments and in transmitting data to data management entities

- Projects to develop instruments that measure factors relevant and important to the conduct of addictions research, such as: the extent of craving and/or of withdrawal, the risk of addiction to a particular substance, the therapeutic alliance between patient and therapist, perceived satisfaction with health care, probabilities of a pain management patient developing dependence/abuse on pain medications, and probability of successfully completing detoxification

- Projects to develop instruments that measure and predict HIV risk behaviors

- Projects that develop and evaluate innovative diagnostic drug screening tests for drug abuse, such as oral swabs

- Projects that develop and evaluate the use of gene chip technology for drug abuse risk factors

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Specific projects could include:

1. *Development of Combination Medication for Emergency Treatment of Opioid Overdose in the Presence of Benzodiazepines.* Suspected opioid overdose—coma, apnea and pin point pupil—is treated by the administration of naloxone, which, while effective, is short-lived. Patients often leave the Emergency Room, return immediately to opioid use, and suffer dire consequences as a result. There is sufficient preclinical and clinical evidence that buprenorphine may be a more effective medication for treatment of opioid overdose in such patients. However, the clinical development of this treatment strategy has been hampered by concerns that many opioid abusers also abuse benzodiazepine, and in such patients the administration of buprenorphine may be hazardous. Fumazinil, a specific benzodiazepine antagonist used to treat benzodiazepine overdose, can be co-administered with buprenorphine and may protect such patients from the ill effects of buprenorphine in cases of overdose involving both opioids and benzodiazepine. The goal is to develop and test the buprenorphine-fumazinil combination medication formulation for the treatment of opioid overdose with suspected concurrent benzodiazepine abuse.
2. *Screening and Development of Partial Agonists at the Human CB1 Receptor for Treatment of Marijuana Dependence or Withdrawal.* NIDA seeks applications to screen and/or develop CB1-receptor partial agonists for application in the pharmacotherapeutic treatment of marijuana dependence or withdrawal. The potential benefits of CB1-receptor partial agonists in the treatment of dependence may parallel those of safe and effective nicotine or opiate partial-agonist replacement therapies, where buprenorphine and varenicline have demonstrated effectiveness in enhancing abstinence from opioid use and cigarette smoking, respectively. As implied by the designations of partial-agonist replacement or substitution therapy, a partial-agonist medication has core biological effects similar to those of the abused drug. Importantly however, there is a ceiling-effect dose with the administration of partial agonists not present with full agonists such that at high doses, partial agonists are less likely to precipitate adverse behavioral or biological events and to have abuse liability compared to full agonists. The phase I project should identify compounds that bind to human CB1-receptors as partial agonists and, in the phase II, the grantee should develop and evaluate selected partial agonists.
3. *Improved Device to Capture and Measure Drug Use in Oral Fluid.* Oral fluid (OF) testing is a promising method to monitor for drugs of abuse. The main advantages of OF is the simplicity and noninvasiveness of sample collection. Aside of patient's/ study participant's comfort and preference compared to urine drug screen, the oral fluid sample collection can be easily observed, obviating the need for special restroom facilities and same-sex collectors and making adulteration of the specimen more difficult. Furthermore, infection risk is lower than for drawing blood. For clinical toxicology applications, including use in clinical trials, drug treatment programs, physician office and emergency room testing, onsite OF testing would offer rapid availability of results for diagnostic or research purposes. At this point, however, Substance Abuse and Mental Health Services Administration approval of OF testing has been delayed because of questions about drug device performance, disposition of drugs in OF, and need for improvement of assays. The greatest current limitation for OF testing is the small number of controlled drug administration studies available to inform interpretation of OF tests. (Bosker, Huestis, 2009) Applications should address current limitations and present methods to remove obstacles for wider usage of OF testing in clinical practice and research.

Reference: Bosker WM, Huestis MA. Oral Fluid Testing for Drugs of Abuse. Clinical Chemistry.2009; 55:11 1910-1931

4. *Improved Technology of Testing Devices to Remotely Capture and Measure Drug Use in Biological Specimens.* There is an ongoing need for more accurate, practical and convenient point-of-collection testing devices for monitoring drugs of abuse. Current devices that test for illicit drugs in urine, oral fluid (saliva), sweat and hair have strengths and limitations. The goal of this solicitation is to develop new technologies/devices that will increase strengths (e.g. accuracy, practicality, and convenience) and decrease limitations (e.g. minimum frequency, contamination, and adulteration) of testing methodologies. New technology might permit testing from remote locations (e.g. patient's or subject's home) while ensuring real time data collection and transfer into medical records/study databases. Risk of adulteration should be minimized to a level comparable with tests provided in drug treatment centers or study sites. The phase I application should explore all tests currently available, especially new technologies allowing for remote collection of the data. In phase II, the grantee should develop and test a prototype.

5. *New Technologies: Integrating Data from Prescription Monitoring Program(s) to Current Clinical Practice.* In some states the prescription monitoring program collects prescription data for controlled substances into a central database that can then be used by a limited number of authorized users to assist in deterring the illegitimate use of prescription drugs. Prescribers and dispensers in some states may query the database to assist in determining treatment history and to rule out the possibility that a patient is "doctor shopping" or "scamming" to obtain controlled substances. Limited time/resources of busy medical offices are a barrier to obtaining and utilizing this information to improve quality of treatment for each individual patient. This initiative will support development and testing of the effectiveness of new technologies that facilitate utilization of data collected by Prescription Monitoring Program(s) in clinical practice. Applications may include, but are not limited to, the development and testing of new and innovative Internet-based systems that provide a) practitioners with current information of their patients' treatment/medication compliance; and b) transfers data automatically to patients chart, etc. The goal is to minimize barriers faced by clinical staff to obtain, record and utilize the data while maintaining strict security requirements (i.e., confidentiality, integrity, and availability). These new technologies should provide a more cost effective way of identifying treatment non-compliance and help adjust a treatment plan according to the needs of individual patients as well as decrease potential diversion of controlled substances. The phase I application will explore and describe current Prescription Monitoring Programs and new technologies allowing development and testing of the application in phase II.

Division of Pharmacotherapies & Medical Consequences of Drug Abuse

The NIDA Division of Pharmacotherapies & Medical Consequences of Drug Abuse (DPMCDA) supports research aimed at the development and testing of pharmacological and behavioral treatments for drug abuse and addiction. This includes the identification, evaluation, development, approvability, and efficacy testing of new and improved pharmacotherapeutic agents, as well as the testing of marketed medications, and of behavioral treatments used alone or integrated with medications.

A. ***Chemistry and Pharmaceutics Branch (CPB).***

1. Synthesis (either using traditional or combinatorial techniques) or discovery (natural products) of new chemical compounds that would have potential as treatment agents for the medical management of stimulant (e.g., cocaine, methamphetamine, or nicotine) addiction. Consideration should be given to the design of partial agonists or pure antagonists that diminish the reinforcing effects of stimulants, as well as full agonists that could function to normalize physiological activity following discontinuation of stimulant use. The CPB supports research in the design (including molecular modeling and structure-activity relationship studies) and synthesis of novel compounds, formulation development, bioanalytical methods development, and pharmacokinetics/ pharmacodynamics aimed at the discovery and development of new

medications for treating drug addiction. Areas that may be of interest to small businesses include, but are not limited to research related to the design and development of new compounds and improved drug products (drug delivery) for the treatment of drug addiction.

2. Compounds of interest include those that are designed to affect dopaminergic (i.e., D1 agonists, D3 agonists and D3 antagonists) activity, CRF antagonists, compounds affecting glutamate activity, GABAergic activity, small molecule neuropeptide antagonists and compounds acting through other mechanisms for which justification has been supplied.
3. Synthesis (either using traditional or combinatorial techniques) of new chemical compounds that would have potential as treatment agents for the medical management of cannabinoid abuse.
4. Development of new immunotherapeutic treatments that would have the potential as treatment agents for stimulant or cannabinoid abuse.
5. Development of heroin/morphine-protein conjugates (heroin/morphine conjugate vaccines) for the treatment of heroin/opiate addiction.

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6. Development of new approaches for the administration of potential addiction treatment drugs (including small molecules, natural products, peptides, proteins, antibodies, etc.) with poor bioavailability.
7. Development of controlled release dosage forms for addiction treatment medications in order to maintain therapeutic drug levels for extended periods of time to alleviate compliance problems associated with addiction treatment.
8. Development of novel dosage forms or chemical/pharmaceutical approaches that eliminate or significantly reduce the abuse potential of prescription drugs/drug products.
9. Development of novel technologies and strategies to deliver potential therapeutic agents (including small molecules and peptides) across blood brain barrier for the treatment of drug addiction.

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B. ***Medications Discovery and Toxicology Branch (MDTB).*** The MDTB supports research on the development of preclinical behavioral models (e.g., of craving, drug-seeking behavior, dependence, or relapse), biochemical assays, gene expressional assays and electrophysiological methods to identify and characterize new medications to treat substance abuse, as well as pharmacological screening of novel compounds to identify potential drug abuse medications. The Branch also supports research on toxicity studies of potential medications for the treatment of substance abuse, and interactions of potential treatment medications with abused substances. Areas that may be of interest to small businesses include, but are not limited to development of new methods for discovery of medications useful in treating drug addiction. Of special interest would be the development of new animal models of addiction, incorporating established drug self-administration techniques that show increased relevance to the clinical setting. Development of relevant biochemical or electrophysiological screening methods is also encouraged.

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C. ***Medications Research Grants Branch (MRGB).***

1. *Develop Novel Treatments for SRDs.* The MRGB seeks to support the development of novel pharmacotherapeutic- and immunological treatments for persons with substance-related disorders (SRDs). The Branch also supports projects aimed at incorporating technological advances that could be used to more effectively treat SRDs.

   This solicitation aims to support small business development of compounds that have completed (or are nearing completion of) successful preclinical evaluation. Treatments should aim to help subjects reduce drug use, become drug free, prolong abstinence/reduce craving, or facilitate survival from drug overdose.

   Therapies that small businesses might consider evaluating include, but are not limited to:

   - A novel (e.g., new chemical entity, novel drug formulation) that could be used to treat SRDs
   - A marketed compound (e.g., SSRIs, anti-epileptic drugs) that could be used to treat SRDs
   - Vaccines for substances of abuse (e.g., cocaine, nicotine)
   - Monoclonal antibodies for substances of abuse (e.g., methamphetamine, PCP)
   - Naturally-occurring compounds (e.g., dietary supplements) that could be used to treat SRDs
   - Or, a rationalized poly-therapeutic combination of pharmacotherapies designed to more comprehensively treat SRDs

   Treatments that concurrently help alleviate associated psychiatric co-morbidities (e.g., depression, schizophrenia, PTSD, anxiety, etc.) and/or are focused upon underserved/vulnerable populations (e.g., pregnant women and their fetuses, adolescents, racial or ethnic minorities, women/gender issues, subjects within the criminal justice system) are especially encouraged.

2. *Development of a Test/Device to More Effectively Diagnose/Manage Patients with SRDs.* This solicitation aims to support the identification and development of an innovative test/device that can be used to help more effectively diagnose and/or manage patients with SRDs. The use of this novel diagnostic tool might help to: (1) expedite the development of-, and/or (2) enhance existing treatments for patients with SRDs.

   Possible diagnostic tests/devices that a small business might consider, but are not limited to, include:

   - An assay/device (e.g., skin sensors, oral swabs) that detects a substance of abuse more reliably than oft-used urinalysis. Optimally, the analytical test/device would be non-invasive and easy-to-use, such that it could be used on an outpatient basis.
   - Discovery/development of a diagnostic test/screen that could help physicians more effectively manage treatments for patients with SRDs.

3. *Discovery / Development of Biomarkers Related to SRD Treatment Outcomes.* Because drug addiction is a brain disease which can change the structure and function of the brain, there is a unique opportunity to develop biomarkers that could reliably predict/assess SRD treatment outcome. To date, evaluations of SRDs often utilize subjective measures (e.g., patient-reported questionnaires) to assess disease progression and primary treatment outcomes. Biomarkers represent a more objective measure of physiological functioning that can be used to predict, diagnose, evaluate the progression of, and/or more accurately assess overall treatment safety and effectiveness.

The goal of this initiative is to support the small business discovery/development of reproducible, quantitative biomarkers related to SRD treatment outcomes. Potential biomarkers might be derived from underlying variations in DNA, gene expression, proteins, metabolism, and/or neuroimages, among others.

4. *Creation of a Data Repository/Software Tool for SRD-related Clinical Research Data.* Clinical data management is currently heterogeneous. Different investigators use different nomenclatures, definitions, timeframes, data-collection instruments, data analysis and reporting methods. This varied (and often inadequate) data management system severely limits the interpretation of results from clinical trials and complicates the ability to make data-based decisions concerning the overall effectiveness of a therapeutic intervention. Appropriate collection and standardization of clinical trial data should permit, for example, more statistically-valid comparisons of treatment outcomes and data integration, meta-analysis, and aid in the development of more effective, individualized clinical treatments for patients with SRDs.

   The purpose of this initiative is to support small business development of repository/software tool that can be used to more efficiently capture and manage (i.e., facilitate/standardize collection, storage, screen/analyze, report) data obtained from NIDA-funded clinical trials. Collection/storage of these data should follow HIPAA guidelines (http://www.hhs.gov/ocr/privacy/index.html) to guarantee the privacy and confidentiality of all study participants.

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Division of Clinical Neuroscience and Behavioral Research (DCNBR)

A. ***Behavioral and Integrative Treatment Branch.*** The Behavioral and Integrative Treatment Branch is interested in research on behavioral and integrative treatments for drug abuse and addiction. The term "behavioral treatments" is used in a broad sense and includes various forms of psychotherapy, behavior therapy, cognitive therapy, family therapy, couples and marital therapy, group therapy, skills training, meditation, guided imagery, counseling, and rehabilitative therapies. The term, “Integrative treatments” refers to treatments that combine behavioral interventions with other treatments, including other behavioral therapies, medications, and/or complementary/alternative therapies. Behavioral and integrative treatment research has been conceptualized to consist of three stages. Stage I, or early treatment development, involves research on the development, refinement, and pilot testing of behavioral and integrative interventions. Stage I may include translational research that incorporates concepts, methods or findings from other disciplines (e.g., neuroscience, cognitive science, etc.) into the development of behavioral and integrative treatments. Stage I may also include research to develop or adapt treatments to become more “community-friendly.” Stage II includes testing treatments that show promise and testing the “dose-response” of treatments. Stage III is research aimed at determining if and how efficacious behavioral treatments may be transported to community settings. Stage III may include studies that test treatments in community settings, with community therapists. Stage III may also include studies that develop or test methods of training treatment providers to administer treatments. Determination of mechanism of action of treatment is relevant to all three stages. Specific areas of interest include:

   1. *Translation from Basic Behavioral or Cognitive Science.* “Stage I” research on the development of behavioral therapies or components of such therapies that are based on developments and findings from the basic behavioral or cognitive sciences.

   2. *Translation of Cognitive, Affective and Social Neuroscience Findings Towards Development of Behavioral Treatments.* “Stage I” research on the development of behavioral treatments or components of such therapies that are based on developments and findings from cognitive, affective, or social neuroscience. For example, one may wish to apply findings on the neural

underpinnings of adolescent risk-taking behaviors to target the developmental needs of substance using youth, or apply findings on the link between early adversity and the impairment of emotion regulatory abilities to address the needs of substance using victims of childhood abuse.

3. *Treatment of Sleep Disorders for Individuals in Drug Abuse Treatment.* Recent research on sleep has shed new light on its importance to psychological and physical health. Sleep deprivation has been linked with impaired cognitive performance, negative mood, and even decreased immune function. Drug abusers often cite insomnia as reason for relapse, and may use drugs to modulate their sleep/waking cycles. However, the treatment of sleep disorders has not been a primary focus of drug abuse treatment research. The development and testing of sleep hygiene interventions, alone or in combination with behavioral interventions, for use in conjunction with drug abuse treatment, as a means of improving treatment for drug abuse is needed. Developmentally and age appropriate, as well as gender sensitive treatment of sleep disorders could impact on the development of more effective treatment interventions.

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4. *Modifying Efficacious Behavioral Treatments to be Community Friendly.* Several behavioral interventions have been found to be efficacious for the treatment of drug addiction. However, there are barriers to implementation of behavioral treatments in community-based settings. Community settings that treat drug addicted individuals are reluctant or unwilling to adopt these interventions for a variety of reasons. Reasons that scientifically-based behavioral treatments are not accepted by community providers could include the excessive cost of implementation, the length of time for administration of treatment, inadequate training available for therapists and counselors, treatments not shown to be generalizable for different patient populations or for polydrug abusing populations, etc. Research aimed at modifying efficacious behavioral treatments to make them more acceptable to community settings is needed. Settings might include, drug abuse treatment facilities, primary care, managed care, after-school or classroom settings, colleges, and the criminal and juvenile justice system. Examples of possible studies are those that are designed to reduce the cost of treatments, reduce the time of administration of treatments, aid in training of therapists, counselors and nurses, adapt individual therapies for group situations, etc.

5. *Treatments to Prevent Escalation from Abuse to Dependence.* Therapies for drug abusers who are not yet dependent on drugs to reduce risk of escalation to dependence and therapies for drug abusers who have not considered or claim little interest in seeking treatment for their drug problems are needed. Treatments for participants in their natural environment, such as treatments delivered over the Internet, cell phone, or in neighborhood settings such as churches and recreation centers are desired. A particular focus on treatments which incorporate engagement strategies for hard to interest groups are requested. Educational games, interactive video content, fluency based learning approaches and other methods to help maintain involvement are encouraged.

6. *Virtual Reality Applications for Drug Abuse.* Development and improvement of treatments using Virtual Reality and other new simulation technologies is needed. New technology may help to make existing treatments more effective, or may make novel treatments possible. Behavioral treatment research to develop, modify, adapt, and test treatments for drug abuse and for co-morbid psychiatric conditions (such as anxiety disorders) using new technologies is of interest.

   Recently virtual reality simulations have been used to train medical personnel in demanding medical procedures such as microsurgery techniques. Virtual training allows trainees to gain familiarity with both the environment in which services are delivered as well as the intervention techniques without the danger of mistakes impacting live patients. Virtual reality interfaces can

assess skill acquisition and provide detailed feedback during procedures to help trainees correct mistakes or avoid making them altogether. In the drug abuse field, training and dissemination efforts have been hampered by a dearth of knowledge about ways to conduct dissemination. Although trainees often practice on actual clients, this approach has drawbacks including its reliance on the client or participant's schedule and willingness to participate in training sessions and potential danger to the client or if the intervention is delivered incorrectly. Libraries of virtual reality simulations of drug users in treatment or "virtual patients" are needed to provide experiential training for treatment providers without relying on existing patients. This will help facilitate the rapid and effective dissemination of proven treatment strategies.

7. *Virtual Clinical Trials Settings for Conducting Behavioral Treatment Trials and Addictions Treatment Provider Education Trials in Cyberspace.* Virtual communities such as Second Life as well as private web forums offer a unique opportunity for behavioral therapy researchers and providers to establish and conduct online psychotherapy and behavioral therapy development research as well as a forum to develop provider "university's" at which various training techniques may be tested for discovering the most efficacious way to deliver continuing education and other training in the latest methods of treating addiction. Applications are encouraged to develop such a forum and test either a provider training or behavioral therapy method in an online trial. As part of this research platform, methods for obtaining consent, maintaining confidentiality, collecting data and where needed, assessing provider adherence and competence are expected.

8. *Remote and/or Mobile Abstinence and Identity Verification.* Methods are needed for at home or mobile abstinence verification which include identity verification. Drug abuse treatment researchers are in the process of developing web-based and mobile phone based treatments which can extend treatment beyond the clinic walls. Additionally, there is growing recognition by providers that drug addiction is a chronic disease which may require multiple bouts of treatment. However, currently there are no means of monitoring abstinence once patients leave formal treatment or validating progress of patients undergoing treatment located outside a clinic which provides onsite testing. Monitoring onsite testing poses barriers to patient privacy but unobserved sample donation may be subject to switching and adulterants. Products are needed which both test for the presence of illicit substances and which accurately identify the donor of the sample and the time of its submission so patients can participate in monitoring outside of formal treatment settings. Blood sampling similar in invasiveness to a skin prick for diabetes testing or other low risk sampling of other tissues and specimens may be acceptable. Scalability and automation of methods are particularly desirable.

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9. *Improving Adherence to Medications and Treatment for Drug Abusers with HIV/AIDS.* The introduction of highly active antiretroviral therapy (HAART) has significantly changed HIV/AIDS clinical care. There is a need for research related to the development and testing of new and improved behavioral interventions(alone, and in combination with pharmacological treatments for drug addiction), in order to facilitate better adherence to antiviral regimens among drug abusers with HIV infection, including HIV positive drug abusers with comorbid medical illnesses and/or psychiatric disorders. There is also a need to develop and test adherence interventions administered or assisted by technological devices such as computers, the internet, expert system models, telephone pagers, or hand-held computers.

10. *Treatment for Emerging or Specific Populations.* Therapies designed to intervene with understudied populations including users of drugs such as methamphetamine, MDMA and other club drugs, marijuana, inhalants, and prescription opioids and psychostimulants, as well as children of substance abusers in need of treatment, and drug abusers with comorbid psychiatric disorders and/or medical illnesses such as HIV/AIDS, hepatitis, etc.

11. *Development of HIV Risk Reduction Interventions.* Research to develop and evaluate behavioral strategies to reduce HIV risk behaviors in HIV-positive and HIV-negative substance abusing treatment populations. Where appropriate, risk reduction interventions should be adapted to patients' age, gender, cultural background and potential cognitive impairments, and should address compliance with medical regimens. The product of such research might be training, supervision, or educational materials, such as manuals or videotapes that describe the intervention and its implementation by treatment staff.

12. *Woman and Gender Differences in the Provision of Behavioral Treatments, and HIV/AIDS Risk Reduction Approaches.* Develop and evaluate specific behavioral treatment approaches targeting drug-addicted women. This may include behavioral therapies, skills training techniques, counseling strategies, and HIV and other infectious disease behavioral risk reduction strategies. This may also include development and testing of training materials that specifically address women and gender differences in drug addiction treatment to promote effective use of research-based treatment approaches. Training materials may involve treatment manuals, training videos, CD ROM or DVD technologies, Internet or computer based programs to manage aspects of treatment administration, or other innovative educational strategies for health professionals using new technologies.

13. *Behavioral Treatments Drawing from Stress Research or Stress-Management Interventions.* Projects are encouraged that apply concepts from stress research (such as appraisal, coping, and social support) to drug abuse in innovative ways, or that test the extent to which stress-management interventions can be applied to the treatment of drug abuse and interventions to reduce risk of HIV and other infectious diseases. Examples of stress-management techniques that may have novel application to drug abuse and HIV risk include techniques that teach problem-solving and affect-management, restore one's sense of purpose and meaning, prevent burnout in the face of chronic stressors, increase self-efficacy for managing stress, inoculate against stressors, train relaxation and meditation, intervene during crises, enlist social support and system support, and others.

14. *Behavioral Strategies for Increasing Medication Adherence.* Research to develop and to evaluate strategies to induce recovering addicts to take medication for a prolonged time, especially opioid antagonist naltrexone; partial opioid-agonist buprenorphine, etc. to encourage HIV infected drug users to comply with medical treatments (HAART) in drug abuse treatment settings; or to adapt existing behavioral strategies to increase patient compliance and cooperation in long-term treatment for drug abuse or for diseases associated with drug abuse such as tuberculosis or hepatitis. An important consideration should be cost and practicality of use in actual clinical practice or in an aftercare program. The product of such research might be a manual, which describes the behavioral strategy, and its implementation by treatment staff or scientific data regarding evaluation.

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15. *Integration of Behavioral Treatments and Pharmacotherapies.* Development of integrated behavioral treatments and pharmacotherapies may enhance the efficacy of both types of therapeutic interventions. For instance, the maintenance and detoxification of heroin addicts could perhaps be optimized by the integration of distinctive behavioral treatments devised specifically for opioid agonists, antagonists or partial agonists determined by the heterogeneity of the subgroup of addicts and the pharmacological differences of the medications. Integration of medications and behavioral treatments could possibly enhance compliance with medication regimens, *increase* retention allowing pharmacological effects to occur and prevent relapse to drug abuse and addiction.

16. *Behavioral Treatment Research for Drug Abuse and Addiction in Primary Care.* Recent research has shown that physicians and other clinicians often fail to recognize drug abuse or addiction among their primary care patients. In addition, a significant number of these clinicians reported that they did not know how to intervene with their patients if drug abuse or addiction was suspected. Drug abuse related illnesses and morbidity often occur in adults and may have begun in adolescence. However, very little research has been done to develop or test behavioral treatment approaches or combined pharmacological and behavioral treatments for drug abuse and addiction in primary care settings. The objectives of this initiative are to encourage research on the development and testing of innovative behavioral treatment approaches e.g. screening and brief interventions, use of web-based or mobile technologies used alone or in combination with pharmacological treatments. Other goals of this research initiative are to encourage additional research on the development and validation of culturally sensitive screening and assessment instruments for use with youth and adults in primary care; and to encourage research on the transportability of efficacious behavioral treatments to primary care settings, as well as research on science-based training approaches for changing primary care clinicians' behaviors regarding their recognition and intervention with drug abusing or addicted patients. While motivational enhancement approaches for some drug abusing populations have been found to be effective, this behavioral approach has not been widely used in primary care.
17. *Using Telemedicine to Deliver Efficacious Treatment to Underserved Populations in Specialty Addictions Treatment and/or General Medical Settings.* Telemedicine programs are being used in urban medical centers to rapidly disseminate science-based information on new medical treatments. In addition, approximately one-third of the rural hospitals are now using telemedicine to improve patient care Studies are needed to modify existing treatments developed by NIDA researchers for deployment and testing as telemedicine treatments at remote locations to underserved populations. These may be delivered in any patient care context including primary care or specialty addiction treatment. Modification of the treatment content to apply to the remote patient population and provider training materials to orient the onsite staff who may not be experienced at delivering the new treatment may be needed.
18. *Youth Smoking Cessation.* Smoking related illnesses usually occur in adults. However, tobacco use and nicotine addiction generally begin in childhood or adolescence. Despite health warnings, adolescents continue to initiate smoking at alarming rates and the majority will continue to smoke as adults. Adolescents who begin to smoke, develop nicotine dependence very quickly and exhibit withdrawal symptoms during quit attempts in a similar fashion to adults. Most adolescents who smoke, express a desire to quite. To date, research on smoking cessation for teen and young adult smokers has not been particularly fruitful. This initiative requests research aimed at the development and testing of smoking cessation treatments tailored to the specific needs of adolescents and young adults. Consideration should also be given to gender and ethnicity.
19. *Complementary and Alternative Medicine Therapies (CAM) for Drug Abuse Treatment.* Research is encouraged on complementary and alternative interventions for drug abuse treatment either as the sole treatment or as an adjunct to enhance the therapeutic potency of existing drug abuse treatments. Any of the five CAM categories: Whole medical systems, mind-body interventions, biologically-based therapies, Manipulative/body-based therapies and energy therapies would be considered for this initiative (for more information, see http://nccam.nih.gov/). CAM therapies are interventions that are commonly used in “real world” settings, but whose therapeutic efficacy has not been scientifically demonstrated. The product of this research might also be a manual or video, which illustrates the intervention and how it is implemented by treatment staff.

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20. *Developing, Evaluating, and Transporting Culturally Sensitive Behavioral Treatments for Racial and Ethnic Minorities.* Minority populations are disproportionately affected by the consequences of drug abuse. Research to develop and evaluate behavioral treatments that are culturally sensitive and relevant for diverse racial and ethnic minority populations is encouraged. This may include studies of behavioral treatments, alone or in combination with pharmacological treatment, or studies of behavioral strategies for increasing adherence to taking medications. In the development and evaluation of the behavioral treatment, attention needs to be directed at examining medical, social, and cultural factors that may influence adherence to the behavioral treatment approach and treatment outcome. Also, little is known about the transportability of efficacious behavioral treatments for minority populations. Research is needed on how to transport science-based treatments to various racial/ethnic populations.

21. *Incorporating Smoking Cessation in Drug Abuse Treatment.* Research is encouraged to develop and test behavioral and combined behavioral and pharmacological treatments for nicotine-addicted individuals who also are addicted to other substances, such as heroin, cocaine, methamphetamines and alcohol. Prevalence of cigarette smoking is extremely high among drug dependent individuals attending drug treatment. Many treatment providers are reluctant to address smoking cessation with clients either because they believe that substance abusers are not interested in quitting or because they fear smoking treatment will have a negative impact on drug abuse treatment outcome. However, studies have shown that many drug abuse clients are interested in quitting smoking and that the concurrent treatment of tobacco dependence and other drug dependencies does not threaten abstinence and might even assist in maintaining it. Research is needed to develop and test smoking cessation treatments that can be incorporated into treatments for illicit drugs of abuse.

22. *Developing Treatments for Smokers with Comorbid Disorders.* Research is encouraged that focuses on the development, refinement, and testing of behavioral treatments for smokers with psychiatric comorbidity, such as depression, schizophrenia, or anxiety disorders. Smoking prevalence is very high in individuals with psychiatric disorders. These populations generally respond poorly to traditional smoking cessation treatments. Similarly, medical comorbidities are widely prevalent and are in need of additional research in adults and in special populations such as youth, LGBT and homeless persons. Research is needed to develop and test innovative behavioral and combined behavioral and pharmacological treatments that address the unique needs of these individuals.

23. *Tobacco Cessation for Pregnant and Post-Partum Women.* Smoking among pregnant women remains an ongoing public health concern. It is estimated that approximately 20-30% of pregnant women smoke. Maternal smoking during pregnancy has been linked to infant mortality, impaired fetal brain and nervous system development, premature and complicated births, and low birth-weight babies. For women who do quit during pregnancy, relapse rates vary, but are reported as approximately 25% before delivery, 50% within four months postpartum, and 70-90% by one year postpartum. Children of smokers continue to be at risk for respiratory illness, middle ear infections, impaired lung function, and Sudden Infant Death Syndrome. Sustained tobacco cessation during pregnancy and the postpartum period reduces health risks to both mothers and their babies. Research focused on the development of innovative behavioral and combined behavioral and pharmacological interventions for nicotine-addicted pregnant and postpartum women is encouraged. Interventions may be tailored to sub-populations of pregnant smokers, such as teenage girls, heavy smokers, ethnic minorities, or low SES populations. Examples of other potential studies may include the development of smoking cessation interventions that address co-occurring issues, such as depression or weight-gain, interventions that include partners or support persons, Internet-based interventions or interventions that can be delivered by primary care physicians.

24 *Behavioral Treatments for Groups.* This includes the development of new psychotherapy approaches, the modification or testing of existing behavioral treatments, and the design and/or testing of innovative clinical training and supervision methods for dissemination of efficacious

treatments to community settings. Examples of relevant projects are: traditional group therapies, such as 12-step and therapeutic community approaches, and newer group therapies such as cognitive-behavioral and acceptance-oriented approaches; groups for various populations, such as adolescents, adults, couple and family groups, gender-specific groups, and groups tailored for racial or ethnic minority populations. Of particular interest are projects that address the recent reports suggesting possible contraindications of group treatments for some populations (e.g., delinquent adolescents), or in some formats (e.g., less-structured, client-led groups).

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25. *Developing Behavioral Treatments for Cognitively Impaired Drug Abusers.* While there are currently many efficacious interventions available for drug addicted individuals in treatment, more can potentially be done to enhance treatments by addressing cognitive impairments that may accompany chronic drug use and HIV infection. Many commonly utilized drug addiction and HIV-risk reduction interventions assume certain basic cognitive capacities and abilities that may be absent, or impaired, in chronic drug abusers who may also be HIV-positive. For substance abusers to benefit from psychological treatment, they must be capable of attending to and receiving new information, integrating it with existing information stores, and translating this input into more concrete behavioral change. Substance abusers with cognitive limitations, who may not comprehend the interventions, are more likely to drop out of treatment, relapse faster, and have poorer long-term outcomes in comparison to cognitively intact substance abusers. Research is needed to develop, modify, and test "cognitive-friendly" drug dependence treatments that could lead to improved treatment response and outcome.
26. *Interventions to Improve Engagement and Retention in Treatment.* Therapies designed specifically to engage and retain individuals in treatment, especially those at high risk for HIV. An example could be a therapy that is: (1) sensitive to the age and motivational level of the client; (2) is specifically designed to respond to the needs of the individual, whatever his or her developmental and motivational level might be; and (3) actively works to increase an individual's desire to remain in treatment.
27. *Development of New or Improved Addiction Assessment Measures and Procedures.* Research directed at the improvement of a currently available measure or the design of a new psychosocial, social or environmental measure appropriate for use in the clinical assessment of youth and adult substance abusing populations. Special consideration should be given to a specific screening or diagnostic tool, or to a specific measure of treatment readiness, treatment compliance, service utilization, therapeutic process or drug treatment outcome.
28. *Marijuana Treatment.* Marijuana is the most commonly used illicit substance in the U.S. However, relative to other drugs of abuse, little research has focused on the treatment of marijuana dependence. Trends in the literature suggest that the types of treatments effective with other substances of abuse are likely to be effective with marijuana dependence. Initial studies also suggest that many patients do not show a positive treatment response, indicating that marijuana dependence is not easily treated. Research is needed toward developing and testing effective interventions for marijuana dependent individuals.
29. *Transporting Behavioral Treatments to Community Practitioners.* There is a need for effective methods of transferring behavioral treatments found to be effective in Stage I clinical trials to clinical practice. Cognitive-behavioral therapy, operant behavioral therapy, group therapy, and family therapy are among the therapies that have been shown to be efficacious in a highly controlled setting and may be helpful treatment approaches in community treatment programs as well. However, community practitioners may have been trained using other approaches and may not have been exposed to these scientifically based approaches. Emphasis should be placed on examining mechanisms to transfer effective research-based drug abuse treatment

information and skills-based techniques to practitioners in the community. This may involve the development and testing of innovative training materials and procedures to use in the training of community practitioners to skillfully administer these treatments, including the development of highly innovative technology transfer and communication approaches. Research testing the transportability of empirically supported therapies to the community is an important component of the Behavioral and Integrative Treatment Development Program.

There is also a need for the development of educational methods to train non-drug abuse health care workers in relating to drug abusers; eliciting medical histories regarding past or present drug abuse; recognition of the signs and symptoms of drug abuse; identification of those at high-risk for HIV and other drug abuse related medical problems such as tuberculosis or hepatitis. Development and validation of a drug abuse screening instrument which can be administered by primary health care providers, and training in administering such an instrument is also needed.

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30. *Treatment Modules for Specific Problems or Populations.* Discrete therapy components that address specific problems common among drug addicted individuals and that can be implemented in conjunction with other therapeutic services. For example, an investigator may wish to develop a four session, highly focused, job seeking skills module that can be easily implemented by a wide range of practitioners to effectively increase appropriate job seeking behavior. Other examples include, but are not limited to, modules to engage ambivalent drug dependent individuals in treatment, modules to increase assertiveness in female drug addicts who feel pressured by others to use drugs, modules to improve study skills and pro-social interactions among withdrawn substance abusing adolescents, or to incorporate effective HIV risk reduction techniques.
31. *Behavioral Treatments for Pre-Adolescents and Adolescents.* Developmentally appropriate behavioral treatments for pre-adolescents and adolescents that incorporate HIV risk reduction counseling as an integral component of the treatment. This includes the development of new, or refinement of existing psychotherapies, behavioral therapies, and counseling (group and/or individual). This also includes the development and testing of manuals as well as other creative, interactive approaches for therapy delivery that may consider different settings for delivery, such as primary care, school-based health programs, juvenile justice settings, etc. Also the behavioral treatments should be culturally and gender sensitive.
32. *Behavioral Treatments for Couples and Families.* This includes the development of new psychotherapy approaches, the modification or testing of existing behavioral treatments, and the design and/or testing of innovative clinical training and supervision methods for dissemination of efficacious treatments to community settings, for youth and adult substance users. Treatments that target domestic violence or other forms of interpersonal abuse along with substance abuse are encouraged.
33. *Innovative Technologies for Drug Abuse Treatment, HIV Risk Reduction, and Training Clinicians.* Relevant research would be directed at the development and evaluation of innovative technologies to treat substance abuse, enhance adherence to medications, and/or reduce risk for HIV infection or transmission. Approaches should be capable of being readily incorporated at reasonable cost into various treatment settings. Areas of interest include Internet-based treatment or training programs, CD-ROM technology, audio delivery devices, photo therapeutic instruments, and hand-held computers. Also of interest are creative approaches for disseminating science-based behavioral treatments and for training therapists to use scientifically based treatments for drug abuse and addiction. Such approaches might include Internet-based education, interactive computer programs, telemedicine, etc. Finally, approaches

which apply therapies with evidence of efficacy through new media such as web-based platforms, over email, or through chat rooms and bullet boards are also desirable.

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B. ***Clinical Neuroscience Research.*** The Clinical Neuroscience Branch (CNB) supports research on the biological etiology (determining the biological basis for vulnerability to drug abuse and progression to addiction, including studies on individual differences and genetics) and clinical neurobiology of addiction (exploring alterations of the structure and/or function of the human central nervous system following acute or chronic exposure of drugs of abuse), and the neurobiology of development (neurobiological effects of drugs of abuse and addiction during various stages of development and maturation, effects of drug exposure on neurobiological processes, development of methodologies and refinement of techniques used in pediatric neuroimaging). The Branch also supports investigations on the cognitive neuroscience of drug abuse and addiction, the neurobiology of treatment, neuroAIDS, and human pain and analgesia. Areas that may be of interest to small businesses include, but are not limited to:

1. *Innovative Technology and Tools for Human Substance Abuse Research.* There is a continuing need for the development of methods, tools, and technology that can be used as markers of or interventions for brain, genetic or behavioral (including cognitive and affective) alterations in humans related to the risk, or reliance (etiology) of, effects of, or recovery from substance abuse. NIDA has a strong interest in facilitating the identification and use of cross-disciplinary research tools and materials that can be applied to human research that will advance our understanding drug abuse. NIDA also has a strong interest in promoting the commercial adaptation and widespread availability of discoveries (“tools”) made in the course of interdisciplinary research to better serve its mission.

   The term research “tool" is being used in its broadest sense to embrace the full range of resources that scientists use in the laboratory and clinicians use as therapeutics; therefore, one investigator’s tool may be another's end product. The value of research tools is difficult to assess and varies greatly from one tool to the next and from one situation to the next. Providers and users are likely to differ in their assessments of the value of research tools. Many research and clinical tools are costly to develop and have significant competitive value to the firms that own them.

   Of particular interest are methods that could be used to determine the effects of drug abuse/ addiction treatments on neurobiological systems in an attempt to understand the neurobiological processes underlying risk and recovery. Also of interest are methods and tools that can be integrated or expend with brain imaging techniques or other brain-related measures that can be used in human subjects.

   Examples include, but are not limited to; Development of stimulus-generating hardware and/or software for use in substance abuse studies, including neurocognitive tasks, presentation of drug-related images for the induction of craving or to probe attentional or affective processes, and “virtual reality” types of dynamic stimuli important in studies of drug abuse and addiction; Remote and mobile based technologies such as PDA’s, “smart phones”, or web-based applications for measuring cognitive and affective function in real world environments; Development or implementation of interventions such as trans-cranial or direct current brain stimulation, real-time neurofeedback, or cognitive training; New infomatic tools for primary data analysis or secondary data analysis would also be appropriate;

   Another example would be methods or technology related to development of the human central nervous system and how drugs of abuse perturb this process. Developmental studies of these populations presents unique challenges when using neuroimaging technology. The development of novel techniques, or the refinement of existing methods, to provide direct noninvasive

measures of brain structure and/or function that are adapted specifically for use in pediatric and adolescent populations is strongly encouraged. Also, neurocognitive and other neurobehavioral tasks for use in these populations, especially where they can be designed to probe underlying neurobiological processes, need to be developed (for developmental issues, contact Cheryl Boyce, Ph.D.).

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2. *Human Brain Neurochemical and Molecular Imaging.* Measurement of brain neurochemistry, neuropharmacology (receptors) and gene expression in humans using non-invasive imaging has lagged behind advances in these areas in pre-clinical research as well as in functional and anatomical neuroimaging in humans. There is a continuing need for development of new ways to measure molecular targets in the human brain. Examples include, but are not limited to novel radioligands for PET and SPECT imaging in human brain for molecular targets (e.g., receptors, intracellular messengers, disease-related proteins), as well as novel methods that use magnetic resonance imaging or other emerging technologies such as optical imaging.. The primary application of these methods will be in basic human research. Ultimately, these measures may also be used as potential biological markers and surrogate endpoints for translational and clinical research, drug discovery and development, and clinical trials. The scope of the projects may encompass pilot or clinical feasibility evaluation in pre-clinical studies, model development, or clinical studies. Alternatively, the focus may be on research and development of new technologies for molecular, neurochemical or neuropharmacological development.

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3. *Neuro-Rehabilitation of Drug-Induced Cognitive Deficiencies.* The increased awareness that the brain is capable of substantial plasticity throughout the lifespan has opened the possibility that intervention can be developed alter brain or cognitive function so as to accelerate recovery of brain and cognitive dysfunction. Such interventions encompass both direct interventions of brain function as well as indirect interventions based on cognitive or behavioral principles.

   Direct interventions include trans-cranial or direct current brain stimulation, real-time neurofeedback, and deep brain stimulation.

   Another complementary approach is based on game technology for “serious (health-related) rather than purely recreational purposes. Serious games can provide a completely controlled, noninvasive, safe and alternative methodology for a variety of important studies of drug abuse and addiction. By involving a person in an interactive computerized situation, designed to be both entertaining yet directive (i.e., in the sense of covertly shaping desired behaviors via highly flexible and programmable sets of scenarios), altered behaviors can be introduced by pre-programming consequences to counteract and potentially reset undesirable neurobiological and neurobehavioral deficits associated with chronic drug abuse.

   Areas of cognitive impairment related to substance abuse that could be enhanced through the use of either direct brain interventions, or “serious” games include diminished decision-making ability, attention/concentration deficits, attentional biases, lack of cognitive flexibility and problem solving abilities, inability to use feedback to monitor/change behavior, memory impairments,.

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4. *Measurement of Psychosocial Stress in Relation to Substance Abuse.* There is the need for development, improvement and/or adaptation of precise and reliable field deployable measurement technologies can detect and quantify an individual's exposure to psychosocial stress and/or one or more drugs. Ideally, the technology could be scalable from selected samples to full population studies. Comprehensive assessment includes measuring acute/chronic/cumulative exposures to psychosocial stress and/or addictive substances with a high degree of temporal and spatial resolution (i.e., as a person moves through environments), and with a high degree of accuracy and sensitivity to detect meaningful variations in extent of and response to exposure across developmental periods (ranging from prenatal to senescence) and among various population groups. Such technologies may include use of emerging remote and mobile technologies such as PDA's, "smart phones", or web-based applications.

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C. ***Human Development Research.*** The Behavioral and Brain Development Branch (BBDB) supports a broad research, research training and career development programs directed toward: (1) an increased understanding of how developmental processes and developmental outcomes are affected by drug exposure and related factors; (2) an increased understanding of developmental processes that are relevant to: (a) drug use, abuse, addiction, treatment and relapse, and (b) risk behaviors related to drug abuse and other health conditions that often accompany drug use (e.g., HIV infection, STDs); (3) the use of translational approaches to increase understanding of these developmental processes; and (4) an increase in effective interventions aimed at preventing or ameliorating negative developmental outcomes resulting from exposure to drugs and related factors across diverse populations (e.g. racial/ethnic minority; rural/urban, etc.).

1. *Develop Improved Technology for Assessment of Prenatal Drug Exposure and Passive Postnatal Drug Exposure.*

   a. Develop and refine methods for the detection and quantification of infant exposure to drugs of abuse during pregnancy, including nicotine cocaine, marijuana, opiates, and methamphetamines.

   b. Develop and refine methods for the detection and quantification of passive exposure to illicit drugs during infancy and childhood including second and third hand exposure to nicotine, marijuana, or other drugs of abuse.

   c. Develop technologies for us in diverse settings (e.g. primary care, emergency rooms, obstetrics/gynecology, etc.) of the assessment of prenatal drug exposure and passive postnatal drug exposure.

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2. *Develop Interactive Database Systems on Human Subjects Issues for Use by Drug Abuse Researchers Studying School-Age Children and Adolescents Drug Use.* Develop systems to assist investigators in obtaining technical and legal information relevant to involvement of children and adolescents in research on drug abuse. Examples of pertinent situations include tracking long-term health and development of children exposed to drugs during pregnancy, and investigating vulnerability and possible pathways to drug abuse including children in primary care and child care settings, and school-age children and adolescents. Human subject issues

addressing family environments, child abuse and domestic violence, and secondary data sources are also of interest. These database systems should address issues such as assent and consent, should provide information on variation in laws and guidelines across jurisdictions, should include the capacity for interactive communication on numerous situations potentially facing clinical research and health care professionals, and should serve as sources of referral for additional assistance.

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3. *Develop Improved Methods of Neuroimaging to Assess Structural and Functional Status of the Brains of Children and Adolescents Exposed to Drugs.* Document the feasibility and accuracy of appropriate and acceptable methods for assessing brain structure and function of children and adolescents, with special attention to any or all of the following groups: those exposed to drugs during pregnancy, those passively exposed during infancy and childhood, This could also include products to improve the tolerability, safety and validity of neuroimaging in children and adolescents, e.g. tools or techniques to reduce head-motion artifacts and image those actively using illicit substances. Documentation should include attention to such matters as technological difficulties and risks, and standardization issues relevant to testing conditions and image analysis.

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4. *Develop and Refine Methodologies and Clinical Tools for Measurement and Effective Interventions of Developmental Factors and Drug Use Among Children and Adolescents.*

   a. Research to develop and refine methodologies for drug use detection and quantification which may address issues of acceptability, reliability, and validity of one or more methods for clinical research and practice (e.g., interviews, computerized questionnaires, and biological indicators such as saliva or sweat). Development of web, hardware and software technology tools to enable refined physiological and behavioral assessment of normal and atypical infant and child development which may inform risk and interventions for drug use are also of interest.

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   b. Research and development of novel, or the enhancement of existing tools to be used in effective preventive or treatment interventions, and information dissemination to or understand drug use and its developmental effects for children, adolescents and their families. These tools might be used by researchers, health professionals and other health care providers, as well as by those in the broader community, including educators, day care providers, family members, etc. These tools must take into account cultural and developmental factor to assure their effectiveness and validity.

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Office of Science Policy and Communications (OSPC)

Science Education. In order to improve science education in the area of drug abuse research (e.g., disciplines such as neuroscience, psychology, epidemiology), efforts are needed to develop innovative methods for improving knowledge of and generating interest in science among school children, the general public, health care providers, and others. These might include but are not limited to:

- Development of innovative curricula using state of the art technology.
- Development of media programs on the science of drug abuse and addiction. These may include television, radio, motion pictures (including CD, and DVD), newspaper articles, magazine articles, books, experiments, computer software, CD-ROMs, web sites, social media or electronic communications instruments or channels, or other written, electronic, or audiovisual presentations designed to educate about the biology of drug abuse and addiction.
- Development of methodologies to present drug abuse and science information to particular groups, such as kindergarten and elementary school students, African Americans, Hispanics, persons with disabilities and health care providers.
- Development of computer based learning systems that allow students to experience the scientific process.
- Development of virtual reality or serious gaming to present neuroscience/drug abuse information for children and others.
- Development of specific materials, activities, or programs that promote science education related to drug abuse, such as exhibits, curriculum materials, coloring books, videos, teacher education workshops, partnership programs with scientists and educators, or workshops for health care providers.
- Development of specific materials, activities or programs that promote the teaching of scientific and research ethics to middle and high school students.

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International Program

NIDA's International Program develops and disseminates important new information on the causes, consequences, prevention and treatment of drug abuse and addiction that will help address the growing problems related to illegal drug use and addiction around the world.

NIDA's International Program is currently interested in supporting US-based small businesses to develop products and services in the following areas:

1. Development of standardized behavioral, physiological, and/or toxicological measures of drug use and drug impairment for use in international comparative studies of drugged driving.
2. Development of a mechanism to enhance international drug abuse researchers' ability to conduct secondary data analyses. While the strategies to address the international phenomenon of drug addiction need to be empirically driven, there are limited funds to support original international drug abuse research which subsequently increases the importance of secondary analyses of existing data sources particularly in low- and middle-income countries. The mechanism to expand the use of

existing data sources that can inform policy is likely be multifaceted and may include: identification of existing data sources, provision of training in secondary data analyses, and interpretation of data analyses for making policy-based decisions. The focus of the research can address any component of drug use, abuse and addiction that is within NIDA's research portfolio.

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NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)

The NIDCD supports research on the normal mechanisms of, as well as on diseases and disorders of hearing, balance, smell, taste, voice, speech and language. The Institute also supports research related to disease prevention and health promotion. The NIDCD addresses special biomedical and behavioral problems associated with people who have communication impairments or disorders. The NIDCD also supports efforts to create and refine devices, as well as develop cellular-based applications that may replace or substitute for lost and impaired sensory and communication functions. For more specific information about areas of interest to the NIDCD, please visit our home page at http://www.nidcd.nih.gov/.

Phase IIB Competing Renewal Awards

The NIDCD will accept Phase IIB SBIR/STTR Competing Renewal grant applications to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA, FCC). Such products include, but are not limited to: medical implants, drugs, vaccines, and new treatment or diagnostic tools that require FDA approval.

The NIDCD will accept applications for up to two (2) years and up to $750,000 per year in total costs. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely.

Please contact your Program Director or Roger Miller, Ph.D., (NIDCD SBIR/STTR coordinator) before beginning the process of putting an application together. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIDCD SBIR/STTR Phase II awards will be eligible for a Phase IIB Competing Renewal award.

Hearing and Balance Program

Research and development related to lost auditory function. Development of treatment modalities to prevent or lessen the effects of hearing disorders; development of new hearing aids, cochlear implants, and other assistive devices; development of systems designed to increase utilization of computers, telecommunication devices, or alerting systems by individuals with hearing impairments; development of improved screening technologies to assess hearing loss, especially in neonates and infants; development

of new or improved batteries for hearing aids and or cochlear implants, including solar rechargeable devices; development of system on a chip technologies (e.g. DSP/VLSI/ASIC) to provide self fitting, self adjusting, or other features that increase performance, accessibility, or affordability of hearing aids; development of better earmolds to address allergy, occlusion effect and/or feedback complaints; development of new outcome measures for assessing the efficacy of treatments for hearing disorders; development of technologies for the study, diagnosis and treatment of tinnitus including development of neural prostheses to treat specific neural deficits; development of technologies for the study, diagnosis and treatment of otitis media including non-invasive diagnostics to identify middle ear pathogens, novel antibacterial strategies, and prophylactic anti-microbial strategies.

Research and development related to lost vestibular function. Development of tests and treatments for balance disorders, particularly for the elderly; development of clinical tests, instrumentation and software systems to assess balance/vestibular function, including otolithic functions and eye movements associated with the vestibulo-ocular reflex; development of instruments and tests measuring head stability and vestibular function during natural stimulation of the vestibular system including during locomotion; development of perceptual reporting techniques and psychological indices for the clinical assessment of the balance-disordered patient; development of tests and new outcome measures for assessing the efficacy of physical rehabilitative regimens for balance disorders; and development of assistive devices for balance disorders, including prostheses involving electrical stimulation of the vestibular system.

Development of new research tools to aid in the study of the auditory and/or balance systems including neuroimaging techniques (e.g. software tools, neuroanatomic tracer; optical and, multielectrode methods of assessing neural activity; new animal models of impaired function; diagnostic tools for inner ear function, including DNA-based assays and biochemical markers of disease. Development of improved tests and instruments for screening and diagnosis of inner ear function; development of technologies to enable gene transfer to the inner ear, including viral vectors; development of cell type specific markers and probes to examine cell lineage in inner ear regeneration; development of relevant software, including computational modeling tools, databases or websites.

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Voice, Speech, and Language Programs

Research on voice, speech, and language disorders focuses on determining the nature, causes, treatment and prevention of communication disorders such as stuttering, spasmodic dysphonia, dysarthria, and aphasia. Emphasis is on research and development of diagnostic measures and intervention strategies for voice, speech, swallowing, and language disorders; development of communication and other assistive devices for individuals with voice, speech, swallowing, and language disorders; development of speech and language assessments and interventions for nonverbal autistic individuals; development of new systems for visual communication by individuals who are deaf or severely hearing impaired; development of new systems of communication for individuals with motor speech impairment, including a brain computer interface (BCI) communication prosthesis; development of innovative treatment delivery systems or intervention protocols; design and development of diagnostic measures or materials for early identification of voice, speech and language impairment in children; development of assessments and treatments for childhood and adult voice, speech and language impairment in multi-cultural populations; development of assessment measures of sign language abilities; development of improved artificial larynges and tracheoesophageal shunts; development of artificial intelligence computer models that simulate normal and disordered voice, speech and language.

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Taste and Smell Program

Research on the development of easily administered diagnostic tools for testing human chemosensory function in population studies; epidemiological studies of the prevalence of taste and smell disorders; intervention strategies for smell and taste disorders; development of bitter taste-blockers targeted toward pharmaceuticals; the development of artificial sweeteners; influence of taste and smell haplotypes on chemosensory sensitivity; chemosensory stem cell biology; human pheromone detection; retronasal olfaction; high-throughput screening of putative chemosensory ligand-receptor interactions; olfactory biomarkers for neurodegenerative disease; chemosensory risk factors affecting diet and health; biosensors and electronic noses for medical and industrial applications; and the development of an inventory of chemicals at exceptional high purity.

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Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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For administrative and business management questions, contact:

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NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR)

The NIDCR conducts and fosters research on the etiology, pathogenesis, prevention, diagnosis, and treatment of oral, craniofacial and dental diseases and conditions. For more specific information about areas of interest to the NIDCR, please visit our home page at http://www.nidcr.nih.gov.

NIDCR's small business programs are highly focused on maximizing translational opportunities – moving rapidly and intentionally toward pushing innovation in basic orofacial biology into useful products. The following are areas of particular interest.

Developmental Biology and Mammalian Genetics

Emphasis is on the understanding of the development of tooth and bone, and on the identification of the genetic and environmental contributions to craniofacial disorders. The objective of this scientific program is to elucidate the underlying causes of craniofacial disorders, thereby advancing the fields of diagnosis, treatment, and prevention. Small business opportunities in this area include but are not limited to:

A. Develop early pregnancy genetic tests to screen fetal cells in maternal blood for genetic mutations involved in inherited syndrome and non-syndrome craniofacial defects.

B. Develop instrumentation to improve the diagnosis and treatment of inherited and acquired craniofacial defects.

C. Develop improved appliances to aid suckling by newborn infants with cleft palate and cleft lip.

Infectious Diseases and Immunity

Research relating to the etiology, pathogenesis, prevention, diagnosis and treatment of infectious diseases of the oral cavity is supported by the NIDCR. This includes research on practical ways to effectively use the host immune system to prevent or treat oral infectious diseases and microbial-induced inflammation. Infectious diseases of the oral cavity include caries, periodontitis, candidiasis, peri-implantitis, pulpitis, and various viral, bacterial, and fungal infections of the oral mucosa and research on the diagnosis and prevention of oral manifestations and malignancies of HIV infection and AIDS. Specific examples of technology development needs include but are not limited to:

A. Develop ways to overcome or eliminate the risk of oral infections in persons who smoke or chew tobacco, drink alcohol, or are immunosuppressed, have diabetes, are malnourished, or are psychologically stressed.

B. Explore novel methods or agents to eradicate oral biofilms (dental plaque) on teeth, oral soft tissues, and dental implants without adversely effecting the normal oral flora.

C. Isolate, synthesize or prepare new antibiotics and antimicrobial agents that can overcome bacterial and fungal resistance to current compounds. Formulate combinatorial drug regimens to attack microbes growing in oral biofilms (dental plaque).

D. Develop controlled release systems for local delivery of synthetic peptides, recombinant proteins, or other chemical or immunotherapeutic agents to prevent, control, and/or treat oral infectious diseases, or the oral manifestations of HIV infection.

E. Develop biological response modifiers or other immunological approaches to reduce or eliminate microbial-induced chronic inflammation or the tissue destruction associated with chronic inflammation in the oral cavity.

F. Develop ways to interfere with microbial colonization and growth through the use of antimicrobial agents and chemotherapy.

G. Identify and exploit the structural features of oral biofilms for increased therapeutics delivery.

H. Develop computer programs to model biologically active peptide regions of oral components that have anti-fungal, anti-bacterial and anti-viral activities. Challenges appropriate for small business applications could include:

I. Develop substitutes of naturally occurring chemicals (phytochemicals) known to have a role in controlling opportunistic infections induced by HIV.

J. Develop synthetic peptides and recombinant proteins of oral components with anti-fungal, anti-bacterial and anti-viral activities including those against HIV.

K. Develop oral topical formulations with combined microbicidal, analgesic, and anti-inflammatory activities to enhance oral mucosal defenses and prevent and/or control oral infections and lesions in HIV-infected and/or immunosuppressed subjects.

Epithelial Cell Regulation and Transformation

Emphasis is on the molecular mechanisms of oral epithelial cell regulation and aberrations of these mechanisms. Research related to early diagnosis, prevention, and treatment of oral neoplasias is particularly relevant for the NIDCR small business program. Some examples include but are not limited to the following areas:

A. Develop imaging techniques for the early detection, diagnosis and prognosis of pre-malignant head and neck lesions including oral salivary gland carcinomas.

B. Develop immunotherapies (e.g. vaccines, gene therapies) effective against viruses suspected to be etiologic agents in the induction of pre-malignant and malignant head and neck lesions.

C. Develop effective pharmacological, immunological and radiological modalities for treatment of pre-malignant and malignant head and neck lesions.

D. Develop novel technologies for the genetic and molecular-targeted therapy of head and neck carcinomas.

E. Develop novel micro and nano-sensor technologies that can release therapeutic agents in tumor cells.

F. Develop regimens for the alleviation of the oral complications of cancer therapy.

G. Develop novel technologies for using stem cells as therapeutics for head and neck cancers.

Mineralized Tissue and Salivary Gland Physiology, Pharmacogenetics and Injury

Emphasis is on the physiology of bones, teeth and salivary glands, craniofacial tissue damage and repair, and pharmacogenetics of agents used for the treatment of craniofacial and oral diseases and disorders. Such technologies that could speed translational research might include but are not limited to:

A. Develop standardized, high-sensitivity, high-accuracy methods, instrumentation, and/or devices to detect oral bone loss, assess alveolar bone quality, and to monitor for bone repair.

B. Develop novel agents and vehicles for local inhibition of bone loss and/or augmentation of bone growth for the treatment of periodontal diseases or craniofacial reconstruction.

C. Develop novel methods and instrumentation to detect and/or treat the earliest signs of demineralized enamel that may develop into carious lesions.

D. Develop systems that effectively remove or neutralize dental caries using non-mechanical means to minimize iatrogenic pulp death.

E. Develop non-invasive devices to assess pulpal health prior to and during treatment; develop means to neutralize necrotic pulps non-mechanically to reduce or eliminate the need for root canal therapy.

F. Develop novel methods and agents to promote scarless repair of cleft lip and scarless cutaneous healing following craniofacial surgery.

G. Develop viral and non-viral vectors for salivary gene therapy and gene therapeutics.

H. Develop non-invasive methods for the determination of efficacy and safety of artificial saliva, sialogogues and of their delivery vehicles used in addressing the diminution or lack of saliva (xerostomia) due to Sjögren's syndrome or head and neck irradiation cancer therapy.

I. Develop apparatus for craniofacial bone distraction for building bone for craniofacial reconstruction or orthodontic procedures.

J. Develop more efficient methods, materials, and devices for prevention of injuries to the teeth, mouth, and face during athletic activities.

K. Develop genetic standards, databases, and diagnostics to predict oral responses to drugs used for the treatment of craniofacial, oral and dental diseases.

L. Develop standardized methodologies for the detection of fluoride load in the body from saliva, serum, urine, nail clippings, and hair.

Molecular and Cellular Neuroscience

Emphasis is on research on chronic disabling diseases of the oral-craniofacial-dental areas including chronic pain, neuropathies and neurodegenerative disorders, diseases of the temporomandibular joint. NIDCR encourages small business applications to:

A. Develop improved techniques for measuring nociceptive, chemosensory, tactile, kinesthetic, or proprioceptive function involving craniofacial structures. Such measures may be useful in screening for deficits, improving diagnosis, or for evaluating responses to dental treatments or interventions.

B. Develop improved measures for assessing oral-motor coordination or oral behaviors (e.g., swallowing, masticatory efficiency).

C. Develop improved biomarkers or treatments for neuropathic conditions or neurodegenerative conditions affecting oral-craniofacial tissues or structures.

D. Develop assays facilitating reliable evaluations of relationships between hormonal or chronobiological variations and other risk factors as these relate to onset or exacerbation of pain symptoms.

E. Discover and develop non-narcotic medications with particular emphasis on chronic orofacial pain disorders.

Biotechnology and Biomaterials

Emphasis is on the development of novel biomaterials and technologies for promoting repair, regeneration, restoration and reconstruction of diseased and injured oral and craniofacial tissues. This includes development of natural and synthetic biomaterials for dental repair and for manufacturing of craniofacial tissue replacement constructs, quantitative methods for evaluating the quality and performance of biomaterials and tissue constructs, as well as their interactions with host tissues. Specific examples of relevant small business applications could include but are not limited to:

A. Develop technologies for design and fabrication of biocompatible biomaterials and tissue constructs to be used for reconstruction and regeneration of oral and craniofacial tissues.

B. Develop non-destructive in vitro and in vivo methods for imaging of cells, tissue constructs and biomaterials.

C. Develop methods for curtailing disease-associated inflammation and promoting wound healing and endogenous regeneration of oral and craniofacial tissues.

D. Develop synthetic analogues of oral and craniofacial tissues and organs for use in high throughput biological assays of tissue function and physiology.

E. Develop sensitive methods for measuring and quantification of biomaterial-tissue biocompatibility and biotoxicity including restorative materials interacting with secondary decay.

F. Develop mathematical and computer algorithms for modeling oral and craniofacial tissue function and physiology.

G. Develop technologies for ensuring sterility of biomaterials and tissue engineered constructs prior to implantation.

H. Develop efficient and non-immunogenic viral and non-viral gene delivery systems to oral and craniofacial tissues.

I. Develop nanotechnology-based implantable biomaterials for dental, oral and craniofacial tissue restoration.

J. Develop improved surgical techniques for replacement of dental, oral and craniofacial tissues and organs.

K. Develop safe and effective technologies for the diagnosis and treatment of temporomandibular joint disorders (TMJDs).

L. Develop safe and effective biomaterials and construct fabrication technologies for repairing TMJDs.

M. Develop new or improved composite biomaterials and adhesive sealants (possibly replacing Bis-GMA resin-based systems) suitable for restoring crowns of posterior teeth and exposed roots of teeth.

N. Develop new effective orthodontic and other prosthetic appliances and constructs.

O. Develop approaches for generating complex tissue/organ structures, such as teeth, periodontal ligament, TMJ, and vascularized and innervated bone and muscle.

P. Develop methods for standardization and comparison of different stem and progenitor cell populations for use in dental and craniofacial tissue engineering.

Q. Develop methods for targeted delivery and release of therapeutic biomolecules to oral and craniofacial tissues.

R. Development of instrumentation for early caries detection and comparison studies on specificity and selectivity with respect to current clinical practice.

Clinical and Behavioral Research

Provides support for the development of evidence-based products related to behavioral and social aspects of oral health, oral health prevention or treatment interventions, and other patient-oriented aspects of oral health. This includes support for clinical trials and patient-oriented research to establish safety and initial efficacy of products. NIDCR is especially interested in applications that significantly improve oral health by: 1) being broadly applicable to many populations, 2) contributing to meaningful oral health improvements for a specific population, 3) expediting translation of research findings into oral health improvements, and/or 4) equipping oral health care providers, educators or researchers with tools to improve public oral health. Examples of studies of interest include, but are not limited to, the following:

A. Develop and test devices or methods to improve time-sampled monitoring of behavioral adherence with preventive or therapeutic regimens specifically relevant to oral diseases/conditions. Such devices or methods could be utilized in a variety of settings, including naturalistic settings, within clinical trials, within oral health care delivery systems, etc.

B. Develop and test novel compliance and survey measures or tools to identify the underlying causes of insufficient preventive dentistry for specific underserved populations.

C. Develop, or adapt for use in a new population or setting, novel measures or methods for identifying individual, family, group, or other processes that explain oral health behavior.

D. Develop and test for safety, efficacy, and/or effectiveness of measures or materials for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders.

E. Develop, or adapt for use in a new population or setting, oral health interventions utilizing technology to improve efficiency of delivery (e.g., management of chronic pain related to temporomandibular joint disorders, etc.).

F. Develop, or adapt for use in a new population or setting, interventions addressing health behaviors highly associated with oral health (e.g., tobacco, alcohol, and other drug use; management of diabetes, HIV infection, or other chronic illnesses; etc.).

G. Develop technologies or modules that utilize existing web-based platforms to improve preventive oral health hygiene for children and adolescents (e.g., social marketing via web-based interaction, virtual reality "worlds", "massively multiplayer online games", etc.).

H. Develop and test innovative methods for facilitating collaborations, referrals, and/or ongoing follow-ups between oral health professionals and other health care professionals.

I. Develop and test web-based training or other innovative approaches for oral health care professionals to accelerate accurate translation of new knowledge regarding oral diseases and their effective prevention or treatment into clinical or public health practice.

J. Develop and test the effectiveness of innovative teaching tools to inform oral health professionals or the public regarding oral cancer prevention and early detection.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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Coordinator, SBIR/STTR Program
Director, Microbiology Program
Integrative Biology and Infectious Disease Branch
Division of Extramural Research
National Institute of Dental and Craniofacial Research-NIH
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For administrative and business management questions, contact:

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NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

The NIDDK supports research in diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; and kidney, urologic and hematologic diseases. For additional information about areas of interest to the NIDDK, please visit our home page at http://www.niddk.nih.gov.

Phase IIB Competing Renewal Awards

NIDDK will accept Phase IIB SBIR/STTR Competing Renewal grant applications from NIDDK supported Phase II awardees that propose to continue the process of developing products that ultimately require 1) clinical evaluation, 2) approval by a Federal regulatory agency, and 3) continuing refinements to durable medical equipment (DME) designs such as cost reduction, testing for safety, durability, and reliability, and meeting or establishing standards. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Such products include, but are not limited to biological products, devices, drugs, medical implants, etc. related to the mission of the NIDDK. The previously funded Phase II SBIR/STTR grant need not have been submitted in response to a particular solicitation, as long as the research is appropriate to the purpose of this solicitation. Budgets up to $1,000,000 total costs per year and time periods up to 3 years may be requested for this Phase IIB Competing Renewal opportunity. These awards are intended to support completion of research needed to obtain an IND or IDE. Applicants must provide evidence that they have consulted formally with the FDA concerning the research needed for the development of a drug, biologic or medical device and that the proposed research will address these regulatory requirements. Such evidence should include FDA correspondence from a pre-IND meeting for an IND application or a pre-IDE meeting for an IDE application, and the status of the project in a timeline related to Federal regulatory approval processes.

Prospective applicants are strongly encouraged to contact NIH staff listed at the end of this NIDDK topics announcement prior to submission of a Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Examples of research that would be considered responsive to this announcement are listed below for illustrative purposes and are not exclusive of other appropriate activities.

- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.

- Assessment of devices with regard to performance standards related to the FDA approval process.

- Clinical and toxicology studies in support of an Investigational New Drug Application to the FDA.

- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

Diabetes, Endocrinology and Metabolic Diseases:

The Division of Diabetes, Endocrinology and Metabolic Diseases supports basic and clinical research on the etiology, pathogenesis, prevention, diagnosis, and treatment of diabetes mellitus and its complications; endocrine diseases; osteoporosis; cystic fibrosis, and other metabolic disorders; as well as research on basic endocrine and metabolic processes. Research topics of potential interest to small businesses include, but are not limited to:

I. SENSORS AND DELIVERY DEVICES:

A. Assessment of non-invasive, minimally invasive or implantable sensors for monitoring blood or interstitial fluid glucose for prevention of hypo- and hyperglycemia in diabetic patients. NIDDK will give priority to research that has already progressed to an in vivo model or to be clinically tested.

B. Integration of glucose sensor and insulin delivery systems to create an artificial pancreas.

C. Development of improved insulin delivery methods or devices.

D. Development of novel and more accurate non-enzymatic based glucose detection technologies.

E. Develop telemedicine approaches that can be incorporated as components/and or adjuvants of an artificial pancreas for better diabetes self management.

F. Development of technologies that may promote and facilitate adherence/compliance by users of glucose control devices.

II. SCREENING TESTS, DIAGNOSTICS AND BIOLOGIC TOOLS:

A. Development of techniques or products useful for predicting, preventing or delaying progression of diabetes, including tests for identifying patients at risk, and methods of monitoring disease progression.

B. Development of diagnostic tools for diabetic foot ulcers. These tests could be used to determine the risk of developing a diabetic foot ulcer or used for choosing treatment strategies.

C. Development of diagnostic tools to measure the autonomic neuropathy that develops in people with diabetes.

D. Development of clinical measures of oxidative stress, advanced glycation end-products and chronic inflammation that result from diabetes.

E. High throughput - Point of care technologies (reliable, accurate, cost-effective, highly sensitive, standardized having rapid turnaround time) for autoantibody detection, T cell –subsets-auto-reactivity and other immune parameters for autoimmune diabetes diagnosis and follow-up.

F. Development of methods to measure changes in the immune status that may be used as markers to follow the immune-modulatory activity and beneficial effect (beta cell mass preservation, reduction of inflammation at the target organ, etc) of biologic agents tested in clinical trials for the prevention and/or treatment of T1D.

G. Development of high throughput assays based on biologic pathways likely involved in the pathogenesis of diabetes and its complications that could be used to screen molecular libraries for novel therapeutic agents.

H. Development and validation of surrogate markers to monitor disease progression and potential therapies for diabetic complications.

I. Development and validation of tools for use by health care providers/systems to improve diabetes care and prevention.

J. Development of techniques and tools to identify islet cell progenitors, methods to predict transplant success with recovered islet preparations, and non-invasive imaging as well as other methods for the in vivo measurement/ evaluation of pancreatic beta cell mass, function or inflammation after transplantation of pancreatic islet/beta cells.

K. Point of care low cost /portable technologies for diabetes and pre-diabetes diagnosis.

L. Development of Innovative technologies to predict and prevent hypoglycemia.

III. INTERVENTIONS AND THERAPIES:

Diabetes

A. Development of immunomodulation/tolerance induction strategies to prevent or slow progression of type 1 diabetes.

B. Development of new therapies or devices to prevent and treat diabetic foot ulcers.

C. Development of new therapies to correct the underlying metabolic defects that result from diabetes, such as reactive oxygen species production and glycation of proteins.

D. Development of methods that protect islet grafts after transplantation, including the evaluation of alternative transplantation sites, minimize the use of immunosuppression through immunomodulation/tolerance induction or immunoisolation/encapsulation of the graft from the host immune system, or support the use of single donors for transplantation.

E. Development of methods that expand the number of human islets during culture while still retaining appropriate functional islet characteristics and the ability to be successfully transplanted.

F. Development of methods utilizing replenishable cell sources, especially stem cells that produce functional islet like cells/tissues that can be successfully transplanted.

G. Development of more reproducible methods that improve yield/viability/function of islets prior to transplantation and the engraftment and long term function of islets after transplantation.

H. Development of educational or psychosocial approaches that increase adherence to recommended diabetes treatment regimens or that reduce co-morbidities and complications (e.g., depression or foot ulcers).

I. Development of novel technologies that may facilitate self management of diabetes and adherence to treatment.

J. New implantable and easy to replace technologies that may mimic the beneficial effect of gastric bypass/bariatric surgery for the treatment of diabetes without the need of a major invasive surgical procedure.

Other Endocrine and Metabolic Disorders

K. Identification of new ligands for previously unclassified (orphan) nuclear receptors and development of partial agonists or antagonists with therapeutic potential for diseases such as diabetes and osteoporosis, hormone-dependent cancers, and for conditions such as obesity.

L. Development of Selective Receptor Modulators (SRMs) with tissue specificity and profiles that provide beneficial effects without the side effects secondary to therapies based on naturally occurring hormones.

IV. GENETIC TESTING AND GENETIC THERAPIES

A. Development of improved methods for the diagnostic, population or newborn screening or prenatal testing for genetic metabolic diseases.

B. Improvements in the construction of gene therapy vectors to increase transduction efficiency, level and duration of expression, and to improve targeting.

C. Development of improved methods of manufacturing gene therapy vectors that are scalable and improve titer and bioactivity of the vectors.

D. Development of new vector systems that improve the ability to transduce nondividing cells such as hematopoietic stem cells, neurons, hepatocytes or epithelial cells.

E. Development of techniques to achieve efficient homologous integration or site-specific integration of introduced genes.

Digestive Diseases and Nutrition

The Division of Digestive Diseases and Nutrition supports research on the function, diseases and disorders of the digestive tract; the esophagus, stomach, intestine, colon, anorectum, pancreas, liver, gallbladder, and biliary tract; basic, clinical and behavioral research on nutrition and obesity as well as information transfer in the field of digestive diseases and prevention of obesity. Innovative investigator-initiated projects that are not mentioned below are encouraged. Areas that may be of interest to small businesses include, but are not limited to:

I. Digestive and Liver Diseases (Clinical)

A. Development of assays to detect biomarkers for genetic predisposition to GI-relevant diseases, e.g., IBD and IBS.

B. Development of new genetic screening methods for detection of inherited digestive and nutritional disorders, e.g., hemochromatosis, Wilson's disease, Crigler-Najjar syndrome, Alagille syndrome.

C. Development of improved means for detecting Barrett's esophagus.

D. Development of a non-invasive means of localizing GI bleeding beyond the duodenum that is more sensitive than the Tc-RBC test.

E. Development of methods for gastrointestinal endoscopy without the need for sedation.

F. Development, using rational drug design techniques, of agents that interact with L-type calcium channels or with delayed rectifying potassium channels to treat motility disorders (pseudo-obstructive disorder, chronic constipation, and slow bowel transit).

G. Development of pharmaceutics from herbal preparations of promise for therapy of digestive diseases, including liver diseases, involving isolation of active components, preparation of pharmacologically pure preparations, and testing for pharmacokinetics and activity in humans.

H. Development of novel antifibrotic therapies for progressive liver failure.

I. Development of agents that would protect the gut epithelium from the damage caused by chemotherapeutic agents.

J. Development of tests of hepatic "reserve" which would be of use, for example, in assessing the risk of surgery in patients with liver disease.

K. Development of agents to promote the repair of gut epithelium barrier function, e.g., as needed following chemotherapy.

L. Development of drugs for dissolving gallstones in vivo.

M. Development of humanized monoclonal antibodies against HCV and HBV to be used for prevention of recurrent disease in liver transplant patients.

N. Development of surrogate markers for liver fibrosis and progression.

O. Development of a rapid, non-invasive diagnostic test for biliary atresia.

P. Development of non-invasive imaging methods to quantitatively assess fatty liver in patients.

Q. Development of non-invasive imaging methods to quantitatively assess liver fibrosis in patients.

R. Development of non-invasive methods to quantitatively assess liver iron content in patients.

S. Develop and validate therapeutic interventions for treatment and/or progression of pancreatitis and its complications.

T. Develop novel and more effective pharmacologic and/or endoscopic approaches to prevent ERCP-induced pancreatitis.

U. Develop more accurate and useful approaches to the diagnosis of chronic pancreatitis by functional, radiologic, endoscopic, or pathologic/cytologic means.

II. DIGESTIVE AND LIVER DISEASES (BASIC)

A. Development of detection methods for non-culturable forms of gut enteric bacteria.

B. Development of molecular probes for the diagnosis of mucosal dysplasia in inflammatory bowel disease.

C. Development of gut immune-modulators, or non-antigenic gliadin in celiac disease.

D. Development of new techniques, including non-invasive imaging, to measure motility/intestinal transit at various sites within the gastrointestinal tract.

E. Development of techniques for the preservation and transplantation of small intestine and pancreas.

F. Development of non-invasive measures of pancreatic exocrine function.

G. Development of a test for determining the hepatotoxic potential of drugs, agents or additives that is more sensitive than testing in mice and reflects the human response to the test compound.

H. Development of animal models to study hepatotoxic agents.

I. Improvements to existing imaging systems, or development of new ones, to allow non-invasive detection of fibrotic, necrotic, inflamed, and fatty livers prior to transplantation.

J. Development of non-invasive techniques to detect liver disease.

K. Development of non-invasive devices/ techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.

L. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.

M. Development of non-occluding stents for use in the biliary tract and in transjugular intra-hepatic porto-systemic shunts (TIPS).

N. Development of cryopreservation techniques for human hepatocytes that would maximize viability and cell culture growth potential of thawed cells.

O. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.

P. Development of molecular standards for Hepatitis B virus quantitation and typing.

Q. Development of an economical, accurate, and fast test for glutens and glidins in foods.

R. Development of humanized mouse models of multi-allelic diseases.

S. Development of measurements to quantitate phenotypic or metabolic markers of disease progression in animal models, thus reducing the numbers of animals needed.

T. Identification of surrogate markers looking at the plasma/sera proteome or metabolome at different stages of digestive or liver disease.

U. Development of novel proteomic or metabolomic technologies designed to study digestive and liver diseases, and their complications.

V. Development of biomarkers or imaging methods that quantitatively measure hepatic regeneration.

W. Development of biomarkers that quantitatively assess the degree to cold and warm ischemia in donor liver organs.

III. NUTRITION

A. Development of a better method for measuring food intake patterns of individuals that could replace recall.

B. Development of better methods for assessing overall nutritional status.

C. Development of a non-invasive breath or blood test to accurately measure dietary fat intake.

D. Development of biological measures, such as serum or urine tests, for long-term dietary consumption of specific nutrients.

E. Development of better means of assessing energy intake and/or energy expenditure (i.e., physical activity), e.g., a device to estimate movement and relate this to calories expended with the goal of impacting behavior and preventing obesity.

F. Development of better means to detect food borne pathogens with the goals of (1) preventing their inclusion in foodstuffs and (2) better treatment of acute infections.

IV. OBESITY AND EATING DISORDERS

A. Development of safe drugs or herbal products that inhibit appetite or increase energy expenditure.

B. Development of computerized interventions for weight-loss/maintenance, prevention of weight gain and/or increasing physical activity such as hand-held computers and web-based programs.

C. Development of devices/equipment/ interventions to encourage “activity” while engaged in sedentary activities (e.g., watching television or sitting at a desk).

D. New technologies for quantitative assessment of intra-abdominal fat; emphasis on technologies that are non-invasive, minimize the use of ionizing radiation, and have the capability of being adapted for use in the usual health care settings.

Kidney, Urologic and Hematologic Diseases

The Division of Kidney, Urologic, and Hematologic Diseases supports research into basic mechanisms of organ and tissue function and into the diseases of the kidney, urologic and hematologic systems. Projects to help develop an understanding of the physiology, pathophysiology, and related diseases of the kidney, urinary tract, and blood and blood forming systems so that rational treatments and means of prevention and/or arrest of diseases may be devised. Support for advances in the technology of cell and molecular biology that will enhance research in kidney, urologic and hematologic diseases is encouraged. Research opportunities of interest to small businesses include, but are not limited to:

I. DEVELOPMENT OF A GENOMIC TOOLBOX FOR STUDY OF KIDNEY, PROSTATE, BLADDER, OR RED CELLS, WHICH WOULD INCLUDE:

A. Library generation and gene identification from whole organ or rare compartments in normal, developing, or injured tissues.

B. Antibodies or phage libraries that will facilitate the prospective identification and purification of renal cell types.

C. Strategies to deal with the anatomical complexity, increase the representation of low abundance transcripts, or decrease the redundant sequencing of over-represented or known genes.

D. Bioinformatics tools.

E. Flexible databases useful for designing organ-specific databases and websites.

F. Techniques for visualizing RNA distribution within cells or tissues.

G. New methods to acquire material from archival samples.

II. APPLICATION OF PROTEOMICS AND METABOLOMICS TO KIDNEY, UROLOGIC AND HEMATOLOGIC DISEASES

A Identification of surrogate markers in the plasma or serum that correlate with acute or chronic kidney disease, urologic diseases of the prostate or bladder, or disregulation of iron metabolism or other hematologic diseases (not leukemia), such as hemoglobinopathies or thalassemia.

B. Identification or development of novel proteomic or metabolomic technologies designed to study kidney, urologic, or hematologic diseases.

III. KIDNEY

A. Development of antibodies or phage libraries specific for the individual cell types of the kidney.

B. Development of both data and cell banks of diabetic kidney disease families and autosomal and recessive polycystic disease families for use by the research community.

C. Development of pharmacological agents that might be used to intervene in acute or chronic renal disorders and in disorders of renal hemodynamics, blood pressure, and extracellular volume regulation.

D. Means to improve physiologic homeostasis in maintenance dialysis therapy through the:

1. Improvement of blood access to permit continuous access to the circulation.
2. Development of means to provide for continuous anticoagulation.
3. Development of reliable, non-invasive, online hemodialysis monitoring systems assessing real-time treatment parameters such as blood volume, access flow, and urea clearance.

E. Studies to improve the efficiency of maintenance dialysis:

1. Development of innovative methods to produce more efficient and less morbid forms of renal dialysis (e.g., GI dialysis, artificial kidney).
2. Studies on biocompatibility of artificial kidney membranes, in surface sensitive proteins, complement, and clotting mechanisms.
3. Development of new agents for sterilizing dialysis membranes.
4. Development of new dialysis membranes to diminish the duration of dialysis treatments.

F. Improved techniques of preservation and storage of kidneys intended for transplantation.

G. Development of material(s) for construction of urinary catheters that may reduce the incidence of infection in the urinary tract.

H. Development of improved renal imaging techniques, differential renal function assessments and diagnostic assessment of benign parenchymal diseases.

I. Development of early diagnostic tools, preventative measures, and treatment modalities for acute kidney injury.

J. Identification of mediators of kidney injury during sepsis and pharmacological means to block these effects.

K. Development of new non-invasive methods for measuring kidney function:

1. Reliable, non-invasive, non-radioactive methods of measuring glomerular filtration rate (GFR).
2. Identification and description of physiologic compounds that are filtered by the kidney, but neither secreted or reabsorbed;

3. Identification of serum factors released by damaged kidney cells.
4. Development of methods / agents to reduce hemodialysis or peritoneal dialysis catheter-related infections.
5. Characterization of changes in kidney hormonal function in kidney disease at various stages of severity.
6. Development of new biomarkers for early detection of kidney dysfunction, prediction of progression, and early indication of recovery.
7. Development of rapid, accurate, and cost effective means of quantifying urine albumin.

IV. UROLOGY

A. Analyses of factors responsible for initiation and progression of benign prostatic Hyperplasia (BPH) leading to the development of a diagnostic tool. Development of animal, computer, or in-vitro models for the study of BPH, including culture conditions for in vitro culture of cells from benign prostatic hyperplasia.

B. Development of diagnostic modes to clinically non-invasively or minimal-invasively measure bladder obstruction before and after surgical or pharmaceutical intervention and/ or treatment devices for bladder outlet obstruction.

C. Prevention, diagnostic, or treatment modalities for urinary tract infections.

D. Kinetics of renal stone formation, such as characterization of growth and dissolution, or crystal growth inhibition, and definition of reliable biochemical profiles of stone forming patients. Development of diagnostic device for biochemical profiling of stones either in-vitro or in-vivo.

E. Development of localization methods through imaging or non-invasive methods or instrumentation using minimally-invasive methods to access stones for therapy. Methods to directly improve access to difficult stones.

F. Development of additional therapeutic agents for prevention and/or treatment of urolithiasis.

G. Development of more real-time diagnostic assessment of bladder and urinary function using non-invasive or minimally invasive measures, which can include neuro-pharmacological/neuro-physiological assessments in urodynamics.

H. Objective and diagnostic measurement devices or methods for assessment of urinary voiding and storage disorders, including stress, urge, and mixed incontinence, both in adults and children.

I. Development of non invasive or minimally invasive treatment methods or pharmacological for urinary incontinence and/or bladder instability.

J. Non-invasive or minimally invasive methods to diagnosis bladder inflammation or bladder epithelial and/ or bladder wall changes of non-cancerous origin.

K. Non-invasive, reduced or non-radiological diagnostic methods for evaluating vesico-ureteral reflux in children and infants.

L. Methods for determining inflammatory cytokines, histamines, or other factors in voided urine, as markers for lower urinary tract inflammatory processes or other urologic disorders, including chronic and acute urologic pain disorders.

M. Development of simple diagnostic kits for evaluating growth factors in urine in a clinical laboratory.

N. Development of new or enhanced methods to derive synthetic or semi-synthetic biological matrices or other tools to treat urologic disease and/or augment the functionality of urologic tissues and organs.

V. HEMATOLOGY

A. Development of methods and equipment for routine high volume isolation of highly purified hematopoietic stem and progenitor populations.

B. Identification of new methods to assay hematopoietic stem and progenitor cells with short- and long-term repopulation models amenable to serial examination.

C. Development of chemically defined reagents that support hematopoietic stem cell proliferation and differentiation.

D. Definition of culture conditions using serum-free medium that will support the ex vivo expansion of hematopoietic stem and progenitor cells.

E. Development of new approaches for identifying, isolating, and genetically analyzing fetal erythrocytes in the maternal circulation.

F. Development of novel methods for the delivery of DNA, proteins, and other compounds to hematopoietic stem cells.

G. Development of rapid, high throughput microarrays for accurate assessment of gene expression profiles of hematopoietic stem cells.

H. Development of non-invasive systems for monitoring the total hemoglobin and hematocrit, suitable for use with adults or neonates.

I. Application of nanotechnology to the measurement of blood parameters and diagnosis of blood disorders.

J. Development of new methods for the non-invasive or minimally invasive measurement of body iron.

K. Adaptation of MRI technology for the non-invasive measurement of body iron:

   1. Develop appropriate MR measurement method(s).
   2. Optimize RF coils for the body region of interest (primarily heart, liver, and pancreas).
   3. Develop magnets of the appropriate magnetic field strength(s).
   4. Develop a reliable method for calibrating, validating, and standardizing organ specific iron concentration measurements as detected by magnetic resonance imaging.
   5. Determine the most appropriate magnetic resonance method for determining relaxation times and susceptibility.
   6. Develop indicator materials for direct MR measurement of iron concentration.

L. Design of therapeutic drugs for inducing fetal hemoglobin synthesis.

M. Development and validation of a sensitive, specific, reproducible, quantitative, and clinically applicable assay method for measuring serum hepcidin levels.

N. Design and validation of novel therapeutic agents that modulate hepcidin expression and/or activity *in vivo*.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

DIABETES, ENDOCRINOLOGY AND METABOLIC DISEASES

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KIDNEY, UROLOGIC AND HEMATOLOGIC DISEASES

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NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

Human health and human disease result from three interactive elements: the environment, genetics, and age. The mission of the NIEHS is to reduce the burden of human disease and dysfunction from environmental causes by understanding each of these components and how they interrelate. NIEHS achieves its mission through a multidisciplinary biomedical research program, prevention and intervention efforts, and a communication strategy that encompasses training, education, and technology transfer and community outreach. NIEHS supports research and training focused on the identification, assessment and mechanism of action of agents in the environment and how they contribute to disease and dysfunction. The ultimate goal of these NIEHS activities is to then transfer this knowledge for the public benefit. The SBIR program uses a combination of research, technology transfer and communication strategies to aid the mission of NIEHS.

For additional information about the areas of interest to NIEHS, visit our home page at http://www.niehs.nih.gov.

Tools for Improved Exposure Assessment

Fundamental to the NIEHS mission is the ability to quantify an individual's exposure, as well as the unique characteristics that account for individualized responses to the exposures. The goal for improved exposure assessment is to develop new technology and assays to generate precise measurements of human exposure to chemical and biological agents that may lead to disease or dysfunction. The desired application of these technologies and assays is in population-based (epidemiological) or clinical research and practice. An emphasis is placed on tools that provide individual exposure metrics either at the point of contact or through measuring internal dose of environmental agents.

It is anticipated that the new technologies and assays, such as those based on micro- and nanotechnology and molecular imaging, may provide sensitive, high-throughput, and potentially portable systems capable of measuring exposure to environmental agents and the impact of the exposures on human biology.

1. Wearable Technologies for Personal Exposure Assessment at the Point of Contact

The NIEHS is interested in developing and validating new products/devices, tools, assays to improve our ability to precisely measure an individual's exposure to environmental agents, with high temporal and spatial resolution. Ideally, the technologies, tools and assays will be of appropriate scale to be field deployable and/or wearable. These point-of-contact devices should be capable of measuring simultaneously and in near real time, multiple agents within a single exposure class (e.g., multiple types of metals, multiple size fractions of particulate matter, multiple components of diesel exhaust) and/or multiple agents across more than one exposure class. Exposures of interest include ozone, particulate matter, diesel exhaust, metals (e.g., arsenic, cadmium, or mercury), volatile organic compounds, polybrominated diphenyls (PBDEs), polycyclic aromatic hydrocarbons (PAHs), mold/microbial toxins, allergens and pesticides/herbicides. Examples include but are not limited to:

A. Novel technologies and assays to generate precise, quantitative measures of human exposure to environmental compounds at the point of contact or in easily obtained biological samples (e.g., skin, breath, saliva, or nasal mucosa). An emphasis is placed on the ability to measure multiple analytes simultaneously.

B. Remote sensing technologies for detecting, quantifying, and monitoring household exposures to toxicants and/or bioaerosols.

2. Technologies for Generating Precise Measurements of Internal Dose of Environmental Agents

The NIEHS is interested in developing technologies and devices to generate precise measurements of internal dose of individual environmental agents and or their metabolites in real time and over time. It would be especially valuable to analyze internal dose over time of multiple agents within a single class or multiple agents across more than one class. The development of a modular design allowing measurement of specific classes of chemical exposures for application in epidemiological studies (e.g., pesticides, endocrine-active chemicals, or components of indoor air pollution) is preferred. Likewise, an emphasis is placed on measuring environmental factors with mixed routes of exposure (i.e., inhalation, ingestion, and dermal exposure) for which biomonitoring is the only comprehensive exposure metric.

Examples include but are not limited to:

A. Development of sensors for measuring the levels of toxicants in biospecimens easily attained for an individual such as finger prick, buccal cells, exhaled breath or urine.

B. The development of integrated devices linking exposure at the point of contact, internal dose, and biological response.

Hazardous Substances Detection and Remediation Program

The NIEHS Superfund Research Program (SRP) is interested in applying biotechnology and bioengineering approaches to develop novel strategies to characterize, monitor, and remediate hazardous substances at contaminated sites. SRP encourages applicants to develop green / sustainable detection technologies and remediation approaches that improve energy efficiency and reduce waste generation.

Examples include but are not limited to:

A. Development of advanced technologies that allow for real-time, on-site monitoring such as nanotechnology–based sensors and probes, biosensors, self-contained miniaturized toxicity-screening kits and miniaturized analytical probes and data analysis tools.

B. Development of methods or devices to detect and measure vapor intrusion or to detect non-aqueous phase liquids (NAPLs) and dense non-aqueous phase liquids (DNAPLs) in the subsurface.

C. Development of assays or devices to determine the extent to which a contaminant is bioavailable.

D. Development of instruments to identify subsurface geological structures and hydro-geological configurations and to sample for the presence of contaminants in these structures.

E. Development of novel technologies for in situ remediation of contaminated sediments, soils, and groundwater.

F. Development of cost-effective devices to detect or remediate chemical mixtures in environmental media.

G. Development of nano-enabled structures, electrochemical methods, photocatalytic processes, thermal treatments, or filtration-based methods of remediation.

H. Development of bioremediation and phytoremediation technologies including the use of genetic engineering approaches.

SRP recognizes the important public health impact of detection or remediation technologies that are applicable to non point-source air pollution and drinking water; however, a higher priority will be placed on remediation and detection technologies with a clear connection to sites impacted by hazardous substances.

Improved Test Systems for Prioritization and Safety Evaluation

The NIEHS is interested in: (1) developing, standardizing, and validating sensitive and specific innovative tests and integrated testing strategies that can reduce, refine, or replace animal use and that will provide improved predictivity, and potential cost and time savings compared to current standard laboratory animal tests (i.e., assays for carcinogenicity, immunotoxicity, reproductive or developmental toxicity, dermal toxicity, and neuro or other organ system toxicity including acute local and systemic toxicity); and (2) developing mid- and high-throughput screens and tests using phylogenetically lower animal species (e.g., fish, worms) to evaluate mechanisms of toxicity to identify mechanisms of chemically-induced biological activity, prioritize chemicals for more extensive toxicological evaluation, and develop more predictive models of *in vivo* biological response. The proposed tests and strategies should use computational and/or biochemical models, cell/ tissue cultures, and/or animal models that are relevant to existing safety assessment databases and human experience, and that can be extrapolated to estimate risks to humans. The endpoints for these tests or assays should take advantage of the new technologies such as genomics, transcriptomics, proteomics, and bioinformatics and of novel endpoints (biomarkers) including those that are non-invasive. Examples include but are not limited to:

A. Biokinetic models that include the integration of toxicodynamic and biokinetic modeling to predict acute and chronic systemic toxicity.

B. In vitro test methods and integrated strategies (e.g., undifferentiated/ differentiated human/mammalian cell model systems, organotypic model systems, biochemical activity (e.g., peptide binding; and computational models) that can be used to prioritize compounds for more extensive testing and/or to predict acute and chronic toxicity by taking into account, for example, metabolism, the ability of chemicals to pass through barriers (i.e., blood brain, kidney, lung, gastrointestinal), and organ specific effects, or which allow the development of endpoints that can be extrapolated to in vivo biomarkers of toxicity. An emphasis is placed on the development of engineered 3D tissue systems that include multiple cell types and that replicate the anatomy and function of intact tissue. Of particular interest are systems that replicate key functions of major organs (e.g., skin, kidney, lung and the gastro-intestinal track) and the ability to incorporate immunological function in these models.

C. Alternative assays and integrated strategies to assess dermal irritation, dermal absorption, dermal hypersensitivity phototoxicity, and ocular toxicity.

D. Non-mammalian or invertebrate models for specific toxicities that utilize endpoint that are conserved across species so the results can be extrapolated to human risk.

E. Identification and validation of predictive biomarkers that can be used to obtain improved mechanistic information and/or serve as the basis for earlier endpoints in toxicological studies.

Other Topics Within the Mission of the Institute

For additional information on research topics, contact:

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NATIONAL EYE INSTITUTE (NEI)

The NEI supports research with respect to blinding eye diseases, visual disorders, mechanisms of normal visual function, preservation of sight, and the special health problems and requirements of individuals with impaired vision. Applications for all areas of vision research are encouraged. Examples that may be of interest to small businesses are provided below, but this list is not meant to be exhaustive.

Phase IIB Competing Renewal Awards

The NEI will accept Phase IIB SBIR Competing Renewal grant applications from NEI-supported Phase II SBIR awardees to continue the process of developing technologies that ultimately require federal regulatory approval or require extraordinary time and effort in the Research and Development phase. Such technologies include, but are not limited to, pharmacologic agents, biological products, and devices related to the mission of the NEI. This renewal grant should allow small businesses to reach a stage where interest and investment by third parties is more likely. The Competing Renewal application must be a logical extension of a previously completed NEI-supported Phase II (R44) SBIR grant. NEI grantees seeking SBIR Phase IIB Competing Renewal funding must submit an application within a period no later than the first six receipt dates following expiration of the previous Phase II budget period. Budgets up to $750,000 total costs per year and time periods up to two (2) years may be requested for this Phase IIB Competing Renewal opportunity.

Potential applicants are strongly advised to contact Dr. Jerome Wujek (contact information provided below) before beginning the process of putting an application together.

The following examples would make appropriate topics for proposed NEI SBIR Phase IIB Competing Renewal projects. These are meant for illustrative purposes only and are not exclusive of other appropriate activities:

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants. Some in vivo or in vitro studies would be expected to have been carried out in Phase I or the initial Phase II grant.
- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or New Drug Application (NDA).
- FDA-required pre-clinical and clinical safety and effectiveness studies of medical devices and tissue engineered products for an Investigational Device Exemption (IDE) or Pre-market Approval (PMA).
- FDA-required evaluation of novel imaging approaches for diagnostic purposes.

General Research Topics

NEI is interested in providing support for the development of new technologies, strategies, research tools, reagents and methods that can be applied to basic and translational research which will benefit vision health. This encompasses research and development of innovative enabling technologies in areas of genomics, proteomics and nanotechnology. More specific topics include drug discovery, high throughput assays, drug delivery systems, gene therapy and cell-based therapies, development of in vitro and in vivo disease models, surgical devices and materials, telemedicine and teaching tools, and design and fabrication of new or improved ophthalmic instruments for diagnosis and treatment of eye disorders.

Retinal Diseases Program

Research and development of new therapeutic approaches for inflammatory and degenerative diseases and for inhibition of abnormal angiogenesis in the retina and choroid; development of better methods of diagnosing and treating diabetic retinopathy and other vascular diseases; development of non-invasive techniques for early diagnosis of macular degeneration and other retinal degenerative diseases; development of instruments and procedures for improved surgical management of retinal detachments; development of retinal prostheses to help restore visual function; development of methods for cell or tissue transplantation.

Corneal Diseases Program

Research and development of new therapeutic agents and drug delivery methods for the treatment of corneal injury, infection, dry eye and other ocular surface disorders; development of new biomaterials for corneal prostheses and corneal transplants; development of instruments and procedures for correcting the refractive power of the cornea and/or measuring the cornea's optical properties or other physiological properties.

Lens and Cataract Program

Research and development of new approaches in the post-operative management of cataract surgery; development of new surgical instruments for cataract extraction and new biomaterials for replacement of the natural lens; development of accommodative intraocular lenses.

Glaucoma and Optic Neuropathies Program

Research and development of new therapeutic agents, instruments, and procedures for the diagnosis and treatment of glaucoma; development of non-invasive methods to measure changes in the optic nerve head and retinal fiber layer.

Strabismus, Amblyopia, and Visual Processing Program

Research and development of new approaches to detect and treat strabismus and abmlyopia; development of new tools and techniques for vision screening; development of innovative techniques to study factors that facilitate regeneration and guidance of nerve fibers.

Visual Impairment and Blindness Program

Research and development of instruments and methods to better specify, measure, and categorize residual visual function; development and evaluation of optical, electronic, and other devices that meet the rehabilitative and everyday living needs of blind or visually-impaired persons.

Myopia and Refractive Error

Research and development of instruments and procedures for diagnosing or treating myopia; development of new or improved methods and materials for correcting the refractive power of the eye and/or measuring the eye's optical properties or other physiological properties; new materials and manufacturing processes for eyeglasses and contact lenses.

Additional Information

The NEI's programs are described in more extensive detail in documents which are available from the Institute. For additional information about the research programs of the NEI, please visit our home page at http://www.nei.nih.gov.

For more information on research topics, contact:

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Research Resources Officer
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National Eye Institute
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For administrative and business management questions, contact:

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Grants Management Officer
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NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

The NIGMS supports research and research training in the basic medical sciences and related natural and behavioral sciences and in specific clinical areas (i.e., clinical pharmacology, trauma and burn injury, sepsis and anesthesiology). The NIGMS also supports health-related research that is otherwise not assigned to another of the PHS components. The three divisions and one center that support research of potential interest to small businesses and their collaborators include:

Division of Cell Biology and Biophysics

Division of Genetics and Developmental Biology

Division of Pharmacology, Physiology, and Biological Chemistry

Center for Bioinformatics and Computational Biology

For additional information about areas of interest to the NIGMS, please visit our home page at http://www.nigms.nih.gov. This site includes staff contact information by program area (http://www.nigms.nih.gov/About/ContactByArea.htm). It also includes links to program announcements that highlight NIGMS areas of special emphasis (http://www.nigms.nih.gov/Research). In some cases, these announcements specifically mention the SBIR and STTR grant mechanisms, in most cases they do not. However, it is clear that small businesses could make contributions to the research objectives described in these announcements.

Phase IIB Competing Renewal Awards

NIGMS will accept Phase IIB SBIR-only Competing Renewal grant applications to continue the process of developing products that ultimately require 1) clinical evaluation, 2) approval by a Federal regulatory agency, and 3) continuing refinements to durable medical equipment (DME) designs such as cost reduction, testing for safety, durability, and reliability, and meeting or establishing standards. This renewal grant should allow small businesses to get to reach a stage where interest and investment by third parties is more likely. Such products include, but are not limited to biological products, devices, drugs, medical implants, etc. related to the mission of the NIGMS. The previously funded Phase II SBIR grant need not have been submitted in response to a particular solicitation, as long as the research is appropriate to the purpose of this solicitation. Budgets up to $750,000 total costs per year and time periods up to 2 years may be requested for this Phase IIB Competing Renewal opportunity. These awards are intended to support completion of research needed to obtain an IND or IDE. Applicants must provide evidence that they have consulted formally with the FDA concerning the research needed for the development of a drug, biologic or medical device and that the proposed research will address these regulatory

requirements. Such evidence should include FDA correspondence from a pre-IND meeting for an IND application or a pre-IDE meeting for an IDE application, and the status of the project in a timeline related to Federal regulatory approval processes.

Prospective applicants are strongly encouraged to contact NIH staff listed at the end of this NIGMS topics announcement prior to submission of a Phase IIB Competing Renewal application. Prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Division of Cell Biology and Biophysics

Research on membrane synthesis, structure, and function; membrane models; membrane transport; cell division; cell organization; cell motility; and biophysics of proteins, nucleic acids, and biological assemblies, including viral entry, packaging, maturation, and release, as well as the development of instrumentation, components, and methods for the analysis of cellular components and macromolecules by imaging, spectroscopy, and diffraction analysis.

SBIR and STTR applications on the application of cell biology, biophysics, biochemistry, physics, mathematics, and chemistry to biomedical problems, and the development of instrumentation to facilitate research in cell biology and biophysics, such as, but not limited to, the topics listed below are welcome.

A. Development and improvement of methods for the expression, solubilization, and purification of milligram quantities of regulatory, cellular, and membrane associated proteins, as well as for the preparation of specifically labeled macromolecules and the recovery of proteins from inclusion bodies.

B. Development of novel ligands, inhibitors, and other probes for spectroscopic and microscopic analysis of cellular assemblies and viral structures, macromolecules and components, their localization and function in vivo and at a single molecule level.

C. Development of instrumentation, devices, and methods for detecting in real time, analyzing, and separating biologically important compounds, macromolecules, and their interactions.

D. Development of new methods and materials directed toward the solution of biological macromolecule structures by, but not limited to, x-ray diffraction, electron diffraction, and NMR spectroscopy.

    1. New methods for the determination of the structures of membrane associated proteins.
    2. New methods for the determination of macromolecular structures in a high throughput mode, including improved detectors, data collection, automated data analysis, and faster software for structure calculations and comparisons.
    3. New methods designed to improve the efficiency of beam line use at synchrotrons.
    4. New methods and technology which enhance the efficiency and reduce the costs of structural genomics protein structure determination pipelines.
    5. New methods to facilitate the structure determination of large macromolecular assemblies.

E. Development of technology for the imaging of molecules and cells, including but not limited to:

1. Reagents, methods, instrumentation and software for existing and potential kinds of microscopy of molecules and cells (including light, electron, X-ray, scanning probe, and others). Improved probes and supporting technologies for dynamic (real-time) imaging of molecules and molecular events in living cells by light microscopy.
2. Reagents, methods, and software for conventional and cryo-electron microscopy, including automated apparatus for controlled and reproducible specimen preparation.
3. Instrumentation, methods and technologies for analysis and manipulation of cells, subcellular components, and single molecules, including atomic force microscopy, atomic forceps and tweezers, and solid state microscopy.
4. Development of analytical systems and tools such as imaging systems and probes, to be used at the nanoscale.
5. Methods, probes, and data analysis for spectroscopy, including magnetic resonance, fluorescence spectroscopy, and EPR.

F. Theoretical methods for, but not limited to:

1. Analysis of macromolecular structures.
2. Prediction of the three dimensional structures of biological macromolecules.
3. Improved methods for structure-based drug design.
4. Improved methods for the simulation and prediction of the dynamics of biological macromolecules.

G. Development of computerized tools that might be used in the presentation of the concepts of cell and structural biology to audiences at a variety of levels.

Division of Genetics and Developmental Biology

Research on developing a better understanding of fundamental processes and mechanisms of development and inheritance in health and disease. Support of basic topics in genetics and developmental biology, including nucleic acid chemistry, the structure of genetic material, the mechanisms of transmission and expression of genetic information, cellular regulation of growth and differentiation, and population genetics. Areas that may be of interest to small businesses include, but are not limited to:

A. Development of computer software for the analysis of the primary and secondary structures of nucleic acids as these relate to genetic problems.

B. Improvement in procedures for the separation and analysis of nucleic acids and proteins as these relate to genetic problems.

C. Improvement of methodology (technology) for genetic analysis (e.g., gene expression, probes).

D. Development of probes for detection of human genetic polymorphisms, including disease genes.

E. Development of improved procedures for cytogenetics and diagnostic array technology.

F. Improvement in procedures (statistical, computational, laboratory) for the analysis of gene flow and gene dynamics in human populations.

G. Development of improved vectors for gene transfer.

H. Development of valid animal models for genetic diseases and birth defects.

I. Development of quantitative approaches to the analysis of complex biological systems.

J. Development of tools and technologies to detect and monitor complex human phenotypes or traits.

K. Development of technology to derive and expand pluripotent cell populations from non-embryonic sources, for example, induced pluripotent stem cells (iPS).

L. Development of improved technology to scale up the growth of induced pluripotent stem cells in culture and to regulate their differentiation state

M. Development of markers, reagents and tools to characterize the unique properties of iPS cell lines and to distinguish them from adult stem cells and more differentiated cells.

N. Development of existing human embryonic stem cell lines and new or existing iPS cells as a model system for drug discovery.

O. Development or improvement of methodology for generation of antibodies or other affinity reagents for proteins and other small molecules in non-mammalian genetic model systems.

P. Development of methods for chemical modifications that improve the properties of nucleic acids for gene silencing.

Q. Improvement in procedures (statistical, computational, laboratory) for the high- and medium-throughput analysis of gene expression patterns and regulatory networks.

R. Development or improvement of methods for high throughput detection of epigenomic changes.

S. Development or improvement of methods for characterizing the metabolic interactions of complex communities of microorganisms particularly those involved in host-microbe interactions.

T. Development of improved or novel methodology for structure/function analysis of very large macromolecular complexes involved in transmission or expression of genetic material.

Division of Pharmacology, Physiology, and Biological Chemistry

Research related to the actions of therapeutics, including anesthetics, and the development of biotechnological methods for their production and investigation. Research on cell signaling molecules and signaling intermediates, particularly those related to G-protein coupled receptors. Research in the field of glycomics, especially tool and methods development for this emerging field. Research on pain management as it relates to anesthesia and the perioperative period. Research on responses to traumatic injury, including burn injury, and methods to mitigate these responses. Research on wound healing and tissue repair. Research on the causes and treatments for common complications of critically ill patients (sepsis, systemic inflammatory response syndrome, multiple organ failure), especially directed towards the role of the inflammatory and innate immune responses. Research leading to new knowledge of physiological functions at the molecular, cellular, and organ systems levels. Research on the structure, function, and biosynthesis of cellular components and cellular metabolism, bioenergetics, and mechanisms of enzyme action, regulation, and inhibition. Research leading to the synthesis of new chemical entities or development of new chemical methods to probe biological phenomena or to alter the behavior of biological systems. Examples include, but are not limited to:

A. Methods for isolation, characterization, and production of natural and bio-engineered products.

   1. Metabolic engineering for the production of biochemicals through genetic and bioengineering manipulation of biosynthetic pathways.
   2. Biosensors for use both in vivo and in vitro in process engineering.
   3. Methods for rapid purification of natural products.
   4. Methods for rapid determination of natural product structures.
   5. Methods for efficient production of natural products.
   6. Universal expression systems for heterologous production of natural products.

B. Development of innovative synthetic chemistry.

1. Catalytic asymmetric methods and methods for large-scale synthesis.
2. New methods applicable to combinatorial library construction, design, analysis, and/or handling.
3. Improved methods for preparation of isotopically labeled amino acids, peptides, proteins, and prosthetic groups, and therapeutic agents.

C. Development of enzymes, catalytic antibodies, ribozymes, artificial enzymes, and host molecules as drugs or synthetic tools.

1. Synthesis of suicide substrates, affinity labeling agents, and transition state analogs as potential therapeutic agents.
2. New enzyme assays to reduce the reliance on radio-isotopes.
3. General approaches for high throughput screening.

D. Isolation, characterization, and development of factors involved in tissue repair and wound healing, i.e., growth factors. Tissue engineering. Development of artificial skin and skin replacements.

E. Development of strategies, methods, or molecular based treatments to improve the speed and outcome of wound healing or to induce regeneration as a substitute to normal wound healing.

F. Metabolomics/metabonomics of injury and/or critical illness.

G. Improved systems for collection, processing, and analysis of real time physiological data from injured or critically ill patients. Application of systems biology or complexity theory approaches towards understanding the physiology of injured and critically ill organisms.

H. Development of tools, software, algorithms, etc. needed to link clinical, demographic, physiological, genomic, proteomic or other datasets of injured or critically ill organisms.

I. Development of strategies, methods, or new technologies to improve the delivery, monitoring, safety and efficacy of anesthesia.

J. Research to improve drug design.

1. Methods for understanding of structure-activity relationships.
2. Mechanisms of drug-receptor interactions.
3. Development of molecular diversity libraries.

K. Research to improve drug bioavailability by improved understanding of factors that influence absorption, metabolism, transport, or clearance of therapeutics and underlying mechanisms.

1. Determination of structure-activity relationships for drug metabolizing enzymes.
2. Determination of structure-transport relationships for active and passive transport of drugs and metabolites.
3. Research on drug transporter structure, function, and regulation.
4. Development and validation of models for prediction of drug bioavailability and metabolism in humans.
5. Research on inter- and intra-individual differences in bioavailability.
6. Methods to improve sensitivity, accuracy, speed, and simplicity for measurements of drugs and their metabolites in complex biological matrices.

L. Application of pharmacokinetic and pharmaceutical principles to the study of large biomolecules, such as proteins, polypeptides, and oligonucleotides.

M. Development of novel targeted delivery systems for both conventional drugs and large molecules.

N. Research to discover, detect, and understand the genetic basis of individual differences in drug responses.

1. Identification of polymorphisms in human drug receptor and drug metabolizing enzymes.
2. Development of laboratory-based and computational approaches for pharmacogenetic and pharmacogenomic mechanistic studies.
3. Development of statistical analysis methods related to research in pharmacogenomics.
4. Development of genotyping and phenotyping tests to support research in pharmacogenomics.
5. Development of proteomic and metabolomic methodologies related to research in pharmacogenomics.
6. Creation of appropriate databases, specimen, and cell culture collections to support research in this area.

O. Development of novel in vivo and in vitro methods to predict toxicities of pharmacologic agents.

P. Development of differentiated hepatic cell lines from human stem cells that are equivalent to adult hepatocytes to characterize metabolic profiles of pharmacological candidates by phase 1 and 2 enzymes.

Q. Development of bioinformatic, mathematical, and/or computational approaches/resources and/or pharmacokinetic modeling programs which utilize ADME parameters of drugs and pharmacogenomic information of individual patients or patient populations to reduce adverse drug reactions in individual patients.

R. Development of ontologies and modules useful for combining and mining databases containing genotype and phenotype information in order to discover correlations for drug effects, either therapeutic or adverse.

S. Development of methods and tools for the field of glycomics including but not limited to:

1. Development of carbohydrate specific databases as well as informatics tools to mine carbohydrate data bases.
2. Development of new facile methodologies to rapidly synthesize and expand defined carbohydrate libraries, especially those applicable for screening for glycomic biomarkers, assessing carbohydrate protein interactions, and development of glycan arrays.
3. Development of linker methods for carbohydrates.
4. Development of methods for exploring glycan-protein, glycan-lipid, and glycan-glycan interactions.
5. Development of well characterized commercial sources of glycosyltransferases and glycosidases that can be used as research tools by the scientific community.
6. Development of methods for high throughput structural analysis of the glycoconjugates of proteins and lipids.
7. Development of defined antibodies as tools for the field of glycomics.

T. Development and application of methods and materials for the elucidation of membrane protein structures at or near atomic resolution.

1. Novel vector and host cell systems for over-expression of membrane proteins, in both unlabeled and isotopically labeled forms.
2. Novel and high purity detergents and non-detergent solubilization agents for the purification and crystallization of membrane proteins.
3. Apparatus to facilitate crystallization and manipulation of fragile crystals for data collection.

4. Reagents for heavy atom derivatization of membrane protein crystals.

U. Development of high-throughput methods for sequencing and resequencing of mitochondrial genes and relevant nuclear genes and for proteomic and/or functional profiling of mitochondria in diagnosis of mitochondrial diseases.

V. Development of methods to create site-directed and knock-out mutations of mitochondrially-encoded genes in higher eukaryotic cells and experimental animals.

W. Development of new metal ion chelators and other tools to probe and/or alter the localization and concentration of metal ions in cells and in whole organisms. Research to exploit metal metabolism and metal-regulated cellular control and cell-cell signaling processes to probe and/or alter cell function. Research to develop investigational and therapeutic applications of metal-complexes and to understand the factors governing their pharmacology and toxicology.

X. Development of high-throughput methods and strategies to characterize the function of proteins and enzymes and/or define the functional interrelationships of proteins and enzymes.

Y. Development of research tools to promote scientific collaboration in any of the above areas of research. For example, applications software for secure peer-to-peer networking to facilitate the exchange of scientific data and research materials or to construct a searchable distributed database.

Z. Development of tools to characterize oxidative stress and oxidative stress related molecules (NO, peroxynitrite, hydrogen peroxide, lipoxidation products modified proteins, DNA modifications, etc.) including the extent and/or localization (by organ/tissue/cell/organelle) of oxidative stress.

Center for Bioinformatics and Computational Biology

A. Development of tools and methods to model complex biological systems that fall within the mission of NIGMS.

B. Development of tools and methods for behavioral and social modeling.

C. Development and enhancement of databases and data formats for activities that fall within the mission of NIGMS.

D. Development of tools and methods for scientific visualization, data mining, and integration and interoperability of different databases and varying modalities of data.

E. Design and development of software and hardware for improving the effectiveness of computational approaches in biomedical research.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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Pharmacology, Physiology, and Biological Chemistry
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NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)

The NHLBI plans, conducts and supports research, clinical trials and demonstration and education projects related to the causes, prevention, diagnosis and treatment of heart, blood vessel, lung, and blood diseases and sleep disorders. It also supports research on the clinical use of blood and all aspects of the management and safety of blood resources. The NHLBI SBIR/STTR program fosters basic, applied, and clinical research on all product and service development related to the mission of the NHLBI.

For more specific information about areas of interest to the NHLBI and a link to the NHLBI Strategic Plan, please visit our home page at http://www.nhlbi.nih.gov.

Research topics of interest include, but are not limited to research and development under the following specific initiatives as well as the topic areas listed under each of the NHLBI Divisions below:

Phase IIB Competing Renewal Awards

The NHLBI will accept Phase IIB SBIR Competing Renewal grant applications from NHLBI-supported Phase II SBIR awardees that propose to perform research required to obtain Food and Drug Administration (FDA) clearance or approval of the Phase II product in the form of a Premarket Notification (510(k)), Investigational Device Exemption (IDE), Premarket Approval Application (PMA), Humanitarian Device Exemption (HDE), Biologics License Application (BLA), Investigational New Drug (IND), or New Drug Application (NDA). This renewal grant should allow small businesses to commercialize their product or get to a stage where interest and investment by third parties is more likely. Such products include, but are not limited to medical devices, biological products, and drugs related to the mission of the NHLBI. The Competing Renewal application must be a renewal and logical extension of a previously completed NHLBI-supported Phase II (R44) SBIR grant. NHLBI grantees seeking SBIR Phase IIB Competing Renewal funding are to submit an application no later than the first six receipt dates following expiration of the previous Phase II project budget period. Exceptions to this submission timing are rare and must first be discussed with NHLBI program staff.

Budgets up to $1,000,000 total costs per year and time periods up to 3 years may be requested for this Phase IIB Competing Renewal opportunity.

NHLBI Phase II awardees planning to apply to this renewal opportunity are expected to have already initiated interactions with the FDA, so that they understand the regulatory process and factor that into

their renewal research plan. Applicants must include a brief description of the FDA regulatory pathway being pursued for their project and a timeline for this pathway in the Experimental/Research Design and Methods Section of the application. An applicant must also submit evidence that they have contacted the appropriate FDA Center and that their research plan and objectives follow FDA requirements or guidance for the further development of their proposed medical device, drug, or biologic. Examples that provide evidence of FDA interaction are letters or emails between the company and the appropriate FDA Center personnel or meeting minutes concerning a presubmission meeting or regarding a 510(k), IDE, PMA, HDE, BLA, IND, or NDA application. Copies of these letters, emails or minutes should be attached in the Letters of Support section in the PHS398 Research Plan Component. Applicants may also provide details of their interaction with the FDA in the description of their regulatory pathway. This should include the FDA contact and date of interaction.

An updated commercialization plan is also required. Providing evidence of partnerships between the SBIR Phase IIB Competing Renewal applicant and third-party investors and or/strategic partners is encouraged.

Prospective applicants are strongly encouraged to contact NHLBI program staff prior to submission of an SBIR Phase IIB Competing Renewal application. Although it is not required, prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Brief project description (less than one page)
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions

Examples of research that would be considered responsive to this announcement are listed below for illustrative purposes and are not exclusive of other appropriate activities.

- FDA-required pre-clinical studies beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants.

- Completion of pre-clinical and clinical studies required by the FDA for an Investigational New Drug (IND) application and New Drug Application (NDA).

- FDA-required pre-clinical and clinical safety and effectiveness studies of medical devices and tissue engineered products for an IDE, 510(k) clearance of PMA approval.

- FDA-required biocompatibility studies of surface materials of putative medical implants or other studies needed for 510(k) clearance or PMA approval.

- FDA-required assessments of novel imaging systems.

If the application results in an award from NHLBI, the grantee will be requested to provide information to their Project Officer about the ongoing status of their interactions with the FDA and any regulatory issues that might come up as the project proceeds. If feasible, grantees should formally invite their Project Officer to participate with them in their interactions with the FDA during the course of the project. NHLBI also encourages the grantee to inform their NHLBI Program Officer when they have received the relevant FDA clearance.

Helpful FDA websites for initiating FDA communication:

Office of Combination Products
http://www.fda.gov/oc/combination/

Center for Drug Evaluation and Research (CDER)
http://www.fda.gov/cder/index.htmlhttp://www.fda.gov/cder/

Drug Approval Databasehttp://www.fda.gov/oc/combination/
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/

CDER "Information for Industry"
http://www.fda.gov/cder/info/industry.htm

Center for Biologics Evaluation and Research (CBER)
http://www.fda.gov/cber/index.html

Center for Devices and Radiological Health (CDHR)
http://www.fda.gov/cdrh/index.html

CDRH Device Advice
http://www.fda.gov/cdrh/devadvice/

Contacts in CDRH, including DSMICA (Division of Small Manufacturers, International, and Consumer Assistance
http://www.fda.gov/cdrh/contacts.html

CDRH User Fee Information
http://www.fda.gov/cdrh/mdufma/index.html

Device Clearances and Approvals
http://www.fda.gov/cdrh/mdufma/index.html Select: “Premarket Approvals:” or Premarket Notifications (510(k))s.

Direct questions about scientific/research issues to:

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Lung and Sleep

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Prevention and Population Sciences

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Cardiovascular Sciences

The NHLBI Division of Cardiovascular Sciences (DCVS) plans and directs research grant, contract, and training programs to support basic, clinical, population, and health services research on the causes, prevention, and treatment of cardiovascular diseases. These programs encompass institute and investigator-initiated basic research, targeted research, specialized centers and clinical trials. The DCVS maintains surveillance over developments in its program areas and assesses the national need for research on the causes, prevention, diagnosis, and treatment of cardiovascular disease. The DCVS ensures that effective new techniques, treatments and strategies resulting from medical research are transferred to the community through professional, patient, and public education programs in a timely manner. DCVS-supported research also includes a broad array of epidemiological studies to describe disease and risk factor patterns in populations and to identify risk factors for disease; clinical trials of interventions to prevent and treat disease; studies of genetic, behavioral, sociocultural, and environmental influences on disease risk and outcomes; and studies of the application of prevention and treatment strategies to determine how to improve clinical care and public health.

The Division is comprised of three programs, in which reside eight branches, and the Office of Research Training and Career Development, and the Office of Biostatistics Research. These are described below.

Adult and Pediatric Cardiac Research Program

Atherothrombosis and Coronary Artery Disease Branch. Supports basic, translational, and clinical research on the etiology, pathogenesis, prevention, diagnosis, and treatment of coronary artery disease and atherothrombosis.

Heart Development and Structural Diseases Branch. Supports basic, applied, and clinical research in normal and abnormal cardiovascular development as well as the etiology, pathogenesis, prevention, diagnosis, treatment of pediatric and adult structural heart disease, and heart transplantation.

Heart Failure and Arrhythmias Branch. Supports basic, translational, and clinical research on normal cardiac function and pathogenesis to improve the diagnosis, treatment, and prevention of heart failure and arrhythmias.

Basic and Early Translational Research Program

Advanced Technologies and Surgery Branch. Supports basic, translational, and clinical research on innovative and developing technologies for the diagnosis, prevention, and treatment of cardiovascular diseases.

Vascular Biology & Hypertension Branch. Supports basic, translational, and clinical research on vascular biology and the etiology, pathogenesis, prevention, diagnosis, and treatment of hypertension and vascular diseases.

Population Sciences Program

Clinical Applications and Prevention Branch. Supports, designs, and conducts research on behavioral, environmental, clinical, and healthcare approaches to reduce occurrence and consequences of cardiovascular diseases.

Epidemiology Branch. Supports, designs, and conducts research in the epidemiology of cardiovascular, lung, blood and sleep diseases and disorders.

Women's Health Initiative Branch. Supports clinical trials and observational studies to improve understanding the causes and prevention of major diseases affecting the health of women. Current studies focus on cardiovascular disease, cancer, and fractures, in collaboration with NCI, NIAMS, NIA, NINDS, and ORWH.

Office of Research Training and Career Development. This office supports research training and career development programs for individuals at many educational levels, from high school to faculty, as well as training programs for individuals from under-represented groups. Many of these programs are designed to take emerging and promising scientific and technological advances from discovery through pre-clinical and clinical studies. A K12 institutional training program, Research Career Development in Vascular Medicine, was established in 2007 to provide comprehensive clinical research training for physicians wanting to specialize in vascular medicine. The office also collaborates with the scientific community and professional organizations to ensure that training programs meet both the current and future needs of the cardiovascular research workforce.

Office of Biostatistics Research (OBR). Provides statistical expertise to members of all Divisions of the NHLBI and performs diverse functions in planning, designing, implementing and analyzing NHLBI-sponsored studies. The OBR is concerned with designing efficient studies and monitoring data while studies are ongoing. The OBR's methodological interest concern survival analysis, longitudinal data analysis, and efficient study designs, including the monitoring of ongoing clinical studies for efficacy and safety. Recently the OBR has made contributions to statistical genetics and has extended its expertise to bioinformatics.

Research topics of interest to the Division of Cardiovascular Sciences include but are not limited to the following:

A. Clinical research/intervention studies designed to improve cardiovascular disease outcomes
    1. Approaches to facilitating adoption of evidence-based guidelines
    2. Approaches to improving care of cardiovascular patients transitioning from hospital to ambulatory or home care
    3. Approaches to improving prevention and treatment of ischemic heart disease (IHD), including prevention of recurring events and optimization of functional capacity in patients with IHD

B. New or improved clinical trial methodologies, including modeling and simulations and "value-of-information" research

C. Novel and improved lifestyle interventions, including matching patients to lifestyle, intervention, or treatment

D. Health-care systems and outcomes research, including development of new quality measures for evidence-based cardiovascular health care

E. Models of behavior modification and other approaches to behavior change

F. Preventative Approaches
    1. Nutrition and dietary interventions and products
    2. Technologies to control weight
    3. Stress reduction interventions
    4. Smoking cessation interventions
    5. Physical activity interventions
    6. Interventions to promote healthy lifestyles, adherence to medications, and cardiac rehabilitation, including stress and exercise

G. New or improved treatment agents or strategies, including medications and devices

H. New or improved methods, tools, and techniques for:
    1. Screening, assessment, and tracking of hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases
    2. Communication of research results
    3. Collection, transmission, management and analysis of clinical data
    4. Population tracking
    5. Communication with minority and low-income populations
    6. Disease self-management, including telemetric monitoring
    7. Assessing polypharmacy, particularly for the elderly

I. New or improved measures, analytical methods, and instruments for:
    1. Gene expression in individuals
    2. Heart failure, including diastolic heart failure
    3. Small vessel disease
    4. Behavioral and lifestyle variables, e.g., diet and physical activity (Note: Measures include survey questionnaires.)

5. Psychosocial assessment, especially in minority populations, including chronic social stress, depression, and discrimination
6. Sleep useful for population based studies
7. Impaired glucose tolerance
8. Nutrition and physical activity
9. Patient responses to behavioral or medical interventions
10. Quality of life and other components of health status
11. Patient adherence/compliance
12. Cell immortalization, storage and distribution service

J. Materials and Devices

1. Angioscopes with increased flexibility and enhanced resolution
2. Medical implants (heart valves, vascular grafts, stents, pacemakers, defibrillators, intracardiac hemodynamic monitors, etc.):
    a. Novel technologies (e.g., nanofabrication), designs and materials
    b. Failure prediction/analysis
    c. Manufacturing
    d. Monitoring
    e. Preservation methods
    f. Quality assurance and quality control
    g. Reference biomaterials for evaluation of biocompatibility
    h. Reliability
    i. Biological response
    j. Devices designed specifically for pediatric patients and/or patients with congenital heart disease
3. Circulatory support systems:
    a. Artificial heart
    b. Ventricular assistance
    c. Automatic control
    d. New animal models for in vivo testing
    e. Percutaneous and transcutaneous transmission of electrical energy
    f. Implantable rechargeable batteries and alternate power sources
4. Percutaneous valve technology
5. Molecular probes
6. Biological, chemical, and mechanical sensors
7. Diagnostic instrumentation for the mouse and rat
8. Devices to improve resuscitation outcomes
9. Point-of-care (POC) devices for monitoring, diagnostics, and personalized medicine

a. Biosensors for detection of early ischemia in the absence of necrosis

b. Minimally-invasive monitoring of heart rhythm, cardiac hemodynamics and/or blood pressure

K. Computing and Informatics

1. New or Improved Software for:

a. Clinical trials

b. Epidemiology studies

c. Literature abstracting

d. Meta-analysis

e. Statistical analysis

f. Shared clinical decision-making

g. Monitoring and providing feedback to patients and providers in clinical care settings

h. Analysis of context-dependent genetic effects

i. Longitudinal data analysis

j. Microarray data analysis

k. Automated systems for genotyping quality control and error checking

l. Sequencing data analysis

2. Computerized systems to support evidence-based clinical practice in prevention and treatment of hypercholesterolemia, coronary heart disease, heart failure, hypertension, and other cardiovascular risk factors and diseases

3. Interactive databases

4. Computational Modeling:

a. Systems biology approaches to study complex disease

b. Mathematical and computer modeling of the cardiovascular system in health and disease. Examples include: vessel wall biology; hemodynamics in complex congenital heart disease; structure, function, and electrical activity of the normal and diseased heart; blood pressure regulation

c. Optimization of implantable defibrillator algorithms for arrhythmia prediction, efficient intervention, device fault detection or early failure detection

5. Informatics:

a. Novel use of information technology to enhance adherence to medical regimens or promote translational research. Examples include: use of the Electronic Health Record (EHR) to improve clinical care; research to interface clinical trial and registry data bases with common source data found in the EHR.

b. Approaches to integrating diverse types of data from cardiovascular research, including genomic data

L. Animal Models

1. Development of phenotypic screening methods in the mouse for cardiovascular diseases

2. Animal models for assessing genetic determinants of disease

3. Animal models of cardiovascular diseases. Examples include: complications of diabetes mellitus, cerebrovascular disease, arrhythmias, aortic aneurysms, and lower extremity arterial disease

M. OMICS Methods and Analytical Approaches

1. Genetics and epigenetics:
    a. Relationship, structure, and function of genes and their products
    b. Technologies for gene discovery, assessment, and diagnostics
    c. Genetics of complex diseases –gene/gene and gene/environment interactions, epigenetics (heritable, non-sequence variations in DNA and its associated proteins)
    d. Pharmacogenetics/Pharmacogenomics and personalized medicine
2. Genomics
3. Metabolomics
4. Proteomics
5. RNA - Development of new and improved antisense agents and RNA interference (RNAi) technologies for cardiovascular disease therapies
6. Sequencing
7. Integration and combined analysis of OMICS data

N. Preventive Approaches

1. Nutrition and dietary interventions and products
2. Technologies to assess energy balance and control weight

O. Transplantation

1. Methods to induce tolerance to cardiac allografts
2. Non-invasive methods to diagnose cardiac allograft vasculopathy and cellular and antibody mediated rejection
3. Strategies to enhance donor utilization such as better preservation methods for cardiovascular tissues or organs
4. Immunosuppression-including renal sparing strategies
5. Pediatric heart transplantation

P. Training and Education

1. Community education and demonstration research studies
2. Studies of cardiovascular disease information, education, prevention, and treatment systems for use in primary medical care and home care, including care by family caregivers
3. Training techniques and modules
4. Interactive web-based programs for health promotion
5. Instructional, research, and clinical computer programs for the normal and abnormal cardiovascular system
6. Educational materials and approaches targeting self-directed or supervised exercise therapy for (1) treatment and management of peripheral arterial disease, coronary heart disease, or heart failure and (2) for children and adults with congenital heart disease to improve exercise capacity and to prevent or treat obesity in this population.

Q. Diagnostic and Therapeutic Approaches

1. Device-Related:

a. Interventions to improve resuscitation outcomes
b. Device-based approaches aimed at preventing cardiac ischemia/reperfusion injury
c. Improved devices and technologies to detect and treat arrhythmias
d. Robotics in treatment of cardiovascular disease. For example: treatment of congenital heart disease
e. Computer-assisted surgery for treating cardiovascular diseases
f. Point-of-care (POC) approaches and techniques
g. Technologies targeting self-directed or supervised exercise therapy for treatment and management of peripheral arterial disease
h. Non-invasive device strategy to monitor ambulatory heart rhythm over extended period

2. Cell or Gene-Based:
   a. Development of gene-based or cell-based therapies for cardiovascular diseases
   b. Tissue engineering and cell or gene-based approaches for repair or replacement of damaged or diseased tissue
   c. Genetic testing or screening for inherited cardiovascular diseases and defects
   d. Biomarkers and surrogate markers for risk assessment, detection, and monitoring of cardiovascular diseases
   e. Biomarkers for long term exposure to environmental factors including diet, physical activity, smoking, alcohol, and contaminants
   f. Development of viral and non-viral vectors for gene therapy for cardiovascular diseases
   g. Pro- and anti-angiogenic and vasculogenic genes, proteins and drugs
3. Other:
   a. Prognostic assays
   b. Approaches and technologies to measure lipid content in the blood
   c. Standardized assays of glycosolated hemoglobin
   d. Non-invasive methods of detecting cardiac rejection, particularly in infants and young children
   e. Non-toxic and selective molecular cages for delivering short-lived vasoactive agents to the vasculature
   f. High-throughput assays or screening for cardiovascular research and disease detection
   g. Non-invasive diagnostic tests. For example: salt sensitivity; vascular and renal tubular fluid dynamics
   h. Heart failure, early detection and treatment strategies
   i. Novel approaches to reduce cardiac ischemia/reperfusion injury following myocardial infarction
   j. Anti-hypertensive drugs from natural and synthetic sources
   k. Vaccines for the prevention or treatment of atherosclerosis or other cardiovascular diseases
   l. Technologies, tools, and/or processes to better study transient molecular complexes that are an integral part of normal cell physiology or that play a role in cardiovascular disease processes

m. Tools to investigate mitochondrial functions and interactions with cell components in vivo or in intact single cells

n. Atrial fibrillation, tools for non-invasive strategy for early detection and management

R. Imaging

1. Molecular and cellular imaging, including imaging to detect gene expression and to track viable implanted stem cells
2. Imaging methods to measure molecular events in living cells in real time. For example: luminescent dyes to measure toxic metabolic intermediates; optical imaging methods for dynamic tracking of reactive species within organelles; echogenic molecular imaging agents that signal early events in calcific aortic valve disease
3. New medical imaging systems, enhancements, equipment, materials, software, and applications
4. Imaging characterizing vessel walls and lesions
5. Clinical imaging in congenital heart disease
6. Neuro-imaging in hypertension
7. Radiologic phantoms mimicking the human cardiovascular system
8. High resolution functional and molecular imaging of the human lymphatic system
9. 3-D fetal echocardiography or magnetocardiography
10. Image-guided therapy: Catheter and imaging guidance system for mapping and ablation to treat cardiac arrhythmias
11. MRI-compatible diagnostic electrophysiology catheters and MRI-compatible ablation catheters
12. New ambulatory imaging of cardiac rhythm to detect irregular or aberrant atrial or ventricular impulses over long (week(s)) period of observation.

Lung Diseases

The NHLBI Division of Lung Diseases (DLD) maintains surveillance over developments in pulmonary research and assesses the Nation's need for research on the causes, prevention, diagnosis, and treatment of pulmonary diseases. Also within the purview of the Division are: technology development, application of research findings, and research training and career development in pulmonary diseases. The DLD plans and directs the research and training programs which encompass basic research, applied research and development, clinical investigations, clinical trials, and demonstration and education research. The Division has three branches: the Airway Biology and Disease Branch, the Lung Biology and Disease Branch, and the National Center on Sleep Disorders Research.

Airway Biology and Disease Branch. Focuses on basic and clinical research, education and training related to chronic obstructive pulmonary disease, asthma, cystic fibrosis, bronchiolitis, lung imaging, and airway function in health and disease.

Lung Biology and Disease Branch. Supports research, education, and training programs in lung cell and vascular biology, including pulmonary hypertension, lung development and pediatric lung diseases, stem cell biology, acute lung injury and critical care medicine, lung immunobiology and interstitial lung diseases, lung transplantation, lymphangioleiomyomatosis, lung imaging, and pulmonary conditions associated with AIDS including tuberculosis.

National Center for Sleep Disorders Research. Focuses on basic research using state-of-the-art approaches to elucidate the functions of sleep including the fundamental regulation of genomic function and circadian timing in peripheral tissues; patient-oriented research to improve the diagnosis and

treatment of sleep disorders; and applied research to evaluate the scope and health consequences of sleepiness and sleep disorders, especially sleep disordered breathing.

Research topics of interest to the Division of Lung Diseases include but are not limited to the following:

A. Diagnostic Tools

1. Computer algorithms for reading and comparing chest radiographs and scans (computed tomography, radioisotopes, etc.) using digitized images
2. Tools to diagnose and treat respiratory abnormalities during sleep in infants, children, and adults
3. Diagnostic proteomics and metabolomics, including methods for early diagnosis of lung disease and characterization of the function/dysfunction of particular cell types
4. Non-invasive measurement of blood gases, hemodynamics and respiratory function in infants, in children, and in adults
5. Non-invasive methodologies for measuring airways inflammation in asthma
6. Non-invasive markers of lung disease activity
7. Non-invasive methods to detect pulmonary thromboembolism, hypertension, and edema
8. Probes to monitor peripheral tissue oxygenation in vivo
9. Probes to non-invasively monitor arterial carbon dioxide
10. Use of ambulatory monitoring techniques to diagnose and manage respiratory disorders of sleep
11. Ambulatory monitoring of oxygenation in infants
12. Computerized tomography to quantify and monitor pulmonary disease processes
13. Virtual bronchoscopy (this is a radiologic 3D reconstruction of the lungs with imaging to approximate bronchoscopy)
14. Novel methods for bioassays
15. Methodologies that provide an objective and semi-quantitative assessment of sleepiness in children and adults
16. Non-invasive imaging technologies to assess neurophysiological and regional brain blood flow changes associated with sleep disorders and other causes of excessive daytime sleepiness
17. Develop placebos for inhaled medications used in clinical trials of lung diseases
18. Detection of injury and repair of the lungs (e.g. after aspiration, near drowning, ARDS)
19. Develop a spectrum of clinically relevant biomarkers (biosensors, bioimaging) on rate-limiting and downstream effects of CF and COPD pathophysiology (mucus production, hydration, inflammation, ion transport, lung disease heterogeneity)
20. Develop new sensitive markers of CF lung disease onset and progression in infants and young children that link to clinically meaningful outcomes and are suitable for showing a response to disease intervention. This might include radiographic (or other imaging) measures of structural lung disease in concert with measures of physiologic function at the macroscopic level

B. Information and Health Education Tools

1. Health information technologies to promote adoption and implementation of asthma clinical practice guidelines in medical practice

2. Health education methodologies for patients, families, or communities to prevent or cope with lung diseases or to reduce their impact, especially among people with asthma who are minorities or living in poverty
3. Information systems to coordinate patient management and monitoring among patients and health care professionals
4. Innovative smoking cessation programs
5. Interventions to reduce passive smoking exposure in infants and children
6. Use of interactive and computer technology to teach self management to asthma and chronic obstructive lung disease patients
7. Educational interventions to reduce the risk of cardiopulmonary disease and improve worksite productivity and school performance through the prevention and management of insufficient sleep and poor sleep environment conditions
8. Methods to improve patient adherence with sleep disordered breathing treatments
9. Develop and test novel and effective approaches to educate the public, physicians, and/or health care systems to increase patient and provider participation in lung and sleep research
10. Develop and test novel and effective approaches to increase patient and/or provider adherence to clinical practice guidelines for management of lung diseases and respiratory sleep disorders
11. Develop and test novel and effective approaches to build capacity for self-management of chronic lung diseases and sleep disorders

C. Materials and Devices

1. Blood substitutes to improve gas exchange
2. Emergency, portable, and servo-controlled ventilatory support devices
3. Improved aerosol delivery systems, particularly for young infants and/or children
4. Improved aerosol delivery systems for ventilated patients
5. Improved devices for continuous oxygen administration, including airline travel
6. Improved extracorporeal or implantable devices for blood gas exchange (artificial lung)
7. New approaches and technologies that can be used to engineer functional tissue, in vitro, for replacement or repair of damaged or diseased lung tissue, in vivo
8. Thrombo-resistant materials for extracorporeal or implantable devices for blood gas exchange and for indwelling catheters
9. Development of miniaturized devices for home monitoring and assessment of periodic breathing, infant apneas associated with hypoxemia, and sleep disordered breathing in adults.
10. Improved CPAP interfaces (i.e., nasal, face masks) for young children and individuals with craniofacial abnormalities
11. Devices to correct congenital disorders of the upper airway
12. Improved low-flow oxygen delivery systems (including cannula) that permit mobility for young children
13. Devices/materials for chest wall disorders (including scoliosis), such as minimally invasive spinal growth modulation instrument; implantable devices for self expansion (child to adult); absorbable biomaterials (rather than metal plates) for fracture repair
14. Develop placebos for inhaled medications used in clinical trials of lung disease

D. Methods

1. "Clean" animal models for Pneumocystis carinii infections
2. Culture Pneumocystis carinii in vitro
3. Determine viability and enumeration of infectious Pneumocystis carinii organisms
4. Development and standardization of in vitro systems for the study of pulmonary epithelial (airway) cells and pulmonary endothelial (vascular) cells
5. Identification of genes causing and modifying lung diseases
6. Identify and detect lung cell specific differentiation markers
7. Identify loss of epithelial integrity
8. Measurement of exhaled nitric oxide
9. Measurement of airway surface liquid
10. Measurement of pH in airways
11. Identify lung stem cell types
12. Identify species and strain differences of Pneumocystis carinii
13. Isolate, identify, and characterize cells found in pulmonary granulomas
14. Three-dimensional static, mathematical, cell culture models of airways and alveoli to define parameters determining aeropollutant absorption, deposition, and effects
15. Develop technologies and tools for use in genomic or proteomic investigations of pulmonary diseases
16. New technologies and instrumentation scaled for high-throughput phenotypic characterization of sleep in animal models
17. Development of high throughput screening methods of pharmaceuticals for lung diseases; for example, using induced pluripotent stem cells derived from lungs of patients with genetic lung disorders
18. High volume, inexpensive assays to assess variations in gene expression related to circadian and behavioral state (sleep and wakefulness)
19. Simultaneous assessment of physical activity and sleep. Dual-purpose ambulatory devices, equally suitable for the objective assessment of physical activity and sleep in population-based cohorts
20. Develop nanotechnology for non-invasive airway sampling

E. Treatments

1. Delivery of specific drugs (e.g., antioxidants, artificial proteinase inhibitors, surfactant) and cell-based reagents to the lungs for treatment of pulmonary and non-pulmonary diseases
2. Gene therapy for cystic fibrosis, alpha-1-antitrypsin deficiency, primary pulmonary hypertension, and other inborn errors of metabolism affecting the lungs
3. Improved aerosol delivery systems
4. Novel pharmacologic and gene therapy approaches for asthma, acute lung injury, idiopathic pulmonary fibrosis, and bronchopulmonary dysplasia
5. Pharmacological means of stimulating growth and repair of alveoli and reparative or restorative elastogenesis in lungs suffering emphysematous changes

6. Countermeasures for excessive daytime sleepiness, including methods that alter the output of the circadian clock to optimize sleep and wakefulness
7. New pharmacological agents for the treatment of sleep disorders, especially sleep disordered breathing
8. New vaccination/immunomodulatory strategies to prevent exacerbations of Chronic Lung Disease
9. Design of new and effective non-viral vectors and delivery systems for gene therapy targeted to lung disease.

Blood Diseases and Resources

The NHLBI Division of Blood Diseases and Resources (DBDR) plans and directs research and research training and career development programs, on the causes, prevention, and treatment of nonmalignant blood diseases, including anemias, sickle cell disease, and thalassemia; premalignant processes such as myelodysplasia and myeloproliferative disorders; hemophilia and other abnormalities of hemostasis and thrombosis; and immune dysfunction. Funding encompasses a broad spectrum of research ranging from basic biology to medical management of blood diseases. The Division has a major responsibility for research to improve the adequacy and safety of the nation's blood supply. It also plays a leading role in transfusion medicine research and applying stem cell biology to the development of new cell-based therapies to repair and regenerate human tissues and organs. The Division has three branches: the Blood Diseases Branch, the Thrombosis and Hemostasis Branch, and the Transfusion Medicine and Cellular Therapeutics Branch.

Blood Diseases Branch. Supports research and training for sickle cell disease, thalassemia, aplastic anemia and other red cell disorders from basic research on globin genes to clinical management.

Thrombosis and Hemostasis Branch. Supports research and training in occlusive disorders involved in deep vein thrombosis, in cardiovascular diseases and stroke, and in bleeding disorders.

Transfusion Medicine and Cellular Therapeutics Branch. Supports research and training in transfusion medicine, blood safety and resources, stem cell biology and disease, clinical cellular medicine; and Resource Programs that provide phenotypically-characterized biospecimens and GMP-grade cell therapies to the scientific community.

Research topics of interest to the Division of Blood Diseases and Resources include but are not limited to the following:

A. Animal models for blood diseases
    1. Anemias including: sickle cell disease (development of larger animal models), thalassemia, Fanconi anemia, Diamond Blackfan anemia, and other anemias
    2. Bleeding disorders including: hemophilia and von Willebrand disease
    3. Inherited and acquired thrombocytopenias
    4. Thrombosis and thrombolysis
    5. Hereditary hemorrhagic telangiectasia
    6. Paroxysmal nocturnal hemoglobinuria
    7. Hemochromatosis
    8. Myelodysplastic syndrome (MDS) and myeloproliferative disorders (MPD)

B. Animal models for complications associated with transfusion of blood products or cell-based therapies

1. Transfusion Related Acute Lung Injury (TRALI)
2. Transfusion-associated immuno and inflammatory complications including alloimmunization
3. Transfusion-transmitted infections such as Transmissible Spongiform Encephalopathy (TSE)
4. Graft versus Host Disease
5. Microoxygenation models to evaluate the effect of RBC transfusion

C. Animal models for the demonstration of safety and efficacy of novel cellular therapies including hemoglobin oxygen carriers (HBOC)

D. Tools, reagents, and assays for investigations of blood diseases and cellular therapies

1. Nanotechnologies
2. Proteomics
3. Glycomics
4. Genomics
5. Non-invasive approaches to analytes

E. Assays and technologies

1. Automated screening of therapeutic agents for blood diseases
2. Anti-thrombotic drug monitoring and thrombosis screening
3. Platelet functional tests
4. von Willebrand disease
5. Thrombotic Thrombocytopenia Purpura (TTP)
6. Multiplexed system for hemostatic factors, cytokines, and inflammatory agents
7. Non-invasive methodology to diagnose DVT and PE
8. Iron overload
9. Blood-borne infectious agents transmitted by blood transfusion, including agents causing babesiosis, dengue fever, malaria, and the transmissible spongiform encephalopathies such as variant Creutzfeldt-Jakob Disease (vCJD)
10. Diagnosis of inherited blood disorders
11. Information systems to manage and monitor continuous anti-coagulation
12. Prolonging the storage of transfusable blood components for therapeutic uses
13. Identification and characterization of microparticles and other bioactive substances in stored transfusable blood components
14. In vitro reduction, inactivation or removal of microorganisms and other infectious moieties from blood, blood components, and plasma derivatives
15. Platelet storage methods that preserve biological efficacy
16. Synthesizing, screening, and evaluating the safety and efficacy of therapeutic oxygen carriers
17. Synthesizing or purifying plasma proteins for therapeutic use
18. Measuring iron non-invasively

19. Non-invasive measurement of blood cell counts or other blood components
20. MHC haplotype determination by methods such as DNA fingerprinting techniques and single nucleotide polymorphisms
21. Tracking of engrafted cells using imaging and/or other techniques
22. Technologies to measure tissue microoxygenation
23. Development of HLA and HNA antibody assays
24. Cord blood collection devices
25. Microfluid assays for blood coagulation assessment
26. Quantitative technologies to predict engraftment of cell therapies including cord blood, peripheral blood and bone marrow

F. Technologies and strategies to improve blood donor screening practices

G. Drugs to Treat Hematologic Diseases and Cytopenic States

1. Anti-coagulants, including novel small molecule compounds
2. Specific agents to reverse the action of anti-coagulants
3. Oral anti-thrombotic agents
4. Dual action: anti-coagulants/anti-inflammatory agents
5. Anti-sickling agents or other pharmacologic approaches to the vasculopathy of sickle cell disease
6. Fetal hemoglobin enhancing agents
7. Fibrinolytic and anti-fibrinolytic agents
8. Iron chelation therapy including modification of existing agents to enhance efficacy
9. Replacement agents for hematologic factor deficiencies

H. Cellular Therapies

1. Expansion of cell populations including ex vivo expansion of cord blood, peripheral blood and bone marrow
2. Production and standardization of immune-modulating cytokines or monoclonal antibodies
3. Directed in vitro stem cell differentiation
4. Development of in vivo techniques to monitor survival, growth and development and differentiation of engrafted cells
5. Reprogramming differentiated cells to increase their lineage potential including the creation of induced pluripotent stem cells

I. Gene therapy vectors and delivery systems for the treatment of hematologic genetic diseases

J. Prothrombotic and hemorrhagic biomarkers and risk factors

K. Computational models for blood diseases and complications associated with transfusion of blood products and cellular therapies

L. Bioinformatics to store and analyze genes, proteins, and biomarkers for hemostasis

M. Equipment and procedures for the collection, separation, processing, preservation, storage, and distribution of blood and blood components and other cell therapies

N. Education

1. Patient and physician health education programs to improve patient management and to prevent or reduce the impact of blood diseases
2. Physician education programs to evaluate effectiveness and improve adherence to transfusion medicine clinical guidelines
3. Physician education materials to evaluate the effectiveness of cell therapies including cord blood, peripheral blood, and bone marrow transplantation

O. Public Health Education

1. Tutorials for community-based providers
2. Community health education programs in sickle cell disease, suitable for use in faith-based organizations or other community settings
3. Community health education programs to increase blood donation

P. Newborn Screening

1. Genetic counseling programs for families of infants with hemoglobinopathies or trait
2. Innovative data or systems to track follow-up and patient outcomes

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NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)

The successful completion of the HGP in 2003 set the stage for making use of the immense potential inherent in knowledge of the complete DNA sequence of the human genome to be applied for the improvement of human health and well-being. In an effort to outline a path forward, the Vision Document (*Nature* 422,835-847 (2003)) broadly outlined three areas that need to be addressed: (1) elucidating the structure and function of genomes; (2) translating genome-based knowledge into health benefits; and (3) promoting the use of genomics to maximize benefits and minimize harms. The latter area relates closely to NHGRI's Ethical, Legal and Social Implications (ELSI) Program. The research topics encompassed by this area have traditionally been included in a separate program announcement. However, given the growing interrelatedness of genomics to research in humans and to applications in health care and other

settings, it has become increasingly clear that the investigation of ELSI issues cannot be separated from the genomic research that generates these issues. As a result, the ELSI research agenda is described in this NHGRI-wide announcement, as well as in a separate ELSI-specific Program Announcement http://grants.nih.gov/grants/guide/pa-files/PA-08-012.html).

The purpose of this document is to provide information to investigators about the breadth of NHGRI's research interests and is very similar the Institute's general funding opportunity announcements (http://grants.nih.gov/grants/ guide/pa-files/PA-07-458.html and http://grants.nih.gov/grants/guide/pa-files/PA-07-459.html). When appropriate, NHGRI will publish Requests for Applications that will be used to stimulate research in specific areas, to fill gaps in research knowledge, or to generate community resources that will further the mission of genomics or ELSI research.

The following are areas of high interest for investigator-initiated applications; they are not listed in priority order.

Technology and Methods Development

Technology development in DNA sequencing and genotyping are examples of activities that have changed the nature of what scientific research questions are practical to address, have enabled new approaches, and have potentiated the development of new community resource data sets. Many areas of critical importance to the realization of the genomics-based vision for biomedical research require continued technological and methodological developments before pilots and then large-scale approaches can be attempted. Accordingly, the NHGRI will continue to support the development of new, fundamental technologies in all areas of genomics. Other important areas in which technology development applications would be responsive to this Program Announcement include (but are not limited to) analyses of gene expression, discovery and characterization of genetic variation; identification of the genetic contributions to health, disease, and drug response; statistical analytic methods for understanding human genomic variation and its relationship to health and disease; and chemical genomics. There is also continued interest in supporting technology development for the comprehensive discovery of functional elements in the human and model organism genomes, and new DNA sequencing technology. Many of these assays would benefit from the ability to work with very small amounts of starting material, to the limit of single cells.

The Institute is also interested in contributing selectively to the development of new and needed technology in related areas, such as proteomics and systems biology research, when NHGRI funding can be used to further a truly unique development that will have a significant impact on the field.

Bioinformatics

Genome databases are essential resources for the biological and biomedical research communities. The creation and maintenance of effective databases are as important a component of research funding as data generation. The NHGRI has been a primary source of support for several major genetics/genomics-oriented databases and will continue to foster technology improvements to develop effective methods for integrating, displaying, and providing access to genomic information. Projects addressing new database technologies to improve the utility of genome databases would be appropriate as applications.

Computational Biology

The NHGRI has supported the generation of many large-scale genomic data sets such as genome sequence, haplotype maps, transcriptome measurements, protein interactions, and functional elements. NHGRI encourages the development of new computational methods and tools to analyze these and other large datasets, and to extract useful biological information from them. Where possible, existing community data standards and methods for data exchange should be used in the development of these new

methods and tools. Further information on programs related to genomic databases and computational biology is available at this website: http://www.genome.gov/10001735.

The development of new sequencing technologies has dramatically increased the amount of data produced for genomics. NHGRI is interested in supporting new computational applications for the production and analysis of data from these new sequencing platforms. These applications would include better computational methods for storage, compression and transfer of large datasets by biomedical researchers along with better analysis methods to interpret these data and integrate with other data types.

Some genomic data analysis and display tools have been developed that already are used in the community that would benefit from additional work to support broader dissemination, for example making them efficient, reliable, robust, well-documented, and well-supported. NHGRI will support projects to extend the support for these informatics tools to make them readily adopted by any biomedical research laboratory that wishes to use genomic technologies to address biological questions.

Population Genomics

This is an emerging discipline that applies genomic technologies, such as genome-wide association testing and sequencing, to population studies to identify gene regions, genes, or variants affecting common etiologically complex conditions and predict individual risk. It also investigates the value of applying genomic methods in clinical care for the diagnosis, treatment, and prevention of complex diseases. The research scope of Population Genomics at NHGRI includes: developing resources and statistical methods for observational studies and clinical trials incorporating advanced genomic technologies; conducting proof-of-principle studies that apply genomic technologies to particular conditions that can be generalized to a broader range of conditions (e.g., translating genomic information to clinical care); and developing research methods and infrastructure needed for future epidemiologic studies of genetic and environmental contribution to disease in the United States, including a large, prospective cohort study of genes and environment. For additional information about Population Genomics within NHGRI, please visit this website: http://www.genome.gov/19518660.

Ethical, Legal and Social Implications

NHGRI supports studies that examine issues and, where appropriate, develop policy options in the following areas: 1) the translation of genomic information to improved human health; 2) the conduct of genomic research—particularly genome-wide association studies, medical sequencing and clinical studies; 3) intellectual property issues surrounding access to and use of genomic information; 4) the use of genomic information and technologies in non-health care settings; 5) the impact of genomics on concepts of race, ethnicity, kinship and individual and group identity; 6) the implications, for both individuals and society, of uncovering genetic contributions not only to disease but also to 'normal' human traits and behaviors; and 7) how different individuals, cultures, and religious traditions view the ethical boundaries for the uses of genetics and genomics. Several of these topics are closely integrated with genomic research, which is why they are described here.

Other Research Topic(s) Within the Mission of the Institute

Individuals interested in any of the above listed areas are encouraged to contact the NHGRI staff listed below. For more specific information about areas of interest to the NHGRI, please visit our home page at http://www.genome.gov/Grants/.

For additional information on research topics, contact:

All Research Topics Except ELSI
Bettie J. Graham, Ph.D.

National Human Genome Research Institute
301-496-7531, Fax: 301-480-2770
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For administrative and business management questions, contact:

Ms. Cheryl Chick
Chief, Grants Management Officer
National Human Genome Research Institute
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NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

The mission of the National Institute of Mental Health (NIMH) is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. Mental disorders constitute an immense burden on the U.S. population, with major depression now the leading cause of disability in the U.S., and schizophrenia, bipolar disorder, and obsessive-compulsive disorder ranked among the ten leading causes of disability. NIMH also takes a leading role in understanding the impact of behavior on HIV transmission and pathogenesis, and in developing effective behavioral preventive interventions. The NIMH conducts a wide range of research, research training, research capacity development, as well as public information outreach and dissemination to fulfill its mission.

For additional information about areas of interest to the NIMH, please visit our home page at http://www.nimh.nih.gov.

NIMH-Supported Program Announcements:
(if the program announcement has expired, please contact Dr. Margaret Grabb for information on new opportunities, and also see: http://www.nimh.nih.gov/research-funding/small-business/small-business-program-announcements-issued-by-nimh.shtml)

1. Lab to Marketplace: Tools for Brain and Behavioral Research (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-08-071.html
2. Competing Renewal Awards of SBIR Phase II Grants for Brain and Behavior Tools (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-08-056.html
3. Innovations in Biomedical Computational Science and Technology (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PAR-09-220.html
4. Development of PET and SPECT ligands for brain imaging (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-08-137.html
5. Pharmacologic Agents and Drugs for Mental Disorders (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-08-142.html
   Also see: http://grants.nih.gov/grants/guide/notice-files/NOT-MH-09-008.html.
6. Development of Biomarkers for Mental Health Research and Clinical Use (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-09-045.html

7. Probes for Microimaging the Nervous System (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-09-062.html.
8. High Throughput Tools for Brain and Behavior
   http://grants.nih.gov/grants/guide/pa-files/PA-08-001.html (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-08-002.html (STTR).
9. Bioengineering Nanotechnology Initiative (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-09-267.html
10. Novel Tools for Investigating Brain-derived GPCRs in Mental Health Research (SBIR)
    http://grants.nih.gov/grants/guide/pa-files/PA-10-081.html
11. Tools to Mitigate and Understand the Mental Health Effects of National Disasters (SBIR)
    http://grants.nih.gov/grants/guide/pa-files/PA-09-117.html
12. Manufacturing Processes of Medical, Dental, and Biological Technologies (SBIR)
    http://grants.nih.gov/grants/guide/pa-files/PA-09-113.html
13. Computational Tools for Research in Neuroscience, Behavioral Science and Mental Health
    http://grants.nih.gov/grants/guide/pa-files/PA-07-424.html (SBIR)
    http://grants.nih.gov/grants/guide/pa-files/PA-07-423.html (STTR)
14. Probes and Instrumentation for Monitoring and Manipulating Nervous System Plasticity (SBIR)
    http://grants.nih.gov/grants/guide/pa-files/PA-08-146.html
15. Robotics Technology Development and Deployment [RTD2] (SBIR)
    http://grants.nih.gov/grants/guide/pa-files/PAR-10-279.html

Phase IIB Competing Renewal Awards

See http://grants.nih.gov/grants/guide/notice-files/NOT-MH-09-008.html and http://grants.nih.gov/grants/guide/pa-files/PA-08-056.html. The NIMH will accept Phase IIB SBIR Competing Renewal grant applications in two categories: 1) to continue research and development of technologies that ultimately require federal regulatory approval (see below and see http://grants.nih.gov/grants/guide/notice-files/NOT-MH-09-008.html, and 2) to continue research and development of complex instrumentation, clinical research tools, or behavioral interventions and treatments (see below and see funding opportunity announcement PA-08-056, entitled “Competing Renewal Awards of SBIR Phase II Grants for Brain and Behavior Tools (R44)” http://grants.nih.gov/grants/guide/pa-files/PA-08-056.html.

Technologies in the former category (those that ultimately require federal regulatory approval) include, but are not limited to: pharmacologic agents and drugs, biological products, medical devices, vaccines, etc., related to the mission of the NIMH. Phase IIB SBIR Competing Renewal grants for such technologies should allow small businesses to get research and development to a stage where interest and investment by third parties is more likely. Companies engaging in drug development for the treatment of mental health disorders may be eligible to submit Competing Renewal applications through the specific funding opportunity announcement PA-08-142 entitled “Pharmacologic Agents and Drugs for Mental Disorders (SBIR [R43/R44])” http://grants.nih.gov/grants/guide/pa-files/PA-08-142.html. For this specific opportunity, budgets up to $1.0 million total costs per year and time periods up to three years may be requested.

Companies that are developing technologies that do not focus on drug development, but that require federal regulatory approval prior to commercialization, may be eligible to submit a Phase IIB Competing Renewal application through the standard SBIR funding opportunity announcement. For this opportunity, budget limits of up to $800,000 total costs per year and time periods up to 3 years may be requested.

Please contact your Program Director or Dr. Margaret Grabb (contact information provided below) before beginning the process of putting an application together. In addition, prospective applicants are strongly encouraged to submit to the program contact a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NIMH SBIR Phase II awards will be eligible for a Phase IIB Competing Renewal grant.

The following examples would make appropriate topics for proposed NIMH SBIR Phase IIB Competing Renewal projects. These are meant for illustrative purposes only and are not exclusive of other appropriate activities:

- Preclinical studies, including pharmacology and toxicology, beyond those conducted under the Phase I (R43) and initial Phase II (R44) grants. Some in vivo or in vitro studies would be expected to have been carried out in Phase I or the initial Phase II grant.

- Completion of studies as required by the Food and Drug Administration (FDA) for Investigational New Drug (IND) or Radioactive Drug Research Committee (RDRC) application.

- Studies in normal healthy volunteers to determine a drug's safety profile, metabolism, etc.

- Clinical studies in patient/disease population to assess the drug's effectiveness.

- Assessment of devices with regard to performance standards related to the FDA approval process.

- Safety and effectiveness studies of novel medical devices.

- Evaluation of novel imaging approaches for diagnostic purposes.

- Clinical studies in support of Pre-Market Approval for biomarkers/medical devices by the FDA.

Although technologies in the latter category (complex instrumentation, clinical research tools, or behavioral interventions/treatments) may not require federal regulatory approval, extraordinary time and effort is needed for their research and development. Therefore, NIMH supports Phase IIB Competing Renewal awards of existing Phase II grants for such technologies. The Phase IIB Competing Renewal award for these would provide up to an additional three years of support at total cost funding levels of up to $800,000 per year. Applicants should apply through the funding opportunity announcement PA-08-056, entitled "Competing Renewal Awards of SBIR Phase II Grants for Brain and Behavior Tools (R44)" http://grants.nih.gov/grants/guide/pa-files/PA-08-056.html.

Direct your questions about scientific/research issues to:

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6001 Executive Boulevard, Room 7201, MSC 9645
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Division of Neuroscience and Basic Behavioral Science

Through research in neuroscience and basic behavioral science we can gain an understanding of the fundamental mechanisms underlying thought, emotion, and behavior and an understanding of what goes wrong in the brain in mental illness. Research sponsored by the Division of Neuroscience and Basic Behavioral Science covers a broad range of neuroscience topics: from both experimental and theoretical approaches, from molecules to whole brains to populations of individuals, from single cell organisms to humans, from across the entire lifespan, and from states of health and disease. This division also supports research on the basic behavioral, psychological, and social processes that underlie normal behavioral functioning. The topics listed below reflect the NIMH interest in technologies related to this broad range, but should not be considered a complete list. Prospective applicants are strongly encouraged to contact Dr. Margaret Grabb (listed below) with questions about the relevance of their interests to the mission of this division.

A. ***Cutting-Edge Technologies for Neuroscience Research.*** Most of the research topics listed after this one are posed from the Division's neuroscience and basic behavioral science mission-oriented perspective, however, the technologies that might be developed to address those mission goals might be quite fundamental. Prospective applicants familiar with such technologies, but not familiar with the mission-related use of these technologies, are strongly encouraged to contact Dr. Margaret Grabb (listed below) for assistance in bridging this gap between their technical knowledge and knowledge of the neuroscience-related mission of NIMH. Technologies and approaches that might be used in products relevant to this mission include, but are not limited to:

1. *Caged Molecules.* These chemical entities could be activated, or could release an active agent, when specified bonds are broken by chemical, biochemical, photic, or other means. Among other uses, such molecules could be used to indicate biochemical or physiological processes or to deliver pharmacologic substances to highly localized brain regions.
2. *Genetically Engineered Proteins.* Such proteins could be put to any number of uses, including to express a fluorophore or chromophore at the occurrence of specific biochemical processes to report the time and location of such processes in brain tissue.
3. *Inducible Gene Expression.* Methods to turn on or off expression of particular genes in animals on the basis of time in the lifespan, location in the brain, or other factors. Such a capability would significantly advance basic brain research, and would have important implications for treatment and therapy of mental illness.
4. *Combinatorial Approaches.* These are high-through-put approaches that can be used to screen and synthesize molecules that affect brain cells.
5. *Biocompatible Biomaterials.* Such research and development relates to the chronic use of electrodes and other probes used in brain research, as well as implanted drug delivery devices.
6. *Nanotechnologies.* This emerging area of technology presents a wide range of opportunities for brain research, from the fabrication of probes to monitor brain physiology to novel means of delivering drugs and other substances.
7. *Informatics Tools.* Such technologies allow brain scientists, clinicians and theorists to make better sense and use of their data. These tools and approaches include those to acquire, store, visualize, analyze, integrate, synthesize and share data, including those for electronic collaboration.
8. *Simulation Technologies.* Computer-based, biologically realistic simulations of parts of neurons, neurons, and circuits.

9. *Mathematical, Statistical and Computer Algorithms.* Such algorithms could be used to analyze large and/or complex data sets. Examples of these data sets include those derived from multiple, single-unit recording studies and functional imaging studies. Among other applications, these could be used to segment images (obtained from electron or light microscopes, or from volumetric imaging instruments such as confocal microscopes and magnetic resonance imagers), filter noise, visualize data or search vast data sets for specified patterns or data (e.g., use of pattern recognition algorithms to search time series data sets obtained from electrophysiological recording of neural activity, or video data obtained from behavioral analysis of genetically altered animals). In addition, digital reconstruction of dendritic and axonal arbors would be of interest.

10. *Telemetry.* Transferring data from one point to another is important for neuroscientists monitoring the physiological signals from the brain. Telemetry, even over relatively short distances (from a few millimeters to a few meters), could, for example, provide a means to obtain data from awake, behaving animals without interfering with the behavior of interest. Examples include telemetry that can be easily implanted/attached to awake behaving animals for measuring peripheral/autonomic responses (this approach could be used to inform stress/emotion research), miniaturized telemetry for use in smaller animals with increased numbers of recording devices/electrodes implanted per animal. Alternatives to telemetry would be considered as well.

11. *Biosensors.* Neurons communicate with each other through thousands of different chemical substances; internally, molecular pathways direct the function of the neuron. Sensors of high specificity and sensitivity for such substances would provide neuroscientists with important new ways to study the brain.

B. ***Instrumentation for Basic Neuroscience Research.*** Modern equipment that uses the most recent technological advances is needed in neuroscience research so that neural substrates of mental illness can be identified and localized. The NIMH is interested in supporting research and development of new or improved approaches relevant to, but not limited to, the following:

1. *Neurophysiology.* Microelectrodes for stimulation and/or recording, smart nanoscaffolds, macroelectrodes, biocompatible coatings, interfaces to electronics, software for data analysis, visualization, etc. Systems with better/easier MR compatibility would also be of interest.

2. *Cell Sorting.* Based on cell size, type, function, morphology, abnormal features, specific membrane proteins, etc.

3. *In Vivo Electrochemical Voltammetry.* More sensitive and selective electrodes, software for data analysis, etc.

4. *High Performance Liquid Chromatography.* Improved reliability, specificity, sensitivity, etc.

5. *Technology to support Multiple Unit Recording Electrode Arrays.* Recording techniques, analysis techniques and raw data storage.

6. *Physiological and Behavioral Monitoring.* Temperature, activity, sleep duration, neuronal activity, EEG activity, EKG, pulse rate, recording, capture and analysis of multiple single unit activity from microelectrodes, automated SWS analysis and coherence of EEG rhythms, and further refinement of High density EEGs.

7. Development of novel technologies for stimulating specific cells or signaling pathways in awake behaving animals.

8. Development of more sensitive fluorescent probes for simultaneous and real time measures of multiple neurotransmitter release and intracellular signaling pathway activities.

9. *Associated Software.*

C. ***Macroscopic Neuroimaging.*** Modern technologies allow for the observation of the structure and function of the intact brain. This capability has the potential to greatly advance understanding of the brain in both health and disease, and across the lifespan. NIMH is interested in advancing this area of technology through enhancing current tools and approaches, as well as developing entirely new ways to image the brain. All modalities are of interest, including, but not limited to: magnetic resonance imaging (MRI) or spectroscopy, positron emission tomography (PET), optical imaging or spectroscopy, single photon emission computed tomography, magnetoencephalography (MEG), diffusion tensor imaging (DTI), etc. While not an imaging technique itself, transcranial magnetic stimulation (TMS) is an associated, important technology. TMS can be used in combination with fMRI as means to further assess physiology and integrity of neural systems both in health and in mental disorders. Due to its greatly increased use in recent years, technologies specifically focused on improving the utility and specificity of fMRI techniques are of particular interest.

1. Innovative agents and/or technologies to visualize brain connectivity, activity, and neural plasticity in situ with minimal invasion.
2. Improvement in the techniques, the design and construction of devices for non-invasive imaging for any modality, for example, improving spatial resolution, quantitative accuracy, signal-to-noise ratio, and electronics.
3. Development and enhancement of non-invasive imaging techniques for evaluating alterations in brain physiology produced by drugs. These would include techniques for monitoring changes in regional blood flow; concentrations of drug and/or tissue metabolites; and the distribution and activity of receptors.
4. Synthesis, or isolation from natural products, of highly selective receptor ligands or indicators of neurochemical processes, which would be labeled for imaging by one or more particular modality.
5. Development of selective hormone receptor ligands for brain imaging.
6. Development of imaging agents to examine the integrity of the blood brain barrier following infection and other environmental challenges.
7. New approaches in radiochemistry that will permit more exact identification of the chemical changes associated with behavioral states (e.g., sleep or arousal) or mental illness as observed with any particular neuroimaging modality.
8. Synthesis of molecules containing stable, rarely occurring isotopes designed to be detected by non-invasive imaging techniques (e.g., fluorine-containing molecules, carbon-13 labeled substrates).
9. Methods and associated products for quantification of imaging data including new statistical approaches for evaluating the data.
10. Methods to integrate routines for greater and more precise computer enhancement of the images, and for combining or overlaying images obtained from multiple modalities.
11. Software needed for the precise quantification of data obtained from these imaging techniques with emphasis on the reliable definition of discrete, anatomically distinct areas within the brain.
12. Novel agents or other tools to increase the ability to correlate features of MR images with histological features (e.g., cytoarchitecture or chemoarchitecture) both identified and those yet to be identified.
13. Generation of physiologic measurements from images of regional radioactivity generated during PET, especially for the study of brain neurotransmitter/neuroreceptor systems.
14. Novel approaches to visualizing data obtained in neuroimaging, such as the computational “unfolding” of three-dimensional images of cerebral cortex.

15. Improved methods for pediatric brain imaging. These would include: software and database products, equipment for creating a “child-friendly” environment and for the behavioral training of children and impaired subjects for cooperation and motion reduction during neuroimaging procedures.
16. Combining of different imaging technologies (e.g., ERPs and fMRI; MEG and fMRI; MEG and EEG, optogenetic methods and fMRI, etc.). The latter example, optfMRI, can be used as means of improving tools for further understanding of neural bases of fMRI signals and to produce connectivity a map of neural cells that can be defined both genetically and topographically with a combination of these two techniques.
17. New tools and devices to simultaneously record hemodynamic signals (BOLD, rCBF, etc.) and neural activity (EEG, LFP, spiking, etc.) to better understand the direct relationship between blood flow variables and neural activity within the brain.
18. Development of equipment, software and other tools for recording and quantifying eye movements, motion, and autonomic reactivity during scanning, applicable to all ages (including young children) particularly in the MRI environment.
19. Methods for relating changes in brain morphology and metabolism associated with age, particularly infancy through adolescence, to changes in hemodynamic responses to neural activity and fMRI signals.
20. Improvements in TMS techniques that will allow for greater specificity in the sites of stimulation and greater control over the effects of the stimulation. In particular, improvements in stimulators that would allow much smaller effective fields of stimulation with more reliable and repeatable stimulator placement would be a significant benefit to the field.
21. Real time fMRI is becoming a research tool of interest with potential clinical/therapeutic neurofeedback applications. Products are needed that would enhance the ability of scientists to use this technology for those neurofeedback applications in an off-the-shelf manner.
22. Development of methods to improve efficiency, specificity and controllability of viruses used in primate tract tracing studies.
23. Development of more sophisticated imaging strategies in rodents.
24. Development of a user-friendly interface to serial reconstruction software capable of generating stackable, 3D images of axonal and dendritic arborizations at the light and electron microscopic level.

D. ***Microscopic Neuroimaging.*** The morphology of individual neurons and the distribution of subcellular components within them, are key to understanding the manner in which these cells function. Advances in the development of agents indicating neuronal structure and function that can be visualized microscopically are important to the NIMH's interest in brain research. This includes enhancements of current agents and ligands to be imaged (agents indicating specific biochemical processes or structures, etc.); development of novel agents and ligands; software to assist interaction with the data; and other related technologies and methods. Examples would include, but not be limited to:

1. Software and hardware for analyzing image data obtained by microscopes, including tools to automatically or semi-automatically. Identify particular profiles (e.g., labeled cell bodies), segment images, reconstruct images into three dimensional representations, perform unbiased counting and measuring, etc.
2. Synthesis and testing of novel or improved probes for microimaging the nervous system.

E. ***Molecular and Cellular Neurobiology and Neurochemistry.*** Manipulating and studying basic molecular, cellular and chemical processes has led to insight to understanding brain function, and has provided the foundation on which pharmacological interventions have been developed for the

treatment of mental illness. NIMH is interested in supporting a wide range of new techniques and tools related to this area. These include, but are not limited to:

1. New low-cost techniques for hybridoma production of monoclonal antibodies specific for “neural antigens” (e.g., neurotransmitters, small peptides, neurotransmitter receptors).
2. Innovative methods for establishing a “monoclonal bank” (frozen cells) for each of the cell lines as a permanent, widely available, reliable, and low cost source of monoclonal antibodies for research on the nervous system.
3. Labeled antibodies or other agents that will readily identify receptors for which there are no ligands (orphan receptors) and which have low densities in the brain.
4. Automated methods for quantifying the low levels of bound ligands for quantifying receptors that are sparsely scattered in the brain.
5. New cell lines that express each of the known neurotransmitter receptors so that each cell line will be homogeneous for one receptor.
6. New cell lines that express each of the above receptors linked to some metabolic function and/or second messenger so that the functional consequences of receptor occupancy can be detected.
7. High volume, inexpensive assay methods for measuring both receptor occupancy and cellular response for each of the receptor types.
8. Develop cell culture models for neurons, including methods of purifying homogeneous populations of non-transformed cells by, for example, developing markers to identify neuronal cell types for use in characterizing cell-type-specific signaling pathways which may be useful in tracking the effects of various drugs.
9. Develop techniques for either activating or deactivating specific ion channels, receptors and signal transduction pathways.
10. Develop dynamic biochemical and imaging assays that allow measurement of variables now obtained only through electrophysiological techniques.
11. Develop tools to facilitate proteomic analysis of CNS neurons.
12. Develop tools to facilitate in vivo studies of protein-protein interaction, folding and aggregation. These technologies could impact our understanding of the basic neurotransmitter receptors chemistry and on developing of more selective small chemical entities with high affinities for CNS targets.
13. New approaches to study the multiple functions of particular proteins.
14. Tools to study post-translational changes in proteins (expression levels, post-translational modifications, etc.) in specified tissue compartments and subcellular domains.
15. Technologies to study functional entities within cells (e.g., green fluorescent protein approaches) and subcellular compartments.
16. Tools and approaches to study coordinate changes in genes and their functional relationship to phenotypes, including phenotypes associated with specific brain disorders.
17. Novel tools and approaches to study protein-protein interactions, especially those with phosphoproteins. Further develop methods and reagents for studying the structures of membrane proteins at atomic resolution. Membrane protein systems that are of particular interest to NIMH include proteins involved in normal function and pathology of cells (neurons and glia) in the central and peripheral nervous system.
18. Develop novel techniques for isolating and identifying the structure of brain-derived membrane proteins.

19. New methods to identify peptide receptors for which traditional biochemical approaches (e.g.: radiolabeling techniques) failed to produce results. This would be relevant for the development of small molecular probes that would target peptide systems that might be altered in mental disorders.
20. Development of new and optimization of the existing methods for non-invasive quantitative detection of hormones and hormone action in awake behaving animals.
21. Development of novel technologies to adapt human induced pluripotent stem cells (iPSCs) to identify molecular and cellular dysfunction underlying mental illness and for high throughput screening assays for candidate therapeutics.
22. Continuing to improve optogenetic techniques (combining optical and genetic techniques to probe neural circuits within intact animals).

F. ***Genetic and Transgenic Technology.*** Advances in genetic and transgenic technologies offer many opportunities to probe fundamental questions about the brain, behavior and pathology. NIMH is broadly interested in these areas; some examples of topics relevant to the mission of this Institute include, but are not limited to:

1. Methods to perform site-directed mutagenesis in cell lines for the study of membrane proteins such as ion channels and neurotransmitter receptors.
2. Development of gene “knockout” or “knockin” animals using such approaches as homologous recombination targeting genes important in neurotransmission, development, and tropic interactions as well as models relevant to psychiatric disease.
3. New methods to delete or alter targeted genes in the preparation of transgenic animals including methods that increase or decrease gene expression.
4. Development of new techniques and apparatus for delivery of synthetic nucleic acids to manipulate endogenous gene expression in specific cell populations and/or brain regions.
5. Develop and validate standardized behavioral tests and apparatuses to assess the gene knockouts and/or gene “knockins” affecting neurotransmission.
6. New approaches for spatially and/or temporally restricted gene activation and/or inactivation.
7. Develop novel markers for elucidating how signaling cascades impact DNA transcription.
8. New ways to assess quantitatively transcription of genes in real time in a manner that is minimally injurious to cells (e.g., non-permeabilizing approaches).
9. Develop new technologies to study gene function and expression, including approaches to studying gene and protein expression at single cell resolution.
10. Develop novel approaches to study the expression characteristics of non-coding (nc) RNA molecules as well as developing methodologies using nc-RNAs to manipulate gene expression in cells and tissues of the nervous system.
11. Development of embryonic stem (ES) cell lines from rodent strains (rats and mice) of relevance to behavioral research.
12. Development of technologies and approaches to facilitate the collection and distribution of ES cell lines containing mutations of potential relevance to behavioral and neural processes relevant to neuropsychiatric disorders.
13. Develop methods for long-term storage of transgenic germ cell lines.
14. Develop technologies and approaches to aid in the renewal of founder colonies of transgenic mice from repositories of transgenic germ cell lines.

15. Develop databases on neurobiological transgenic animals produced to date, including information such as the origin of the transgenic animal, key features of the biological and behavioral mutant, availability and location of germ cell lines, and existence of breeding colonies.
16. Develop gene transfer technologies such as viral vectors and non-viral (e.g. polymer-based) systems to produce long-term, stable gene expression in the brain.
17. Develop methods to analyze and manipulate DNA structure to study epigenetic modifications and chromatin remodeling in brain tissue and neuronal populations.
18. Development of selective gene silencing strategies to ablate neurons in one circuitry in order to examine its specific behavioral consequences.
19. Technology development in epigenetics:
    a) development of novel and highly accurate tools to analyze proteomics of histones
    b) development of antibodies for immunochemical studies of histone modifications that selectively target a specific DNA modification site
    c) develop and apply tools for epigenetic research to determine how, when, and where experience affects gene expression.
20. Technology development in Microbiome research: a) development of tools for high throughput genomic analysis of human microbiome; b) development of informatics tools to study the huge amount data that will result from these studies; and c) development of methods to determine the interaction between microbial community genes and host genetics as a potential contributing factor for mental disorders.

G. ***Neuroimmunology.*** Research on the interplay between the brain, neuroendocrine system, and, immune system has revealed important links between these major homeostatic system components. Examples of NIMH-relevant topics in this area include, but are not limited to:

1. Development of new tools to explore the specific properties of the blood-brain barrier responsible for the selective delivery or retention of cytokines, immune cells, and drugs affecting immune activity in the brain.
2. Development of assays for identifying potential autoimmune components of psychiatric disorders.
3. Identification of critical molecules, processes, and pathways mediating signals from the peripheral immune system to the brain.
4. Development of novel cytokine ligands and antagonists, and neuroimaging agents.

H. ***Pharmacology.*** Pharmacological intervention represents a major force in the treatment of mental illness, and NIMH is interested in supporting research and development in this area. However, pharmacologic agents that primarily act on molecular targets which replicate those of currently-marketed pharmaceuticals used in the treatment of mental disorders would not be of interest for this program. Relevant pharmacology topics include, but are not limited to:

1. New chemical entities with high, selective affinities for CNS targets. Examples include, but are not limited to, receptors, transporters, ion channels, enzymes, kinases, or second or third messenger systems.
2. Methods to evaluate old and new chemical entities (including complex mixtures of crude extracts from natural products) for possible therapeutic usefulness using “in vitro” and “in vivo” assays and model systems.
3. Methods for extraction, fractionalization, and isolation of active compounds from natural products. Water-soluble compounds are of particular interest due to the difficulty of the procedures.

4. Computer algorithms that model receptors to evaluate theoretical permutations of known molecules to find the molecule with the maximum probability of having the highest affinity for a specific receptor as well as those that have the potential for the most desirable “on” and “off” rates.
5. Computer models of the blood brain barrier and evaluate potential and actual drug molecules for their ability to cross or penetrate this barrier.
6. Strategies for evaluating pharmacological agents (e.g., animal behavioral testing, computer simulation) within specific domains of cognitive function.
7. Behavioral “models” similar in animals and humans; behavioral pharmacological effects that may serve as “surrogate” markers in humans.
8. Development of models for evaluating drug effects within functional brain circuits relevant to mental disorders.
9. Development of novel drug delivery systems.
10. Tools for Drug Development including neuroimaging (e.g., radiolabeled compounds) and development of animal models.
11. Pharmacological profiling (in vitro and in vivo) for potential therapeutic drugs.
12. Methods for evaluation of long-term effects of psychotropic drug administration in animal models or human subjects. If clinical populations are being tested, the technology would be appropriate for either the Division of Developmental Translational Research (DDTR) or the Division of Adult Translation Research (DATR) at NIMH.
13. Improving existing, and developing new, vectors for delivery of genes to the brain.
14. Development of novel therapeutic approaches targeting gene expression through effects on promoter activity or epigenetic mechanisms.
15. Development of novel high throughput screening (HTS) assays for drug development. Examples include, but are not limited to, in vitro functional assays, toxicology screens, blood-brain barrier permeability assays, and circuit based or behavioral assays.
16. Development of novel molecular targets for drug development to treat mental illnesses.

I. ***Tract Tracing Methods and Tools.*** Little is known about the details of the connectivity of the human nervous system, because the best tract tracing techniques are invasive and require the deposit of substances in vivo. Methods that would be applicable to post-mortem tissue would allow significant progress in connectional studies of human tissue, as well as non-human tissue, particularly with regard to the development of c, quantu onnections and the connections of structures not easily accessed in vivo. Examples include the development of improved physical, chemical and/or biological markers for neuroanatomical tract-tracing (e.g. m dots, caged molecules, viral delivery agents, etc.).

J. ***Educational Tools.*** Neuroscience, basic behavioral science and human genetics are compelling areas of science that not only touch upon a diverse array of disciplines, but also provide insights to the essence of what it is to be human. Products aimed at teaching the substance of these fields to students of all ages would be useful in disseminating this information and these insights. Examples include, but are not limited to: software and other interactive media used to convey fundamental concepts about the brain to children; computer simulations of neuroscience experiments; updateable media that presents state-of-the-art information on particular topics for use by experts; website or other online, interactive electronic vehicle to allow for sharing of information about the brain and its functions, including technologies for holding interactive research conferences related to basic behavioral sciences, basic neuroscience, or clinical neuroscience.

K. ***Neuroinformatics.*** Data generated by brain research are diverse, vast, and complex. The diversity of data is due to the fact that neuroscience data are obtained from: theoretical, experimental and clinical approaches; from levels of biological organization that span molecules to populations of individuals and from single-cell organisms to humans; and from states of health, disease, and models of disease. The quantity of data in brain research is the result of tens of thousands of neuroscience laboratories working around the world. The complexity of data reflects the high level of interconnectedness of the data, and their high dimensionality. Neuroinformatics is a new area of science that draws upon neuroscience, information science, computer science, statistics, applied mathematics, and a variety of engineering fields to develop tools that will let neuroscientists make better sense and use of their data. These tools include software and hardware for digital data acquisition, visualization, analysis, integration, and sharing (e.g., through tools for electronic scientific collaboration). Such tools can address data of any type or from any area of neuroscience; examples include, but are not limited to:

1. Databases, querying approaches, and information retrieval tools for neuroscience and neuroscience-related data. An example would be the development of a web-based database for sharing, analyzing and comparing the pharmacological responses of a variety of CNS active compounds in preclinical studies relevant to mental health.
2. Tools for neuroscience data visualization (and other forms of presentation) and manipulation (probabilistic atlases of brain structure or function, new statistical approaches for analyzing data, etc.).
3. Software for integration and synthesis of neuroscience data (computational models of neurons to integrate data about structure and function, environments to merge data from multiple imaging modalities, etc.).
4. Tools for electronic collaboration to allow neuroscientists to interact with colleagues, data, and instruments at a distance (this could include novel types of “groupware”, etc.).
5. Tools that bridge existing neuroscience and biology information tools and resources, such as databases and informatics tools associated with genome mapping efforts.

For further information on basic neuroscience or basic behavioral science research topics, contact:

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The Division of Developmental Translational Research

The Division of Developmental Translational Research directs, plans, and supports programs of research and research training leading to the prevention and cure of childhood psychopathology. This long-term goal will be accomplished through an integrated program of research across behavioral/psychological processes, brain development, environment and genetics. The topics listed below reflect the NIMH interest in technologies related to this research area, but should not be considered a complete list. Prospective applicants are strongly encouraged to contact Dr. Margaret Grabb (listed below) with questions about the relevance of their interests to the mission of this division.

A. ***Technologies for Clinical Pediatric Research.*** It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior, as well as normal and abnormal physiological and biochemical functions, in human development. Computer-based methods of accomplishing this are also needed to increase the

accessibility and reliability of information made available to the research community. Examples include:

1. *Measurements of Alterations in Pediatric Development in Patients with Mental Health Disorders Using Physiological and Behavioral Measures.* Research studies indicate that some mental health disorders, such as autism, may begin to develop as early as infancy. Therefore non-invasive modern equipment that use the most recent technological advances are needed to isolate specific physiological and behavioral changes during development, to identify potential diagnostic markers of mental health disorders. A priority for this program is to support research and development of hardware and software tools to measure pediatric development. Examples of technologies needed include:

    a. Psychophysiological measures to evaluate infants, children or adolescents.

    b. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).

    c. Telemetry capability for non-invasive devices so that children can be monitored for prolonged periods without interfering with their behavior.

    d. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.

2. *Pediatric Assessment Tool.* Diagnosis of mental health disorders in children and adolescents is vital to providing early interventions to treat the disorder. In addition, a better understanding of the concept of functioning in psychopathology, and its appropriate measurement, is needed in pediatric populations. In the future, diagnostic tools may even help detect the initial onset of illness in children at risk, before symptoms occur. A priority for this program is to develop novel diagnostic tools to detect mental health disorders in children and adolescents. Of particular interest to this division are methods that can be used with children and adolescents with limited verbal communication (i.e., very young or developmentally disabled). Biochemical, genetic, physiological and psychological tool development is welcomed.

    a. Technologies to assess CNS effects of psychosocial or pharmacological interventions.

    b. Development of reliable and stable biomarkers/biosignatures that can identify at-risk individuals prior to disease onset, biological and behavioral indicators or predictors of treatment response, measures of disease progression, measures to identify dose ranges prior to clinical studies, preclinical or clinical efficacy testing, toxicity measures for drug development, defining patients to enroll in the clinical study, identifying CNS abnormalities, etc.

    c. Assessment tools for pediatric mental health disorders that are sensitive to developmental change, gender and cultural diversity, variation in cognitive and behavioral functioning, hearing and/or speech impairment, and co-morbid disorders.

    d. Innovative approaches to assessing mental disorders using new statistical and psychometric techniques such as Item Response Theory.

    e. Computerized methodologies for assessing various mental disorders suitable for use in primary care settings, e.g. they would need to function rapidly and reliably.

    f. Biological and behavioral measures to define and assess specific impairment-related components of psychiatric disorders, e.g., cognitive dysfunctions in schizophrenia.

    g. Development of valid and reliable measures that operationalize functioning within and across developmental periods, and that can be used in a variety of service settings. Such measures can lead to more accurate diagnoses, a better understanding of the impact of psychiatric disorders, and better tracking of treatment effectiveness.

3. *Behavior Monitoring and Analysis of Pediatric Mental Health Disorders.*

a. Improve or create new video devices to monitor human behavior and ease analysis of behavior.

b. Computer software to ease analysis of behavior monitored by video or telemetry systems.

c. Automated methods to detect specific emotional states using behavioral and autonomic indicators: This Division is specifically interested in technologies that can identify children with heightened or dampened emotional states that could be associated with particular mental health disorders, including children with limited verbal skills (i.e., very young or developmentally disabled). If the technology will primarily be used to investigate basic mechanisms of behavior, the Division of Neuroscience and Basic Behavioral Science at NIMH would be the most appropriate division to contact.

4. *Intervention Development for Childhood-Onset Mental Disorders.*

a. Strategies (e.g., animal behavioral testing, computer simulation) for evaluating, in early developmental periods, the effects of pharmacological agents on specific functional domains and brain circuits associated with mental disorders.

b. Strategies (e.g., animal behavioral testing, computer simulation) for evaluating, in early developmental periods, the effects of cognitive or behavioral interventions (e.g., cognitive rehabilitation, attention training) or device-based protocols (e.g., transcranial magnetic stimulation or direct current stimulation) on specific functional domains and brain circuits associated with mental disorders.

c. Methods for evaluation of long-term effects of psychotherapeutic drug administration or brain stimulation protocols in developmental animal models.

5. *Methodological Research and Development.* There is a need to devise new ways of data collection, analysis, management and dissemination. Examples include:

a. Technologies that use the most recent technological advances to identify aberrations in the CNS during development, associated with mental disorders. Once these aberrations are identified and localized, rational therapies can be developed and evaluated.

b. Innovative, computer-based methods to monitor preventive and treatment intervention efforts and correlate them with outcome measures are needed. Results should be accessible to other interested parties without compromising the privacy of the individual.

c. Development of innovative software for addressing the integration of distributed cross-disciplinary data sources into coherent knowledge bases. The data should focus on pediatric mental health disorders.

d. Computer-based intervention development for parents or for school settings.

e. Development of databases containing detailed genetic and behavioral information on pediatric populations and their families, as resources for the field in investigations of gene x environment interactions.

f. Mathematical, statistical and computer algorithms that could be used to analyze large and/or complex data sets. Examples of these data sets include those derived from functional imaging studies. Among other applications, these could be used to segment images such as those obtained from magnetic resonance imagers, filter noise, visualize data or search vast data sets for specified patterns or data (e.g., use of pattern recognition algorithms to search time series data sets obtained from electrophysiological recording of neural activity, or video data obtained from behavioral analysis of genetically altered animals). Improved techniques for path analysis when examining functional imaging datasets would also be of interest.

B. ***Child and Adolescent Treatment and Preventive Intervention Research.*** An estimated one in ten children and adolescents in the United States suffers from mental illness severe enough to cause some level of impairment. Yet, it remains unclear what treatments are the best and safest for

these developing age groups. A priority for this program is to support research and development of novel psychopharmacological or psychosocial approaches for the treatment and prevention of mental illness in childhood and adolescence, in subjects aged 18 and below.

The goal of this research is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, and the range of outcomes measured. Disorders studied include all mental and behavioral disorders. Interventions studied include pharmacologic approaches (individual and combination medications), somatic approaches, behavioral and psychotherapeutic approaches. Research is supported on individual and combined approaches. Research that translates findings on basic physiological or behavioral processes into novel preventive or treatment interventions is especially encouraged. Effectiveness studies that focus on interventions of known efficacy are assigned to the Division of Services and Intervention Research.

Human subjects include child and adolescent age groups covering the full range of mental disorders individually and in complex patterns of comorbidity with other mental disorders and behavioral problems (e.g., anxiety and depression) and substance abuse (e.g., depression and alcohol abuse).

1. *Pharmacologic Treatment Intervention.* Clinical testing of novel mechanism therapeutics is the principle aim of this technology development section. This includes Phase IIa and proof of concept studies in pediatric subjects. It is expected the pharmacologic agents selected for these studies be IND-ready and based on novel molecular targets identified through basic and clinical research, preclinical research and animal model research relevant to understanding developmental aspects of mental illness.
2. *Combined Intervention.* Areas include all research that combines different treatment modalities in a single combined or comparative protocol (e.g., pharmacologic plus psychosocial intervention).
3. *Psychosocial Intervention.* Areas include development and application of new psychotherapeutic, behavioral, and psychosocial treatments, based on the latest advances in development neuroscience.
4. *Preventive Intervention Program.* Areas include preventive intervention studies in which efficacy has not been demonstrated, including those designed to reduce the risk of onset or delay onset of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (e.g., prevention of relapse, recurrence) or side effects (prevention/ minimization of tardive dyskinesia, etc.). Prevention studies that focus on behavioral problems, without a focus on a specific mental health disorder or a specific domain of function that significantly impacts a mental health disorder (e.g. cognitive function) should contact NICHD.
5. *Development and Maintenance of Clinical Trial Networks.* Areas include the development of hardware/software to facilitate research collaborations in conducting clinical trials, technologies to facilitate data sharing, merging of multiple data sets, and the development and maintenance of common protocols across research sites working on a common pediatric preventive or treatment intervention.

C. ***Science Education in Mental Disorders.*** There is a critical need for improvement in science education, particularly in areas specifically related to brain, behavior and mental illness. Examples include:

1. Research on the best ways to present neuroscience and behavioral science information, in the context of mental health disorders, to particular groups of students (e.g., kindergarten through sixth grade).
2. Computer-based systems to teach students how to observe scientific phenomena related to the brain, behavior and mental illness, and to report them clearly in writing.

3. Research on better ways to communicate new knowledge and directions of scientific growth in the area of neuroscience and mental illness to teachers and curriculum developers.

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Division of Adult Translational Research and Treatment Development (DATR)

The DATR is responsible for planning, directing and supporting programs of research, research training, research dissemination and resource development aimed at understanding the pathophysiology of mental illness and hastening the translation of behavioral science and neuroscience advances into innovations in clinical care. The Division supports a broad portfolio of pre-clinical and human clinical studies that focus on the phenotypic characterization and risk factors for major psychiatric disorders. In addition , the Division studies psychiatric disorders of late life. The division is comprised of four branches. These branches are: The Adult Psychopathology and Psychosocial Intervention Research Branch, The Clinical Neuroscience Research Branch, the Geriatrics Research Branch and the Experimental Therapeutics Branch. This division also includes a program on Traumatic Stress Disorders Research. Their respective functions are as follows:

Adult Psychopathology and Psychosocial Intervention Research Branch. This branch promotes the integration of basic behavioral and neuroscience findings into translational research on the foundations of psychopathology and functional disability. The branch targets new science based assessment, prevention, treatment and rehabilitation practices including research on causal risk and protective factors for mental disorders, mechanisms that convert vulnerability into psychiatric symptoms and disability and use of modern psychometric and statistical theories to advance nosology and assessment. Other specific areas of emphasis include mood, eating disorders, anxiety disorders and schizophrenia.

Clinical Neuroscience Branch. The focus of this branch is on the understanding of the neural basis of mental disorders. Human and animal studies are supported on the molecular, cellular and systems level of brain function designed to elucidate the pathophysiology of mental disease and to translate these findings to clinical diagnosis, treatment and prevention. These approaches are applied to the spectrum of mental disorders including schizophrenia, depression, bipolar disorder, anxiety disorder and other brain disorders. Areas of emphasis include: identification of valid and unique neurophysiological markers or complexes of markers for the major mental disorders and development of animal and or computational models that accurately mimic complex neurophysiology or behaviors characteristic of mental illness.

Geriatrics Research Branch. This branch focuses on research and resource development in the etiology, pathophysiology and course of mental disorders of late life as well as in the treatment and rehabilitation of persons with these disorders. Disorders studied include mood, anxiety and personality disorders, psychotic disorders and schizophrenia, psychiatric syndromes and behavioral disorders in Alzheimer's Disease and related dementias, suicide, and eating disorders. Selected areas of emphasis include: development of more reliable and valid phenotypes, assessments and biological and behavioral markers for late-life mental disorders; development of improved treatment and preventive intervention techniques for use in geriatric care settings; and identification of genetic, brain imaging and other predictors of variability in older adults' treatment response.

Experimental Therapeutics Branch. This branch supports multidisciplinary research on novel pharmacological approaches to the treatment of mental disorders, evaluation of existing treatments of

mental disorders, development and assessment of putative biomarkers of psychiatric disease and treatment response and development and testing of novel treatments. Studies supported include early phase clinical studies of new medications, studies to predict treatment response and studies to validate biomarkers or predictors of therapeutic response to pharmacological intervention. Side effects of therapeutic agents are also given emphasis.

Traumatic Stress Disorders Research Program. This program supports integrating basic behavioral and neuroscience findings into translational research on psychopathology associated with trauma exposure. Areas of emphasis include developing disorder and risk assessment tools based on individual differences, the development of treatment and preventive interventions for posttraumatic disorders, and identifying mechanisms of therapies and mechanisms of disorder that are impacted by therapies. This program also supports a broader continuum of research (basic science, clinical practice, and health care system factors) focused on the mental health consequences of mass trauma and violence (e.g. war, terrorism, natural and technological disaster), including interventions and service delivery in children, adolescents, and adults impacted by mass trauma.

All applications relevant to the mission of the Division of Adult translational Research and Treatment Development will receive full consideration. Possible areas for future research include:

A. ***Instrumentation for Clinical Research.*** Up-to-date hardware/software systems that use the most recent technological advances are needed to identify CNS dysfunction(s) related to mental disease. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.

   1. *Physiological and Behavioral Monitoring:* Technologies are needed to continuously monitoring physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate) with behavior, noninvasively and without impacting behavior. These monitoring devices should be designed for use with subjects that have a mental illness.

   2. *Data Analysis from Complex Data Sets:* Computational tools are needed to record, catalog, categorize and identify interrelationships between several of the above measures.

   3. *Deep Brain Stimulation Technologies:* Improvements in deep brain stimulation technology in human subjects/patients is increasingly important as this technique becomes more common as a potential treatment option for Obsessive Compulsive Disorder, depression, and other disorders.

B. ***Technologies for Adult Clinical Research.*** It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer-based methods of accomplishing this aim are needed to increase the accessibility and reliability of information made available to the research community.

   1. *Assessment Tools.*

      a. Technologies to assess CNS effects of psychosocial variables and interventions.

      b. Innovative approaches to assessing mental disorders using new statistical and psychometric techniques such as Item Response Theory.

      c. Computerized methodologies for assessing various mental disorders suitable for use in primary care settings.

      d. Inexpensive methodologies or techniques for assessing adherence to medication regimens.

      e. Innovative technologies for identifying and directing clinical attention to potentially adverse psychotropic drug interactions, particularly in vulnerable patients with complex regimens involving multiple medications.

      f. Simple-to-use tools for assessing individual risk profiles for the development of various mental disorders.

2. *Methodological Research and Development.* There is a need to devise new ways of data collection, analysis, management and dissemination.

    a. New relatively culture-free taxonomies and/or measures of basic behavioral and social phenomena that can be employed in research across socio-cultural contexts.

    b. Innovative computer-based observation techniques, and computer software and hardware that allow on-line methods for characterization of interpersonal interactions in groups.

    c. Low cost microcomputer software for the recording and analysis of patterns and sequences in observed social interactions.

    d. Causal modeling methodology as applied to correlational longitudinal data sets.

    e. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.

    f. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection for experiments on perception and cognition.

    g. Development of improved standardized instruments and methods for assessing assets, deficits, and disorders in adult and late life.

C. ***Adult Treatment and Preventive Intervention Research.***

1. Development of novel methods to enhance efficiency of early phase clinical trials.
2. Development of novel assessments of psychopathology suitable for use in clinical research.
3. Identification of causal risk and protective factors for mental disorders.
4. Development of standardized assessments of psychiatric and comorbid disorders.
5. Develop psychometrically sound methods for assessing the cognitive, affective and behavioral response systems believed to underpin clinical symptoms and functional impairments.
6. Identify valid markers of illness onset.
7. Develop new definitions and measures to assess functioning in people with psychiatric disorders including self-reports, tests that simulate real-world tasks and new approaches to ratings by observers.
8. Creation and validation of new measures of functional capacity.
9. New approaches to assess the functional effects of drug or psychosocial interventions to treat mental disorders.
10. Identify valid and unique neuropsychological markers for the major mental and personality disorders.
11. Identify more reliable and valid phenotypes, assessments and behavioral markers for late-life mental disorders.
12. Development of techniques for maintaining or restoring mental capacities in older adults who experience declining learning and memory abilities due to age-related brain disorders.

D. ***Experimental Therapeutics Research.***

1. Early phase clinical studies of new medications targeting major mental illnesses or symptom domains now lacking adequate treatments.
2. Development of novel somatic treatments or medical devices for the treatment of mental illness.
3. Development of reliable and stable biomarkers/biosignatures that can identify at-risk individuals prior to disease onset, biological and behavioral indicators or predictors of treatment response,

measures of disease progression, measures to identify dose ranges prior to clinical studies, preclinical or clinical efficacy testing, toxicity measures for drug development, defining patients to enroll in the clinical study, identifying CNS abnormalities, etc.

Examples of side effect issues include:

a) Development of new approaches to understand and predict the types, rates and pathophysiology of adverse effects of psychotropic medications.

b) Development of new techniques to predict emergence of later abnormalities in body weight and disorders of glucose and lipid metabolism during treatment with psychotropic drugs.

c) New methods to predict and assess the effects of psychotropic medication on cerebrovascular and cardiovascular function.

4. New approaches to understand age-related changes on the emergence of adverse effects from psychotropic medications.

5. New approaches, including pharmacological to prevent or reduce the negative metabolic, vascular and other side effects of psychotropic medications.

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Division of AIDS Research (DAR)

The DAR supports research to develop and disseminate behavioral interventions that prevent HIV/AIDS transmission, support HIV/AIDS treatment and care, and understand and alleviate the neuropsychiatric consequences to HIV/AIDS infection. Specific topics related to these research areas are listed below. Inquiries are encouraged.

THE CENTER FOR MENTAL HEALTH RESEARCH ON AIDS:

A. ***Technologies to Facilitate Research in HIV/AIDS Prevention and Care***

1. Innovative approaches for assessing HIV sexual risk behavior among research participants and at-risk populations, including biomarkers of risk behavior.

2. Development of electronic, on-line archives of validated HIV/AIDS research instruments.

3. Development and validation of novel self-report, computer-assisted, and virtual reality HIV/AIDS research instruments and assessments.

4. Development of methods to assess functioning in families in which there is an HIV infection in order to develop improved treatment modalities.

5. New tools and methods that physicians and researchers could use to monitor patient adherence to prescribed HIV/AIDS antiretroviral medication regimens in real time.

6. Computational systems that physicians and researchers can use to model the development of drug resistance based on degree and pattern of patient adherence to HIV/AIDS antiretroviral medications.

7. Technologies to assist the merging of multiple forms of HIV/AIDS data sets (e.g., community- or clinic-level data, pharmacy claims, patient self-reports, etc.) and to facilitate innovative and complex analytic strategies.
8. Causal modeling methodology as applied to correlational longitudinal data sets collected in HIV/AIDS research.
9. The development and advancement of innovative research trial designs (e.g., fixed adaptive, encouragement, partially randomized preference) for HIV/AIDS prevention and care research.
10. Technology and electronic systems that will facilitate participant scheduling, tracking, and retention in HIV/AIDS clinical trials and longitudinal studies.
11. The application of modern technology to enhance the science, operation, and management of multi-site HIV/AIDS clinical trials and behavioral research.
12. A data translation and communication package for collecting, archiving, and making available existing HIV/AIDS behavioral data sets to the scientific community for secondary or meta-analyses.

B. ***HIV Prevention Interventions.*** CMHRA seeks innovative technologies and strategies that will help reduce HIV transmission risk behavior, especially among populations at high risk for HIV infection (such as ethnic minority populations and young men-who-have-sex with men), as well as among individuals who are infected with HIV.

1. Development of methods to reduce, prevent and/or change HIV-associated and STD risk behaviors.
2. Development of school-based HIV prevention curricula, including innovative uses of emerging technologies.
3. Curricula, computer software and virtual reality programs that provide communication skills, training and role-play exercises for HIV risk reduction.
4. Methods to increase use of HIV testing and that facilitate effective test result obtainment, confirmation and counseling.
5. Novel approaches to address the issue of relapse prevention of HIV-associated risk behaviors.
6. Development of new behavioral strategies to reduce high-risk HIV transmission behavior among persons recently infected.

C. ***HIV/AIDS Educational Tools, Curricula, and Scientific Training***

1. Development of computer-based or online HIV/AIDS prevention curricula and interventions for parents, foster parents and guardians, schools, or community settings.
2. Research on the best ways to present HIV/AIDS science and prevention information in an age-appropriate manner to particular groups of students.
3. Development of print and/or computer based materials to assist primary care practitioners in informing their patients about HIV risk and prevention.
4. Innovative approaches to the development of curricula for training in multicultural issues and development of cultural competence in HIV risk assessment.
5. Develop and test technologies designed to modify the practice behaviors and decision-making process of health care providers to improve the quality of screening, counseling, prevention, and treatment services for HIV positive persons or individuals at-risk for HIV.
6. Video and computer-assisted methods to train health and mental health care providers in the psychosocial and neuropsychiatric aspects of HIV infection and AIDS.

7. Development of materials and programs to assist health care practitioners in improving patient adherence to HIV/AIDS medical regimens.
8. Development of training materials to increase awareness regarding the neurodevelopmental consequences of HIV infection in children in developing countries.
9. Development of strategies and systems to encourage entry and retention of individuals with non-HIV/AIDS science backgrounds (engineers, computer scientists, medical anthropologists, law, business) or perspectives (individuals from under-represented communities) into the HIV/AIDS research field.
10. Development of systems to keep established researchers and practitioners up-to-date on the findings and implementation of HIV research.

D. ***Systems to Advance the Dissemination and Implementation of HIV/AIDS Interventions***

1. Web-based networks and software for the dissemination, identification, and tailoring of efficacious HIV/AIDS behavioral interventions targeting at-risk populations.
2. Development of technological approaches to increase the sustainable uptake of scientifically based HIV/AIDS prevention interventions across diverse community settings.
3. Development of strategies or application of technology to assist organizations in identifying and implementing proven HIV prevention strategies and in addressing health disparities.
4. Novel methods of disseminating HIV prevention materials to be used in community based outreach programs for special populations (school dropouts, homeless, street youth, incarcerated youth).
5. Development of innovative approaches to link researchers with community providers in the implementation of research-based HIV prevention efforts at the community level.
6. Systems that build the capacity of HIV/AIDS community-based organizations to conduct program evaluations and document intervention outcomes for the purposes of maintaining and enhancing ongoing intervention programs.

E. ***Technologies to Support HIV/AIDS Mental Health Services***

1. Use of technology to develop and disseminate curricula for training clinicians and other health care practitioners in the prevention and treatment of HIV-related mental disorders.
2. Development of novel programs to help people recognize and access treatment of mental health problems arising from living with HIV/AIDS as a long-term chronic condition.
3. Develop rehabilitative approaches to alleviate HIV-associated neurodevelopmental abnormalities that may restrict children's academic achievements and quality of life.
4. Development of innovative approaches to reduce stigma often expressed toward individuals with HIV/AIDS.
5. Develop and test interventions for appropriate HIV status disclosure to relationship partners, family members, and health care providers, in an effort to optimizes the likelihood of positive outcomes.

F. ***Tools to Monitor and Improve Patient Adherence to HIV/AIDS Treatment***

1. Development of novel methods to expedite and enhance linkage to primary medical care for individuals who receive HIV-seropositive test results in community-based settings.
2. Technologies that will electronically monitor HIV/AIDS patient adherence to antiretroviral medications and that will use wireless technology to radio this data back to providers and/or researchers for real-time monitoring of adherence.

3. Clinic-based systems that will screen HIV/AIDS patients for medication adherence while they await medical appointments and that will immediately integrate these patient reports into the electronic medical record so this information is routinely available to physicians during their appointments with patients.
4. Development of novel tools or methodologies designed to improve patient adherence to HIV/AIDS drug therapies.
5. Systems that improve adherence to HIV/AIDS medical care by enhancing the ability of patients to monitor and manage scheduled medical appointments, routine prescription refills, and daily medication doses.
6. Novel systems for distributing, dispensing, or administering antiretroviral drugs that are designed to enhance patient adherence to these regimens.
7. Biologically-based technologies that will aid medical doctors in determining how a particular individual may respond to a particular HIV/AIDS medication, i.e. "individualized medicine." For example, genomic and phenotypic information combined could be used in determining whether a drug will be an effective treatment for an individual. Likewise, genomic and phenotypic information may help to identify which patients are at risk for drug-induced side effects.

G. ***Research Tools and Treatments for Neuro-AIDS: HIV-1 Infection and the Nervous System***

1. Development of novel non-invasive (e.g., neuroimaging) approaches to assess and study mechanisms of neurologic and neurocognitive dysfunction associated with HIV infection.
2. Development of in-vivo and in-vitro models to assess mechanisms of HIV-1 trafficking into and out of the CNS, mechanisms of neuropathogenesis and therapeutic strategies for eradicating HIV-1 in the CNS.
3. Development of novel molecular markers for NeuroAIDS using proteomics, microarrays and neuroimaging.
4. Development of novel molecular approaches to study compartmentalized viral evolution in the CNS.
5. Development of improved anti-retroviral therapeutic strategies for targeting CNS infections including: nanotechnologies, facilitated entry of anti-retroviral therapeutic agents through the blood-brain barrier by manipulation of transporter systems and development of novel anti-retroviral therapeutic agents that readily pass through the blood-brain barrier.
6. Development of novel therapeutic approaches to block or reverse CNS dysfunction associated with HIV infection.
7. Discovery and development of novel tools and cost effective methods for detecting the efficacy and neurological and neuropsychiatric side effects of anti-retroviral medications.
8. New approaches to reduce transmission risk or neuro-cognitive impairment in persons with recent HIV infection (0-6 months post exposure).
9. Novel therapeutic and diagnostic instrumentation development for the detection and treatment of neurological manifestations of HIV co-infections such as tuberculosis, hepatitis C, toxoplasmosis, that can be used in developing countries.
10. Development of novel or refinement of existing cell-based assays designed to screen compounds (small molecule, large molecule, bioproduct, etc.) targeted to treat neurologic and psychiatric disorders that are associated with HIV/AIDS.
11. Development of novel or refinement of existing animal models to test the efficacy and toxicity of new agents targeted specifically towards eliminating/eradicating HIV or its sequelae in the brain.

12. Discovery and development of small molecular inhibitors or enhancers targeted to mechanisms that play critical roles in viral replication pathways especially in the CNS.
13. Improvement/validation/characterization of the existing in vitro and animal models that are used for screening compounds that have therapeutic potential for NeuroAIDS and its associated complications.
14. Novel compounds or adjunctive therapies that have the potential to protect/ameliorate/treat the long-term neurologic and psychiatric side effects of ARVs in the presence or absence of psychotropic medications.
15. Novel models or methods for the pharmacokinetic/pharmacodynamic studies to detect long-term neuropsychological adverse effects of ARVs.
16. Applications that assess the neuroprotective potential or inhibition of HIV replication in the brain with FDA-approved drugs that are currently registered for other indications (off-label validation studies).
17. Development/improvement of cost effective methods, assays, or instruments that detect currently approved ARVs plasma concentrations in relationship with disease progression.
18. Discovery and development of biomarkers designed to detect drug efficacy, measure viral load, or provide evidence that agents are directed against the targets in the CNS or peripheral nervous system (PNS).
19. Development of technology (IT or other) to optimally study/analyze/report on adverse effects of ARVs in the presence of other medications, especially psychotropic medications, drugs of abuse, or medications to treat drug abuse.
20. Develop or adapt neurological/ neuropsychological/neurobehavioral assessments to evaluate HIV associated abnormalities in adults/children in resource poor environments that are adaptable to different cultures and languages.

For information related to programs supported by the Center for Mental Health Research on AIDS please contact:

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Division of Services and Intervention Research

The Division of Services and Interventions Research supports research, research demonstrations, research training, resource development, and research dissemination in prevention and treatment interventions, services research, clinical epidemiology, and diagnostic and disability assessment. The division is composed of three branches: Services Research and Clinical Epidemiology Branch, Adult Treatment and Preventive Intervention Research Branch, and Child and Adolescent Treatment and Preventive Intervention Research Branch.

The Division supports two critical areas of research:

- Intervention research to evaluate the effectiveness of pharmacologic, psychosocial (psychotherapeutic and behavioral), somatic, rehabilitative and combination interventions on mental and behavior disorders-including acute and longer-term therapeutic effects on functioning across domains (such as school, family, peer functioning) for children, adolescents and adults.

- Mental health services research

The interventions focus is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, and the variety of community and institutional settings in which treatment is provided. It includes clinical trials evaluating the effectiveness of known efficacious interventions, as well as studies evaluating modified or adapted forms of interventions for use with additional populations (such as women, ethnic and racial groups), new settings (public sector, pediatric primary care, schools, other non-academic settings, communities at large) and people with co-occurring disorders. Other foci include: identifying subgroups who may be more likely to benefit from treatment, evaluating the combined or sequential use of interventions (such as to extend effect among refractory subgroups), determining the optimal length of intervention, establishing the utility of continuation or maintenance treatment (that is, for prevention of relapse or recurrence), and evaluating the long-term impact of efficacious interventions on symptoms and functioning.

Services research covers all mental health services research issues, across the lifespan and disorders, including, but not limited to:

- Services organization, delivery (process and receipt of care), and related health economics at the individual, clinical, program, community and systems levels in specialty mental health, general health, and other delivery settings (such as the workplace).

- Interventions to improve the quality and outcomes of care (including diagnostic, treatment, preventive, and rehabilitation services.

- Enhanced capacity for conducting services research

- The clinical epidemiology of mental disorders across all clinical and service settings.

The Division also provides biostatistical analysis and clinical trials operations expertise for research studies; analyzes and evaluates national mental health needs and community research partnership opportunities; and supports research on health disparities.

The priorities for 2011 should focus on technologies that advance the scientific opportunities and recommendations of "The Road Ahead: Research Partnerships to Transform Services, A Report by the National Advisory Mental Health Council's Workgroups on Services and Clinical Epidemiology Research." "The Road Ahead: Research Partnerships to Transform Services, A Report by the National Advisory Mental Health Council's Workgroups on Services and Clinical Epidemiology Research," and the NIMH Strategic Plan. Examples are listed below:

1. **Clinical Trials Methodologies:** The development, testing and refinement of methodologies, instruments and statistical approaches to facilitate collaborative clinical trials for the prevention, treatment and rehabilitation of individuals with mental disorders; the development of innovative trials design (e.g., fixed adaptive, encouragement, partially randomized preference) the application of modern technology to enhance the science, operation, and management of multi-site mental health clinical trials; and the development of mental health clinical trial archives. The development of portable clinical trial management systems such as serious adverse event (SAE) oversight and monitoring software. Adaptation of existing clinical trial methodologies to study mental health disorders. Development of common data elements to enhance uniformity across clinical trials with and amongst disorders.

2. **Science Training and Education:** SBIR applications must focus on DSIR's research priorities. Develop, modify and test new and existing technologies, strategies and approaches to: (1) enhance science and research training across the educational/ career pipeline; (2) improve scientific literacy for clinicians and service/ organizational providers; (3) encourage entry and retention of individuals with non-mental health science backgrounds (engineers, computer scientists, medical anthropologists, law, business) or perspectives (individuals from under-represented communities) into the mental health services and interventions field; (4) keep established researchers and practitioners up-to-date on the findings, implementation, and methods of services and interventions research; and (5) facilitate *participatory* research with individuals, families and communities. This can include the development of science/ research education materials, curriculum, methodologies and web-based programs relevant to the mission of the division; the development of networking and collaborative approaches to research training in mental health interventions and services research; and the development of multi-media approaches (combined with traditional strategies) to improve the level of scientific and career mentoring that mental health services and interventions researchers receive.
3. **Public Health Oriented Pharmacoeconomics:** Develop and test simulation models for estimating the amount of total out-of-pocket expenditures (co-payments) for the most frequently prescribed psychotropic drugs under different insurance benefit scenarios and/or under different pharmacy benefit management scenarios. Models should also be developed to accommodate common combined pharmaceutical approaches.
4. **Dissemination:** Development of technological approaches to increase the sustainable uptake of scientifically based treatments and services across diverse community settings. This could include web-based interactive tools for state/county mental health or related (e.g., schools) agencies around implementation of evidence-based practices. Development of innovative ways (e.g., new technology, use of multi-media) of disseminating information to stakeholders. Development of new approaches to the dissemination and implementation of evidence based mental health interventions to underserved populations (e.g., rural/frontier, aging individuals with neuropsychiatric disorders). Development of technology to enhance conduct of clinical trials and the dissemination of their results.
5. **Implementation:** Application of new technologies, approaches and strategies to identify and utilize active therapeutic ingredients in complex community-based services and programs that optimize functioning and sustain community reintegration of people with mental disorders. Use of technologies and strategies to assist service systems to more adequately plan for transitions (e.g., child to adult system, prison to community) and seamlessly integrate mentally ill individuals moving between these sectors.
6. **Merging Multiple Data Sets:** Merging multiple data sets (e.g., claims, trials, pharmacy etc.) for innovative and complex analytic strategies.
7. **Community Outreach to Diverse and Underserved Populations:** Application of new technologies and strategies to develop, test, and refine culturally appropriate materials and approaches to: foster help-seeking and engagement of diverse and underserved populations in research-based mental health treatment and prevention; to foster participation in community based research by diverse and underserved populations; and to inform diverse provider groups about state-of-the-art mental health treatments and services in order to facilitate their implementation of these interventions.
8. **Computerized Methodologies for Mental Health Services Research:** Applications need to focus on computerized methods to assess mental disorders in primary care settings including screening devices for identifying mental disorders across the life-span; development of computer software and hardware that allow conducting computer assisted interviews with severely mentally ill people for research purposes to obtain information on their quality of care; design work to move assessment as rapidly as possible to computerized adaptive testing (CAT); apply audio and video technologies to assess patient's treatment preferences.

A. ***Services Research and Clinical Epidemiology Branch.*** The branch supports research on the organization, financing, delivery, effectiveness, and appropriateness of mental health care in everyday settings in order to find ways to improve the effectiveness, efficiency, and equity of mental health services (including preventive services) in community and other settings. Also supported are studies on pharmacoeconomics, pharmaco-epidemiology, and the distribution, determinants, and course of mental illness in the context of various clinical settings. Mental health services include mental health care provided in specialty mental health and general health care settings, including primary care, hospitals, nursing homes, and other residential care settings, as well as in educational settings and various legal system settings, such as jails, juvenile detention and correctional facilities, prisons, and probation and parole programs. Other services often needed by mentally ill persons include social services, vocational and rehabilitation services, welfare, and housing. Relevant services include those provided to children and adolescents with emotional disorders, adults and elderly adults with mental disorders, and persons with mental illness that co-occurs with physical illness and with alcohol and/or drug abuse disorder. Research methodologies include ethnographic studies, surveys, and analyses of secondary data, randomized controlled trials, quasi-experimental designs, cohort, and case-control studies.

Advances in clinical epidemiology, mental health treatment and services research fields have made it imperative that intensive work continue in the areas of assessment/screening technologies, outcome assessment measurement and measurement packages, dissemination technologies, data analysis techniques, and the training of clinicians and providers. The translation of efficacious and effective treatments into primary care, community mental health centers, and managed care settings is both a major challenge and opportunity to develop technologies and systems that will improve the care and rehabilitation of patients and enable them to profit from the research advances that have been made. Research is needed on the dissemination of empirically supported treatments or services.

1. *Methodological Research Program.* Supports studies that involve development, testing, and refinement of methodologies and instruments to facilitate research on services for mentally ill persons, including measures of severity of illness, family burden, social support, quality of care, effectiveness of care, direct and indirect cost of mental disorders, and short-term and long-term outcome measures; studies submitted by statisticians, psychometricians, and other experts in research methodology and scientific data analysis for work on the design, measurement, and statistical challenges inherent in conducting mental health services research.

2. *Outcomes and Quality of Care Research.* This program is concerned with strengthening the theoretical and empirical base for mental health services research by including approaches that derive from sociology, anthropology, and the behavioral sciences in general. The program supports research relating to issues of culture, social systems, and social networks as they relate to help seeking, use, and provision of services, effectiveness, quality, and outcomes of services.

3. *Systems Research Program.* Supports studies on organization, coordination, and collaboration of mental health and related services both within and across care settings in order to improve mental health outcomes and prevent or treat co-occurring substance abuse, physical problems, and other behavioral health disorders. Service sectors of interest include: the criminal justice system, housing and other social services, community support, post-trauma services, and adult autism services. Also relevant are studies to establish the effectiveness of legal mechanisms relevant to persons with mental illness, such as outpatient commitment, community monitoring, and guardianship; and the development of the role and expertise of social workers in mental health research activities.

4. *Disparities in Mental Health Services Program.* Plans, stimulates, disseminates, and supports research on the complex factors that influence disparities in mental health services, particularly across special population groups such as racial and ethnic groups, as well as women and children, and persons living in rural and frontier areas. The program addresses care delivered in

a variety of settings such as the specialty mental health sector, the general medical sector, and community settings (such as schools). Also, it supports research that examines innovative services interventions (such as community-based participatory methods, faith-based) to overcome mental health disparities related to mental health service delivery and use.

5. *Sociocultural Research Program.* Is concerned with strengthening the theoretical and empirical base for mental health services research by including approaches that derive from sociology, anthropology, and the behavioral sciences in general. The program supports research relating to issues of culture, social systems, and social networks as they relate to help seeking, use, and provision of services, effectiveness, quality, and outcomes of services.

6. *Child and Adolescent Services Research Program.* Includes research on the quality, organization, and content of services for children with mental disorders and their families. The program focuses on child mental health services provided in multiple sectors and settings, such as schools, primary care, child welfare, juvenile justice, and mental health. Program emphases include practice research within child service systems, research testing the outcomes of innovative child service delivery models, and studies that examine the adaptability or sustainability of child mental health services.

7. *Financing and Managed Care Research.* Supports research on economic factors affecting the delivery of mental health services including the economic burden of mental illness; financing and reimbursement of public and private mental health services; impact of various forms of managed care and physician payment methods on the cost of mental health care; pharmaco-economics; evaluation of the impact of insurance coverage including mandated coverage and mental health insurance parity on access, cost, and quality; cost-benefit, cost-effectiveness and cost-utility analysis of mental health service interventions; and economic analysis of practice patterns of different mental health providers. The goal of the program is to expand understanding of the role of economic factors in the delivery and use of mental health services and assist in the development of improved mental health financing methods promoting high quality, cost-effective care for people suffering from mental disorders.

8. *Primary Care Research.* Includes studies on the delivery and effectiveness of mental health services within the general health care sector; recognition, diagnosis, management, and treatment of mental and emotional problems by primary care providers; coordination of general medical care with and referrals to mental health specialists; provision of psychiatric emergency services, consultation/liaison psychiatry, and other psychiatry, psychology, and social work services within the general medical care sector; studies that improve understanding of how best to improve care for people with mental disorders and co-occurring physical conditions.

9. *Clinical Epidemiology Research.* Includes epidemiologic studies of mental disorders in clinical settings, that is, the distribution of treatments and services in a population; studies to determine usual or best practices and the relationship to patient, provider, and system factors, as well as to outcomes; pharmaco-epidemiology studies; research to identify factors for the development of mental disorders in clinical settings, factors important in the natural history of mental disorders, including comorbid conditions, and the rates of occurrence of mental disorders in clinical and services populations.

10. *Disablement and Functioning Research Program.* Supports studies on the development of methodologies for assessing disablements and functional status, and the development of global and specific measures of disablements and functional status; the identification and assessment of disablements/functional status in clinical investigations and in clinical epidemiological surveys. In addition, it supports studies of the relationship of rehabilitative and traditional mental health services and service systems; impact of disability benefits and insurance; factors affecting impairments and disabilities during and as an outcome of rehabilitation and other treatments; rehabilitative services focused on specific domains of disabilities, such as work and social relationships; and, factors that influence and sustain community reintegration.

11. *Dissemination and Implementation Research Program.* Includes studies that will contribute to the development of a sound knowledge base on the effective transmission of mental health information to multiple stakeholders and of the process by which efficacious interventions can be adopted within clinical settings. Research on dissemination will address how information about mental health care interventions is created, packaged, transmitted, and interpreted among a variety of important stakeholder groups. Research on implementation will address the level to which mental health interventions can fit within real-world service systems. Related topics include multilevel decision-making perspectives about services and interventions in community settings, with special focus on translating behavioral science into applied research in these areas.

B. ***Adult Treatment and Preventive Interventions Research Branch.*** This Branch supports research evaluating the therapeutic (acute, maintenance, and preventive) and adverse effects of psychosocial, psychopharmacologic, and somatic interventions of proven efficacy in the treatment of mental disorders in adults. It includes trials evaluating and comparing the effectiveness of known efficacious interventions, as well as studies evaluating modified or adapted forms of interventions for use with specialized populations (such as women, or specific ethnic or racial groups), new settings (public sector, or computer based), new methods of treatment delivery (e.g., web or computer – based), and people with comorbid physical or mental disorders.

1. *Somatic Treatments Program.* Areas include electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (RTMS), bright light, physical exercise, and similar nonpharmacologic approaches for which efficacy has been demonstrated.

2. *Adult Psychotherapy Intervention Program.* Areas of program responsibility include evaluation of the effectiveness of psychotherapeutic, behavioral, and pspychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and applications of psychotherapy treatments.

3. *Adult Psychopharmacology Intervention Program.* Areas of program responsibility include research involving psychotropic medications of demonstrated efficacy. Examples include evaluation of long-term effectiveness of pharmacotherapy and treatment of subpopulations of recognized diagnostic groups.

4. *Adult Integrated Treatment Program.* Areas of program responsibility include the use of combined or sequential treatment approaches to improve long-term outcome. A major focus is improvement of efficacious psychopharmacological interventions to maximize symptomatic relief while minimizing adverse reactions. For example, medications may be combined with the full range of therapies in individual, conjoint, or group settings.

5. *Preventive Interventions Program.* Areas of program responsibility include studies evaluating the effectiveness of preventive interventions, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (such as prevention of relapse, recurrence, inappropriate resource use) or side effects. A specially designated programmatic focus is the area of suicide prevention.

6. *Rehabilitative Interventions.* Areas of program responsibility include evaluation of the effectiveness of psychotherapeutic, behavioral, and psychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and applications of psychotherapy.

C. ***Child and Adolescent Treatment and Preventive Intervention Research Branch.*** The branch supports research to evaluate the effectiveness of mental health preventive, treatment and rehabilitative interventions- alone or in combination-for children and adolescents (including those co-occurring with other conditions). The Branch also supports research addressing the long-term effectiveness of known efficacious interventions, including their role in the prevention of relapse and recurrence of mental disorders.

Areas of emphasis include: Research on the effectiveness of treatment interventions for childhood and adolescent mental and behavioral disorders in practice and community settings to determine the real life therapeutic benefit short-and-long term; Research to prevent mental and behavioral disorders in children and adolescents; Research to build new methodologies that can be effectively used to evaluate the safety of interventions in community settings; Research to determine whether treatment of mental and behavioral disorders in children results in improved outcomes as adolescents and young adults and prevents the negative functional outcomes associated with those disorders (such as substance abuse, academic failure, higher medical costs, co-occurring mental disorders). juvenile justice facilities.

1. *Pharmacologic Treatment Intervention Program.* Areas of program responsibility include evaluation and comparison of efficacious pharmacological and other somatic treatments for children and adolescents with mental disorders.
2. *Combined Intervention Program. Child and Adolescent Combined Intervention Program.* Areas of program responsibility include all research that combines different treatment modalities in which efficacy has been demonstrated in a single combined or comparative protocol.
3. *Psychosocial Intervention Program.* Supports research evaluating the effectiveness of psychosocial interventions on children's and adolescents mental and behavior disorders, including acute and longer-term therapeutic effects on functioning across domains. It includes trials evaluating the effectiveness of known efficacious interventions, as well as studies evaluating modified or adapted forms of interventions for use with additional populations, new settings, and people with comorbid disorders.
4. *Preventive Intervention Program.* Areas of program responsibility include research examining the effectiveness of preventive intervention studies, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems with asymptomatic subclinical populations.

D. ***Clinical Trials Operations and Biostatistics Unit.*** This Unit serves as the operations focal point for collaborative clinical trials on mental disorders in adults and children. The Unit has responsibility for operations and oversight of both contract-supported and cooperative agreement-supported multisite clinical trial protocols, as well as operations focus on special clinical trial research projects that may be undertaken by the Institute. In addition, the Unit has general leadership responsibility for over-arching matters related to clinical trials operations, such as the coordination of the ancillary protocols across the large trials, development of long-term strategies for clinical trials research (such as clinical trials research networks), improvement of the quality of clinical trials by development and monitoring of operations guidelines, and implementing the NIMH policy for dissemination of public access datasets. Unit staff serves as primary liaison with the Data and Safety Monitoring Boards for all matters related to the operation and conduct of the clinical trials. The Unit provides consultation to Institute staff and grantee/contractor staff on biostatistical matters related to appropriateness of study design, determination of power and sample size, and approaches to statistical analysis of data from clinical trials supported by NIMH.

For further information on Services and Intervention Research contact:

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NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES (NIMHD)

The mission of the National Institute on Minority Health and Health Disparities (NIMHD) is to promote minority health and to lead, coordinate, support, and assess the National Institutes of Health (NIH) effort to reduce and ultimately eliminate health disparities. In this effort, the NIMHD conducts and supports basic, clinical, social and behavioral research, facilitates the development of research infrastructure and training, fosters emerging programs, and reaches out to racial/ethnic minority and other health disparity communities.

NIMHD particularly serves as the focal point for targeted, hypothesis-driven, patient-oriented research and targeted applied, outcomes- and problem-driven studies that meet at least two of three criteria: (1) participating health disparity population(s) is/are over sampled; (2) the participating health disparity population(s) is/are specifically targeted with or without within-group comparisons; and/or (3) the research focus is within the scope of NIMHD programmatic interests. NIMHD's programmatic interests include surveillance, explanatory, and translational research in health disparity populations. Specific topics include health promotion and disease prevention and intervention; pathogenic mechanisms underlying escalations in the susceptibility to disease and illness; and health services research - the impact of socioeconomic, cultural, and other environmental factors on health outcomes.

PROGRAM AREAS OF INTEREST

Summary

Priority Populations: Minorities, Low-Income, and Rural

Diseases where significant health disparities exist: Infant Mortality, Obesity, Depression, Cancer, Heart Disease, Diabetes, Sexually Transmitted Infections, and HIV/AIDS

Interventions that address: Behavioral Change, Prevention, Social Determinants of Health, and Health Literacy

Applications that are: Transformational, Trans-disciplinary, and Translational

Natural History of Disparities in Health Outcomes

Disparities in health outcomes are believed to result from the interaction of a plethora of interactive factors such as environmental exposures and genetic traits, and/or the accrual over time of stable phenotypic traits and lifestyle behaviors that contribute to but are insufficient individually to cause the onset of disease or illness. The etiology of disparities in health outcomes with particular emphasis on identifying and deconstructing the array of interactive risk factors—environmental, socioeconomic, stereotyping, bias, clinical uncertainty, and gene-related factors—that contribute to escalations in the susceptibility to disease and illness and may contribute to health disparities. Examples include, but are not limited to:

1. Multidisciplinary basic research approaches that lead to biological probes and starting points for therapeutic interventions;
2. Innovative high throughput screening approaches to identify compounds that are active in target- and phenotype assays and to use these approaches to develop bioactive probes for application in vitro and potentially in vivo studies;
3. Methodological and technological innovation that will integrate behavioral and social science with biomedical research, including gene related and environmental components.
4. Differential pharmacologic drug metabolism; and

5. Impact of dietary decision making in diverse populations and effect on health disparity outcomes.

Health Promotion and Prevention Research in the Health Disparities Communities

High priority is given to activities designed to empower health disparity communities to achieve health equity through health education, disease prevention, and partnering in community-based hypothesis, outcomes- and problem-driven research. Examples of such activities include, but are not limited to:

6. Efficacy of therapies in local populations;
7. Motivating positive behavioral changes in diverse populations;
8. Health outcomes related to health seeking, lifestyle, risk taking, protective behaviors and/or socioeconomic status;
9. Incorporating research into health promotion and disease prevention initiatives, applying new knowledge in a culturally appropriate manner in intervention/disease prevention initiatives; and
10. Distribution of health structures and adverse health effects, and the sufficiency of healthcare frameworks in accommodating diverse social, cultural, political and economic factors.

Innovations in Health Disparities Research

Studies that promote and advance evidence-based transformation in medical decision-making and health policy; demonstration projects that implement evidence-based, culturally sensitive intervention/disease prevention therapies and diagnostics; and activities designed to build capacity for health disparities research are of high priority. Examples of such studies include, but are not limited to:

11. Development of health disparity group-specific methodologies and diagnostics;
12. Development of technologies targeted for health disparity groups (i.e., gene chips, other novel assay systems, animal models, specialized instruments, etc.); and
13. Demonstration projects that build capacity for health disparities research (e.g., regional hospital-based registries for disease areas of emphasis, etc.) or implement the translation/application of research results in a culturally sensitive manner.

For additional information about the areas of interest to the NIMHD, please visit our home page at http://www.ncmhd.nih.gov.

Broad Area of Research that NIMHD Supports

Studies on the biological and biobehavioral risk factors for disparities in health and health outcomes; cultural, environmental, and societal dimensions of disparities in health status, including the impact of health processes; development and refinement of research tools, survey instruments, and databases that are culturally sensitive and specifically for racial and ethnic minority populations and other health disparity populations, in particular the medically underserved which includes the rural and urban poor.

For additional information on research topics, contact:

Mr. Vincent A. Thomas, Jr., MSW, MPA
Program Manager
National Institute on Minority Health and Health Disparities, NIH
6707 Democracy Blvd.
Suite 800, MSC 5465
Bethesda, MD 20892-5465
301-402-2516, Fax: 301-480-4049
Email: vt5e@nih.gov

For administrative and business management questions, contract:

Ms. Priscilla Grant, J.D., C.R.A.
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NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)

The mission of NINDS is to reduce the burden of neurological disease—a burden borne by every age group, by every segment of society, by people all over the world. To this end, the Institute supports and conducts research on the healthy and diseased brain, spinal cord, and peripheral nerves. Hundreds of disorders afflict the nervous system. Common disorders such as stroke, epilepsy, Parkinson's disease, and autism are well-known. Many other neurological disorders are rare and known only to the individuals and families affected, their doctors, and scientists.

The NINDS SBIR/STTR program funds small business concerns to conduct innovative neuroscience research or neuroscience research and development (R/R&D) that has both the potential for commercialization and public benefit. NINDS is committed to helping small business concerns commercialize their technologies through its grant funding, technical assistance program participation, and outreach at meetings. NINDS encourages all Phase II applicants to apply to the NIH Commercialization Assistance Program (CAP) to gain assistance in transferring their products to the marketplace. The CAP program is open to all Phase II grants that were active in the past six years. NINDS is increasingly tracking the progress of its funded small business concerns and the products they develop. Funding priority will be given to those small business concerns that show not only their ability to develop products but their growth as a small business concern towards independence from the SBIR/STTR program.

LIMITED AMOUNT OF AWARD

For budgetary, administrative, or programmatic reasons, NINDS may decrease the length of an award and/or the budget recommended by a review committee, or not fund an application. Generally, NINDS does not fund Phase I applications greater than $350,000 total cost per year for up to 2 years or Phase II applications greater than $1,000,000 total cost per year for up to 3 years. Applicants considering a requested budget greater than these limits are strongly encouraged to contact program staff before submitting an application.

Phase IIB Competing Renewal Awards

In addition to the traditional Phase I and II applications, NINDS will accept Phase IIB SBIR/STTR Competing Renewal grant applications to continue the process of developing products that require approval of a federal regulatory agency. Such products include, but are not limited to: medical implants, drugs, biologics, and new treatment or diagnostic tools that require FDA approval.

NINDS will accept applications for up to three years that do not exceed $1,000,000 per year in total costs.

The following examples would make appropriate topics for proposed SBIR or STTR Phase IIB Competing Renewal projects. This list is not meant to be all-inclusive, and applications for other appropriate activities will be accepted.

1. Studies for preclinical discovery and development of drugs to treat neurological disorders. Appropriate areas of effort may include the following (but are not limited to): medicinal chemistry structure-activity relationship (SAR) studies to develop drug candidates, pharmacology studies aimed at evaluating the potential therapeutic activity and side effect profile of drug candidates, medicinal chemistry and pharmacology studies aimed at synthesizing and evaluating compounds as potential drug leads and as preclinical drug candidates, and studies aimed at evaluating drug metabolism and pharmacokinetic behavior in rodents. These efforts should extend beyond those conducted under the initial SBIR Phase I and Phase II grants. The studies conducted under the previous grants should be sufficient to provide a sound rationale for continued development.
2. Completion of studies as required by the FDA for an IND application.
3. Safety and effectiveness studies of novel medical devices.
4. Human clinical trials/studies to determine the safety profile, metabolism, and/or efficacy of a drug.

Please contact Ms. Stephanie Fertig (contact information provided below) before beginning the process of preparing an application. Prospective applicants are strongly encouraged to submit a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review. It is expected that only a portion of NINDS SBIR/STTR Phase II awards will be eligible for a Competing Renewal grant.

Any Phase IIB Competing Renewal applications that do not propose to develop products that require regulatory approval, or that exceed the total cost budget cap, will be withdrawn from consideration prior to peer review.

For more information on Competing Renewal Awards of SBIR Phase II grants for Brain and Behavior Tools: http://grants.nih.gov/grants/guide/pa-files/PA-08-056.html.

Ms. Stephanie Fertig, M.B.A.
Project Manager, Small Business Programs
301-496-1447; Fax: 301-480-1080
Email: fertigs@ninds.nih.gov

For general questions related to the small business program, email: nindssmallbusiness@mail.nih.gov.

RESEARCH TOPICS OF INTEREST TO NINDS

General Areas of Interest

The NINDS accepts a broad range of small business applications that are significant, innovative, and relevant to its mission. Examples of research topics within the mission of NINDS that may be of interest to small businesses are shown below. This list is not all inclusive and some research areas fall into multiple categories.

1. Therapeutics and Diagnostics Development for Neurological Disorders, including biomarker and diagnostic assays, therapeutics (drugs, biologics, and/or devices) for treatment of neurological disorders, and technologies/methodologies to deliver therapeutics to the central nervous system.

2. Clinical and Rehabilitation Tools, including intraoperative technologies for neurosurgeons, rehabilitation devices and programs for neurological disorders, and brain monitoring systems
3. Technology and Tools, including imaging technologies to image the nervous system, neural interfaces technologies, and tools for neuroscience research and drug development.

In addition to the research topics listed, NINDS also solicits applications in specific program areas. For additional information about NINDS program announcements, please visit our small business home page at: http://www.ninds.nih.gov/funding/small-business/.

Clinical Trials

The NINDS is committed to identifying effective treatments for neurological disorders by supporting well-executed clinical trials. NINDS may decline funding of a clinical trial application for programmatic or administrative reasons. SBIR applicants are strongly encouraged to contact Joanne Odenkirchen (contact information provided below) within the NINDS Office of Clinical Research for advice about potential clinical trial applications ***prior*** to submission in order to determine the relevance of the proposed research to NINDS and its potential for translating discoveries to clinical interventions for neurological disorders. For more information about what is generally required before trials are funded, applicants are encouraged to review the NINDS Office of Clinical Research webpage (http://www.ninds.nih.gov/research/clinical_research/index.htm).

Joanne Odenkirchen, M.P.H.
Clinical Research Project Manager, Office of Clinical Research
301-496-3104
Email: jo21x@nih.gov

NINDS Cooperative Program in Translational Research

Although translational research is supported through the general SBIR/STTR program announcement, the NINDS also has a Cooperative Program in Translational research (PAR-08-235). The NINDS Cooperative Program encourages Phase II and Fast-Track applications that directly address the identification and pre-clinical testing of new therapeutics for neurological disorders. The program will facilitate solicitation, development, and review of therapy-directed projects to accelerate the translation of basic research discoveries into therapeutic candidates for clinical testing. This program is specifically directed at projects that include therapeutic leads with demonstrated activity against the intended disease target. The program supports pre-clinical optimization and testing of these leads and projects must be sufficiently advanced that an IND or IDE application to the FDA can be submitted by the end of the project period. The program does not support early-stage therapeutic discovery activities such as high throughput screening. The program also excludes clinical research, basic research, and studies of disease mechanism. This is a milestone-driven cooperative agreement program involving participation of NINDS staff in the development of the project plan and monitoring of research progress. For more information on the NINDS Cooperative Program in Translational Research-Small Business Awards (SBIR[U44]): http://grants.nih.gov/grants/guide/pa-files/PAR-08-235.html.

Due to the unique requirements of the NINDS Cooperative Program in Translational Research, applicants are strongly encouraged to consult with Dr. Tom Miller at least three months prior to the next receipt date.

Dr. Tom Miller, Ph.D., M.B.A.
Program Director, Office of Translational Research
301-496-1447
Email: millert@ninds.nih.gov

Countermeasures Against Chemical Threats

NINDS manages the NIH Countermeasures Against Chemical Threats (CounterACT) program. CounterACT supports research and development on new and improved therapeutics or diagnostic technologies to prevent or mitigate the toxic effects from exposure to chemical threats, defined as toxic chemical agents that could be used in a terrorist attack against civilians, or those that could be released at toxic levels by accident or natural disaster. This includes the development of new (or support of existing) partnerships between small business and not-for-profit laboratories engaged in this research. The scope of research supported includes early screening for compounds with the desired biological activity, advanced preclinical and efficacy testing, through clinical research with promising candidate therapeutics. For more information on this program, including specific program announcements, please see: www.ninds.nih.gov/counteract. Applicants are strongly encouraged to consult with Dr. David Jett to determine the programmatic relevance of their proposed research.

David A. Jett, Ph.D.
Program Director, NIH CounterACT Research
301-496-6035
Email: jettd@ninds.nih.gov

For additional information on research topics, contact:

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or for general questions related to the small business program, email: nindssmallbusiness@mail.nih.gov

For administrative and business management questions, contact:

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NATIONAL INSTITUTE OF NURSING RESEARCH (NINR)

The National Institute of Nursing Research (NINR) supports research focused on biological and behavioral aspects of critical health problems that confront the Nation. Emphasis is on seeking ways to reduce the burden of illness and disability by understanding and easing the effects of acute and chronic illness, improving health-related quality of life by preventing or delaying the onset of disease or slowing its progression, establishing better approaches to promote health and prevent disease, and improving clinical environments by testing interventions that influence patient health outcomes and reduce costs and demand for care.

For additional information about areas of interest to the NINR, please visit our home page at http://www.nih.gov/ninr/.

Research and Development of Technologies for Health Promotion and Alleviation, Adaptation to, or Management of Symptoms

A. Technologies to be used in the hospital, long-term care, hospice, assisted living facility, or home setting that improve symptom evaluation in persons with chronic conditions. Conditions of interest include congestive heart failure, cystic fibrosis, organ failure, cognitive impairment, renal disease, asthma, diabetes, or mobility impairments.

B. Devices that improve the acceptance and use of assistive and monitoring devices, e.g., child peak flow measurement in the home and at school; nightly use of continuous positive airway pressure (CPAP).

C. Devices to diagnose and screen for COPD early in the course of the disease, particularly targeting young adults.

D. Technologies to assist in adolescent health promotion and prevention activities such as smoking cessation devices or obesity prevention technologies.

E. Devices to assist in providing palliative care for patients with life threatening illnesses through the disease trajectory whether in active treatment or at the end of life.

F. Technologies to assist individuals in reducing environmental exposures, i.e., chemical and viral agents, and indoor/outdoor allergens.

G. Devices to facilitate resource sharing such as: technologies that will enable valid and reliable measurement tools/instruments to be readily available and shared by research scientist focused on similar issues in a variety of populations.

H. Adaptation of existing or development of new technologies that will link under-represented populations with available resources to sustain healthy life styles and eliminate health disparities.

Research and Development of Technologies to Enhance Self Care and Clinical Care

A. Technologies to assist patients to adhere to chronic regimens such as reminding children to take steroid inhalers during the day for asthma; alerting obese adults when high calorie and fat content foods are about to be eaten; adhering to medication regimens; and prompting sedentary adults to exercise.

B. Devices that improve delivery of care to persons who have restricted or impaired movement due to (1) conditions of neurological disease or injury, peripheral vascular disease, rheumatoid disease, or intractable pain, (2) life sustaining equipment, such as dialysis machines or left ventricular assist devices, or (3) orthopedic fixation devices.

C. Devices to enable providers and or research scientists to monitor successful adherence to complex medication regimens (e.g., Highly Active Anti-Retroviral treatment).

D. Technologies that monitor short and long term self-care behavior changes.

E. Biological and behavioral monitoring devices for patients in at-risk and underserved populations in rural and frontier areas that will enable access to clinical care.

F. Telehealth technologies to improve patient outcomes through increasing quality, type, and speed of health information sharing, e.g., assessing traumatic injury severity at remote sites and transmitting this information to acute care settings for assessment and evaluation; communicating signs and symptoms of clients at home to health care providers in distant locations; tailoring care for diverse patients in a wide variety of settings, and promoting community interventions to eliminate health disparities.

G. Technologies to treat chronic wounds that fail to heal, specifically decubitus ulcers, venous stasis ulcers, and diabetic ulcers.

H. Technologies to be used in the hospital or home care setting to monitor or assess preterm, low-birth weight or other high-risk infants.

I. Technologies to assist informal caregivers in providing care or assistance to family members in the home.

J. Noninvasive devices to assess exposure to chemical and viral agents for children and adults and transmit this information to health care personnel for assessment and evaluation.

K. Technologies to disseminate research information (i.e., biobehavioral responses, communication of risk, bioethics) to nurses practicing in emergency settings and in the community.

Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

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NATIONAL CENTER FOR RESEARCH RESOURCES (NCRR)

NCRR provides laboratory scientists and clinical researchers with the environments and tools they need to understand, detect, treat, and prevent a wide range of diseases. This support enables discoveries that begin at a molecular and cellular level to move to animal-based studies, and then are translated to patient-oriented clinical research, resulting in cures and treatments for both common and rare diseases. Through the small business Phase I, Phase II, Fast-track and Competing Renewal awards, NCRR supports primary research to create and develop critical resources, models, and technologies; including high-throughput informatics technologies that provide comprehensive answers to complex questions.

A description of NCRR program topics follows the description of our Phase IIB Competing Renewal Awards. For additional information, please visit our home page at http://www.ncrr.nih.gov.

NCRR Phase IIB Competing Renewal Awards

NCRR will accept Phase IIB SBIR Competing Renewal grant applications to continue research and development of complex instrumentation and tools for basic, translational or clinical research where extraordinary time and effort is needed for their research and development. The Phase IIB Competing Renewal award is intended to allow small businesses the opportunity to reach to a stage where interest and investment by third parties would be more likely. Such products are expected to have a broad applicability, consistent with the mission of NCRR. Budgets that do not exceed $1 M per year in total costs (for up to 3 years), may be requested for this Phase IIB Competing Renewal opportunity, although it is expected that in most cases the requested budget would not exceed the final year budget of the applicant's previous phase II award. This opportunity is available for the SBIR program only.

Please contact your Program Officer before beginning the process of preparing a Phase IIB Competing Renewal application. In addition, prospective applicants are strongly encouraged to submit to the Program Contact (listed above), a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating organizations
- Funding Opportunity Announcement Number (e.g., PA-10-XXX)

A letter of intent is not required, is not binding, and does not enter into the review of a subsequent application. It is expected that only a few of NCRR SBIR Phase II awards will be eligible for a Phase IIB Competing Renewal grant.

RESEARCH TOPICS OF INTEREST TO NCRR:

Biomedical Technology Research and Development

New or improved instruments, devices, and related methodologies to facilitate biomedical or behavioral research. Instrumentation includes, but is not limited to mass spectrometry, nuclear magnetic resonance, imaging, optical or laser spectroscopies, X-ray absorption/diffraction/scattering, detectors, electron or confocal microscopies, electrophoresis and other separation techniques, bioreactors, centrifugation, and flow cytometry.

A. ***Information Technology:*** Development of information and communication technology, computer and other mathematical sciences in support of biomedical or behavioral research. This may include:

   1. Interactive tools and technologies for meaningful and intuitive exploration of biomedical and health-related data and information that (a) create cognitively useful spatial mapping of not inherently spatial datasets; (b) synthesize methods and approaches from computer graphics, human-computer interaction, cognitive psychology, semiotics, graphic design, statistical graphics, cartography, art and other relevant fields; (c) utilize visualization, statistics, information modeling, artificial intelligence (AI), semantics, ontology merging, natural language processing (NLP), data mining, personalization, malleable interfaces, serious games, uncertainty modeling; (d) enable personalized information delivery and communication of complex concepts across scientific disciplines; (e) have proven useful in other scientific domains.
   2. Creating resources for clinical and biomedical research such as (a) long-term sustainable environments for scientific databases, and tools for data federation; (b) online environments for scientific collaborations, data sharing, behavioral and population studies, and social network analyses.
   3. Developing computational and conceptual infrastructures that enable the transformation of biomedical, clinical, and other health-related data into evidence-based knowledge about human health. These may include methods and tools for (a) identifying knowledge gaps; (b) creating computed or synthesized knowledge; (c) creating coherent information from multi-modal diverse sources of varying reliability and accuracy; (d) assessing data, information, and knowledge provenance; (e) integrating heterogeneous data sources with the use of interdisciplinary methods (e.g. graph theory, principal component analysis, differential geometry, etc) to enable meaningful exploration of high-dimensional data spaces; (f) knowledge discovery and validation, computable abstracts; (g) assessing datasets and models for re-purposing and re-use.
   4. Computer simulations and modeling.

B. ***Technology for Systems Biology:*** Development of novel technologies for proteomics, glycomics, metabolomics, and other aspects of systems biology for discovery and clinical applications, (e.g., sample handling, separations, mass spectrometry, and computational tools for protein identification, data curation and mining).

C. ***Technology for Computational Biology:*** Development of computational biology software packages for integrative analysis of genomics data, especially ones relevant to applications of new

sequencing technologies. The proposed work should apply best practices and proven methods for software design, construction, and implementation to promote adoption by a broad biomedical research community.

D. ***Technology for Structural Biology:*** Development of detectors and cameras for studying the structures of biomolecules in the size range of peptides to cells, using synchrotron radiation and multiple types of microscopy.

E. ***Imaging Technology:*** Development of non-invasive imaging techniques and methodologies to facilitate understanding of biological systems at the molecular, cellular or organ levels. Imaging modalities include, but are not limited to, magnetic resonance imaging/spectroscopy (MRI/MRS), positron emission tomography (PET), single photon emission tomography (SPECT), X-ray computer tomography (CT), ultrasound (US) , diffuse optical imaging (DOI), magnetoencephalography (MEG), transcranial magnetic simulations (TMS), electroencephalography (EEG) and other integrated modalities (such as PET/MRI, PET/CT, etc). Areas of interest may include:

1. Contrast agent development including but not limited to (a) exogenous or endogenous imaging agents to detect structural, functional or molecular signatures of disease progression; (b) imaging agents capable of crossing biological barrier for diagnostics or therapeutic interventions.
2. Hardware development to improve image accuracy, spatial/temporal resolution, and signal-to-noise ratios and to broaden imaging capabilities to cellular and sub-cellular levels.
3. Software development such as (a) image processing software for high-throughput, integrative and robust data interpretation in preclinical and clinical settings; (b) image acquisition protocols to enhance image quality/specificity, monitor biochemical activities or functions in biological systems.

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Proteomics, Mass Spectrometry

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Research and Development in Comparative Medicine

A. Development of improved reagents and cost-effective methods to accurately screen and diagnose selected laboratory animal diseases, and for performing overall assessments of animal quality and health status. An urgent need currently exists for the development of improved methods for the detection of active tuberculosis in nonhuman primates.

B. Development of improved reagents and techniques for isolating and propagating stem cells, from laboratory animals. Improved methods for inducing pluripotent stem cells and stem cells of animal to differentiate along specific pathways *in vitro* and *in vivo*.

C. Development of improved reagents, techniques, and equipment for genomic and transcriptomic analysis and data mining from tissue or cells of laboratory animals and animal models of human diseases.

D. Development of new technologies to rapidly phenotype large number of animals.

E. Development of vaccines and new therapeutic agents for the prevention and/or control of selected laboratory animal diseases. One high priority need is for the development of methods to control and prevent Herpes virus B in nonhuman primates.

F. Development of commercially valuable reagents for lower organisms or established cell cultures.

G. Development of cost-effective husbandry and colony management techniques, equipment, and/or new approaches to improve laboratory animal welfare and assure efficient and appropriate research use.

H. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control.

I. Identification, development, and characterization of spontaneous and engineered vertebrate animal models for studies on various types of human disease. A need exists for a small animal model of Hepatitis C virus infection in humans.

J. Development and refinement of high throughput technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.

K. Development of technologies for improved embryo transfer within a single animal species or of intraspecific embryo transfer to allow preservation of rare, unique, or endangered animal species that may have unique value as animal models for human disease.

L. Development of improved reagents, techniques, and equipment for performing and analyzing “omics” (genomics, transcriptomics, phenomics, proteomics, glycomics, epigenomics, metabolomics) in normal and disease conditions animal models.

M. Development of biological tools and reagents for reconstruction, remodeling, repair and regeneration of tissues damaged by injury or disease.

N. Development of computational science-based technologies to create fast, effective community access to preclinical animal models-based raw data, processed data, and processing tools.

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Clinical Research Technology Applications

A. Innovations to accelerate the utilization of personalized medicine:

1. Biomedical materials and medical devices;
2. Medical drug, biologics and product development;
3. Therapeutics;
4. Drug/product delivery;
5. Drug-device combination products;
6. Integrated bio-engineering and pharmacogenomic/genetic research.

B. Innovative Health Informatics for Clinical and Translational Researchers including:

1. Data Repositories for Research: Innovations in the creation and maintenance of large scale data repositories, designed specifically to support translational research use cases; including patient-centered outcomes research.
2. Participant Recruitment Tools and Strategies: Innovations in Informatics to enhance and accelerate participant recruitment for clinical studies.
3. Clinical Information Systems and Research Study Management Systems: New means to identify, link and export research-relevant data from electronic health records.
4. Research Portal Innovations: innovations in the creation and maintenance of research portals that facilitate investigator-initiated identification of research resources and potential collaborators. Support and document concierge-based navigation and access to institutional core resources; track investigator use of services; and provide dashboards to monitor project-specific financial information and progress of regulatory reviews.

C. Innovative technologies that enable use of electronic medical records (EHR) and personal health records (PHR) for clinical and translational research purposes. Elements could include:

1. Interoperability and mapping among technologies;
2. Development of software to process data from multiple clinical and translational research sites;
3. Security systems development to protect storage and transmission of confidential medical data;
4. Development of standardizing agreements for patient privacy and protection.

D. Innovative biomedical technologies to enhance the feasibility or improve the quality of clinical research, conducted in the neonatal intensive care unit.

E. Innovations in the development of vectors for gene therapy, with improved:

1. Targeting of specific cells and/or tissues;
2. Transduction and expression;
3. Delivery to patients; and/or
4. Production and purification.

F. Innovative vehicles for drug delivery.

G. Innovations in tools used by patients or for patients in Mobile Health (mHealth) and TeleHealth technologies for communication, diagnosis, monitoring, evaluation, medical management, tracking, training, and treatment.

H. Innovations in specialized medical devices and robotics for clinical use as implantable sensors, surgical instruments, and imaging devices for medical diagnostics and treatment improvements.

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Human Stem Cell Technologies, Methods, and Tools

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Development of Innovative and Inquiry-Oriented Software and Tools for Science and Health Education

Funding opportunities are available for the development of discovery-oriented educational software and the application of educational technology and tools for health science topics that target K-12 students, families, students from community, tribal, undergraduate colleges and the general public. Topics can range from basic biological science to specific human diseases. Examples include; but are not limited to regenerative medicine, bioengineering, and how different parts of the body work across the lifespan, healthy living and lifestyle, mental health, and prevention of heart disease, diabetes, and other chronic diseases. Development of software, technology, or tools may be directed towards new products or adaptation of existing products designed to be more efficient, cost-effective, and user-friendly in promoting interactive learning, dissemination and promotion of health science. This effort is intended to yield efficient and user-friendly, culturally appropriate and effective educational units that can be extended to enhance the health science literacy of the general public. A broad dissemination is strongly encouraged.

Examples of responsive applications may include but are not limited to:

A. Web-based, stand-alone computational tools, instructional software or other interactive media for dissemination of science education;

B. Curriculum materials, Interactive teaching aids, models for classroom instruction, and teacher education workshops; and

C. Development of health promotion and disease prevention/intervention materials such as informational videos and/or print materials and programs which are culturally appropriate for populations and special communities.

Projects that target the following constituencies are strongly encouraged:

D. K-12 students;

E. Students of community colleges, tribal colleges, undergraduate colleges and minority-serving institutions; and

F. Patients and families with health conditions that disproportionately affect minorities and other medically underserved populations, including members of disadvantaged urban and rural communities.

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Other Research Topic(s) Within the Mission of the Center

NCRR's Division of Research Infrastructure supports programs such as Research Centers in Minority Institutions (RCMI) and Institutional Development Award (IDeA) that support and foster health-related research to build capacity at minority serving institutions and in underserved states, respectively. These programs support a wide variety of biomedical research, including clinical and translational research to reduce health disparities experienced by disadvantaged groups and medically underserved populations. Applications involving partnerships with minority-serving institutions and IDeA-eligible institutions are strongly encouraged. Topics of special interest include:

A. Development and/or refinement of culturally appropriate survey instruments, tools and databases to promote community based research engaging minorities, rural and other medically underserved populations;

B. Development of methodologies, diagnostics, technologies, equipment, assay systems and portable devices that can be used in community settings, such as health centers, neighborhood clinics, doctors offices, public schools, libraries, and rural and remote locations to facilitate biomedical and behavioral research;

C. Development of culturally appropriate educational materials for health promotion and disease prevention/intervention such as: software, videos, printed material to facilitate translation and dissemination of evidence-based health information; and

D. Innovative applications of health information technology, including telemedicine/telehealth tools and technologies, to facilitate electronic health information exchange, enable clinical research at the point of care, and improve access to quality health care for hard to reach populations.

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NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM)

The mission of the National Center for Complementary and Alternative Medicine (NCCAM) is to explore complementary and alternative healing interventions in the context of rigorous science; educate and train complementary and alternative medicine (CAM) researchers; and disseminate authoritative information to the public and professionals. CAM encompasses those healthcare and medical interventions that are not currently an integral part of conventional medicine. For a detailed description of NCCAM mission, please see http://nccam.nih.gov/about/plans/2005/index.htm.

The following narrative indicates the scope of projects suitable for the SBIR/STTR program that fit within the mission of NCCAM. For additional information about areas of interest to NCCAM and a listing of NCCAM's currently funded applications, please visit http://www.nccam.nih.gov/research. Business concerns interested in exploring SBIR/STTR grant opportunities with NCCAM are strongly encouraged to contact NCCAM Program Officers prior to submitting an application.

Topics of Interest to NCCAM

NCCAM encourages innovative technological research and development of commercializable CAM products that would fulfill the mission of NCCAM. The application may include basic, pre-clinical, and early phase clinical studies that can ultimately lead to a commercial CAM product. The areas of interest to NCCAM include but are not limited to development and validation of:

- technology for standardization and characterization of biologically active CAM products;
- tools for the analysis of polysaccharides and polyphenols;
- novel botanical or botanically derived products with useful therapeutic potential;
- methods for the sustainable production of low yield natural products of commercial interest;
- methods for standardization and characterization of active elements of mind-body medicine interventions;
- innovative biomarkers for measurement of stress in studies also testing efficacy of CAM therapies;
- standardized, reliable and economical tools that correlate with brain imaging to assess brain function;
- technical imaging tools or instruments for studying manual therapies;
- CAM-based tools for pain management;
- innovative tools, technology and instruments for the accurate assessment of adherence to the use of CAM practices, interventions, and products;
- tools to improve patient-reported outcome measures of CAM clinical investigations;
- tools to improve biological and physiological outcome measures of CAM clinical investigations.

Topics That Are of Less Interest to NCCAM

The NCCAM Office of Communications is responsible for disseminating CAM information to the public. Therefore applications addressing software development or educational materials and courses (including Continuing Medical Education courses or CD's) will not be considered relevant to the NCCAM SBIR/STTR program. Also not eligible for support are applications seeking to develop cookbooks for special diets or instructional materials for clinical practice. NCCAM does not fund clinical practice other than as a component of funded clinical research.

Although applications to support the development of databases are not widely encouraged, these applications will be considered if they are limited to aiding the taxonomic and phytochemical characterization of medicinal plants/fungi. Applicants are encouraged to contact the appropriate NCCAM Program Officer before submitting any SBIR applications related to database development.

Other Research Topic(s) Within the Mission of the Center

For additional information on research topics, please contact:

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NATIONAL LIBRARY OF MEDICINE (NLM)

The National Library of Medicine (NLM) offers support for research and development projects in biomedical informatics. NLM defines biomedical informatics as the science of optimal organization, management, presentation and utilization of information relevant to medicine and biology. The informatics projects of interest to NLM involve the application of computer and information sciences to information problems in a biomedical domain. For additional information about areas of interest to NLM and a listing of NLM funded applications, please visit http://www.nlm.nih.gov/ep. Business concerns interested in exploring SBIR/STTR grant opportunities with NLM are encouraged to contact the NLM representatives prior to submitting an application.

NLM's SBIR/STTR grant programs are focused on areas of particular interest from small business. Examples of research areas of interest that fit within the mission of NLM include, but are not limited to:

- Tools for managing interactive publications and /or large datasets
- Modeling tools for climate and environmental effects on human health
- New technologies for disaster information management
- Tools to enable communities to use health indicators, such as the HHS Health Indicators Warehouse, to improve a community's health

Other Research Topic(s) Within the Mission of the Center

For additional information on research topics, contact:

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CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)

CDC will accept SBIR grant applications on the April 5, August 5, and December 5, 2011 submission dates.

CDC's mission is to create the expertise, information, and tools that people and communities need to protect their health – through health promotion, prevention of disease, injury and disability, and preparedness for new health threats.

CDC seeks to accomplish its mission by working with partners throughout the nation and the world to:

- monitor health,
- detect and investigate health problems,
- conduct research to enhance prevention,
- develop and advocate sound public health policies,
- implement prevention strategies,
- promote healthy behaviors,
- foster safe and healthful environments,
- provide leadership and training.

Those functions are the backbone of CDC′s mission. Each of CDC′s component organizations undertakes these activities in conducting its specific programs. The steps needed to accomplish this mission are also based on scientific excellence, requiring well-trained public health practitioners and leaders dedicated to high standards of quality and ethical practice.

In realizing its mission, CDC is focusing on public health priorities with large-scale impact on health and with known, effective strategies to intervene. The charge under these priorities, known as Winnable Battles, is to identify optimal strategies and to rally resources and partnerships to accelerate a measurable impact on health.

To date, CDC has identified the following winnable battles based on the magnitude of the health problems and CDC′s ability to make significant progress in improving outcomes.

Healthcare Associated Infections (HAIs) – CDC is committed to eliminating preventable infections that occur as a function of medical or surgical conditions. HAIs are one of the top 10 leading causes of death in the United States, accounting for an estimated 1.7 million infections and 99,000 associated deaths each year.

HIV – CDC provides leadership in reducing new HIV infections through awareness of HIV status, prevention for positives, prevention for high risk negatives, and elimination of health disparities.

Motor Vehicle Injuries – CDC actively supports evidence-based interventions such as primary restraint laws, graduated driver licensing, and DUI interlock devices to drive down deaths and injuries from motor vehicle crashes.

Obesity, Nutrition, Physical Activity and Food Safety – CDC is committed to addressing the epidemic of obesity and overweight in the U.S. and improving the public's health through the promotion of good nutrition, physical activity, and a safe food supply.

Teen Pregnancy – CDC works to prevent teen pregnancies that contribute to poor health and negative social outcomes through evidence–based strategies, policies, and systems change.

Tobacco – CDC is dedicated to reducing the death and disease caused by tobacco use and exposure to secondhand smoke.

By identifying priority strategies and clear targets and by working closely with our public health partners, we can make significant progress in reducing health disparities and the overall health burden from these diseases and conditions.

In addition CDC continues to focus on other high burden public health topics where it can make a significant impact in preventing illness, injury and disability and death.

For additional information about CDC, please visit our home page at http://www.cdc.gov.

Questions of a general nature about the CDC SBIR program should be directed to:

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CENTER FOR GLOBAL HEALTH (CGH)

For additional information about CGH, please visit their website at: http://www.cdc.gov/globalhealth/.

1. Field Optimization of an Inexpensive Colorimetric Assay to Measure Cyanopyrethroid Insecticides on Treated Fabrics and Walls

Background: Insecticide-based interventions are used in many vector control programs worldwide for managing diseases such as malaria and dengue. Insecticide-impregnated fabrics, (e.g. bed nets, curtains and clothing), as well as insecticide spraying onto walls (indoor residual spraying) have been shown to be effective in reducing vector-borne disease transmission by providing an insecticidal barrier against disease-transmitting vectors . Monitoring of insecticide levels provides critical information about the quality of vector control interventions, for formulating strategies and focusing control efforts. However there is currently no rapid field-deployable assay(s) to monitor the effectiveness of insecticides used in these control methods. Pyrethroids are commonly used in indoor residual spraying (IRS) programs and deltamethrin/ permethrin are the only two pyrethroids approved for treated fabrics. Gas or high-performance liquid chromatography provides the most sensitive means of pyrethroid analysis. The standard WHO cone bioassays for evaluating efficacy of insecticides in IRS and for bed nets requires access to a colony of susceptible mosquitoes. These techniques are neither practical nor affordable (labor/resource intensive and/or require highly trained personnel) in countries where insecticide-treated materials or IRS are being implemented. A sensitive quantitative colorimetric assay with an innovative sampling technique (simple rubbing of filter paper on material surface) to measure cyanopyrethroid (e.g. deltamethrin, λ-cyhalothrin, α-cypermethrin, cyfluthrin, etc.) levels on bed nets has been developed at the CDC Entomology Branch and has proven to be robust and sensitive (Trop. Med. & Int. Health Vol 14, pp 1-8, 2009). The next step is to further develop this technique into field-usable assay(s) capable of determining and quantifying pyrethroid levels for monitoring vector-control interventions.

Public Health Impact: Insecticides are still the mainstays of vector-borne disease control. With malaria elimination back on the global agenda, there has been an expansion of IRS and a dramatic increase of insecticide-treated bed net distribution for vector suppression and reducing transmission. Technical and operational obstacles for successful vector control operations include technical quality of IRS, effective life of the insecticide on sprayed surfaces and levels of pyrethroids in bed nets. Sub-optimal levels of insecticides also increase the potential of insecticide resistance developing in the vectors. Field-usable assays are key to accurately and rapidly monitor insecticide-based approaches and to prevent resistance to the insecticide.

Examples of specific research areas of interest include, but are not limited to: Development of field-usable assay(s) capable of determining and quantifying pyrethroid levels for monitoring vector-control interventions. The assay(s) should be easy to operate, inexpensive, portable, use heat stable reagents and have no special storage requirement. The focus of current cyanopyrethroid assay has been for deltamethrin in treated bed-nets. However another cyanopyrethroid, α-cypermethrin, and a non-cyanopyrethroid, permethrin is also used for bed nets. In addition a number of pyrethroids are used for IRS. Of particular interest to CDC are assays capable of detecting pyrethroids currently used on bed-nets, and pyrethroids detection assays that can be used for monitoring IRS programs used for different housing materials.

2. Novel and Simple Diagnostic Tools for Malaria Parasite Detection in the Field and Innovative Tools for the Detection of Drug Resistant Malaria Parasites in the Field

Background: Malaria continues to be a global public health challenge contributing to at least an estimated 800,000 deaths and more than 240 million clinical illnesses affecting mostly young children in Sub-Saharan Africa and other tropical countries. Development of resistance to cheap antimalarial drugs such as chloroquine and sulphadoxine-pyrimethamine has led to adoption of artemisinin based combination therapy (ACT) which is more expensive. Recently the World Health Organization has recommended evidence based treatment (based on confirmed diagnosis of parasites) for malaria instead of basing treatment on symptoms. However, microscopic diagnosis is not feasible in many endemic countries setting and there is a greater need for alternative diagnostic tools for malaria. Although immunochromatographic rapid diagnostic tests (RDTs) have been used for malaria diagnosis, these tests have limitations in correctly identifying malaria species and recently the emergence of parasite populations lacking the most commonly used diagnostic antigen HRP-2. In addition, there is a concerted effort through various public and private efforts (such as U.S. President's Malaria Initiative, U.N. Millennium Development Goals, Gates Foundation etc) to reduce malaria burden to very low levels, including elimination of malaria wherever possible. As these efforts progress there is increased realization that there is a need for more sensitive field diagnostic tools to diagnose low density infections that contribute to ongoing transmission but which are not detected by RDTs or microscopy.

Since 2006, 38 countries in sub-Saharan Africa and most other endemic countries have adopted an ACT regimen for the primary treatment of uncomplicated malaria due to *P. falciparum* infection. Although it was hoped that ACT would remain efficacious for a number of years until the next generation of antimalarials would become available, very recent surveillance data from the Thailand-Cambodia border have raised the alarming specter of declining efficacy of ACTs. Initially it was hoped that resistance was due to declining efficacy for the artemisinin partner mefloquine. Unfortunately, additional recent research has shown that resistance to artemisinin has emerged. In the past molecular markers have proven to be useful molecular tools for tracking resistant parasites and there is greater need to adopt simpler field usable platforms for conducting molecular surveillance for monitoring emergence and spread of resistant parasites. Currently, there are no available molecular markers for artemisinin resistance. In addition, available molecular tools are expensive and not available for use in endemic countries, requiring shipment of samples to developed countries for analysis. Therefore, there is a need to develop field usable immunologic, molecular and other tools for malaria diagnosis and for detecting resistant parasites.

Public Health Impact: Availability of diagnostic tests with greater sensitivity can help to identify subclinical infections, reduce transmission, and monitor success of control programs. Development of field usable tools for the surveillance of drug resistant parasites will help to develop appropriate public health policies to combat resistance.

Examples of specific research areas of interest include, but are not limited to: 1) Development of highly sensitive, specific and field usable tests for malaria parasite detection for use in malaria control programs for mass screening. 2) Development of molecular tools that can simultaneously detect several molecular markers of drug resistant malaria parasites using simpler platforms that can be used in the field.

3. Diagnostic Needs for NTD Programs

Background: Neglected tropical diseases (NTDs) are bacterial and parasitic infections that disproportionately affect poor and marginalized populations around the world. A subset of NTDs, including lymphatic filariasis, onchocerciasis, schistosomiasis, trachoma and intestinal helminth infections, can be targeted effectively through mass chemotherapy. These NTDs are not considered to cause appreciable mortality; however, they are associated with high levels of morbidity because of the chronic nature of many of the infections. Blindness and disability due to these NTDs increase in prevalence with age, reducing the productivity of adults. Intestinal helminths, among the commonest of infections, have profound effects on the growth and cognitive development of children. The past five years have seen significant increases in the number of countries implementing NTD programs and in the number of persons being treated. These increases are the direct result of generous donations of drugs from pharmaceutical manufacturers and new funding support from USAID and DFID, among others. Reducing the morbidity caused by NTDs is an objective of the Global Health Initiative and the global elimination of lymphatic filariasis and trachoma are specific GHI targets. Available diagnostic tools for lymphatic filariasis, trachoma, schistosomiasis, onchocerciasis and intestinal helminth infections do not at present meet the needs of the control programs.

Public Health Impact: Development of improved diagnostic tools would enhance the commitment of donors and policy makers to the control and elimination programs for NTDs by providing higher quality information and increased confidence that public health goals are being met. Significant savings in human and financial resources could be obtained through the development of improved diagnostic tools.

Examples of specific research areas of interest include, but are not limited to: For diseases addressed by mass drug administration (MDA), diagnostic tests are needed to guide programmatic decisions on community treatment. Despite the molecular revolution in biology, little of the new found knowledge of parasite genes and gene products is being translated into tools than can be used in the field to guide program decisions. Tools for mapping and monitoring program impact are still conventional parasitologic methods, based on microscopy. These tests lack sensitivity and are not adequate for NTD programs with elimination endpoints. New antibody tests could provide more sensitive tools to monitor transmission, facilitate decision-making and conduct surveillance. The potential advantages of antibody-based tests for post-MDA surveillance argue that increased efforts also should be made to develop a standard platform for such tests, opening opportunities for integrated surveillance for NTDs.

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NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP)

For additional information about NCCDPHP, please visit their website at: http://www.cdc.gov/chronicdisease/index.htm.

1. Comfortable and Inexpensive Life Jacket to Increase Wear

Background: In 2008, the U.S. Coast Guard received reports for 4,789 boating incidents; 3,331 boaters were reported injured, and 709 died. Among those who drowned, 9 out of 10 were not wearing life jackets (personal floatation device or PDF). Most boating fatalities that occurred during 2008 (72%) were caused by drowning with 90% of victims not wearing life jackets (Centers for Disease Control and Prevention. Wide-ranging OnLine Data for Epidemiologic Research (WONDER) [online]. (2010) Available from URL: http://wonder.cdc.gov/mortsql.html).

For those who take to the water for occupational purposes, the U.S. Coast Guard (USCG) estimates during 1982-1987 the annual occupational fatality rate for U.S. commercial fishermen was 47 deaths per 100,000 workers. The major cause of these deaths was drowning. According to information gathered by CDC's Alaska Activity, the occupational fatality rate for commercial fishermen in Alaska during 1991-1993 was 195 deaths per 100,000 workers -- nearly 30 times the average annual rate for all U.S. workers. Of these 195 deaths, 91% were caused by drowning. Data clearly show that PFDs greatly increase the chances of survival for fishermen: 63% of fishermen wearing PFDs when they jumped or fell into the water survived, whereas only 12% of those without PFDs survived. These conclusions and recommendations may apply to all commercial fishing operations in the United States.

Public Health Impact: Studies have shown that the majority of drowning incidents were precipitated by unexpected entry into the water, which means the victim had no time to grab a life jacket before entering the water. Many of the drowning incidents could have been prevented by wearing a PDF. Common reasons given for not wearing a life jacket include being 1) uncomfortable and 2) expensive. A newly designed life jacket that addressed these issued has the potential to increase use and decrease morbidity and mortality from drowning. It is believed that a wide array of retail and commercial outlets (specialty outdoor retail stores, warehouse stores, and convenience stores) will have an interest in this product.

Examples of specific research areas of interest include, but are not limited to: To develop a comfortable, lightweight, compact, inexpensive, and easy to use life jacket that could be worn for recreational and/or occupational activities (boating, kayaking, fishing, etc.) to reduce the risk of drowning.

2. Design and Test Standing Desks to Prevent Childhood Obesity

Background: Childhood obesity affects 23 million children in the United States. Seventy percent of overweight and obese youth become overweight and obese adults, which significantly increases the risk

of hypertension, type 2 diabetes, kidney problems, heart disease, and certain types of cancer (Power, Lake & Cole, 1997; Dietz, 1998). Most school-based childhood obesity interventions target some aspect of energy balance—either reducing the calories consumed by removing soda machines in schools or providing healthy meal choices, or by increasing physical activity through recess, physical education classes, after school, or weekend programs. Although physical education and recess time will help address the issue, a process to engage in physical activity *during the entire duration of the school day* may provide additional benefits (see description of winnable battles, obesity, at http://www.cdc.gov/obesity/causes/index.html). Results from a pilot study of 71 first-graders in five classrooms showed a 17% increase in calories burned for the treatment group compared to control group ($p = 0.022$). Children whose weight was higher than the 85th percentile for their age group and gender showed a 32% increase in calories burned (1.56 kcal/min vs. 1.18 kcal/min). Research conducted in work settings has used dynamic environments as well, including a stand/sit workstation, to reduce weight and improve productivity, which suggests that this may translate to children's school environments with similar effects.

Public Health Impact: Standing desks for schools children may provide a relatively low-cost, low-effort method of combating childhood obesity in an institutional setting in which most American children spend a great deal of time. Schools and school districts could be encouraged to purchase standing desks for their classrooms based on increased calorie burn, increased academic performance, and improved behavior in the classroom. For example, after learning of the pilot study's success in five classrooms, the Edinburg Consolidated Independent School District in south Texas decided to purchase standing desks for four new elementary schools and one new middle school in the next few years. As new schools are built and older schools are renovated, districts may consider standing workstations as better alternatives to traditional classroom furniture.

Examples of specific research areas of interest include, but are not limited to: Develop a standing desk (workstation) for use in elementary school classrooms as a strategy to change the physical environment to prevent childhood obesity. Characteristics of an effective desk include usability, comfort, likeability for students and teachers, and sustained across a variety of classroom types. Ideally a well designed standing desk would increase students' caloric burn, decrease body fat percentage and body mass index, and improve academic performance.

3. Where's the Salt? Purchasing of Lower Sodium Wholesale Products Made Easier

Background: The majority of the U.S. adult population consumes more than 2 times their recommended maximum of daily sodium. Higher consumption of sodium strongly increases the risk of having high blood pressure which currently affects nearly 1 in 3 adult Americans, the majority of whom do not have it under control. High blood pressure is a leading risk factor for heart disease and stroke, the first and third leading causes of death, as well as kidney disease. The vast majority of sodium consumed in the United States comes from restaurant and processed foods. Two scalable strategies to help reduce the amount of sodium in the American diet include: 1) reducing the amount of sodium in restaurant and processed foods and 2) informing the public about recommended sodium intake levels, the sodium content of the foods they purchase.

Currently for wholesale purchasers, there are no readily accessible non proprietary (or non commercial) datasets that provide nutritional value or food quality information, such as sodium, sugar or fat content of wholesale food products. High volume food purchasers need such tools to make seeking out and purchasing healthier food products easy and convenient.

Public Health Impact: Improving nutrition by reducing sodium intake is one of CDC's Winnable Battles and one that will save lives. Recent research has advised that reducing sodium levels in packaged foods and restaurant foods in half would save tens of thousands of lives per year from fatal heart attacks and strokes. Reducing average population intake to the recommended 2300 mg per day may reduce cases of hypertension by 11 million and save $18 billion health care dollars.

The nutritional datasets have the potential to be marketed to restaurateurs as well as to large food service providers in government, education, and business as a commercial product. There are over 500,000 private industry food and drink establishments in the US that could benefit from this tool. High volume food purchasers are key points of leverage in changing the nation's food supply. By shifting purchases to healthier products, these businesses would not only provide healthier foods to their constituents, but send a powerful message to wholesalers that consumers demand healthier products.

Examples of specific research areas of interest include, but are not limited to: Develop an accessible nutritional information system for low sodium products to be used by restaurants and wholesale food purchasers. The system should include geocoding and a search tool. Elements of developing the nutritional information system may included identifying the structure and key variables in the food supply chain in the US, cataloguing the nutrient content of products available from suppliers, development of a web-based search tool to enable purchasers to search for vendors servicing their geographic area that provide lower sodium food products. Future use could be expanded to include information related to reduced fat, trans fat, calorie, and sugar products.

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THE NATIONAL CENTER FOR EMERGING AND ZOONOTIC INFECTIOUS DISEASES (NCEZID)

For additional information about NCEZID, please visit their website at: http://www.cdc.gov/ncezid/.

1. Cervical Cancer Control and Global Health: Rapid Point of Care Test for Human Papillomavirus Typing

Background: With nearly 500,000 new cases and 274,000 deaths annually, cervical cancer is the second most common cancer among women worldwide. The understanding that persistent infection with one of ~15 high risk (HR) Human Papillomavirus (HPV) is required for cervical carcinogenesis led to the successful development of vaccines to prevent HPV infection as well as to recommendations to incorporate HPV testing into cervical cancer screening algorithms. Cervical cancer control strategies ideally will include a combination of screening and vaccination. However 80% of the deaths from cervical cancer occur in regions of the world with the lowest resources. With Gates Foundation funding, PATH developed CareHPV, an adaptation of the FDA approved Digene HPV test for use in low resource settings. This has promise for screening, but does not provide type-specific information needed to monitor HPV vaccine impact. Due to the long natural history of cervical cancer, impact of the vaccine on this endpoint will not be seen for decades after widespread vaccine uptake. The ability to detect an impact on an early biologic endpoint is helpful to ensure the commitment of ministries of health to ongoing expensive HPV vaccination.

Public Health Impact: A simple point of care test for HPV typing would facilitate cervical cancer control in low resource settings by supporting both vaccination and screening. In developed countries the test would reduce loss to follow-up by allowing definitive treatment decisions to be made at one visit. With increased recognition of the role of HPV in anal and oropharyngeal cancers, the test may have impact on cancers at those sites as well. There is an expanding market for HPV tests. While HPV typing assays are available, all are highly complex and expensive requiring at least one day turnaround.

Examples of specific research areas of interest include, but are not limited to: Develop a point-of care device for rapid detection and typing of HR HPV from a variety of biological samples such as cervical, anal and penile swabs. The device should incorporate simplified methods for sample handling, and may utilize target and or signal amplification to identify 14 high risk HPV types (e.g., HPV 16, 18, etc.). CDC is interested in the application of biosensors, microfluidic platform, and nanoparticles in the successful development of a fully integrated system for point of care HPV typing.

2. Improving Hospital-Based Antimicrobial Use to Prevent Antimicrobial Resistant Healthcare-Associated Infections

Background: Healthcare-associated infections have been estimated to occur in about one of every 20 hospitalized persons; an increasing proportion (about 20%) of HAIs are caused by pathogens demonstrating increased resistance to traditional antimicrobials, leaving clinicians with fewer treatment choices and putting other patients at risk for infections through transmission between patients. Over the past decade, researchers have demonstrated that use of a comparative measure of inpatient-antimicrobial use by pharmacists and providers improves the appropriateness of antimicrobial prescribing by providers in hospitals that use these measures. To facilitate this prevention strategy, CDC's National Healthcare Safety Network (NHSN) (http://www.cdc.gov/nhsn/index.html) is launching an Antimicrobial Use Surveillance Option in January, 2011 to allow facilities to report such data and compare facility-specific usage rates to a national risk-adjusted comparative benchmark; however, facilities are required to submit these data electronically using specifications consistent with the NHSN electronic reporting standards. Complying with these standards will require vendors of "Electronic Medication Administration Records" (eMAR) used in acute-care facilities to modify the applicable software to allow such reporting. After initial modification and piloting of the reporting from a few facilities to NHSN, expansion of such reporting as a tool for reducing antimicrobial-resistant HAIs within acute-care facilities nationally can occur. As more vendors enable their products to report these data electronically to CDC's NHSN, CDC will be able to provide the comparative data to drive practice change locally at each reporting facility and to reduce unnecessary antimicrobial use through this enhancement of antimicrobial stewardship activities. Research has suggested that facilities can reduce unnecessary antimicrobial use through activities such as these within 6 months, and observe reductions in antimicrobial-resistant infections within 2 years.

Public Health Impact: Successful piloting of submission of data from eMAR systems to NHSN would provide facilities utilizing the vendor's software to report and receive comparative antimicrobial use data as a tool to drive local HAI prevention activity. HAIs are reportable in over 22 States, and antimicrobial use stewardship is mandated in California. Commercialization potential for antimicrobial use reporting is going to increase as mandates become more common.

Examples of specific research areas of interest include, but are not limited to:

1. Develop a technical prototype for aggregating antimicrobial use metrics (as outlined in NHSN – website) using eMAR systems and reporting to NHSN within the CDC clinical document architecture specifications (http://www.cdc.gov/nhsn/CDA_eSurveillance.html).
2. Evaluate (1) the validity (i.e., accuracy) of the data reported to NHSN and (2) the usability by hospital-based pharmacists.
3. Define a scalable solution and business plan to enhance utilization of the reporting capabilities by all acute-care facilities using electronic medical administration record systems.

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NATIONAL CENTER FOR HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION (NCHHSTP)

For additional information about NCHHSTP, please visit their website at: http://www.cdc.gov/nchhstp/.

1. Technologies to Reduce Unsafe Injections and Sharps Injuries

Background: The needle-syringe (N-S), invented 150 years ago, while invaluable in medicine, also pose several risks, primarily through intentional or inadvertent unsterile re-use, as well as through needlestick injury and improper waste disposal. These pose a substantial burden in resulting transmission of blood-borne pathogens (BBPs) in healthcare workers, patients and others exposed to these sharps.

The World Health Organization estimates that unsafe injections result in 260,000 human immunodeficiency virus (HIV), 21 million hepatitis B virus (HBV), and 2 million hepatitis C virus (HCV) infections and 9.2 million Disability-Adjusted Life Years (DALYs) lost annually.

Fundamentally, the N-S is "over-engineered" for its routine use. For a medical procedure that is low pressure and takes a few seconds, one is left with an almost indestructible stainless steel needle and a durable plastic syringe. In some developed countries, the solution has been to use sterile, disposable N-Ss only once, activate their needletip-shielding devices, and then discard each in a safety container (and ultimately incinerated). Such safety syringes are uncommon among diabetics and intravenous drug users (IDUs), however; therefore safe disposal of used N-S in these two populations remain an issue.

In developing countries, N-S with safety features is usually unavailable due to their higher cost. Logistical constraints result in interruptions in the supply of new N-Ss to remote clinics, and make more difficult maintaining proper sharps waste disposal systems. Supply interruptions and limited funds encourage improper recycling of what should be single-use-only N-S. Auto-disabling syringes used in some settings in developing countries (e.g., immunizations) do not yet have needle-shielding features, and are not yet universally available and used to prevent improper re-use. These problems extend to almost all other sharps needed to provide modern health care.

Public Health Impact: Reduction in the number of unsafe injections and sharps injuries will help prevent the spread of HIV, hepatitis B, and hepatitis C.

Examples of specific research areas of interest include, but are not limited to: Development of appropriate and affordable technologies that may contribute to solving the problems of unsafe injection and unsafe sharps disposal. Examples of such technologies -- not to the exclusion of others, which may be materials, methods, techniques, instruments, or devices – include: a) plastic needles to replace steel ones to simplify sharps disposal; b) noncorrosive sterilants without the disadvantages of bleach, or other equipment for effective sterilization of reusable medical instruments; c) locally-fueled melter ovens or other simple, practical sharps waste encapsulation or disposal systems; and d) needle-free devices for administering off-the-shelf formulations of existing vaccines and drugs.

2. Controlled Antiretroviral Drug Release Systems for Systemic HIV Pre-exposure Prophylaxis

Background: The HIV/AIDS pandemic remains among our greatest public health challenges. More than a quarter century after the description of the first cases of AIDS, HIV has spread to virtually every country in the world infecting 65 million people and killing 25 million. The ongoing high incidence of HIV infection and the incomplete coverage with basic HIV prevention tools underscore the need for new, highly effective biomedical HIV interventions to complement existing prevention strategies. In the absence of a vaccine, the administration of antiretroviral (ARVs) drugs before HIV exposure (pre-exposure prophylaxis or PrEP) has gained considerable attention as a strategy to protect high-risk HIV-negative people from becoming infected. PrEP is a proven concept for other infectious diseases such as malaria, and multiple lines of evidence suggest that it might also be a feasible strategy to prevent HIV infection. ARVs drugs effectively prevent HIV transmission at birth, during breastfeeding, and after occupational exposure, and as topical gels can prevent vaginal transmission. Several clinical trials with daily oral PrEP are now ongoing in high-risk populations. A reasonable next step would be to evaluate more practical, less costly drug delivery systems for humans.

Public Health Impact: Mathematical models estimate that over the next 10 years an effective PrEP program with daily ARVs could prevent 2.7 to 3.2 million of the 11 million new HIV-1 infections projected to occur in sub-Saharan Africa. Model simulations have also shown that an effective PrEP program could substantially reduce the incidence of HIV transmission in populations at high risk of infection in the United States. This potentially significant public health benefit of PrEP requires a very high efficacy of the drugs and a high degree of adherence to the PrEP regimen. However, prophylactically giving people daily ARVs drugs may be costly and impractical, even if confined to a high-risk population. Thus, special emphasis should be made on evaluating long-acting drug delivery systems including injectable biopolymers that entrap and slowly release ARVs systemically over prolonged (weeks-months) periods of time. If effective, these systems could substantially decrease the frequency of ARV dosing, improve adherence, and

minimize costs. PrEP with long-acting drug formulations may also provide an attractive prevention strategy against postnatal HIV acquisition in breast-fed babies.

Examples of specific research areas of interest include, but are not limited to: The development of novel long-acting drug delivery systems for systemic PrEP including injectable bio polimers that entrap and slowly release ARVs. Designs should include systems for controlled release of attractive drug candidates for PrEP including HIV reverse transcriptase, entry, and integrase inhibitors. Initial studies may incorporate drug pharmacokinetic and efficacy studies in non-human primates. Experimental design may include ways to measure drug levels in blood and tissues and explore correlates of protection. Studies should be designed with the long-term goal of providing information that will guide human clinical trials.

3. Development of a Cross-platform Desktop/smartphone App for Real-time Biomedical HIV Prevention Information Dissemination

Background: The National HIV/AIDS Strategy tasks CDC to extend access to post-exposure prophylaxis (PEP) to reduce HIV incidence in the US. DHAP will also introduce pre-exposure prophylaxis (PrEP) should trials soon show substantial efficacy and safety as expected. Effective use of biomedical HIV prevention requires that clinicians and other potential users have means readily available to learn about them and the guidelines for their use, and to identify accessible sources for provision of them. Mobile devices (e.g., smart phones) and desktop applications are commonly used to find information quickly as needed. According to one recent survey, 1 in 6 mobile subscribers own a smart phone. The ability to rapidly update information on these “apps” is more efficient than notifying users to access websites or paper forms. A cross-platform desktop/smartphone app could provide an important new method of transferring PEP and PrEP information to clinicians, public health staff, and potential users in near real-time mode. One state health department provided a PEP widget for download to emergency room desktops across the state www.ceiwidget.com, to ensure ready clinician access to guidance and materials (e.g., consent forms). The next step would be to extend this approach to provide a nationally available resource for additional topics (e.g., PrEP), audiences (e.g., potential users and referral providers), delivery modes (e.g., smart phones), and features (e.g., zip code lookup of service providers).

Public Health Impact: A cross-platform desktop/smartphone application would allow for more rapid update and dissemination of HIV prevention information to clinicians, and public health staff.

Examples of specific research areas of interest include, but are not limited to: Develop a cross-platform widget architecture, which can be rapidly modified to add emerging topics and updated materials to provide a method of transferring PEP and PrEP information to clinicians, public health staff, and potential users in near real-time mode. The development of this cross-platform “widget” architecture initially should include three biomedical HIV prevention methods (e.g., PEP, PrEP, prevention of mother-to-child transmission). Future additions could include other clinical prevention activities such as viral hepatitis, sexually transmitted diseases.

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NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

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1. Traffic Innovations to Drive the Death Rate Down

Background: Traffic crashes account for half of all unintentional injury deaths, are the leading cause of death for people ages 5–34 in the United States, and result in nearly 5 million serious injuries. In one-year, the cost of medical care and productivity losses associated with traffic injuries in the United States exceeded $99 billion. Globally, road traffic injuries kill 3,000 persons daily.

The risk of motor vehicle crashes is highest among teen drivers age 16- to 19-year-olds. Alcohol is a contributing factor in 37% of fatal motor vehicle crashes. In 63% of fatal crashes, the occupant killed was not wearing a seat belt. Excessive speed has been identified as a key risk factor in traffic injuries, influencing both the risk of a crash and the severity of the injuries that result.

Motor vehicle crashes result from a combination of environmental, human behavioral, and vehicle-related factors. Modifying any or all can substantially alter the risks of a crash, and the chances of survival. The ecological approach that modifying any one factor can influence all others, and that feedback loops about the performance of the vehicle, road and environment, and driver fitness will reduce risks and errors, but this requires adaptive technology. Currently, there are no readily accessible means to warn the driver of impending dangers such as perceptual deficits, driver error, hazardous road conditions and environments, and suboptimal vehicle performance that may influence crash risks. Nor are there convenient accessible databases to find affordable alternative transportation options. Drivers need such tools to make life-saving decisions easier and more automatic.

Public Health Impact: Improving safe and efficient travel is a universal goal. Reducing traffic crashes and the injuries that result is a primary goal in public health and one of CDC's *Winnable Battles*. Reducing speeding, increasing safety belt use, reducing traffic exposure, and eliminating alcohol-impaired driving, fatigue and driver distraction as factors in traffic crashes could save tens of thousands of lives annually and reduce disabling injuries by more than half, in addition to saving billions in health care costs.

Examples of specific research areas of interest include, but are not limited to: CDC is particularly interested in the development of improved environmental, engineering, and human factor controls (including retrofit vehicle solutions and information technology to access to alternative forms of transportation) with the potential to reduce motor vehicle crashes and the injuries that result. Development of real-time technologies that deliver to interventions, such as "cues to safe action", while driving, based on driver fitness, vehicle performance characteristics, environmental conditions, and road - based information. Technology that can be applied in both occupational driving and private vehicle use in domestic and global settings is of high interest, along with applications of this technology to assist persons with cognitive or psychomotor limitations (e.g. distracted, drowsy, alcohol impaired or drug impaired driving).

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NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)

For additional information about NIOSH, please visit their website at: http://www.cdc.gov/niosh/.

1. Occupational Traumatic Injuries from Motor Vehicle Crashes and Incidents

Background: The risk of roadway crashes and incidents associated with on-the-job operation of motor vehicles affects millions of U.S. workers. Motor vehicle-related incidents are consistently the leading cause of work-related fatalities in the United States. Of approximately 5,700 fatalities annually reported by the Bureau of Labor Statistics, 35% are associated with motor vehicles.

The public health toll from 2002 to 2008 included:

- 1354 workers died each year from crashes on public highways
- 324 workers died each year in crashes that occurred off the highway or on industrial premises.
- 358 pedestrian workers died each year as a result of being struck by a motor vehicle.

High-risk exposures include emergency response, highway construction zones, operation of farm equipment on roads, and off the highway use of commercial vehicles.

An important goal of the NIOSH Traumatic Injury Program is the reduction of injuries and fatalities due to highway motor vehicle crashes and incidents.

Public Health Impact: Application of evidence-based interventions may have a large impact on reducing the incidence occupational motor vehicle crashes and incidents. Workers sustaining fatal or serious injuries represent a huge toll on future years of productive life. In addition, their families are adversely affected. Any reduction in occurrence will have tremendous public health importance. In addition, reductions in occurrence will also have beneficial impacts on reducing workers' compensation and health insurance premiums and improving the productivity of American businesses. Given the extremely short induction period between exposure and injury occurrence, CDC can make a measurable difference in a very short period of time (< 4 years).

Examples of specific research areas of interest include, but are not limited to: An important priority is the development of innovations to apply evidence-based interventions for occupational occurrences of motor vehicle crashes and incidents. Priorities include developing new design concepts and standards that may be used by national standardization groups to update or develop design standards for specific motor vehicles, enhancing effective interventions for driver education and behavior to reduce motor vehicle incidents and crashes among professional drivers, evaluating intervention strategies for their effectiveness in reducing the number or severity work-related motor vehicle incidents and crashes, and enhancing engineering controls for the prevention of crashes and incidents or reducing the severity of traumatic injury associated with such crashes and incidents.

2. Control Technology and Personal Protective Equipment

Engineering controls, administrative policies, and personal protective equipment are needed to manage exposures to occupational hazards. Engineering controls include substitution of a safe material for a hazardous one, design changes to equipment, or modification of work methods to eliminate or reduce hazards. Changes in work practices and management policies and training programs are examples of administrative controls. In some cases where it is not otherwise possible to maintain a healthy work environment, personal protective equipment such as respirators and protective clothing can be used to isolate workers from the hazard. Research is needed to develop and evaluate control strategies for specific hazards and to assure their practicality and usability in workplaces.

A. Improve the effectiveness of existing or proposed engineering controls (including retrofit solutions).

B. Develop control measures for new workplace hazards.

C. Develop products or approaches that reduce/eliminate the specific hazardous parts of a job that contribute most to the actual exposure, including personal hygiene where contamination of surfaces, clothing, or skin may occur.

D. Develop personal protective equipment that will fit the anthropometric diversity in today's workforce.

E. Develop alternatives to pesticide application and hazardous waste remediation.

F. Develop micro sensing devices to notify workers before chemicals break through protective clothing and identify failures in containment systems for hazardous materials.

G. Develop new materials for clothing to protect against chemical and physical hazards.

H. Develop information dissemination methods to help businesses learn about and implement occupational safety and health programs.

I. Develop training materials to teach hazards and risks, demonstrate solutions, measure changes in behavior and practices, and improve injury and illness rates.

http://www.cdc.gov/niosh/programs/ppt/

3. Exposure Assessment Methods

Exposure assessment is a multi-disciplinary field central to deciding whether and how to use resources for reducing workplace exposures, and to defining exposure-response relationships in epidemiologic studies. Rapid, inexpensive measurement tools and improved data analysis methods are needed for the collection of adequate exposure data and for effective intervention. At least three major gaps in current methods will drive development of exposure assessment methods in the next decade: (1) the lack of sufficiently precise exposure assessments to support accurate epidemiologic studies in the complex environments of today's workplaces, (2) the lack of practical measurement techniques that can be applied at reasonable cost in many workplaces where hazards may exist, and (3) the lack of validated methods for measuring relevant exposure and total dose data directly from biological samples obtained by relatively noninvasive techniques.

A. Develop computer models to extrapolate information from historical data of limited exposure measurements to apply to large study populations, and to incorporate short-duration but high-intensity exposures such as leaks or spills into the models.

B. Develop easy-to-use, direct-reading instruments and test kits to measure exposures rapidly and inexpensively in a variety of workplaces for routine monitoring, evaluating the success of control technologies, and providing data for research studies.

C. Improve the measurement of low concentrations of chemicals and biomarkers in biological specimens such as blood, urine, saliva and sweat so that such concentrations can be linked to internal dose at the target organs.

D. Design laboratory analytical methods for inexpensively measuring numerous chemicals in a single sample.

E. Formulate exposure survey designs and methods for exposure data analysis to obtain more meaningful data for health risk assessments.

F. Improve exposure assessment methods so that at-risk workers can be identified.

http://www.cdc.gov/niosh/programs/expa/

4. Intervention Effectiveness Research

The goal of intervention research is to develop practical strategies and techniques that effectively reduce or prevent workplace injuries and illnesses. Workplace safety and health interventions include but are not limited to developing and implementing specific engineering control technologies, process and work organization changes, information dissemination and health communication practices, worker/management participatory safety and health programs, safety and health training, selective use of personal protective equipment, and inspection and enforcement of protective exposure limits. Intervention research involves the testing and evaluation of interventions, programs, and policies. Although many intervention strategies have been applied to industrial settings, knowledge about what works best is limited. Corporate safety and health programs, regulatory requirements and voluntary consensus standards, workers' compensation policies and loss-control programs, engineering controls, and educational campaigns are among the types of interventions that need to be developed, implemented, and evaluated.

A. Develop techniques to evaluate the effectiveness of implemented control technologies.

B. Develop materials and methods for increasing the acceptance of new control technologies and develop approaches to eliminate or alter these barriers, including economic feasibility.

C. Develop intervention efforts in the areas of greatest need.

5. Surveillance Research Methods

Surveillance systems describe where occupational hazards, injuries, or illnesses are found, how frequently they are found, whether they are increasing or decreasing, and whether prevention efforts have been effective. The public health community relies on surveillance information to set research and prevention priorities, but critical gaps in current systems limit their usefulness. These systems need to be updated and expanded, and new systems and methodologies need to be developed.

A. Develop approaches for implementing comprehensive, integrated national systems utilizing data sources and models of surveillance that exist in the public and private sectors.

B. Formulate methods to assess nationally or locally the impact of intervention efforts on worker safety and health.

C. As restructuring of health care delivery systems occurs throughout the United States, develop linkages among the systems to identify, track, and target occupational safety and health problems and provide information for decisions to develop interventions or to improve related medical care.

D. Investigate hazard surveillance systems as a means of identifying risks and exposures at worksites and industries, including risks associated with prototypes of new technologies, before injuries and illnesses occur.

http://www.cdc.gov/niosh/programs/surv/

6. Construction

Each day, construction workers face injury hazards from falls, machines, electricity, motor vehicles, and other equipment and circumstances. Health hazards posed by construction work can include dusts, fumes, noise, and chemicals. Musculoskeletal disorders can arise from excessive exertion of force, working in awkward positions, repetitive motions, exposure to vibrating power tools, environmental extremes, and other physical and organizational risk factors. NIOSH researchers identify causes of and develop programs and solutions to prevent injuries and fatalities in construction. NIOSH and construction stakeholders have identified fifteen strategic goals identifying specific needs. These are available at http://wwwdev.niosh.cdc.gov/niosh/nora/default.html and they provide additional ideas for innovation research. Some examples of innovation needs include:

A. Development of new designs or controls to reduce various hazards such as noise, vibration, dust emissions, welding fumes, high force exertion, or awkward postures.

B. Development of improved tool designs to reduce various hazards such as noise, vibration, or awkward postures.

C. Information tools to facilitate hazard recognition (e.g. for scaffolds, cranes, excavations) and implementation of precautions on job sites.

D. Development of design approaches for prevention or minimization of hazards and commercialization of these interventions to help get them into use.

E. Development of engineering interventions that reduce fall, electrical, overexertion, or struck-by hazards and commercialization of these interventions to help get them into use.

http://www.cdc.gov/niosh/programs/const/

7. Agriculture, Forestry, and Fishing

Agriculture ranks among the most hazardous industries. Farmers are at high risk for fatal and nonfatal injuries, work-related lung diseases, noise-induced hearing loss, skin diseases, and certain cancers associated with chemical use and prolonged sun exposure. Farming is one of the few industries in which the families (who often share the work and live on the premises) are also at risk for injuries, illness, and death.

A. Develop and evaluate devices that improve ladder safety.

B. Design and test improved safety and health training modules for Latino farmers.

C. Safe use of pesticides for limited English speaking and other minority farmers.

D. Roll over protection devices and roll over warning systems for older tractors.

http://www.cdc.gov/niosh/programs/agff/

8. Mining

The mining industry is one of the more challenging occupational sectors with regards to health and safety. Miners must deal with adverse natural conditions while working in restricted spaces with limited visibility. The industry also deals with a variety of unknown conditions, including the physical characteristics of the material being mined as well as the surrounding strata which ultimately form the mine complex. All health and safety topics for the mining industry are eligible for consideration. Some example topics include exposure of mine workers to diesel exhaust, hearing loss prevention in miners, reduction of injuries from materials handling, reduction of injuries and fatalities from powered-haulage equipment, controlling coal and silica dusts, prevention of musculoskeletal disorders, health and safety during construction and maintenance operations, control of chemical hazards and toxic substances, assessment of intervention effectiveness, and dissemination of proven interventions into the mining workplace. The chief requirement for all projects is a focus on reducing the risks of injuries and illnesses directly related to working in a mining environment. Advancements in technology and knowledge which address any of the above concerns would be beneficial to improving mine-worker health and safety. The advancements could be achieved through developing new and innovative technologies, enhanced understanding of the working environment, and improved approaches and strategies for dealing with the issues.

A. Develop new approaches, technologies, or strategies for dealing with excessive exposures in the mining environment.

B. Develop new approaches, technologies, or strategies for assisting in mine escape and/or mine rescue operations. Particular interest is for underground coal mines.

C. Determine the effectiveness and/or development of improved approaches for training used to protect the health and safety of mine workers.

D. Determine a methodology for evaluating the safety culture of the mining community and develop an improved model which enhances the overall safety of surface and underground mining operations.

http://www.cdc.gov/niosh/programs/mining/

9. Healthcare and Social Assistance (HCSA)

Workers are at risk for illness and injuries because of long hours, changing shifts, physically demanding tasks, violence, and exposures to infectious diseases and hazardous chemicals. The HCSA sector comprises workplaces providing health care and social assistance for individuals. The industries in this sector are arranged on a continuum starting with those workplaces providing medical care exclusively, continuing with those providing health care and social assistance, and finally finishing with those providing only social assistance. The services provided by workplaces in this sector are delivered by trained professionals. Many of the industries in the sector are defined based on the educational degree held by the practitioners. Emerging issues identified include: stress from chronic understaffing and long hours due to shortages in nursing and other health care professions; an aging workforce of nurses and other HCSA workers, in the face of increasing demand; potential exposures to unknown hazardous agents contaminating emergency responders; emerging infectious diseases such as SARS and avian influenza; exposure to a variety of antibiotic-resistant pathogens; risk from a dramatic increase in workplace violence perpetrated by clients, their families, and co-workers; and hazardous chemical use and the exposure to potentially hazardous new technologies which are continuously being introduced into healthcare settings.

A. Identify an emerging issue or an existing issue and develop technology to measure or predict exposure of HCSA workers present in workplaces providing health care and social assistance for individuals.

B. Determine the effectiveness and/or develop improved approaches for training used to protect HCSA workers.

C. Develop information tools to facilitate hazard recognition.

http://www.cdc.gov/niosh/programs/hcsa/

10. Manufacturing

The Manufacturing sector includes workplaces engaged in the mechanical, physical, or chemical transformation of materials, substances, or components into new products. The assembling of component parts of manufactured products is also considered manufacturing, except in cases where the activity is appropriately classified as Construction North American Industry Classification System (NAICS) Web site (Code 31-33, Sector 23). Workplaces in the Manufacturing sector are often described as plants, factories, or mills and characteristically use power-driven machines and materials-handling equipment.

The Manufacturing sector includes industries that manufacture durable and non-durable goods including food and food products, beverage and tobacco products, textiles and textile products, apparel, leather and allied products, wood products, paper and paper products, printing and related support activities, petroleum and coal products, chemicals, plastics and rubber products, nonmetallic mineral products, primary metals and fabricated metal products, machinery, computer and electronic products, electrical equipment, appliances and components, transportation equipment, furniture and related products, medical equipment, jewelry, sporting goods, toys, office supplies, signage, and other products. Manufacturing workplaces may process materials or may contract with other workplaces to process their materials for them. Both types of workplaces are included in manufacturing.

A. Identify an emerging issue or an existing issue and develop technology to measure or predict exposure of manufacturing workers present in workplaces engaged in the mechanical, physical, or chemical transformation of materials, substances, or components into new products.

B. Determine the effectiveness and/or develop improved approaches for training used to protect manufacturing workers.

C. Develop information tools to facilitate hazard recognition.

http://www.cdc.gov/niosh/programs/manuf/

11. Public and Private Services

This sector includes workers in the following fields: information and publishing industries; finance and insurance; real estate; professional, scientific, and technical services; management; education; arts, entertainment, and recreation; accommodation and food services; repair services; personal services; and public administration.

Emerging issues in the services sector include Infectious disease such as Avian influenza and SARS may place workers in the hospitality industry at risk as they make contact with travelers and their discarded materials; Needle stick injuries are increasing outside medical clinics and hospitals. More and more patients are injecting medications for diabetes, arthritis and other common ailments at home. Needles from illicit drug use also get placed in domestic solid waste. Workers in waste handling, hospitality, and housekeeping experience increased injury and infection risks as they handle contaminated discarded needles; Wireless technology is changing the locations where work can be completed especially for information industries. Miniaturization of some electronic devices may result in increased musculoskeletal disorders and in hearing loss with long-term use; Ergonomic interventions have reduced muscle strain from lifting but have increased the loads that are pushed or pulled by workers. These new job demands may have long-term health risks that have yet to be recognized; Violence is an increasing risk for many in the service sector, especially those in public safety and food and alcohol service; and, Work Organization changes have led to increasing responsibilities with less control over work factors in many industries and jobs. Increased reliance on electronic measures has created productivity pressures on workers in the information sector.

A. Identify an emerging issue or an existing issue and develop technology to measure or predict exposure of Public and Private Services workers present in workplaces potentially exposed to infectious disease, needle sticks, muscle strain, or violence.

B. Determine the effectiveness and/or develop improved approaches for training used to protect Public and Private Services workers.

C. Develop information tools to facilitate hazard recognition.

http://www.cdc.gov/niosh/programs/pps/

12. Transportation, Warehousing and Utilities

Transportation and Warehousing includes industries providing transportation of passengers and cargo, warehousing and storage for goods, scenic and sightseeing transportation, and support activities related to modes of transportation. Establishments in these industries use transportation equipment or transportation related facilities as a productive asset. The type of equipment depends on the mode of transportation. The modes of transportation are air, rail, water, road, and pipeline. Utilities is comprised of establishments engaged in the provision of the following utility services: electric power, natural gas, steam supply, water supply, and sewage removal.

A. Identify an emerging issue or an existing issue and develop technology to measure or predict exposure of Transportation, Warehousing and Utilities workers engaged in activities that may cause musculoskeletal disorders. Intervention effectiveness projects regarding obesity or sleep disorders in truckers will also be welcomed.

B. Determine the effectiveness and/or develop improved approaches for training used to protect Transportation, Warehousing and Utilities workers.

C. Develop information tools to facilitate hazard recognition.

http://www.cdc.gov/niosh/programs/twu/

13. Wholesale and Retail Trade

This sector includes both wholesale and retail trade. Both wholesale and retail trade are comprised of establishments engaged in the sale of merchandise, generally without transformation, and rendering services incidental to the sale of merchandise.

Some of the emerging issues include the following: (1) long work hours, (2) shift work, and (3) work stress from serving the public, either in direct or telemarketing sales. Health and retirement benefits are disappearing, which can cause work-related stress in managing illnesses. Just in time shipping and order filling is increasing causing time pressure and lack of work control. Psychosocial problems are increasing that can fuel workplace violence. Musculoskeletal disorders continue to be a burden to workers, but the stress loads are shifting from the low back and legs to the upper extremities and shoulders/neck. This is occurring as a consequence of materials handling equipment reducing the lifting burdens but increasing the need to use keyboards and monitoring systems. Researcher will need to be sensitive to low force and high speed repetitive activities and static postures. It is expected that as the research agenda for the Wholesale and Retail Trade sector is developed, more emerging issues will be identified that will require continuing research.

A. Identify an emerging issue or an existing issue and develop technology to measure or predict exposure or to measure intervention effectiveness of wholesale and retail trade workers present in their workplaces.

B. Determine the effectiveness and/or develop improved approaches for training used to protect wholesale and retail trade workers.

C. Develop information tools to facilitate hazard recognition.

http://www.cdc.gov/niosh/programs/wrt/

14. Other Research Topic(s) Within the Mission of the Institute

Because of the diverse nature of occupational safety and health issues, many other research topics are supported by NIOSH in addition to the National Occupational Research Agenda (NORA) topics. In addition, NIOSH supports research to reduce occupational injuries and illness in sector specific areas including construction, agriculture, and mining. Visit the NIOSH homepage for more information on NIOSH's research program areas http://www.cdc.gov/niosh/homepage.html.

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FOOD AND DRUG ADMINISTRATION (FDA)

FDA will accept SBIR grant applications on the April 5, August 5, and December 5, 2011 submission dates.

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get accurate, science-based information they need to use medicines and foods to improve their health.

For additional information about areas of interest to the FDA, please visit our home page at http://www.fda.gov.

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER)

CBER is responsible for ensuring the safety, efficacy, potency and purity of biological and related products intended for use in the treatment, prevention or cure of diseases in humans as well as the safety of the nation's supply of blood and blood products. The primary responsibility of CBER is to review the

quality, safety and efficacy of vaccines, blood products, certain diagnostic products and other biological and biotechnology-derived human products.

CBER's activities include: evaluating the quality, safety and effectiveness of biological products before marketing, and monitoring the pre-clinical and clinical testing of new biological products; licensing biological products and manufacturing establishments, including plasmapheresis centers, blood banks, vaccine and biotechnology manufacturers; AIDS program and policy activities, including research on AIDS therapeutic products, diagnostic tests and vaccines; research to establish product standards, develop improved testing methods and assess the safety of biological products; compliance, lot release program and post market surveillance; meeting PDUFA goals, new research programs, and new regulatory initiatives (managed review process for all products).

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

CDER develops FDA policy with regard to the safety, effectiveness, and labeling of all drugs for human use; evaluates new drug applications and investigational new drug applications; develops standards for the safety and effectiveness of all over-the-counter drugs; monitors the quality of marketed drugs through product testing (bioavailability/bioequivalence testing), post marketing surveillance, and compliance programs; develops guidelines on good manufacturing practices; conducts research and develops scientific standards on composition, quality, safety, and efficacy of human drugs.

Drug regulatory research as conducted in CDER is directed at the discovery of new knowledge relevant to drug development, post marketing drug experience (patterns of drug use and safety), and drug regulation to enhance FDA regulatory decisions. These drug regulatory decisions impact on the development of regulations, guidelines and guidance for the regulated industry and provide clarity and consistency in application of CDER regulatory requirements. These drug regulatory decisions also impact public health by ensuring that marketing drugs are safe and efficacious and that their risk: benefit profile remains acceptable during the market life of a drug. Specific areas of research conducted by the Center include: Pharmacology/toxicology, microbiology/virology, clinical pharmacology, pediatric issues in drug therapy, post marketing drug safety, evaluation of effectiveness of regulatory actions, patterns of drug use, including off-label, signal detection methodologies (e.g., data mining techniques), epidemiologic studies of therapeutics using population-based data, regulatory compliance, product quality, and active surveillance methods.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Develop a system for gathering real-time data on physician prescribing behavior, understanding and compliance with drug product labeling and frequency of off-label prescribing.

B. Develop and evaluate the effectiveness of new methods and tools for managing the known risks of marketed drug products (e.g., communicating newly identified risks to health care practitioners and patients).

C. Develop methods for timely active surveillance of newly approved drug products in large populations to identify both expected and unexpected outcomes.

D. Develop methods for actively collecting information on all cases of classically drug-associated events (e.g., acute liver failure, blood dyscrasias, severe desquamating skin disorders) to augment the FDA’s current passive surveillance system.

E. Develop improved clinical markers and methods with potential for bed-side application for detection of the early onset of adverse drug events.

F. Develop surrogate potency methods for biotech drug products to replace traditional animal testing.

G. Development of psychochemical and in-vitro biological tests to evaluate pharmaceutical equivalence of complex drug substances and drug products.

H. Research into approaches to handle informative missing patient data in clinical trials, including innovations in study designs and statistical methods of analysis.

I. Statistical and computational methods and strategies for the design, analysis and interpretation of microarray, genomic and proteonomic data.

CENTER FOR FOOD SAFETY AND APPLIED NUTRITION (CFSAN)

The FDA is responsible for the safety of the vast range of food Americans eat; about 80 percent of all food sold in the United States. This includes everything except for the meat, poultry, and processed egg products that are regulated by the USDA. Consequently CFSAN seeks research designed to complement and accelerate efforts aimed at the detection, prevention, and control of contamination that may be responsible for illness or injury conveyed by foods, colors, and cosmetics. CFSAN conducts research, and develops regulations, guidance and standards related to the composition, quality, nutrition, and safety of food, food additives, colors, and cosmetics. The Center evaluates FDA's surveillance and compliance programs relating to foods, colors, and cosmetics; reviews industry petitions, and develops regulations for food standards to permit the safe use of color and food additives.

CFSAN maintains an active research program that is focused on the following priorities; ensuring the safety of food, dietary supplements and cosmetics; improving nutrition; and promoting the security and integrity of the food supply. The Center's research activities are intended to; support the FDA's regulatory activities; reduce the incidence of foodborne illness by improving our ability to detect and quantify foodborne pathogens, toxins, and chemicals that could jeopardize the safety and security of the food supply; find new and improved ways to control these agents; and safely produce, process, and handle food and food products. FDA is committed to reducing the incidence of foodborne illness to the greatest extent feasible while at the same time protecting the nation's food supply. Mission-critical knowledge gaps are addressed through translation research focused on the risks associated with FDA regulated products throughout their life cycles, from production to consumption. Ideally extramural research is sought that complements the Center's intramural research efforts, and which will enhance the Agency's and the Nation's ability to reduce the incidence of foodborne illness and protect the integrity of the nation's food supply. FDA's mission-critical needs require that the research not simply end with the generation of new knowledge and technologies, but extend to the validation of new approaches by using realistic conditions that accurately reflect the diversity of the food industry and offer potential solutions that can be accept by appropriate sectors of the food industry.

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)

CDRH develops FDA policy and solves problems related to public health and safety of medical devices and radiation-emitting electronic products. It evaluates applications for premarket approval of medical devices, approves products development protocols and exemption requests for investigational devices. It classifies devices into regulatory categories, develops safety effectiveness standards and good manufacturing practices regulations, operates post market surveillance and compliance programs, and provides technical, non-financial assistance to small manufacturers. The Center also conducts programs to reduce human exposure to hazardous ionizing and nonionizing radiation, through an electronic product radiation control program and other programs designed to control and limit radiation exposure. The Center develops and conducts research and testing programs in the areas of physical, life, and engineering sciences related to the human health effects of radiation and medical device technologies, provides expertise and analyses for health-risk assessments, and also develops new or improved measurement methods, techniques, instruments and analytical procedures for evaluating product performance and reliability.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Examine the setup, documentation and optimization of our Sun Grid Engine (SGE). The architecture of this networking application is particularly suited to managing surge capacity in high performance computing. The modeling of many physiologic functions and bioinformatic analyses can take months or even years to run on a standard desktop computer. The SGE takes the overall problem and distributes it to a cloud of computers on a network so that no user knows, or cares, if a computation is performing in the background on their machine. As FDA rolls out laptops with multi-core CPU's and which are equipped with prodigious amounts memory this experiment in "cloud computing" could become a reality on the Whiteoak Campus. The scope of work would be to develop, document, and provide training systems for developers, network architects, and users on working methodologies for the integration of cloud computing with the existing FISMA compliant conventional networking.

B. Develop a high-speed, low light spectral CMOS linear imaging system to measure complete spectra of multiple variables from living tissue. Complete spectra of fluorescence signals (including auto-fluorescence and FRET) could be measured along a line at high speeds (10 kHz) with a rectangular CMOS grid (e.g. 10 x 1,000 pixels -> 10 sites 1000 wavelengths).

C. Develop bioassays/biosensors to identify injurious levels of nerve stimulation utilizing bioluminescence and neurotransmitter detection technologies. Research capabilities needed include voltage clamp, current clamp and extracellular techniques in peripheral nerves and brain slices to explore stimulation protocols that release neuroactive substances released in injury and inflammation which are not normally evoked under normal physiological conditions.

D. Design, build, and validate a phantom that is traceable to a national metrology institute (NMI) such as NIST (or any other NMI) to improve the accuracy and clinical utility of bone mineral density measurements made using dual energy X-ray absorptiometry (DXA). The calibration phantom should be constructed using biosurrogate materials with known/tabulated data for body tissue and tissue substitutes.

CENTER FOR VETERINARY MEDICINE (CVM)

CVM is a public health organization that enables the marketing of effective drugs, food additives, feed ingredients, and animal devices that are safe to animals, humans, and the environment. The Center, in partnership with Federal and state agencies and other customers, ensures animal health and the safety of food derived from animals. The Center makes timely, quality decisions and takes regulatory actions to ensure that these products provide for quality health care of animals, minimize the transmission of zoonotic diseases, and increase the efficiency of production of animal-derived food and fiber. Regulatory decisions are supported by research, the monitoring of product safety, and efficacy, and the continual improvement of processes.

Research and development opportunities within the Center for Veterinary Medicine that lend themselves to performance by small businesses include, but are not limited to, the following areas of interest:

A. Development, for the specific purpose of obtaining approval or conditional approval, of products for the treatment, control or prevention of diseases or conditions occurring in minor species or small numbers of major species.

B. Development and validation of high throughput/screening quantitative and qualitative analytical methods for analyzing drugs, additives, and contaminants in animal tissues and feeds.

C. Development of methods to determine absorption, distribution, metabolism, and excretion of drugs, feed additives and contaminants (microbial and chemical) in food animals, including minor species.

D. Development of new biomarkers and models for determining the safety and effectiveness of veterinary drugs and food additives in domestic animals, including minor species.

E. Development of methods to determine the effects of drugs, food additives, and contaminants (microbial and chemical) on immunological and physiological functions of domestic animals, including minor species.

OFFICE OF CRITICAL PATH PROGRAMS

The Office of Critical Path Programs, in FDA's Office of the Chief Scientist, coordinates the cross-agency Critical Path Initiative (CPI), FDA's strategy for transforming the way medical products are developed, evaluated, and manufactured. CPI activities are under way throughout the Agency, from the product centers to the Office of the Commissioner. For details, see http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/default.htm. Collaboration is key to the CPI initiative because bringing safe, effective, and innovative therapies to the American public requires FDA to leverage the resources and expertise of all stakeholders, including other Federal agencies, academia, healthcare professionals, patient and consumer groups, regulated industry, and health-related organizations. In 2008, CPI collaborations involved 84 government agencies, universities, industry leaders, and patient groups from 28 states and 5 countries on a raft of groundbreaking research projects.

Research and development opportunities within FDA that lend themselves to performance by grantees include, but are not limited to, the following:

A. Studying the immunological correlates of TB immunity and developing tools to evaluate TB vaccine efficacy

B. Developing study models for testing combination-antimicrobials as a strategy to prevent the development of drug resistance

C. Developing new approaches to preclinical safety testing

D. Identifying biomarkers for safety and efficacy evaluation of medical products

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT

The Office of Orphan Products Development was established to identify and facilitate the development of orphan products. Orphan products are drugs, biologics, medical devices and foods for medical purposes, which are indicated for a rare disease or condition (i.e., one affecting fewer than 200,000 people in the United States). These products may be useful in a rare disease/disorder but lack commercial sponsorship because they are not considered commercially attractive for marketing. A subcategory of orphan products are those marketed products in which there is evidence suggesting usefulness in a rare disease/disorder but which are not labeled for that disease/disorder because substantial evidence of safety and effectiveness for that use is lacking.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

A. Development of products for the treatment of rare diseases or disorders including but not limited to neurological, metabolic, genetic, ophthalmologic, hematologic, and dermatological diseases or disorders for the specific purpose of obtaining marketing licensure.

B. Development of products for use in diagnosis of rare diseases for which the diagnostic tool would be used in fewer than 200,000 persons annually in the United States.

C. Development of vaccines for the prevention of rare diseases to be used in fewer than 200,000 persons annually in the United States.

Other Research Topic(s) Within the Mission of FDA

For additional information on research topics and administrative and business information, contact:

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Food and Drug Administration
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ADMINISTRATION FOR CHILDREN AND FAMILIES

The Administration for Children and Families (ACF), within the Department of Health and Human Services (HHS) is responsible for federal programs that promote the economic and social well-being of families, children, individuals, and communities. ACF partners with State and local governments, for-profit and non-profit organizations, faith- and community-based organizations, American Indian Tribes and Native American communities to design, administer and promote programs in areas such as child welfare, childcare, Head Start, healthy marriage, Temporary Assistance for Needy Families (TANF), and responsible fatherhood.

The Office of Planning, Research and Evaluation (OPRE) facilitates ACF's SBIR investments. The Office provides guidance, analysis, technical assistance, and oversight to ACF programs on strategic planning aimed at measurable results; research and evaluation methodologies; demonstration testing and model development; statistical, policy and program analysis; synthesis and dissemination of research and demonstration findings.

The focus of the research topics for SBIR should reflect the research and programmatic interests of ACF. Particular areas of interest for ACF include but are not limited to:

Adoption and Foster Care
Child Abuse & Neglect
Child Care
Child Support
Developmental Disabilities
Early Head Start
Energy Assistance
Family/Domestic Violence
Fatherhood and Healthy Marriage
Head Start
Native American and Tribal Programs
Refugee Resettlement
Human Trafficking
Temporary Assistance for Needy Families
Youth Development

For additional information on ACF programs and research, please visit the ACF website at http://www.acf.hhs.gov and the Office of Planning, Research and Evaluation's website at http://www.acf.hhs.gov/programs/opre/index.html.

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