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

SMALL BUSINESS INNOVATION RESEARCH (SBIR)

AND

SMALL BUSINESS TECHNOLOGY TRANSFER (STTR)

GRANT APPLICATIONS

NIH, CDC, and FDA Program Descriptions and Research Topics

SUBMISSION DATES

APRIL 5, AUGUST 5, AND DECEMBER 5, 2007

National Institutes of Health (SBIR and STTR)

Centers for Disease Control and Prevention (SBIR)

Food and Drug Administration (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-07-280.HTML

SMALL BUSINESS TECHNOLOGY TRANSFER PROGRAM PARENT ANNOUNCEMENT (STTR [R41/R42])
HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/PA-FILES/PA-07-281.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)

NIH SBIR/STTR INTERNET GUIDE (MS WORD)

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, and FDA 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 proposals, including the co-funding of such proposals 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 cost 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 II Competing Renewal Awards

Some NIH Institutes/Centers (ICs) offer Phase II SBIR/STTR awardees the opportunity to apply for a Phase II Competing Renewal award. 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 II Competing Renewal award. Moreover, this opportunity is only for Phase II awardees that propose to continue the process of assessing and improving drugs or devices or propose to conduct preclinical studies of drugs or devices that ultimately require: 1) clinical evaluation, 2) approval of a Federal regulatory agency, and/or 3) continuing refinements to durable medical equipment (DME) designs such as cost reduction, testing for safety, durability, and reliability, and meeting or establishing standards. Such products include, but are not limited to, devices, drugs, vaccines, therapeutics, and medical implants related to the mission of the IC. The product being developed must be one for which Federal regulatory approval (e.g., FDA) is a required step toward commercialization. Prospective applicants are strongly encouraged to contact NIH staff prior to submission of a Competing Renewal application. 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 II Competing Renewal awards: **NIA, NIAAA, NIAID, NICHD, NIDA, NIDCD, NIDDK, NHLBI** (SBIR only and only Competing Renewals of NHLBI-supported Phase II awards), **NIMH** (SBIR only), **and NINDS.**

Bioengineering Nanotechnology Initiative

See Program Announcement at http://grants.nih.gov/grants/guide/pa-files/PA-06-009.html (SBIR R43/R44) and http://grants.nih.gov/grants/guide/pa-files/PA-06-008.html (STTR R41/R42)

The NIH invites grant applications for nanotechnologies useful to biomedicine. Nanotechnology is defined as the creation of functional materials, devices and systems through control of matter at the scale of 1 to 100 nanometers, and the exploitation of novel properties and phenomena at the same scale. Nanotechnology is emerging as a field critical for enabling essential breakthroughs that may have tremendous potential for affecting biomedicine. Moreover, nanotechnologies developed in the next several years may well form the foundation of significant commercial platforms.

The following list describes some of the priority areas for nanoscience and nanotechnology research support at NIH. The list is not exhaustive, nor are the topics mutually exclusive. Their presentation here exemplifies important scientific areas in which research at the nanoscale has the potential to make enormous contributions to solving biomedical problems.

- Nanomaterials (enabling): development of synthetic nanoscale building blocks for the formulation of bottom-up approaches to complex and multi-functional nanomaterials. These materials are expected to find use in applications towards pharmaceutical delivery, towards the development of contrast and biological agents, and multi-functional medical devices.
- Nano-bio interfaces: science of controlling the interface between biomolecular systems and nanoscale synthetic materials, which involves ability to control the interface architecture and transduction of the control signal through this interface.
- Nanoimaging: real-time imaging of subcellular structure, function, properties and metabolism.
- Cell biology: nano-scale research on cellular processes, including biophysics of molecular assemblies, membranes, organelles, and macromolecules.

- Molecular and cellular sensing/signaling: technologies to detect biological signals and single molecules within and outside cells.
- Prosthetics: mechanical, chemical, and cellular implant nano-technologies to achieve functional replacement tissue architectures.
- Environmental and health impact of nanotechnologies: ramifications of nanomaterial processing, use, and degradation on health and the environment.
- In-vivo therapeutics: development of nanoparticles that enable controlled release of therapeutic agents, antibodies, genes and vaccines into targeted cells.
- Sensor technologies: detection and analysis of biologically relevant molecular and physical targets in samples from blood, saliva and other body fluids, or for use in the research laboratory (purified samples), clinical specimens, and in the living body.
- Nanosystem design and application: fundamental principles and tools to measure and image the biological processes of health and disease and methods to assemble nanosystems.
- Bioinformatics for nanotechnology: algorithms and computer software to enable and support all of the above.

Manufacturing Processes of Medical, Dental, and Biological Technologies (SBIR [R43/R44] and STTR [R41/R42])

http://grants.nih.gov/grants/guide/pa-files/PA-06-012.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-013.html (STTR)

The NIH encourages research related to advanced processing in the manufacture of biomedical products and the implementation of new technologies in medical care. New methods, procedures, measures, and controls are needed for manufacturing a broad range of technologies and products with unsurpassed quality and to lower manufacturing costs for existing and/or new processes. Research is also encouraged that can contribute to the containment and reduction of health care costs and that can improve the cost effectiveness, quality, and accessibility of the health care system.

Because manufacturing-related R&D is extremely broad in scope, the following examples of research topics may be of interest but are not meant to be exhaustive.

Flexible computer-assisted integrated manufacturing equipment and intelligent processing equipment adaptable to the varied needs of biomedical research and medical care device and material production.

Systems engineering and management tools needed for the development of biomedical product manufacturing plants with particular emphasis on the requirements to meet GMP requirements for FDA approvals.

Technology for the manufacture of research instrumentation, such as highly sensitive, high resolution spectrometers, highly selective electrodes, microarray devices, and microfluidic devices.

Technology for the manufacture of clinical diagnostic devices and reagents.

Technology for the manufacture of novel diagnostic imaging devices for both invasive and non-invasive techniques.

Technology for the manufacture and delivery of therapeutic drugs, including for example, synthetic process chemistry, separations methods, formulation, and dosage delivery.

Technology for the manufacture of implantable devices and materials, including drug delivery pumps, prosthetic organs, artificial tissues, electronic sensors and electrical stimulators.

Technology for the production of natural products derived from plant, animal, and microbial sources, such as antibiotics, anticancer drugs, and other therapeutic agents, and useful synthetic starting materials.

Technology for the production and isolation of biotechnology products, such as proteins, antibodies, nucleic acids, vaccines, and vectors for genetic engineering and gene therapy.

Technology for the production of new materials relevant to biomedical research and medical care delivery, including nanomaterials, carbon fibers,

polymeric materials, self-assembled monolayers, controlled size, shape, and porosity particles, filters, membranes, silicon substrates for microarrays, superconducting materials for NMR and MRI magnets, and implantable magnetic materials for external magnetic manipulation.

Technology for manufacture of medical device power sources, such as high energy density, long life-time batteries, solar cells, and fuel cells.

Technology for the fabrication of medical care instruments and devices such as minimally invasive and magnetic field tolerant surgical instruments, orthopedic implants, prostheses, and enabling devices for the injured and disabled.

Rapid prototyping and manufacture technology suitable for remote site and on demand production processes.

Technology to promote the recovery, reuse, and remanufacture (recycling) of medical materials and equipment.

Technology for the manufacture of biomedically specialized computational and information technology equipment and software.

Development of innovative products that facilitate the safety and health training of hazardous materials workers, emergency responders, and skilled support personnel. (See also NIEHS Worker Education and Training Program at http://www.niehs.nih.gov/wetp/home.htm.)

Development of Synthetic and Natural Biomaterial Reference Materials

The NIH invites applications for the development of synthetic or natural biomaterial reference materials (RMs). RMs are used for standardization of studies of interactions between materials and blood and tissues, for calibration of physicochemical test methods, and/or for reference controls in physical, chemical, and materials structure characterization tests. All innovative developments of biomaterials and devices also need measurements to demonstrate their innovation and improvement. Because RMs lie at the heart of measurement technology, funding for their development could play a key role in future advances in biomaterials and biomedical material device technologies.

Industry uses biomaterial RMs for quality assurance and traceability. The Food and Drug Administration considers them useful for comparing new biomaterials, or new uses of biomaterials, with existing standards and materials. In order to have maximum utilitarian value, it is intended that these biomaterial RMs be stored at, and distributed by, the National Institute of Standards and Technology (NIST). Hence, they must be produced to meet the stringent requirements of the NIST Standard Reference Material Program. *It is important for applicants to contact NIST (Dr. John A. Tesk, 301-975-6799; Email: john.tesk@nist.gov) to obtain detailed information on requirements of that program prior to preparing and submitting their applications.*

Biomaterial RMs may be synthetic polymers, ceramics, metals, or mixtures of these, or may be derived from living tissues. The choice of RM to be developed is up to the applicant but must be fully justified based on the applicant's knowledge of the magnitude of the current or potential utilization of the biomaterial. RMs of known particular value include: (1) silica-filled poly(dimethylsiloxane), (2) aliphatic polyether urethane, (3) poly (vinylchloride), (4) poly(methylmethacrylate), (5) expanded poly (tetrafluoroethylene) of varying standardized internodal distances, (6) oxygen permeability standards, and (7) carbon materials used in mechanical heart valve designs.

RMs must be of appropriate size and shape. The form in which the reference material is produced and the tests necessary to characterize the material are the decision of the applicant based on the end use of the material. The applicant may consider NIST as a potential subcontractor for measurement and other professional services.

For additional information on this topic, please contact:

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Research Supplements to Promote Diversity in Health-Related Research

(See Funding Opportunity Announcement at http://grants.nih.gov/grants/guide/pa-files/PA-05-015.html)

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 the diversity of the research workforce by supporting and recruiting students, postdoctorates, and eligible investigators from groups that have been shown to be underrepresented. 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 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.

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.

A currently funded Principal Investigator can submit one application on one topic. 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-05-015 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.

Questions and additional information about these programs is available by contacting the NIH SBIR Office at sbir@od.nih.gov or 301-435-2713.

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 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. With the assistance of the participant, a contractor will help identify niches and potential partners. The contractor will do the due diligence and provide 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 information about the FY 2007 Niche Assessment Program, see the Notice (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-089.html) that was published in the *NIH Guide for Grants and Contracts* on August 2, 2006.

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 participate in this program.

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

The Commercialization Assistance Program (CAP) is designed to assist small businesses 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.

The program is two-phased and runs sequentially. The first phase includes one-on-one business counseling organized around topics that will contribute to the development of a business plan or licensing package specific to each product being developed. The second phase is an investment event where the participants present their business opportunities to a targeted group of potential investors and/or partners.

Participation in the CAP is limited to NIH SBIR Phase II awardees (grants and contracts) awarded in the previous five years. Applications to participate are typically announced in the *NIH Guide for Grants and Contracts* and on the NIH Small Business Funding Opportunities Web site and accepted in late spring/early summer. Other than travel expenses for two required workshops, the cost to participate in CAP is free.

Manufacturing Assistance Program (For NIH SBIR Phase II awardees)

The goal of the Manufacturing Assistance Program is to provide individual technical assistance in manufacturing to SBIR Phase II awardees as they prepare to commercialize their SBIR-developed products. Through an effort with the National Institute of Standards and Technology's (NIST) Manufacturing Extension Partnership (MEP) program and their national network of non-profit centers, technical support will be provided to companies as they move to a developmental stage that requires decisions in manufacturing transition strategies. This includes but is not limited to: method of scale up, cost estimation, quality control, prototyping, design for manufacturability, facility design, process development/ improvement, vendor identification and selection, plant layout and other similar issues. Upon completion, it is anticipated that participating companies will be able to make better manufacturing and operational decisions converting their research into products by: (1) decreasing development costs and cycle time to market; and (2) minimizing anticipated operational expenses and increasing product quality.

Participation in this program is limited to NIH SBIR Phase II awardees (grants and contracts) and participants must be willing to commit a minimum of 200 – 300 man hours over a six-month period. NIH initiated this program as a pilot program in FY 2007; and, if successful, NIH will implement the Manufacturing Assistance Program as a trans-NIH program in late summer/early fall of 2007.

NATIONAL INSTITUTE ON AGING (NIA)

The NIA supports 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 grant research under four established programs: Behavioral and Social Research, Biology of Aging, Geriatrics and Clinical Gerontology, and Neuroscience and Neuropsychology of Aging.

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 II Competing Renewal Awards

NIA accepts Phase II Competing Renewal grant applications from Phase II SBIR/STTR awardees to continue the process of developing products, primarily compounds for pharmaceutical agents, that require approval by a Federal regulatory agency, namely the Food & Drug Administration (FDA). NIA will consider requests for other products requiring FDA approval, such as medical implants and treatment or diagnostic tools, but will emphasize and direct a majority of its CY 2007's Phase II Competing Renewal resources toward pharmaceutical development, particularly in the development of

therapeutic agents for treatment of Alzheimer's disease.

NIA will accept applications for up to two (2) years and up to $750,000 per year in total costs. The Phase II 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 II Competing Renewal applicants are 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
- Participating institutions
- Funding Opportunity Announcement Number (e.g., PA-07-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 II Competing Renewal award.

The following examples would make appropriate topics for Phase II Competing Renewal projects. These are meant only as indications of potential Phase II Competing Renewal projects and are not exclusive of other appropriate activities. Research and development efforts can be focused on medications to treat, delay the progression of, or prevent age-related cognitive decline, 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 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 II Competing Renewal applications, please contact:

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

Behavioral and Social Research

Research on basic and translational social and behavioral research on aging processes and the place of older people in society. The program focuses on how people change with age, on the interrelationships 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. Emphasis is placed upon the dynamic interplay between the aging of individuals and their changing social and physical environments. Special emphasis areas are Aging Minds (see *The Aging Mind: Opportunities in Cognitive Research*, http://books.nap.edu/catalog/9783.html); Genetics, Behavior and the Social Environment; Health Disparities; Health, Work and Retirement; Increasing Health Expectancy; and Interventions and Behavior Change. Areas that may be of interest to small businesses include, but are not limited to:

A. Cognitive and human factors interventions on the individual and environment to maintain independence, maintain functioning, increase well being, and prevent disease/disability. Such interventions can include behavioral technologies, environmental modifications and redesign, training and teaching efforts, or new programs, products and services. Interventions can be developed for home, community, health-care or work-place settings.

B. Research Innovation: Innovations and new products that improve data collection, data analysis, and data dissemination are encouraged. Examples of areas of interest in data collection include, but are not limited to: experience sampling methodologies; improved performance-oriented measures of cognitive and physical functioning suitable for use in field settings or in cross-national research; the development of miniaturization devices to improve real-time data collection, blood spot assay technology for large volume field-based

and survey research, technology for the adaptation and validation (for use in field-based settings) of platforms that allow for simultaneous measurement of multiple analytes using a small quantity of sample (e.g. cardiovascular, metabolic, immune, endocrine, reproductive, cognitive and endocrine markers), real time salivary cortisol measure, and the development of computer-assisted personal and telephone instrument modules to use with older respondents. New and innovative methods for improving the measurement of well-being and physical functioning (alternatives to ADL/IADLS) in the older populations (both across subgroups and internationally), are particularly encouraged.

C. Social, behavioral, environmental and/or technical interventions on the individual for health maintenance and disease/disability prevention. Such interventions can include self management of chronic diseases including behavioral change technologies, enhancing compliance, especially for less educated patients with chronic diseases requiring strict adherence to complex regimens, or new programs, products and services to increase the health, functioning and well-being of older people. Interventions can be developed for home, community, health-care or work-place settings.

D. AIDS and aging. The development of intervention strategies which are designed to prevent the spread of AIDS in middle-aged and older populations. These strategies may include health education programs to inform the health care providers and public about risks of AIDS in older people.

E. Multi-Level Interventions are interventions that influence multiple levels. Levels include the social, community, family, institutional, and individual. More information about the use of multilevel methodology in the social sciences can be found in *People and Pixels: Linking Remote Sensing and Social Science* (http://books.nap.edu/openbook/0309064082/html/index.html). Other valuable information about social science interventions can be obtained from *New Horizons in Health an Integrative Approach* (http://books.nap.edu/openbook/0309072964/html/index.html). Interventions and technologies that address multiple levels are of particular interest to the Behavior and Social Research Program.

Anneliese Hahn
301-402-4156, Fax: 301-402-0051
Email: hahnan@nia.nih.gov

F. Interventions for care provision. Development of strategies for care providers (both professionals and families) to deal with burdens of care associated with chronic disabling illness or disease (including Alzheimer's disease). Interventions include new forms of adult day care, and family interventions. Development of work site programs to supply information on caregiving (including community respite and daycare facilities) and to enable advance planning by employees.

G. Death and dying. Programs that deal with decreasing the trauma and difficulty of elders, their families, and care providers faced with end-of-life decisions and those events that surround the end of life.

H. Long-term adherence. Development of strategies and technologies to enhance long-term adherence to medical regimes for chronic conditions and behavior-change interventions for health promotion in older adults. Adherence advances might target the healthcare provider, caregiver or patient, or a larger group, such as a social network.

Dr. Sidney M. Stahl
301-402-4156, Fax: 301-402-0051
Email: StahlS@nia.nih.gov

I. Forecasting. Development of mathematical, economic, demographic and epidemiological 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 effects of public health interventions, changes in health-care financing and insurance, social security, pension coverage or changes in the retirement age. For example, micro- and macro-simulation models of changes in health and economic status and methodological enhancements to existing models that takes into account health, intergenerational transfers, changes in family composition, and other characteristics of future cohorts. The program is interested in both domestic and international projections.

J. Measurement instruments and database support. The program supports collection of numerous large datasets and is therefore interested in technologies which lead to products that will facilitate distribution of data

while ensuring the confidentiality of NIA supported longitudinal studies are of particular interest. Information on supported datasets can be found at: http://www.nia.nih.gov/ResearchInformation/ExtramuralPrograms/BehavioralAndSocialResearch/Resources.htm.

1. Development of new instruments using existing demographic and economic data and theory that yield defensible estimates of quality of health plans, hospitals, nursing homes, etc. The program is interested in both domestic and international estimates.
2. Development of improved performance-oriented measures of cognitive and physical functioning suitable for use in field settings or in cross-national research.
3. Development of new technologies which improve large scale longitudinal surveys in the US and abroad. Including the development of computer-assisted personal and telephone instrument modules, including expert systems, to use with older respondents, in order to determine information such as occupational status, migration, housing issues, disability status, and family structure.
4. Development of new databases (e.g., from administrative data) and database support to satisfy data and research needs on aging, and innovative data archives and methods for accessing archives to make current statistical and epidemiological data more accessible to researchers.
5. Development of innovative methods and software to provide improved high performance remote analytic access to complex longitudinal studies or surveys that cannot be placed in open data archives because of issues relating to confidentiality and the need to prevent re-identification of subjects or respondents. Such software would increase the ease with which data analysts could perform sophisticated analyses with a wide range of statistical software programs, while automatically preventing any analyses or remote requests that could compromise data security.
6. The development of high quality micro or macro simulations models that measure the impact of interventions on health expenditures, well-being and other outcomes.

K. Dissemination and teaching materials. Development of innovative teaching and dissemination tools (e.g., dataset-based computer programs, simulations/games, videotapes and other heuristic devices) to teach dynamics of population aging and convey results of aging research. For example, teaching modules for secondary data analysis for high school and college students using, for example, data from the US Census Bureau, the National Center for Health Statistics, or an NIA sponsored study (see NIA website http://www.nia.nih.gov/ResearchInformation/ExtramuralPrograms/BehavioralAndSocialResearch/Resources.htm for available data sets) and projection data.

L. Interventions on the health-care system. Development and evaluation of strategies to improve health-care organization and delivery including attention to assisted living and new forms of in-home care.

Ms. Georgeanne Patmios, MA
301-496-3138, Fax: 301-402-0051
Email: PatmiosG@nia.nih.gov

M. Development of indicators and measures of progress in the behavioral and social sciences, including bibliometric measures of citations and impact of research, measures of the rate of change and the formation of new research areas, and measures of the impact of behavioral and social research on public policy and well-being.

Dr. Richard Suzman
301-496-3131, Fax: 301-402-0051
Email: SuzmanR@nia.nih.gov

N. Development of miniaturized devices to be used in behavioral and social research to improve real-time, remote monitoring, virtual data collection for instant, continuous, and/or interactive feedback system, and reliable data storage/retrieval.

O. Evaluation of studies (feasibility and sustainability) related to cost effectiveness and efficacy of health promotion/intervention programs in a population that combine innovative disease management tools, multiple intervention/implementation strategies including but not limited to use of health risk appraisals/assessments of individuals, enhanced educational materials relevant to disease management, resource networks for maintenance/dissemination, continuous implementation technology/tools, etc. that show

health improvement and cost savings within one year of intervention.

Ms. Angie Chon-Lee, MPH
301-594-5943, Fax: 301-402-0051
Email: Chon-LeA@nia.nih.gov

Biology of Aging

Research on the physiology, molecular, and cellular basis of aging processes. NIA 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, for example, human fetal lung fibroblasts. Areas 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. Anna McCormick
301-496-6402, Fax: 301-402-0010
Email: am38k@nih.gov

or

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

Dr. Jill Carrington
301-496-6402, Fax: 301-402-0010
Email: carringtonj@nia.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 model 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. Felipe Sierra
301-496-6402, Fax: 301-402-0010
Email: sierraf@mail.nih.gov

Neuroscience and Neuropsychology of Aging

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, immune, disease states); degenerative processes or pathological changes in the aging brain in the context of understanding normal age-related changes; and the sensory, perceptual and cognitive processes and changes that occur with aging as related to their underlying biological mechanisms. An important component of this program is the support of studies on Alzheimer's disease and related dementias of aging. Areas that may be of interest to small businesses include, but are not limited to:

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

B. Development of sensitive, specific and standardized tests for diagnostic screening of cognitive decline and dementia, for example, the development of biochemical and neuroimaging criteria for the diagnosis of cognitive decline and Alzheimer's disease.

C. Discovery, development and/or evaluation of drugs, delivery systems, or treatments to enhance cognitive functioning in normal aging and to treat the cognitive deterioration and/or behavioral symptoms associated with Alzheimer's disease as well as to slow and/or reverse the course of the disease, or prevent it entirely.

Dr. Neil Buckholtz
301-496-9350, Fax: 301-496-1494
Email: nb12s@nih.gov

D. Nutritional interventions to restore brain biochemical changes in aging and neurodegenerative diseases.

E. Biosensors and prosthetic devices to aid sensory and memory dysfunctions.

Dr. Andrew Monjan
301-496-9350, Fax: 301-496-1494
Email: monjana@mail.nih.gov

F. 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.

Dr. Andrew Monjan
301-496-9350, Fax: 301-496-1494
Email: am39m@nih.gov

G. 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 anesthetized animals.

Dr. Molly Wagster
301-496-9350, Fax: (301)496-1494
Email: mw203d@nih.gov

H. 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.

I. Development of technology such as non-invasive methods, to identify neural stem cells and to monitor their function in the adult and aged nervous system Development of novel markers of stem cell 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

Dr. D. Stephen Snyder (Alzheimer's disease and other dementias of aging)
301-496-9350
Email: ss82f@nih.gov

Geriatrics and Clinical Gerontology

The Geriatrics and Clinical Gerontology (GCG) Program supports research on health and disease in the aged and research on aging over the human life span and its relationships to health outcomes.

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. Research on better ways to prevent injuries and deaths associated with the use of currently available bed rails in older patients; this will include improved designs of bed systems for use in the home, nursing home and hospital.

B. 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.

C. Techniques for preventing or treating urinary incontinence.

Dr. Susan Nayfield
301-496-6761, Fax: 301-402-1784
Email: nayfiels@nia.nih.gov

D. 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.

E. 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.

F. 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.

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

G. Improved instrumentation (e.g., accelerometers) for assessment of physical activity, and improved monitors for visually and/or biomechanically characterizing falls in older patients.

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

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

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

K. Measurement of deficits in muscle strength and balance among older persons.

1. Instrumentation for biomechanical assessment of ambulation and falls.
2. Quantitative methods of assessing postural perturbations relevant to activities of daily living.

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

L. Techniques and methods for screening, diagnosis, and treatment of cancer in older persons.

1. Development of geriatric assessment instruments and/or methodology to assist oncologists in patient evaluation and diagnostic work-up to determine the older patient's overall physical and physiologic health status.
2. Techniques to promote effective pain management in older-aged cancer patients. This includes documentation and assessment of pain intensity and its characteristics prior to and after pharmacologic and non-pharmacologic interventions.
3. Development of innovative teaching tools for physicians, nurses, and other health professionals in the following areas: (1) to convey benefits of screening and early detection of cancer for use with older-aged persons; (2) to assist in teaching older-aged patients in self-examination for early warning signs of cancer; and (3) to teach older aged patients how to care for themselves after cancer surgery (e.g., ostomy patients).
4. Development of methods to be used as guidance for physicians to estimate proper medication dosage in elderly cancer patients given body composition, size, age, other health problems, kidney functioning, and other physiologic parameters. This includes estimates of an initial or loading dose of therapeutic drugs and daily maintenance for continuance of therapeutic concentration of drugs in the patient's bloodstream.

Dr. Rosemary Yancik
301-496-5278, Fax: 301-402-1784
Email: ry3e@nih.gov

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

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

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

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

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

Dr. Michael-David ("MD") A.R.R. Kerns
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: mk417e@nih.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
Bethesda, MD 20892
301-496-1472, Fax: 301-402-3672
Email: lw17m@nih.gov

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

The NIAAA supports research on the causes, prevention, control, and treatment of the major health problems of alcohol abuse, alcoholism, and alcohol-related problems. Through its extramural research programs, the 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. The 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 II Competing Renewal Awards

NIAAA will accept competing renewal Phase II SBIR/STTR 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-07-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 competing renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase II 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:

Max Q. Guo, Ph.D.
Telephone: 301-443-0639
Fax: 301-594-0673
Email: qmguo@mail.nih.gov

Pharmaceutical Development for Alcoholism Treatment

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 attenuate drinking behavior.

C. Development of agents to treat acute alcohol withdrawal.

D. Development of agents to treat the protracted withdrawal syndrome.

E. Development of neurotransmitter agonists and antagonists, or drugs that enhance the efficacy of neurotransmission, which are capable of improving or reversing alcohol-induced cognitive impairments.

F. Development of agents to induce sobriety in intoxicated individuals (amethystic agents).

G. Development of agents to diminish drinking by treating associated psychiatric disorders and/or drug abuse.

H. 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.

I. Development of drugs for the treatment of alcoholic hepatitis, cirrhosis, pancreatitis, and cardiomyopathy.

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

For clinical questions, contact:

Joanne B. Fertig, Ph.D.
301-443-0635
Email: jf75t@nih.gov

For pre-clinical questions, contact:

Mark Egli, Ph.D.
301-594-6382
Email: me114r@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 methodology to translate diagnostic instruments for alcohol use disorders and associated disabilities into relevant different languages (e.g., various Hispanic languages).

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

D. Development of computer software for utilization of assessment instruments in a clinical setting. Development and testing of detailed audio, visual, or printed training modules to accompany diagnostic instruments.

E. Application of statistical and mathematical analyses to develop models designed to increase our understanding of (1) etiologic relationship between alcohol use disorders and their associated disabilities, and (2) the factors that influence the initiation and maintenance of alcohol use disorders.

F. Identification, validation, and assay of physiological and/or biochemical measures capable of identifying individuals at risk for becoming alcoholics or individuals who already exhibit alcohol problems. The accurate measurement of acetaldehyde conjugates or abnormal glycoconjugates in blood is one promising approach.

G. Development of biochemical/physiological methods for early detection of alcohol-derived pathology, e.g., alcoholic hepatitis or cirrhosis. Development and characterization of markers

to accurately predict vulnerability to alcohol-derived pathology.

Cherry Lowman, Ph.D.
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Treatment of Alcoholism

A. Development and evaluation of innovative treatment approaches. These approaches can include outreach, shelter, detoxification, treatment and recovery, and alcohol-free housing, as appropriate.

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.

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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, 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.
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Promoting Adherence to Medical, Pharmacologic, and Behavioral Treatments

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.
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Prevention

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. 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 inform the elderly about 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 educational materials designed to provide information on date rape, spouse abuse, child abuse, and other types of violence that have been found to be associated with alcohol use and/or abuse. The development of strategies for preventing victimization would also be appropriate.

D. Development of instruments and educational materials designed to improve the effectiveness of employee assistance programs, especially with respect to assessment, referral, and health promotion as it relates to alcohol use and abuse.

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

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

D. Development 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 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 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 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.

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Fetal Alcohol Syndrome (FAS) 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 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:

Laurie Foudin, Ph.D.
301-443-0912
Email: lf29z@nih.gov

For prevention research questions, contact:

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

Science Education

The NIAAA Science Education program is intended to: (1) supplement in-service education of health

professionals and paraprofessionals with respect to their recognition and treatment of alcohol-related medical problems; (2) stimulate the interest of both precollege and college students, especially among underserved populations, in career opportunities in the biomedical and behavioral sciences generally and the alcohol field specifically; (3) enhance precollege education in the classroom, both directly and via support to teachers, in the life sciences and in education regarding science-related personal and societal challenges; and (4) improve public understanding of science generally and with particular regard to the role of and need for alcohol research. The NIAAA Science Education program complements, but does not duplicate, the education and training components described under other NIAAA topics.

Efforts in science education might include, but are not limited to:

A. Development of methodology to transfer new alcohol research knowledge and directions of scientific knowledge growth to curriculum developers and science teachers, consistent with the National Research Council's National Science Education Standards (1996).

B. Development and testing of specific science education materials, activities or programs to implement one (or more) of the four stated objectives of the NIAAA science education program. The creative use of emerging educational and telecommunications technologies in this regard is of special interest.

C. Development and testing of methodology to present science and alcohol abuse-related curricula and educational materials to particular underserved group(s) in culturally relevant ways, and/or to obtain community support for education in science-related and alcohol-related topics that may be culturally sensitive.

D. Development of resource materials on scientific career opportunities in fields of interest to NIAAA, reflecting activities (e.g., focus groups) and research on motivational factors influencing high school students' career choices, and reflecting economic and social projections of career outlooks for the 21st century.

Roger Hartman
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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.

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

E. Development of ligands for alcohol-relevant neurotransmitter systems 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 instruments that simulate driving, piloting aircraft, or using other complex machinery under hypothetical or actual drinking handicaps and are designed to predict fatal and nonfatal accident involvement.

G. Development of computational, statistical or bioinformatics tools to organize and manage high throughput data obtained by proteomics, metabolomics, or functional genomics strategies.

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

I. Development of non-invasive or minimally invasive alcohol detection biosensors with sensitivity and specificity appropriate for laboratory research with humans or animals (see also Alcohol Biosensors and Data Analysis Systems).

Laurie Foudin, Ph.D.
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Development and 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.

For clinical questions contact:

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301-443-0636
Email: rlitten@niaaa.nih.gov

For pre-clinical questions, contact:

Laurie Foudin, Ph.D.
301-443-0912
Email: lf29z@nih.gov

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

For additional information on research topics, contact:

Max Q. Guo, Ph.D.
National Institute on Alcohol Abuse and Alcoholism
5635 Fishers Lane

Bethesda, MD 20892
For Federal Express delivery, use:
Rockville, MD 20852-1705
Phone: 301-443-0639
Email: qmguo@mail.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: js182a@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 High-Priority Areas of Interest, please visit http://www.niaid.nih.gov/ncn/sbir/sbirareas.htm.

Limited Amount of Award (Total not Annual)

For budgetary or programmatic reasons, NIAID may decrease the length of an award or the amount of an award recommended by a review committee. 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 II Competing Renewal Awards

The NIAID will accept Phase II SBIR/STTR Competing Renewal SBIR/STTR grant applications to continue the process of developing products that require approval of a Federal regulatory agency (e.g., FDA). Projects that are particularly encouraged include those in the NIAID Small Business High Priority Areas of Interest (http://www.niaid.nih.gov/ncn/sbir/sbirareas.htm) and also:

- therapeutics (drugs or antibodies) to treat HIV infections
- therapeutics (drugs or antibodies) for HIV-related opportunistic infections
- anti-inflammatory therapeutics
- transgenic transplantation strategies
- new or improved vaccines, antiviral or antimicrobial agents for infectious diseases

NIAID will accept Phase II 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. SBIR Phase II Competing Renewal grant applications may exceed this guideline, however, when well justified and when those costs are necessary to support clinical studies or trials 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. NIAID will only support investigator-initiated clinical trials through a two part grant process: (1) a clinical trial planning grant (http://grants.nih.gov/grants/guide/pa-files/PAR-06-384.html) followed by (2) a clinical trial implementation cooperative agreement (http://grants.nih.gov/grants/guide/pa-files/PAR-05-113.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 II 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 2153, 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. Ed Tramont
301-496-0545
Email: et89f@nih.gov

BIOSTATISTICS RESEARCH BRANCH

Stimulate innovative research in statistical methods to advance the study of HIV/AIDS vaccines, therapies and pathogenesis.

Dr: Misrak Gezmu
301-435-3722
Email: mgezmu@niaid.nih.gov

BASIC SCIENCES PROGRAM

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

Director: Dr. Carl Dieffenbach
301-496-9112
Email: cdd@nih.gov

A. ***Epidemiology Branch.*** Population-based research of HIV transmission and associated biological, behavioral, and environmental factors including correlation between immunologic and virologic events and clinical outcome trends in natural history; correlation between immunologic and virologic events and clinical outcome; and trends in natural history.

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.

Contact: Ann Namkung, M.P.H.
301-496-9176
Email: an107z@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 to pilot clinical studies in humans; (4) preclinical discovery and development of topical microbicides and other entities for non-vaccine prevention strategies; and (5) animal models for evaluating new therapeutic entities, regimens, and strategies.

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; 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. Isaac Rodriguez-Chavez
301-496-4738
Email: icrodriguez@niaid.nih.gov

B. ***Preclinical Research and Development Branch.*** Support of applied preclinical development of candidate AIDS vaccines, delivery methods, 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

THERAPEUTICS RESEARCH PROGRAM

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

Director: Dr. Sandra Lehrman
301-496-8210
Email: slehrman@niaid.nih.gov

A. ***Clinical Research Management Branch.*** Management of grants and contracts supporting therapeutic clinical trials.

Chief: Ms. Margaret Matula
301-402-2302
Email: mmatula@niaid.nih.gov

B. ***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 -OI compounds; immunologic, virologic, and pharmacologic research related to the design and conduct of clinical trials.

Contact: Dr. Mike Usserv
301-402-0134
Email: musserv@niaid.nih.gov

C. ***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.

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

D. ***Complications & Co-Infections Research Branch.*** Preclinical and clinical research to develop improved therapies for the treatment and prophylaxis of AIDS-associated opportunistic infections and other complications, including Pneumocystis carinii pneumonia, tuberculosis, Mycobacterium avium disease, hepatitis C, and cryptococcosis. Research on metabolic complications of anti-retroviral therapy, emergence of resistance to existing therapies and drug-drug interactions.

Chief: Dr. Barbara Laughon
301-402-2304
Email: blaughon@niaid.nih.gov

E. ***Pediatric Medicine Branch.*** HIV therapies in children and adolescents, strategies to reduce transmission from mother to infant or fetus.

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

F. ***Prevention Science Branch.*** 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. Basic research on mechanisms of HIV transmission supportive of 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.

Acting Chief: Sheryl Zwerski, MSN, CRNP
301-402-4032
Email: szwerski@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, molecular basis of hypersensitivity, basic studies of asthma and allergy mechanisms, new therapies for asthma and allergic diseases, food allergies, epidemiology and prevention, phagocyte biology, 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, 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: 301-402-2571
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, technologies for MHC typing.

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

Division of Microbiology and Infectious Diseases

The Division of Microbiology and Infectious Diseases (DMID) supports research to control diseases caused by all infectious agents, except HIV, through basic investigation of microbial physiology and antigenic structure, pathogenesis, clinical trials of drugs and vaccines, and epidemiologic studies. 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 research.

Director: Dr. Carole Heilman
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A. ***Bacteriology and Mycology Branch.*** Research areas: (1) Products to address public health needs in medical bacteriology and mycology including early stage development of vaccines/adjuvants (target identification and characterization, device or apparatus development, novel delivery, and preclinical evaluation), therapeutics (drugs and novel antimicrobials interfering with host-pathogen interactions, probiotics, immune modulators with broadly protective or pathogen-specific potential, etc.), and multiplex medical diagnostics; (2) Products to combat antibacterial and antifungal drug resistance; (3) Application of proteomics and genomics technologies; (4) Host-pathogen interactions; (5) Genetics, molecular, and cell biology; and (6) Microbial structure and function. Research focused on the following bacterial diseases is strongly encouraged: anthrax and other zoonotic infections (plague, tularemia, glanders, melioidosis, brucellosis, leptospirosis), Lyme disease, rickettsial and related diseases: ehrlichiosis, anaplasmosis, bartonellosis, typhus, Q fever, tickborne spotted fevers, actinomycete infections, sepsis, enterococcal infections, staphylococcal infections, urinary tract infections, nosocomial and other healthcare-associated infections, and vector-borne bacterial infections. Research in the following areas is of particular interest:

- Vaccines, therapeutics, and medical diagnostics for glanders, melioidosis, typhus and Q fever
- Novel approaches for the diagnosis of Lyme disease

Research focused on the following fungi and fungal diseases is strongly encouraged: aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, Pneumocystis carinii, and other primary and opportunistic fungal infections. The Bacteriology and Mycology Branch does not support applications covering environmental detection and decontamination.

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B. ***Enteric and Hepatic Diseases Branch.*** Special emphasis areas include development of a single diagnostic tool for the simultaneous identification of multiple diarrheal pathogens; pediatric vaccines to prevent the major causes of worldwide diarrhea; more stable vaccines and formulation improvements; vaccines against hepatitis C virus; novel therapeutics for chronic hepatitis B and C; improved therapies and vaccines for botulinum neurotoxins; and therapies and diagnostics for *Clostridium difficile*. Research areas of the Branch include the following organisms and diseases: astrovirus, Bacteroides, Campylobacter, enteric Clostridia including botulinum neurotoxin, commensals, Crohn's Disease, diarrhea, enterotoxins, enteric *Escherichia coli*, gastroduodenal disease, gastroenteritis, Guillain-Barré, Helicobacter, Listeria, normal flora, Noroviruses including Norwalk, ricin toxin, rotaviruses, Salmonella, Shigella, Staphylococcus, toxins, ulcers, Vibrio, enteric Yersinia, and hepatitis viruses A, B, C, D, and E. Studies encompass: (1) basic virology and bacteriology, genome sequencing, natural history and pathogenesis; (2) immunology of infectious diseases including mechanisms of recovery and persistence, protective immune responses and immunopathogenesis in humans and in animal models; (3) vaccine research and development including novel approaches and delivery systems to prevent infection as well as to control and treat disease; (4) development and evaluation of adjuvants and vaccine vectors; (5) identification of new therapeutic targets and development and evaluation of therapeutics; (6) immunotherapy discovery and development; (7) epidemiology, ecology, zoonoses, and transmission; (8) antimicrobial resistance of these organisms in non-nosocomial settings; (9) development of tools for rapid medical diagnosis of organisms, specific targets, disease, and markers of disease outcome; (10) development of model systems to study infection and disease and evaluate vaccines and drugs; and (11) characterization and exploitation of the role of normal flora in disease preventive therapy.

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C. ***Parasitology and International Programs Branch.*** Research areas: (1) protozoal infections, including amebiasis, cryptosporidiosis, cyclosporiasis, giardiasis, leishmaniasis, malaria, trypanosomiasis, toxoplasmosis; helminth infections, including cysticercosis, lymphatic filariasis, schistosomiasis, onchocerciasis, others (e.g., roundworms, tapeworms, and flukes); Invertebrate vectors/ectoparasites, blackflies, mosquitoes, ticks, snails, mites; (2) parasite biology (genetics, genomics, physiology, 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 control; mechanisms of pathogen transmission.

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D. ***Respiratory Diseases Branch.*** Research areas: (1) viral respiratory diseases, including those caused by: human coronaviruses (including SARS), orthomyxoviruses (including influenza A, B and C), and paramyxoviruses (including parainfluenza viruses and respiratory syncytial virus); (2) bacterial respiratory diseases, 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 and Klebsiella pneumoniae; (3) Otitis media; (4) mycobacterial diseases, including those caused by: M. tuberculosis (tuberculosis), multi-drug resistant M. tuberculosis, M. leprae (leprosy),

and M. ulcerans and other non-tuberculous mycobacterial diseases. Areas of emphasis include: development of vaccines and therapeutic agents for treating and preventing the respiratory diseases described above, including influenza vaccines with improved effectiveness in the elderly and other high risk populations; maternal immunization strategies; and development of better and more rapid multi-plex point-of-care diagnostic tests or other screening tools that can detect infection prior to active disease.

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E. ***Sexually Transmitted Infections Branch.*** Development of medical diagnostics, drugs, topical microbicides, and vaccines for sexually transmitted infections (STIs) and other reproductive tract syndromes, such as bacterial vaginosis; molecular immunology; vaginal ecology and immunology; epidemiologic and behavioral research; 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.

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F. ***Virology Branch.*** Acute viral infections and zoonoses, dengue and other arthropod-borne viral diseases (mosquito-borne encephalitis, including West Nile, yellow fever, etc.), hantaviruses, hemorrhagic fevers (Ebola, Lassa, South African hemorrhagic fevers, etc.), measles, polio, coxsackie virus, and other enteroviruses, poxviruses, rabies, rubella; persisting viral diseases and viruses: adenoviruses, bornaviruses, coronaviruses, herpesviruses, parvoviruses, prion diseases; emergence of viral disease; mechanisms of replication, permissiveness, persistence, and latency; vaccines; immune protection and evasion and viral vectors; epidemiology and viral evolution; structure and function of viruses and viral proteins; molecularly targeted approaches to identify and characterize antiviral targets and agents; chemical design and synthesis of novel antiviral agents; in vitro screening and evaluation of antiviral activity; preclinical therapeutic and some prophylactic evaluations of human viral infections in animal models; clinical trials of vaccines and therapies for viral infections; research of civilian defenses for potential bioterrorist use of viruses; and development of rapid medical diagnostic systems. The Virology Branch does not support applications covering environmental detection and decontamination.

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

The NIAMS supports research in arthritis and musculoskeletal and skin diseases. Such research is directed at basic understanding of the causes and development of rheumatic diseases, connective tissue diseases, musculoskeletal and skin disorders and diseases. Basic investigations involve immunology; purine metabolism; skeletal muscle structure, function, metabolism and physiology; the structure, function, production, biochemistry and physiology of collagen, elastin, and other proteins of connective tissue; metabolic and hormonal changes in bone; prevention and treatment strategies for osteoporosis and related bone diseases, structural and biochemical changes in osteoarthritic cartilage and cartilage repair; novel imaging modalities for bone, cartilage, and connective tissues; new treatments for fractures and other musculoskeletal

tissues including tissue engineering and gene therapy; orthopaedic implant science (materials, design, wear, osteointegration); bioimaging of musculoskeletal tissues; computer-assisted orthopaedic surgery and other computer-assisted musculoskeletal bioimaging and treatment interventions; the biomechanics of normal, arthritic and prosthetic joints; the structure, function, barrier properties, metabolism, and physiology of the skin. Exercise research related to musculoskeletal function, including the development of tools or behavior modification programs to enhance exercise in normal individuals or those with chronic diseases, and related behavioral and prevention research.

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

Arthritis and Musculoskeletal and Skin Diseases

A. ***Rheumatic Diseases Branch.*** Supports basic and clinical research in the normal function and components of connective tissue and the immune system and their dysregulation in rheumatic, genetic, and inherited diseases of connective tissue. The goals are increased understanding of the etiology and pathogenetic mechanisms involved in rheumatic and degenerative disease of the joints and in the translation of these basic research findings to prevention, diagnosis, and treatment of disease. The research supported by the Program utilizes approaches emanating from relevant areas of genetics, biochemistry, cellular and molecular biology, biophysics, enzymology, immunology, pathology, physiology, behavioral medicine, and epidemiology.

   A description of other areas of research under investigation may be found at http://www.niams.nih.gov/rtac/funding/grants/ep3.htm.

B. ***Musculoskeletal Diseases Branch.*** Supports studies of the skeleton and associated connective tissues. Research areas supported through the Musculoskeletal Diseases Branch include bone diseases, bone biology, and orthopaedic research. Broad areas of interest include skeletal development, metabolism, mechanical properties, and responses to injury. Osteoporosis, a disease afflicting many of the Nation's growing population of older people, is particularly emphasized for investigation under this program. Among other diseases and skeletal disorders under investigation are osteogenesis imperfecta, a genetic disorder that leads to fragile, easily fractured bones; Paget's disease of bone, which results in irregular bone formation and subsequent deformity; genetic disorders of bone growth and development, such as osteopetrosis and the osteochondrodysplasias; vitamin D refractory diseases; and rickets and osteomalacia. Other studies focus on the causes and treatment of acute and chronic injuries, including carpal tunnel syndrome, repetitive stress injury, low back pain and clinical and epidemiological studies of osteoarthritis. The Program supports development of new technologies with the potential to improve treatment of skeletal disorders and facilitate the repair of trauma in the normal skeleton. These include drugs and nutritional interventions, joint replacement, bone and cartilage transplantation, and gene therapy. In addition, bioengineering, sports medicine and musculoskeletal fitness are areas of special research emphasis.

   A description of other areas of research under investigation may be found at http://www.niams.nih.gov/rtac/funding/grants/ep5.htm.

C. ***Skin Diseases Branch.*** Supports basic and clinical studies of the skin in normal and disease states. The wide range of skin diseases under study with NIAMS support includes 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.

   A description of other areas of research under investigation may be found at: http://www.niams.nih.gov/rtac/funding/grants/ep3.htm.

   1. Determinations of drug effects.
   2. Determinations of effects of other therapies, including occupational and physical therapy modalities, spinal manipulation, bracing, transcutaneous nerve stimulation, acupuncture, and topical agents (e.g., capasicin).
   3. Preventive strategies.
   4. Development and validation of animal models for rheumatic, musculoskeletal (especially for herniated intervertebral disc

and spinal stenosis), muscle and skin diseases.

5. Improvement and refinement of immunogenetic determinants of rheumatic diseases.
6. Development of novel and improved diagnostic methods and treatments for muscle, tendon, ligament, bone, and joint injuries, including overuse and repetitive motion disorders.
7. Devices and activities designed to prevent muscle, tendon, ligament, and joint injuries, including overuse and repetitive motion disorders.
8. Assessment techniques for musculoskeletal and skin diseases.
9. Functional and metabolic measures of the musculoskeletal system in normal, diseased and active states.
10. Development of novel implant designs, materials and surface coatings for musculoskeletal implants. Development of assessment strategies to detect implant failure, loosening, and osteolysis, and the development of novel technologies to prevent them.
11. Computer modeling, relevance to the musculoskeletal system.
12. Improved topical treatments of skin diseases and disorders.
13. Devices and computer programs for diagnosis or assessment of skin diseases.
14. Tissue culture models for skin diseases.
15. Artificial skin.
16. Photoprotective agents.
17. Improved treatment for bone diseases.
18. Measurement techniques for bone diseases.
19. Preventive measures for fractures.
20. Delivery systems for dietary supplements.
21. Novel delivery systems for therapeutic agents.
22. Development of novel or improved technologies for bone healing and repair. This includes, but is not limited to, the development of osteoinductive, osteoconductive, or a combination, technologies to facilitate bone healing/repair, and the development of improved or novel approaches to the use of autogenous, allograft, and bone graft substitutes.
23. Development of novel or improved technologies to facilitate the repair of articular cartilage, including, but not limited to cartilage cell transplantation, use of stem cells, biodegradable scaffolds, growth factors, and refinements of currently existing technologies.
24. Development of novel technologies to improve the diagnosis, prevention, and treatment of acute and chronic low back pain.
25. Development of novel assessment technologies for identifying biomechanical inputs on bone and cartilage tissue at the cellular level, and identification of the corresponding physiological response.
26. Development of novel technologies leading to the use of gene therapy for selected musculoskeletal diseases and injuries.
27. Development of novel, non-invasive technologies to assess joint tissues, including articular cartilage and subchondral bone.

Markers of Osteoarthritis

The NIAMS seeks applications for the development and validation of standardized, sensitive assays for osteoarthritis markers in body fluids or tissue specimens. Osteoarthritis is the most prevalent musculoskeletal disorder, characterized by joint pain, tenderness, and functional disability. The percentage of Americans over 65 years of age is the fastest growing segment of the population, which is expected to reach 68 million people by the year 2010. A biochemical test for osteoarthritis would be particularly useful for early detection, assessment of disease severity and progression, and to monitor the effects of therapies.

Advances in the molecular biology, biochemistry, and metabolism of cartilage have stimulated the quest for appropriate markers of degradative and regenerative processes in osteoarthritis. Important new studies indicate that molecular fragments of cartilage-derived matrix molecules are present in the blood and joint fluid in osteoarthritis that have the

potential to represent disease-specific markers. The increased rates of cartilage degeneration increase the concentration of matrix components in tissue and body fluids, thus reflecting changes in the rates of cartilage catabolism. Further, cartilage degeneration in osteoarthritis changes the type or structure of the molecules being synthesized by the chondrocytes. Thus, the presence of these neo-epitopes may be a marker of degenerative events within the tissue. Markers of metabolic changes in subchondral bone or other joint tissues in osteoarthritis are also be of potential interest.

The NIAMS is soliciting applications to test the potential application of a marker for osteoarthritis diagnosis, prognosis or severity and the standardization of a clinically relevant test. Successful applicants will provide a rational approach for the development of a practical and reliable assay for osteoarthritis disease marker(s) and determination of the sensitivity and specificity of the marker(s) in patient populations. The applications must include the rationale for the selection of the marker to be employed in the study. If a battery of markers will be utilized the basis of this approach must be clear and well justified. The assay systems as well as the methods of sample collection, storage, and handling must be clearly delineated. Marker levels must be validated against other methods of monitoring osteoarthritis, such as imaging techniques. The expected outcome of these studies is an osteoarthritis test that can be used in larger scale human trials.

Muscle Biology, Exercise Physiology and Sports Medicine

A. ***Muscle Biology Branch.*** Supports research on skeletal muscle, its diseases and disorders, and its central role in human physiology and exercise. Topics include the molecular structure of muscle and the molecular mechanisms that produce force and motion. An aim is understanding the alterations in muscle resulting from increased exercise regimens and, conversely, the atrophy that follows immobilization during injury or illness. Some of the specific areas of research covered by the Muscle Biology Branch include Muscle Physiology, Molecular Architecture, Muscle Membranes, Muscle Development and Specialization, Musculoskeletal Fitness and Adaptive Biology, Muscle Diseases, and Sports Medicine, Muscle Injury and Muscle Repair. Areas that may be of interest to small businesses include but are not limited to:

1. Muscle Structure and Function.

   Research on the application of biochemistry, molecular, and cell biology to muscle biology, including studies of membrane structure, function, and biosynthesis, lipid metabolism, membrane models, membrane transport, sub-cellular organization, organelles, cytoskeletal components, and cell division. Development of new instruments and methods to facilitate studies on muscle function and physiology. Specific examples might include, but are not limited to, the following:

   a. Development of methods and materials directed toward the solution of muscle cytoskeletal and membrane protein structures by x-ray diffraction, electron diffraction, and NMR spectroscopy.

   b. New methods for the purification and reconstitution of muscle membrane proteins.

   c. Development of monoclonal and/or recombinant antibodies to cytoskeletal and membrane proteins exhibiting high specificity and affinity and broad cross-species reactivity.

2. Muscle Fitness and Sports Medicine.

   a. Improve measurement of muscle strength and balance, including refined instrumentation for biomechanical assessment of normal movement and posture.

   b. Develop quantitative methods of assessing postural perturbations and forces relevant to activities of daily living.

   c. Improve imaging and analytical techniques to measure skeletal muscle properties, (e.g., through MRI Imaging and Spectroscopy).

   d. Imaging techniques which allow simultaneous imaging of muscle morphology and metabolism and blood flow.

   e. Development of novel assays or modifications of currently existing assay of muscle metabolism for use with human biopsy samples.

f. Develop biosensors to detect changes in pressure, temperature, or physiological parameters associated with muscular activity.

g. Development of treatments for wound healing and improve general understanding of the natural healing process for muscle.

h. Develop antioxidant interventions to prevent oxidative damage during muscle use and overuse.

i. Develop cell culture models for rapid testing of treatments for muscle injury and wasting.

3. Development and Genetic Diseases.

a. Develop animal models that mimic the pathophysiology of the genetic human muscle diseases.

b. Develop gene vectors (viral and non - viral), promoter and enhancer elements and related methodologies that could be used for in vivo and ex vivo gene therapy for muscular diseases.

c. Develop cell lines and tissue cultures for replacement of muscle that has been damaged or destroyed.

d. Develop markers for muscle satellite cells and use them to characterize availability for muscle repair.

e. Develop techniques, equipment, and software to enable improved imaging of muscle development and specialization.

A description of other areas of research under investigation may be found at: http://www.niams.nih.gov/rtac/funding/grants/ep5.htm.

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

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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.

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

Areas of high programmatic interest include:

- intelligent systems design and smart modeling
- enabling nanotechnologies for designed drug and gene delivery vehicles
- in vivo optical imaging
- activatable imaging agents
- multiscale modeling in biomedical systems
- sensor and lab-on-a-chip devices for point-of-care testing
- imaging informatics
- development of engineered 3D human tissue model systems for drug discovery and development
- image-guided interventions
- *in vivo* microimaging of internal organs
- techniques for characterization and modification of biomaterial interfacial properties
- high-field and high speed (parallel) MRI
- high-frequency and very high-frequency ultrasound imaging and other applications
- novel sensing technologies
- enabling technologies for tissue engineering and regenerative medicine
- high-intensity focused ultrasound (HIFU) therapies or interventions
- computational analysis and simulation methods

For additional information on research topics, contact:

Mr. Todd Merchak
National Institute of Biomedical Imaging and Bioengineering
301-496-8592, Fax: 301-480-1614
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NATIONAL CANCER INSTITUTE (NCI)

In its attempt to eliminate suffering and death due to cancer by 2015, the National Cancer Institute promotes research that crosses the discovery, development, and delivery continuum and that addresses barriers to progress, forging partnerships, opening access to datasets and tissue resources, and more fully utilizing emerging technologies in genomics, proteomics, communications, and delivery of clinical and public health interventions. To achieve these goals, NCI seizes extraordinary scientific opportunities and creates and sustains funding mechanisms that support translational research.

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 homepage: http://www.cancer.gov/ and http://otir.nci.nih.gov/smallbusiness/small_sbir.html .

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.nci.nih.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.

For additional information, please email our SBIR/STTR Program Director at Taylorem@mail.nih.gov.

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 and applied 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; serves as the focal point for the Federal Government on the synthesis of clinical, epidemiological and experimental data concerning biological agents relating to cancer; and maintains the necessary scientific management capability to foster and guide an effective research program. 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 in this solicitation 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.

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 transformatioin, 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 in this solicitation 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 in this solicitation 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 in this solicitation 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 in this solicitation 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 in this solicitation 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 updated 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.
  - Development of consumer friendly software which creates 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 studies, including those focused on rare cancers.
  - 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.

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

B. ***Multimedia Technology and Health Communication in Cancer Control.*** The NCI promotes communication about and dissemination of information about cancer. Toward these efforts, the Behavioral Research Program (BRP) uses its SBIR/STTR Multimedia Technology Health Communication Program to fund translational research using a variety of multimedia.

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. This list replaces previously listed research categories. This site also provides important program requirements and SBIR information.

For questions, contact the Program Director at cd34b@nih.gov.

Division of Cancer Treatment and Diagnosis

The Division of Cancer Treatment and Diagnosis (DCTD) 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 Diagnostic Biomarkers and Technology 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 that are likely to control, retard or kill cancer 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.
    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, 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.

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. Specifically:

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 that would be responsive to this solicitation include:

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-ongogene 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, and infectious agent, 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://dcp.nci.nih.gov/.

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 animals 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:

   a) In vivo animal models, including transgenics and knockouts, to examine the cancer prevention effects of essential and non-essential nutrients.

   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-immunity interactions.

   e) New models/approaches for examining diet and angiogenesis interactions.

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

   g) New and improved diagnostic markers for nutritional status.

   h) New methods to detect and identify anticarcinogenic nutrients in foods.

   i) New methods for the isolation and preparation or synthesis of candidate nutrients in quantities suitable for preclinical and clinical screening.

   j) Valid, more facile and effective methods for assessing the content of bioactive food components in foods and dietary supplements.

   k) Transgenic/knockout food models for testing the physiological significance of bioactive food components within the food matrix.

   l) Combinations or blends of bioactive food components for cancer prevention, including the importance of the food matrix.

   m) Bioinformatics tools for the study of bioactive food components as regulators and modulators of genes associated with cancer prevention.

   n) New bioengineering tools for the study of bioenergetics and obesity.

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

   p) New methods 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

For additional information on research topics, contact:

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

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 II Competing Renewal Awards

(See http://grants.nih.gov/grants/guide/pa-files/PA-06-029.html STTR and http://grants.nih.gov/grants/guide/pa-files/PA-06-030.html SBIR.)

NICHD will accept Phase II 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. 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 either NICHD SBIR/STTR Phase I or Phase II support and who are currently Phase II awardees are eligible.

You are strongly encouraged to contact Dr. Louis Quatrano (contact information provided below) before beginning the process of putting a Phase II 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-07-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 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:

1. Development of reagents to facilitate study of reproductive and developmental processes.
2. Development of improved methods of growing and differentiating stem cell lines in vitro, including feeder cell-free approaches.
3. Development of novel assays, kits, and devices to monitor fertility and treat infertility and gynecological disorders.

4. Use of genomics and proteomics to develop novel diagnostics and treatments for reproductive diseases and disorders.
5. Development of high resolution technologies to provide invasive or noninvasive assessments of reproductive and developmental competence.
6. Development of experimental animal models that would be useful for studying the physiology and pathophysiology of reproductive processes.
7. Development of improved and novel technologies for the preservation of human gametes.
8. Development of improved technologies for preimplantation genetic diagnosis.
9. Development of improved technologies for the reprogramming of cells, including embryonic stem cells or adult cells, into eggs and sperm.

Dr. Richard J. Tasca
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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:

1. 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.
2. 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.
3. 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.
4. 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.

Dr. Steven Kaufman
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Email: sck@nih.gov

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 teenage childbearing, AIDS, single-parent families, racial and ethnic differentials in infant mortality, legal and undocumented immigration, and the well-being of children. Applications are encouraged in these areas:

1. Technological innovations/inventions to help collect biomarker data, such as wearable technology for large surveys.
2. 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.
3. Innovative use/implementation in integrating geographical information systems, spatial network analysis, and/or

simulation methods for demographic research.

4. Innovative approaches to analyzing and disseminating large-scale data sets.
5. Development of effective tools for prevention research and intervention programs related to STD/HIV, pregnancy, divorce, child health, and other mission-related topics.
6. Innovative approaches to teaching population studies and other behavioral and social sciences at the undergraduate and graduate level.
7. 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.

- Reading, Writing, and Related Learning Disabilities: relative contributions of environmental, experiential, instructional, cognitive, linguistic, genetic, and neurobiological contributions 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.

- 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.

- 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.

Dr. Peggy McCardle
301-435-6863, Fax: 301-480-7773
Email: pm43q@nih.gov

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.

Dr. Gilman D. Grave
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Email: gg37v@nih.gov

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

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 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.
- 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.

Dr. Kevin Ryan
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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.*** Research on 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.

Dr. Tonse Raju
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B. ***Development Biology, Genetics, and Teratology.*** Biomedical research on the cellular, molecular, and genetic aspects of normal and aberrant embryonic and fetal development and including early embryogenesis, limb formation, development of the nervous system, developmental and reproductive immunology, and causative factors in teratogenesis. Applications to develop and apply new animal model systems or innovative and high throughput genomic and proteomic technologies to advance the study of embryonic development, structural birth defects, and newborn screening are particularly welcome.

Dr. Lorette Javois
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C. ***Mental Retardation and Developmental Disabilities.*** Biomedical 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 social, economic and cultural influences on the occurrence of mental retardation and developmental disabilities (MRDD); and research leading to the assessment, prevention, and amelioration of MRDD, including screening and prenatal diagnosis.

Dr. Mary Lou Oster-Granite
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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:

A. Enabling technologies for restoration of function.

B. Promoting behavioral adaptation to functional losses.

C. Assessing the efficacy and outcomes of medical rehabilitation therapies and practices.

D. Developing improved assistive technology.

E. Promoting rehabilitative outcomes in pediatric critical care.

F. Understanding whole body system responses to physical impairments and functional changes.

G. Developing more precise methods to measure impairments, disabilities, and societal limitations.

H. Training health professionals in the field of medical rehabilitation.

I. Development of Home Centered Rehabilitation care systems.

J. Promoting profession structured/directed self care and wellness.

K. Development of tools to assist and facilitate families in their involvement in rehabilitation.

Investigators proposing budgets exceeding the guidelines should contact program six weeks prior to submitting the application. Study section approval of projects exceeding the guidelines may not be supported at the level requested.

For additional information on research topics, contact:

Nancy Shinowara, Ph.D.
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or

Dr. Louis A. Quatrano
301-402-4221, Fax: 301-402-0832
Email: lq2n@nih.gov

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

For additional information on research topics, contact:

Louis A. Quatrano, Ph.D.
National Institute of Child Health and Human Development
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For administrative and business management questions, contact:

Mr. Bryan Clark
Grants Management Branch
National Institute of Child Health and Human Development
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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 II Competing Renewal Awards

(See http://grants.nih.gov/grants/guide/pa-files/PA-06-036.html.)

NIDA will accept competing renewal Phase II SBIR/STTR 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.

Please contact Dr. Cathrine Sasek (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 type 2 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-07-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 NIDA SBIR/STTR Phase II

awards will be eligible for a competing renewal grant.

The following examples would make appropriate topics for proposed SBIR or STTR Phase II 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 systems. 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. *Real-Time EMA Data Collection.* Paper and electronic diaries have long been used as tools to record events, environment, mood and experiences. Recent technological advancements have made it possible to use a PDA-like device to record Ecological Momentary Assessments (EMAs). These devices are carried by the subject, and prompt the completion of a series of questions throughout the day. They also provide a time/date stamp. Additionally, questions can be tailored to the time of day, such that they can be morning, afternoon and/or evening relevant (e.g., drug craving upon awakening).

   Although PDA devices that are used to collect EMAs have great potential as research and therapeutic tools, they are limited to manual data downloads. NIDA is looking for proposals that develop a PDA-like device that performs EMA data collection, and then has a "real-time", automatic download capability, such that researchers are able to track performance during the day. This may also include the pairing with physiological sensors that integrate into the real-time data collection platform. The goal of this solicitation is to stimulate the creation and evaluation (including feasibility, reliability, and validity) of such technology.

Phase 1 will be for technology development, and Phase 2 will be for application trials (e.g., human studies).

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2. *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 proposals 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 proposal should demonstrate the feasibility of developing new metabolomics technology and phase II should focus on the application of this technology in drug abuse research.

Hari H. Singh, Ph.D.
301-443-1887
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3. *Development of Alternate Drug Delivery Dosage Forms for Drugs Abuse Studies.* The SBIR proposals are being 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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4. *Discovery of New Chemical Probes.* The SBIR proposal are being 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, mecamylamine, SNC 80, NCS-382, U50,488H, DALDA, DSLET, Dynorphins, DALCE, Orphanin FQ, Kaffiralin 1 and 2, etc. All probes for cannabinoids, neuropeptides, nicotinic acetylcholinergic receptors and related probes for drug abuse study are encouraged. In addition proposals 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.

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5. *Discovery and Study of Psychoactive Components of Botanicals.* NIDA is looking for proposals 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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6. *Virtual Reality for Treatment of Pain.* Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) exposure can reduce reported pain during wound care. Grant proposals 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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7. *Virtual Reality for the Treatment of Drug Abuse.* Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that 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 proposals 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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8. *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 proposal 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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9. *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.

Proposals 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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10. *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 could 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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11. *Genetic Studies.* The National Institute on Drug Abuse is interested in SBIR proposals 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. Design, development, and marketing of behavioral apparatuses to conduct rapid behavioral 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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12. *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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13. *Research Resources.* The National Institute on Drug Abuse is interested in SBIR proposals 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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14. *Predisposition to Cardiovascular Complications Associated with Abused Substance(s).* The National Institute on Drug Abuse is interested in SBIR proposal that are designed to develop experimental animal models that can assess a genetic predisposition or increased sensitivity to cardiac and vascular complications associated with abuse of illicit drugs. Areas of interest include, but are not limited to, investigations involved with biochemical, physiological and pathological indices of cardiovascular system function.

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15. *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, study, and treatment 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. Marketing evidence-based prevention interventions for substance abuse and related HIV prevention.
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.

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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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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 on going 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 polices 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

Specific projects could include:

1. *Development of Innovative Techniques/Tools for the Screening, Recruitment, and Follow-up of Participants in Drug Abuse Trials.* Screening and recruitment of participants for multi-center clinical trials pose a number of problems. Tracking devices/programs are needed to document and manage a patient's interaction throughout a clinical trial. This would include screening tools, recruitment strategies that could be followed, and steps to increase and document follow-up practices. Validated materials/tools applicable to diverse populations for use in education and counseling of potential participants are needed. These tools would be applicable across trials and would provide a strategy for management to improve clinical trial performance. These recruitment concerns are particularly relevant for community practices, which often do not have the resources of larger hospitals or academic institutions. Both the participants and the research clinicians administering the trial would benefit from this product. Approaches are needed to develop innovative techniques and/or tools for the screening, recruitment and follow-up of clinical trial participants in drug abuse trials. These tools or techniques can be from the standpoint of clinicians who are running the clinical trials, to patients who are participants in the drug abuse trials. Tools can include software for following up on participants, reminder tools for clinical trial participants, technological devices for clinician or patient use. The ultimate goal is to make the trial management more efficient and effective.

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2. *Development of Practical Training Materials for Evidence-Based Treatment.* States have initiated the requirement that community treatment programs provide evidence-based treatment or risk losing their public funding if they don't comply. The onus is on the publicly funded program to provide their staff with training in evidence-based treatment modalities. Current staff training opportunities in evidence-based treatments are expensive and frequently require repetition because of high rates of staff turnover. The level of staff training and education varies across agencies. Certification in evidence-based treatment has not been standardized. Externally presented training is not timely or efficient. Computers with Internet capabilities are not always available for staff learning opportunities. It is important to offer alternatives to the delivery of training that are easy for staff to access and that meet requirements to provide evidence-based treatment. There is a need for practical, non-computer and interactive, self-administered computer versions for training counseling staff in evidence-based drug abuse treatments. Such programs should include competency testing to meet local and state requirements for certification, such as, motivational incentives, motivational interviewing, cognitive-behavior therapy, and other proved therapies.

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3. *Innovative Diagnostic Drug Screening Tests for Drug of Abuse.* Drug screening and the detection of drug use/abuse prior to and during treatment episodes are an important factor in defining treatment progress and outcome. Rapid results from the tests are important in addressing a patient's behavior in a clinically effective manner. The time and personnel resources required to perform this function are costly and cumbersome. Current urine tests often require visual corroboration from a staff member of the same gender as the participant in order to ensure that the urine samples are legitimate. This takes staff time away from other duties and requires a separate facility for patients to give urine samples. Clinics have to schedule enough male and female employees to observe these tests. Effective and cost-efficient approaches to testing using oral swabs, patches, and/or other methods would be welcomed by the treatment clinics. To date the newer technologies are not cost effective for most programs. Additionally, immediate or less than 24-hour results are not available as is true with most urine screens. Innovative and inexpensive technologies and/or products are needed that provide for on-site, rapid drug screening, are minimally invasive for the patient, and are gender neutral for the program staff.

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4. *Automation of the Development of Electronic Data Capture (EDC) System for Clinical Trials Data Collection and Management.* Information is captured in clinical trials by using either electronic or paper Case Report Forms (CRFs), which consist of multiple pages and sections. Each section is referred to as an individual CRF. It is not unusual for a trial protocol to require 20 CRFs. Based on the individual CRFs, the Electronic Data Capture (EDC) system is developed for users to collect data elements for data management and data analysis. Each CRF has a data dictionary, which specifies the characteristics of each data element, such as data name, data type, length, valid response, logic checks, etc. Currently, the time required for a programmer to develop an EDC system is around two to three days per CRF. Therefore, it would take more than two months to program the EDC for the average trial. A more automated system, which can read the information specified in the data dictionary and create the corresponding EDC system minutes for one CRF, would be of great use. Such an EDC system should run within the UNIX and Microsoft Windows environments, and the database should be compliant with CDISC (Clinical Data Interchange Standards Consortium) standards.

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5. *Development of Drug Use Patch.* It is difficult to accurately track a patient's drug use when they are outpatients in a program or study. Relying on a weekly or monthly urine test is not always reliable. History indicates that patients are more likely to abstain from illegal drug use when their behavior is observed. This initiative

is for the development of a cost effective and tamper proof patch to detect drug use that can be worn by patients. The patch should be one that can be worn for 1-2 weeks. After it is applied and worn for a length of time, the patient would come into the clinic, and the patch would be and analyzed for drug use. The patch should be contain chemical profiles for at least 4 major categories of illicit drugs and be easily worn for up to a month and non-irritating to the skin.

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6. *Internet Based Program for Patient Referral.* Electronic health information is widely used by patients and families to seek treatment options. For drug abuse, development and testing of an internet-based program for individuals to assess their own levels of drug use/misuse/addiction using up-to-date measurement tools would be useful. The program should then provide contact and descriptive information of treatment options appropriate for the individual's level of abuse and provide contact and descriptive information for treatment settings available in the individual's specific location. The system should incorporate and integrate modern healthcare informatics technology into conventional evidence based behavior prevention/intervention medicine.

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7. *Development of eHealth Tools.* eHealth, the healthcare practice supported by electronic processes and communication, offers the potential to increase quality, enhance reach, lower cost, resolve time/distance concerns, and customize patient care. Information technology can be implemented to support a broad of applications. We are looking for unique, state-of-the-art eHealth tools that can promote the following applications:

   - **Health Information** — includes the development of electronic medical records, data mining of a variety of health care databases, etc.

   - **Telemedicine** — includes the online communications via Internet for efficient interaction among consumers, patients, and providers about health concerns and treatments.

   - **Clinical Trials Management** — includes the development of systems to promote and manage the clinical trials life cycle, such as the integrated clinical trials information management systems, systems for more effective and efficient recruitment, workflow management to streamline the processes, etc.

   - **Behavior Change/Prevention** — includes products that can support a specific behavior change in clinical trials.

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8. *Development of Instruments To Assess Co-morbidities.* Drug and alcohol treatment centers lack a brief assessment instrument to screen their patients for mental health disorders. There are diagnostic instruments available; however, they require specialized training and can be time consuming to administer. For this reason and others, co-morbid conditions such as depression, ADHD or PTSD often go undiagnosed and untreated in this population. If clinicians had a proper instrument to screen these patients, they could then refer them for further evaluation. This initiative is for the development and validation of an instrument to be used in community practices to screen for mental health disorders when patients present themselves for drug and/or alcohol treatment. The instrument should be easy to use either by the clinician (as an interview) or by the patient (as a self assessment) and could be either in paper format or computerized.

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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).*** 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*:

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.

   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.

2. 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.

3. Development of new immunotherapeutic treatments that would have the potential as treatment agents for stimulant, opioid or cannabinoid abuse.

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4. Development of new approaches for the administration of potential addiction treatment drugs with poor bioavailability.

5. 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.

6. Development of novel dosage forms or chemical/pharmaceutical approaches that eliminate or significantly reduce the abuse potential of prescription drugs/drug products.

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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).*** The MRGB supports investigations of the use of therapeutic agents (including

vaccines and monoclonal antibodies) for the treatment of substance related disorders, with the aim of assisting in reducing drug use, becoming drug free, prolonging abstinence, decreasing associated psychosocial, medical or legal problems, or surviving drug overdose. In general, therapeutic agents are expected to be investigated using a platform of appropriate psychosocial interventions. The program funds extramural grants in the following areas:

- Clinical trials to test the safety, find the optimal dose, and/or obtain preliminary efficacy data for new agents or new indications of marketed medications. This phase includes interaction studies to test the safety of the agent when used in combination with drugs of abuse.

- Clinical trials to assess the efficacy of new agents or marketed medications for the treatment of substance related disorders. In general, these types of trials use a randomized double blind placebo controlled design.

- Clinical studies of the efficacy of medications for the treatment of the comorbidity of substance related disorders (e.g., alcohol and cocaine dependence) or the comorbidity of these disorders with other medical or psychiatric conditions.

- Clinical evaluation of the efficacy of medications for the treatment of substance related disorders in specific groups of the population. For example, adolescents, the elderly, women of childbearing age, pregnant and/or postpartum women, as well as racial and ethnic minorities.

- Evaluation of biological and/or psychosocial factors that may affect the outcome of the pharmacotherapy of substance related disorders.

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

1. *Pharmacogenetics and Substance Use Disorders.* The emergence of new genetic techniques may allow the use of genetic information to improve the safety and efficacy of treatments. The field of pharmacogenetics focuses on the genetic determinants of response to medications and other therapies in humans and animals. The goal is to discover novel single nucleotide polymorphisms (SNPs) and test their relevance to the underlying genetic differences that determine the safety and efficacy of medications for the treatment of SUD. It includes the study of genes encoding drug metabolizing enzymes, transporters, receptors and other drug targets, polygenic determinants of drug disposition and effects in humans, the role of genes in the clinical response to and medical safety of medications, and application of genetic information to disease prevention and to optimize treatments in humans. It also includes novel methods for phenotyping the diagnosis, safety and treatment outcome of SUD. Ultimately, it is expected that pharmacogenetics research will help clinicians to individualize the treatment of their patients based on their genetic information. Research is needed to study the genetic factors that may be associated with drug abuse treatment safety and outcome.

2. *Medications Development for the Treatment of Drug Abuse in Adolescents.* Drug abuse among adolescents is a significant and growing public health concern. It is known that the pharmacokinetics and pharmacodynamics of some medications are different in adolescents. Therefore, adolescents may present overdoses, underdoses or lack of efficacy, or different safety profiles when administered medications at the doses studied only in adults. Unfortunately, little is known about the safety and efficacy of medications for the treatment of drug abusing adolescents because most of the drug abuse medication research has focused on adults. Research is needed to test medications for the treatment of nicotine and drug abuse in adolescents.

3. *Medications for the Treatment of Comorbid Medical or Mental Disorders and Drug Abuse.* Co-morbid medical and psychiatric conditions are frequently found among substance abusing patients. Co-occurring mental disorders, such as depression, post-traumatic stress disorder, and anxiety disorder, and medical conditions such as hepatitis C, AIDS related disorders, and pain, are common among substance

abusing patients. Unfortunately, there are presently no commonly prescribed safe and effective medications for the treatment of substance abusing patients with other co-morbid medical and psychiatric conditions. Research is needed to study the safety and therapeutic profiles of medications for treatment of substance abuse in patients with other comorbidities. There is also a need to study the effects of medications for the treatment of substance use disorders in patients taking medications for other comorbid conditions and the necessary dose adjustments.

4. *Development of Software for Data Management of Medical Safety Data from Clinical Trials.* Recent policies for the protection of human subjects participating in clinical trials are requiring increasing levels of medical safety monitoring. Currently, adverse event and serious adverse event data management (collection, storing, analysis, and reporting) is heterogeneous. Different investigators use different nomenclatures, definitions, timeframes, data collection instruments, and data analysis and reporting methods. This heterogeneous and often inadequate data system limits the interpretation of safety results and the ability to make sound decisions about the safety (and often the efficacy) of clinical trials. In some instances, external reviewers may misinterpret the reported signs or symptoms and may provide wrong recommendations. Furthermore, inadequate safety data does not allow comparing the adverse events and serious adverse events results across multiple clinical trials, which hinders the scientific progress, and increases costs. The purpose of this initiative is to stimulate research on innovative medical safety data management tools for clinical trials testing interventions for drug addiction, while guaranteeing the privacy and confidentiality of study participants. Appropriate management of medical safety data will enhance the protection of human subjects, optimize the reviews by IRBs, DSMBs, funding and regulatory agencies, promote the trust of participants and the community in clinical trials, enhance scientific progress, and lower research costs.

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5. *Medications for the Treatment of Pregnant and Post-Partum Drug Abusing Women and Their Children.* Little is known about the safety and efficacy of medications for the treatment of substance abusing pregnant women and their children. There is a need for safe and effective medications for the treatment of nicotine and drug abuse/dependence among pregnant and post-partum women and the effect of these medications on their children. Research is also needed to study the effects on the newborn of the medications taken by the mother and medications for treatment of children born to substance abusing mothers who may present drug withdrawal and other symptoms.

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6. *Immunotherapy for Addiction Treatment.* The MRGB supports research on the advanced stage development of monoclonal antibodies and vaccines for the treatment of drug and nicotine addiction and/or overdose. Monoclonal antibodies have been reported as possible treatment agents through passive immunization for PCP, methamphetamine, MDMA, and cocaine overdose and may also serve to minimize abuse and prevent relapse. New vaccines are being developed as therapies for drug or nicotine cessation and relapse prevention. New technologies, such as the production of antibodies in plants, are emerging as cost-effective and efficient ways for the large scale manufacture of immunotherapy agents, represent another facet of this area for development.

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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.
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.
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, 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. *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.

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6. *Behavioral Strategies for Increasing Compliance in Taking Treatment Medication*. Research to develop and to evaluate strategies to induce recovering addicts to take medication for a prolonged time, especially antagonists such as Naltrexone; to induce 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.

7. *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.

8. *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, or to incorporate effective HIV risk reduction techniques.

9. *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 brief behavioral treatment approaches, alone or

in combination with pharmacological treatments that may be used in various primary care patient populations and primary care settings. Other goals of this research initiative are to encourage additional research on the development and evaluation of culturally sensitive screening and assessment instruments for use 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.

10. *Using Telemedicine to Disseminate Drug Addiction Research Findings to Primary Health Care Providers*. 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. Health care professionals need science-based information on drug abuse prevention and treatment. Research to develop and evaluate telemedicine programs to transport science-based information on drug addiction to the primary health care community is encouraged.

11. *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.

12. *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 drug abusers with comorbid psychiatric disorders and/or medical illnesses such as HIV/AIDS, hepatitis, etc.

13. *Treatment 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. For these populations treatments are needed which interest and engage the potential client and intervene with them. Treatments for participants in their natural environment, such as treatments delivered over the Internet or in neighborhood settings such as churches and recreation centers are desired.

14. *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.

15. *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. Research is needed to develop and test innovative behavioral and combined behavioral and pharmacological treatments that address the unique needs of these individuals.

16. *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.

17. *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, or ethnic minorities. 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.

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 smokers has not been particularly fruitful. More research is needed to develop interventions for young

smokers. This initiative requests research aimed at the development and testing of smoking cessation treatments tailored to the specific needs of adolescents. Consideration should also be given to gender and ethnicity.

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19. *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.

20. *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.

21. *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 motivational level of the client; (2) is specifically designed to respond to the needs of the individual, whatever his or her motivational level might be; and (3) actively works to increase an individual's desire to remain in treatment.

22. *Complementary and Alternative Medicine Therapies (CAM) for Drug Abuse Treatment*. Research is encouraged on complementary and alternative interventions for drug abuse treatment. CAM interventions could be the sole treatment or could be adjunctive strategies to enhance the therapeutic potency of existing drug abuse treatments. An example of an adjunctive CAM intervention might be where the intervention reduces withdrawal symptoms thus enhancing retention in treatment. Included would be interventions that are commonly used in "real world" treatment settings, but whose therapeutic efficacy has not been scientifically demonstrated. Such interventions include acupuncture, bioelectrical stimulation, exercise, biofeedback, meditation, among others. The product of this research might be a manual or video, which illustrates the intervention and how it is implemented by treatment staff.

23. *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 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.

24. *Behavioral Treatments for Pre-Adolescents and Adolescents.* 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.

25. *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. Treatments that target domestic violence or other forms of interpersonal abuse along with substance abuse are encouraged.

26. *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).

27. *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.

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. This solicitation requests research aimed at developing and testing effective interventions for marijuana dependent individuals.

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29. *Transporting Behavioral Treatments to Community Practitioners*. There is a need for effective methods of transferring behavioral treatments found to be effective in 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. This is a call for proposals that examine 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.

30. *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.

31. *Virtual Reality Applications for Drug Abuse*. Development and improvement of treatments using Virtual Reality and other new 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 comorbid 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.

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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. *Development of Novel Approaches in Human Neuroscience.* Development of innovative, noninvasive research methods or novel approaches are needed to identify various neurobiological markers of brain alterations in humans induced by acute or chronic exposure to drugs of abuse. This may include the identification of neurobiological (including genetic) markers that might be associated with risk for, or resilience to drug abuse and addiction. Of particular interest are noninvasive methods (e.g., brain imaging) 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 therapeutic efficacy.

   In recent years, there has been an increase in studies employing functional magnetic resonance imaging (fMRI) to understand brain processes and functional neuronal systems. In particular, these neuroimaging techniques are being used to probe how drugs of abuse alter brain functioning. Consequently, there is a need for the development of stimulus generation hardware to be used within an fMRI magnet that can display stimuli important in drug studies. As the studies of brain function become more sophisticated, task-related assessments of brain activation are increasingly important. Shielded goggles or other types of stimulus-generating hardware and software are necessary for presentation, for example, of neurocognitive tasks, drug-related images for the induction of craving, or other "virtual reality" types of dynamic stimuli important in studies of drug abuse and addiction. Responses to this type of stimulation then could be correlated with brain measures using neuroimaging techniques. These types of studies will provide new insights into drug-brain-behavior interactions.

   Development of the human central nervous system and how drugs of abuse perturb this process is of great interest. Little is currently known about the effects of exposure to drugs of abuse, either prenatally or during childhood or adolescence, on the development of the human nervous system. Further, the application of newly emerging technologies (such as neuroimaging) to these populations presents unique challenges due to the fact that the central nervous system, and its capabilities, are changing rapidly. 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 Laurence Stanford, Ph.D.).

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2. *Virtual Reality for the Neurobiological Study of Drug-Brain-Behavior Interactions and Drug Abuse Treatment.* Virtual Reality (VR) is an emerging technology useful in a variety of research-related, therapeutic and instructional settings. By immersing a person's senses in a synthetic world or Virtual Environment (VE) that characterizes VR, a highly flexible and programmable set of stimuli can be used to enhance the standard approaches used in assessment of neurobiological and neurobehavioral processes.

Collection of real-time data and bulk data recording can provide a correlation of a stimulus reference signal with simultaneously collected fMRI scanner and physiological data over time. Unlike most computer access systems that accept only one or two modes of precise and/or discrete input at a time, VR systems have the potential to monitor movement or action from any, or many, neurobiological functions at once. In addition, the multimodal feedback inherent in VR provides a way to vary nonvisual stimulus components (e.g., resistance, temperature, pitch) in a way that is impossible to achieve via standard computer systems. Finally, VR systems provide a bypass for keyboard entry or direct manipulation environments (e.g., pointing instruments like the mouse), by allowing the manipulation of multi-sensory representations of entire environments by natural actions and gestures.

VE can provide a completely controlled, noninvasive, safe and alternative methodology for a variety of important studies of drug abuse and addiction. For example, VR allows for the presentation of a variety of complex, multi-sensory stimuli for neurocognitive tasks or, alternatively, the dynamic stimuli important for producing drug-related images for the induction of craving. VR can also be tested as an alternative to traditional behavioral therapies in the treatment of drug abuse. Responses obtained as a result of the above can then be correlated with brain measures using state-of-the-art neuroimaging techniques. We, therefore, invite studies employing VR, especially to probe brain processes in drug abuse/addiction combined with neuroimaging methods or to be developed or applied as a potential treatment for substance abuse.

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3. *Development of Interactive Computer Applications for Neuropsychological/ Neurocognitive Assessment to Determine Functional Brain Deficits in Acute and Chronic Drug Abusers.* In addition, a neurobehavioral test battery to assess other neurobehavioral/neurocognitive deficits resulting from drug abuse/addiction is encouraged. Of particular interest is the development of such assessments for use in children and adolescents exposed to drugs of abuse to better define and understand the effects of early exposure on brain function and development (for developmental issues, contact Laurence Stanford, Ph.D.).

Steven Grant, Ph.D.
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or

Laurence Stanford, Ph.D.
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4. *Development of Ligands for Brain Imaging.* Development of novel radioligands for PET and SPECT imaging in human brain for molecular targets (e.g., receptors, intracellular messengers, disease-related proteins) is of broad interest to the neuroscience and drug abuse research community. The primary application of these radiotracers will be in basic neuroimaging research. Ultimately, these radiotracers 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 radiotracer development.

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5. *Novel Approaches in the Clinical Neurobiology of Drug Addiction.* Many scientists involved in behavioral and neurobiological research are faced with growing difficulties in identifying approaches, devices (e.g., research tools) and/or strategies to broaden the within-discipline knowledge base for understanding, preventing and treating

drug abuse. NIDA has a strong interest in facilitating the identification and use of cross-disciplinary research tools and materials that are being used and have proven efficacious in research unrelated to drug abuse (e.g., virtual reality, transcranial magnetic stimulation, deep brain stimulation). 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.

Advances in biomedical science continuously yield new research findings that play a critical role in the furtherance of knowledge and innovation in both the public and private sectors. For the purpose of this solicitation, the term research tool may include methods, laboratory equipment and machines, databases and computer hardware and software. From a clinical perspective, interactive games and emerging game technologies are being used successfully in a variety of health education situations; therefore, applications proposing introducing these "tools" as adjuncts in the prevention and treatment of drug abuse will be accepted. NIDA has solicited and continues to solicit proposals using virtual reality to increase our understanding of the neurobiology of addiction, (e.g., drug cues, craving), comorbidity (e.g., post-traumatic stress disorders) and pain (e.g., distraction). Additional novel approaches, devices and strategies are now being sought to further our understanding of the cognitive neuroscience of drug abuse and addiction, neuroplasticity and repair, the neurobiology of treatment (including training tools, assessment and neurolobiologic correlates of treatment outcome) and neuroAIDS.

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6. *Development of Serious Games for Neuro-Rehabilitation of Drug-Induced Cognitive Deficiencies.* Health-related gaming is an emerging industry useful in a variety of research-related, therapeutic and instructional settings. 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.

   It is hypothesized that changes in behavioral contingencies as a consequence of varying time and/or rate of the stimulus-response-reinforcer sequence (e.g., designing a game that involves differential rates for low responding (DRL) schedule) may alter brain activity (pattern changes noted using state-of-the-art neuroimaging techniques) and, thus, correlate with the improvement of neurocognitive deficits

   Neurocognitive deficits are generally drug-specific. For example, chronic methamphetamine abusers loose their decision-making ability, and suffer attentional bias in a visual discrimination task. Cocaine abusers lack cognitive flexibility, the ability to use feedback to monitor/change behavior, have slower reaction times on match-to-sample and increased errors (both omission and commission) along with attention/concentration deficits. Chronic use of opiates produces an increase in

auditory, visual, and associative reaction times, impaired vigilance, attention, information processing, short-term visual memory, delayed visual memory, short-term verbal memory, long-term verbal memory and problem solving. Although in controversy, marijuana may decrease one's ability to focus, sustain, and shift attention as well as decrease memory and motivation.

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7. *Development of Field-Deployable Tools for Quantifying Exposures to Psychosocial Stress and to Addictive Substances.* This announcement encourages the development, improvement and/or adaptation of measurement technologies for the purpose of creating field-deployable tools that can detect and quantify personal exposure to psychosocial stress and/or addictive substances with maximum precision and reliability. Ideally, the technology could be applied in large-scale population studies to comprehensively measure multiple addictive substances and psychosocial stress events, either singly or jointly. 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.

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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.

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 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.

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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 among school-age children and adolescents. 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 investigators, 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, and 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 for Drug Use Measurement Among Adolescents.* Research to develop and refine methodologies for drug use detection and quantification, with special application to the adolescent with HIV infection or at high-risk for HIV infection. This research should address issues of acceptability, reliability, and validity of one or more methods (e.g., interviews, computerized questionnaires, and biological indicators such as saliva or sweat).

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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 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 methodology to transfer new knowledge and directions of scientific growth to teachers, curriculum developers and health care providers.
- Development of computer based learning systems that allow students to experience the scientific process.
- 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 accurate and culturally-appropriate translations of valid and reliable questionnaires, surveys, interviews, and other instruments for use in domestic and international settings. Other instruments may include assessment, quality of life, and outcomes measures.
2. To facilitate research collaborations between U.S. and international researchers, and to respond to the demand for science based drug abuse information, there is a need for the development of a series of information and

training modules specially targeted to foreign trainees and investigators. Proposed topics for the modules include, but are not limited to: Drug Abuse Treatment Approaches, Understanding the Neuroscience of Addiction, Tools and Guidelines for Assessing and Evaluating Drug Abuse Treatment Programs and Treatment Approaches with HIV-Positive Drug Abusers.

3. Development of standardized behavioral, physiological, and/or toxicological measures of drug use and drug impairment for use in international comparative studies of drugged driving.

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

NIDA encourages applications in other areas of research that may not be listed.

For additional information on research topics, contact:

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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 II Competing Renewal Awards

The NIDCD will accept Phase II 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 Lynn Luethke (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-07-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 Competing Renewal grant.

Hearing Program

Research and development related to lost auditory function. Development of new cellular and tissue-based applications, hearing aids, cochlear implants, and other assistive devices (e.g., systems designed to improve access to and to increase utilization of computer and other information technologies, telecommunication devices, alerting systems) for individuals with hearing impairments; development of new or better materials for earmolds to address allergy, occlusion effect and/or feedback complaints; development of molecular technologies, including viral and non-viral vectors to enable gene transfer to the inner ear; development of cell type specific markers and probes to examine cell lineage in inner ear regeneration; development of research tools such as software and imaging technologies; development of relevant web or other databases; development of assays (including DNA-based assays), tests and instruments for the screening and diagnosis of hearing impairment, especially in neonates and infants; development of treatment modalities to prevent or lessen the effects of hearing disorders; development of new outcome measures for assessing the efficacy of treatments of hearing disorders; development of new research tools to aid in the study of the auditory system (e.g., imaging techniques, neuroanatomic tracers, electrophysiologic technology, new animal models); 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.

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Balance/Vestibular Program

Research on balance and vestibular function, including development of tests and treatments for balance disorders. Balance disorders affect a large proportion of the population, particularly the elderly. The vestibular system, with its receptor organs located in the inner ear, plays an important role in maintaining orientation in space, controlling balance while the body is immobile and in motion, and visual fixation of objects during head movement. Emphasis is on research and development of treatments for balance disorders; development of neuroimaging techniques, computational modeling, genetic tools and biochemical markers of disease in the vestibular system; 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.

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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 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; identification and development of computer and animal models for research in communication disorders; 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 impairment; development of innovative treatment delivery systems or intervention protocols for adult aphasia design and development of diagnostic measures or materials for early identification of speech and language impairment in children; development of tests for the assessment of childhood and adult 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 speech and language.

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Taste and Smell Program

The study of the chemical senses of taste and smell will lead to a better understanding of how individuals communicate with their environment and interact socially. Taste and smell perception regulates food consumption and plays an important role in maintaining a nutritious healthy diet. In addition, both the olfactory (smell) and gustatory (taste) systems offer special approaches for understanding fundamental mechanisms of neurogenesis, plasticity and regeneration in the brain. Innovative approaches for obtaining functional expression of mammalian taste or odor receptors in heterologous cells will help determine ligand-receptor specificities and taste and smell quality perception. The olfactory receptor neuron represents a model system for the study of the biological processes related to stem cells. Advances in molecular and cellular biology, biophysics, and biochemistry of the olfactory and gustatory systems are paving the way for improved diagnosis, prevention, and treatment of chemosensory disorders. Research on the development of readily administered diagnostic tools for testing human chemosensory function in population studies, intervention strategies for smell and taste disorders, biosensors and electronic noses for medical and industrial applications, and the development of an inventory of chemicals at exceptional high purity have high priority.

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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 might include:

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 and fungal infections of the oral mucosa and research on the diagnosis and prevention of oral manifestations of HIV infection and AIDS. Specific examples of technology development needs include:

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 therapeutic agents to prevent and/or control 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 proposals 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, specifically HIV, activities.

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.

A. Develop imaging techniques for the early detection, diagnosis and prognosis of pre-malignant head and neck lesions including oral 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 novel techniques for the evaluation of chromosomal changes in head and neck cancers.

D. Develop effective pharmacological, immunological and radiological modalities for treatment of pre-malignant and malignant head and neck lesions.

E. Develop novel technologies for the genetic and molecular-targeted therapy of head and neck carcinomas.

F. Develop novel micro and nano-sensor technologies that can release therapeutic agents in tumor cells.

G. Develop regimens for the alleviation of the oral complications of cancer therapy.

H. 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:

A. Develop standardized and more sensitive 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 better methods and instrumentation to detect and/or treat the earliest signs of demineralized enamel that may develop into carious lesions.

D. Develop novel methods and agents to promote scarless repair of cleft lip and scarless cutaneous healing following craniofacial surgery.

E. Develop viral and non-viral vectors for salivary gene therapy and gene therapeutics.

F. 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.

G. Develop apparatus for craniofacial bone distraction that is contained entirely within the oral cavity for use in the restoration of large bony defects and/or building bone for orthodontic procedures.

H. Develop more efficient methods, materials, and devices for prevention of injuries to the teeth, mouth, and face during athletic activities.

I. Develop genetic standards, databases, and diagnostics to predict oral responses to drugs used for the treatment of craniofacial, oral and dental diseases.

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 proposals specifically to:

A. Develop improved techniques for measuring 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 natural and synthetic materials to be used for the repair, regeneration, restoration and reconstruction of oral tissues and organs; on the development and improvement of evaluation and measurement systems for the characterization of implanted

material properties; on their interactions as well as on their performance under the conditions of the biological environment; and finally on the development and/or improvement of new dental restorative materials that are mercury free. Specific examples of relevant small business proposals could include:

A. Develop strategies for the fabrication of site-specific repair and regeneration systems (e.g., smart implants to specifically attach the appropriate reparative cells).

B. Develop non-destructive methods for the characterization of properties of materials used for tissue/organ reconstruction in vivo and in vitro.

C. Develop synthetic analogues of oral/craniofacial tissues and organs for use in high throughput screening and drug development.

D. Develop more sensitive methods to determine and measure the interactions of materials with biological systems (e.g., material biocompatibility and bioactivity in the oral environment).

E. Optimize imaging techniques for describing the architecture of oral tissues and structures.

F. Develop computer and mathematical modeling systems capable of mimicking biological tissues and of evaluating material designs.

G. Develop novel techniques for ensuring sterility of engineered structures prior to implantation.

H. Develop delivery systems that are compatible with host immunity; consider hybrids and artificial vectors as well as viral and non-viral gene delivery systems with cell-type selectivity.

I. Develop in vitro methods that predict immunogenicity to vectors used for gene transfer as well as for biomaterials.

J. Develop improved implantable materials, designs through nanotechnology principles.

K. Develop improved surgical techniques for artificial implants to support replacement of dental, oral and craniofacial tissues and organs.

L. Develop new and improved instruments and techniques for the diagnosis and treatment of TMJDs.

M. Develop safe and effective biomaterials or procedures useful in repairing the temporomandibular joint (TMJ) following trauma, degenerative or inflammatory diseases processes, or iatrogenically-induced pathology (e.g., failed TMJ implants).

N. Develop improved composite materials and adhesive sealants suitable for restoring crowns of posterior teeth and exposed roots of teeth.

O. Utilize nanoscience- and nanotechnology-based materials and/or principles in the improvement or development of new composite and/or ceramic dental restorative materials.

P. Design and development of orthodontic and other prosthetic appliances based upon the application of new materials or engineering principles.

Q. Develop tissue engineering and regenerative approaches to building complex structures (e.g. teeth, ligaments, peridontum) in the oral cavity.

R. Develop or use of highthroughput assays for drug discovery and/or pharmacogenomics.

Clinical, Epidemiological, and Behavioral Research

Provides support for clinical trials and patient-oriented research on the safety, efficacy, and effectiveness of measures for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders, as well as for research on the distribution of such disorders, risk and protective factors, oral health disparities, and basic and applied behavioral, social science and health services research relevant to oral diseases and their prevention or treatment. NIDCR is especially interested in applications that have broad, enabling utility, including:

A. Develop and test web-based training or other innovative approaches to accelerate accurate translation of new knowledge regarding oral diseases and their effective prevention/treatment into clinical or public health practice.

B. Develop and test the effectiveness of innovative teaching tools to inform oral health professionals or the public regarding oral cancer prevention and early detection.

C. 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 either within clinical trials or oral health care delivery systems.

D. Develop novel compliance and survey tools to examine the underlying causes of avoidance of preventive dentistry in underserved populations.

E. Develop effective electronic outreach tools (e.g. console or web-based video games, simulations, virtual reality) to increase oral health literacy, and prevention of caries and gum disease.

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

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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 II Competing Renewal Awards

NIDDK will accept Phase II SBIR/STTR 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 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 II Competing Renewal opportunity. 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. 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-07-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.

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. 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.

F. Development and validation of surrogate markers to monitor disease progression and potential therapies for diabetic complications.

G. Development of tools to support the application of behavioral approaches to risk reduction in the development of type 2 diabetes or to the improved treatment of diabetes. An important consideration should be cost and practicability of use.

H. Development and validation of tools for use by health care providers/systems to improve diabetes care and prevention.

I. 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.

J. Development of simple inexpensive test for diagnosis of diabetes and pre-diabetes that do not require fasting or timed blood sampling.

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.

Other Endocrine and Metabolic Disorders

H. 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.

I. 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.

Cystic Fibrosis and Inborn Errors

J. Development of potential therapeutics for CF including agents to improve trafficking and function of mutant CFTR, to enhance activities of channels which can serve as alternatives to CFTR, and to increase transcription or translation of CFTR RNA.

K. Production of stabilized biologically active proteins or peptides useful for enzyme replacement therapy.

L. Development of small molecules that improve folding and activity for enzymes defective in inborn errors.

M. Development of products useful in assessing or improving nutritional status in patients with CF including improved pancreatic enzyme preparations.

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.

F. Development of approaches to gene transfer for cystic fibrosis by improving gene delivery systems, improving tropism for target cells, increasing efficiency and duration of transgene expression and minimizing toxic effects.

V. APPLICATION OF PROTEOMICS AND METABOLOMICS TO DIABETES, ITS COMPLICATIONS, AND OTHER ENDOCRINE AND METABOLIC DISEASES

A. Identification of surrogate markers looking at the plasma/sera proteome or metabolome at different stages of diabetes its complications or other endocrine or metabolic diseases.

B. Development of novel proteomic or metabolomic technologies designed to study diabetes its complications or other endocrine or metabolic diseases.

C. Identification of novel drug targets or novel therapeutic agents using proteomic approaches that might be relevant to diabetes its complications or other endocrine or metabolic diseases.

D. Use of high throughput proteomic and metabolomic technologies for toxicology studies of drugs that might be relevant to diabetes.

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.

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 imaging methods to assess fatty liver in patients.

L. Development of non-invasive devices/ techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.

M. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.

N. Development of non-occluding stents for use in the biliary tract and in transjugular intra-hepatic porto-systemic shunts (TIPS).

O. Development of cryopreservation techniques for human hepatocytes that would maximize viability and cell culture growth potential of thawed cells.

P. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.

Q. Development of molecular standards for Hepatitis C virus quantitation and typing.

R. Development of molecular standards for Hepatitis B virus quantitation and typing.

S. Development of an economical, accurate, and fast test for glutens and glidins in foods.

T. Development of humanized mouse models of multi-allelic diseases.

U. Development of measurements to quantitate phenotypic or metabolic markers of disease progression in animal models, thus reducing the numbers of animals needed.

V. Identification of surrogate markers looking at the plasma/sera proteome or metabolome at different stages of digestive or liver disease.

W. Development of novel proteomic or metabolomic technologies designed to study digestive and liver diseases, and their complications.

X. Identification of novel drug targets or novel therapeutic agents using proteomic approaches that might be relevant to digestive and liver diseases, and their complications.

Y. Use of high throughput proteomic and metabolomic technologies for toxicology studies of drugs that might be relevant to digestive and liver diseases, and their complications.

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 and/or increasing physical activity such as hand-held computers and web-based programs.

C. Development of devices/equipment/ interventions to encourage “activity” while performing sedentary work.

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.

E. Development of more economical methods to produce 18-labelled oxygen for use in energy expenditure studies and/or body composition studies using doubly labeled water.

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. Bioinformatic 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 distinction between benign and malignant parenchymal diseases.

I. Development of early diagnostic tools, preventative measures, and treatment modalities for Acute Renal Failure.

J. Identification of mediators of renal failure 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. Characterization of changes in kidney hormonal function in kidney disease at various stages of severity.
5. Development of new biomarkers for early detection of kidney dysfunction, prediction of progression, and early indication of recovery.
6. Development of rapid, accurate, and cost effective means of quantifying urine albumin.

IV. UROLOGY

A. Study of the effect of growth factors, hormonal concentrations and other biochemical stimuli on the growth of prostatic tissue. Analyses of factors responsible for initiation and progression of Benign Prostatic Hyperplasia (BPH).

B. Development of animal or in-vitro models for the study of stromal - epithelial interactions in BPH.

C. Assessment of factors responsible for Benign Prostatic Hyperplasia (BPH) induced uropathy.

D. Host-parasite and bacteria-urothelial cell interactions involved in urinary tract infection.

E. 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.

F. Development of additional therapeutic agents for prevention and/or treatment of urolithiasis.

G. Neuropharmacological-neurophysiological assessments in urodynamics.

H. Development of culture conditions for in vitro culture of cells from benign prostatic hyperplasia.

I. Development of serum or urine markers that correlate with prostate size to evaluate rate of growth.

J. Development of non-invasive instrumentation that can detect early onset of bladder instability associated with diabetes mellitus.

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 and validating iron concentration 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.

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

For additional information on research topics, contact:

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NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

Human health and human disease result from three interactive elements: environmental exposures, genetic susceptibility 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.

Exposure Biology Program

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 of this

exposure biology program 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. Indeed there is an overall NIH effort in Exposure Biology which is part of a larger Gene and Environment Initiative (GEI). Applicants in the exposure biology aspect of the NIEHS SBIR program should also examine the GEI website as there are additional RFAs available in this area (http://www.gei.nih.gov/exposurebiology).

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 environmental exposures and the impact of the exposures on human biology. Ideally, such technologies and assays will provide exposure measurements with a high degree of temporal and spatial resolution; that is, they will provide real-time measurements of exposure (high temporal resolution) as an individual moves from location to location (high spatial resolution). Additionally, the technologies and assays will be able to provide precise, quantitative measurements of both current (and ongoing) exposures and/or past exposures, depending on the exposure agent measured.

1. TECHNOLOGIES FOR GENERATING PRECISE MEASURES OF ENVIRONMENTAL EXPOSURES

The NIEHS is interested in developing and validating new products/devices, tools, assays to improve our ability to precisely measure environmental exposures to individuals 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 airborne/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, mercury), volatile organic compounds, polybrominated diphenyls (PBDEs), polycyclic aromatic hydrocarbons (PAHs), mold/microbial toxins, allergens and pesticides/herbicides. Examples include:

A. Novel technologies and assays to generate precise, quantitative measures of human exposure at the point of contact (e.g., skin, breath, nasal mucosa).

B. Remote sensing technologies for detecting, quantifying, and monitoring household exposures to toxicants and/or bioaerosols.

C. Micro- and nano-scale technologies, such as lab-on-chip sensors, for detecting and quantifying simultaneously multiple environmental exposure agents in a specific chemical or biological class in environmental samples collected in the personal environment (e.g., breathing zone, clothing).

D. Field deployable diagnostic devices capable of assaying biomarkers indicative of specific exposures in biological samples encountered in a mass casualty situation.

2. TECHNOLOGIES FOR GENERATING PRECISE MEASURES OF BIOLOGICAL RESPONSE TO ENVIRONMENTAL EXPOSURES

The NIEHS is interested in developing technologies and devices to generate precise indicators (or markers) of the biological response to environmental exposures. The indicators may reflect compensatory biological responses and/or early (preclinical) responses to the exposure agent. The goal is to develop quantitative indicators (or markers) that can be measured in easily accessible biosamples (blood, urine, saliva, buccal samples, nasal mucosa or exhaled breath) for human population-based and clinical research and practice. The exposure markers may reflect either acute or chronic responses related to toxicity or preclinical disease. Examples include:

A. Development of high-throughout and sensitive technologies and assays for the detection and quantification of molecular changes in genes (genomics), proteins (proteomics), or metabolites (metabolomics), that are reflective of the early response to environmental exposure.

B. Development of biomarkers of response to environmental agents that will define a pattern of response at a single level (i.e. a molecular signature) or at multiple levels (i.e. molecular, cellular, and/or physiological responses).

C. Comparison of panels of biomarkers in multiple tissues progressing from invasive to noninvasive specimens.

D. Identification of early (preclinical) response markers in animal models that have direct application to marker development and validation in population-based and clinical studies.

E Devices for assessing not only biomarkers of exposure but also distinguishing those exposed individuals at risk of developing life-threatening symptoms or long term chronic sequelae from their exposure.

F. Comparison of patterns of response to environmental agents across species including humans.

3. 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. As with the external exposure sensors throughput should be an important component of the product.

Examples include:

A. Development of sensors for measuring the levels of toxicants in bio specimens easily attained by an individual such as finger prick, buccal cell, exhaled breath or urine.

B. The development of biocompatible in vivo sensors for measuring target organ distribution of specific agents.

C. The development of integrated devices combining the functionality of external exposure sensors, internal exposure sensors and biological response sensors.

Hazardous Waste Assessment, Evaluation and Remediation Program

The NIEHS is interested in applying biotechnology and bioengineering approaches for the development of novel strategies that can be used to characterize and monitor contaminants at waste sites, and to reduce exposure via remediation technologies. In addition there is interest in developing products for better site characterization that includes improved monitoring capabilities to assess the extent and amount of contaminants present at sites, as well as to monitor the effectiveness of remediation technology in reducing the amount and toxicity of contaminants. Examples include but are not limited to:

A. Development of nano structures, electrochemical methods, photocatalytic processes, thermal treatments or filtration-based methods of remediation.

B. Development of bioremediation and phytoremediation technologies including the use of genetic engineering approaches.

C. Development of model organisms for site characterization that monitor genomic responses to environmental exposures, with a special interest in metals.

D. Development of technologies to determine the extent to which a contaminant is bioavailable .

E. Development of methods/instruments to detect and measure non-aqueous phase liquids and dense non-aqueous phase liquids in the subsurface.

F. Development of instruments to identify subsurface geological structures and hydro-geological configurations and to sample for the presence of contaminants in these structures.

Predictive Test Systems for Safety Evaluation Program

The NIEHS is interested in developing, standardizing, and validating sensitive and specific new and novel tests or batteries of tests that will provide faster and less expensive alternatives to the use of 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). The proposed tests should use cell cultures or animal models that are relevant to human experience and can be extrapolated to estimate risk to humans. The NIEHS is interested in developing both high throughput screens that can be used to prioritize chemicals for definitive testing and in developing specific tests that meet regulatory requirements for toxicity tests. The endpoints for these 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 systemic toxicity.

B. In vitro test methods (e.g., undifferentiated/ differentiated human/mammalian cell model systems, organotypic model systems) that can be used 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.

C. Alternative assays to determine 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.

Educational and Training Resources Program

The NIEHS is interested in developing educational and training resources for students of all ages, educators, health care professionals and the lay community to enhance their knowledge of environmental health sciences. These resources are an important part of our communication strategy that encompasses training, education, and community outreach. Resources may be directed at all levels of education: Kindergarten through 12th grade, undergraduate, graduate, adult education, health care professional training, and community outreach. Products may include:

A. Web-based interactive lessons, training modules and educational games that can be used in the classroom as well as in the home.

B. Innovative communication strategies for distance learning (e.g. satellite broadcasting, video conferencing, webcasting, Personal Digital Assistant programs, etc.) to enhance educational and training opportunities.

C. Video and DVD-based educational outreach materials that can be used in the classroom, at community meetings, or for professional development, including continuing medical education courses.

D. Educational television shows (e.g., PBS Kids, NOVA, etc.) with accompanying lessons or activities (accessible via internet or print) that can be used by teachers, parents or professional development coordinators.

Resources on subjects of particular interest include, risk assessment, hazards in our environment, use of pesticides, endocrine disruptors, air/soil/water quality, susceptibility/gene-environment interactions, ethical, legal, and social implications of environmental health research, health disparities, and intervention/prevention strategies.

Educational and training materials must be aligned with state and federal standards. Training materials and activities for health care professionals should include continuing education units. Partnerships are encouraged among small businesses, environmental health scientists, and educators, health literacy experts or training specialists.

For more information on NIEHS Science Education activities, visit www.niehs.nih.gov/science-education/.

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. Proposals for all areas of vision research are encouraged. Examples

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

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; identification and characterization of factors regulating retinal cellular proliferation and development that will facilitate retinal regeneration and 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; 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; new materials and manufacturing processes for eyeglasses and contact lenses.

Lens and Cataract Program

Research and development of therapeutic agents for the prevention of cataract; 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 using imaging techniques, such as PET and MRI, to localize lesions and test the functioning of specific parts of the visual system, especially those involved in higher order visual processing and oculomotor processing; 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 persons who are blind or have low vision.

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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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, 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/StaffContacts.html). 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.

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 proposals 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. Bioinformatics, including but not limited to:

1. Development of databases relative to structural and cellular biology.
2. Development of methods for linking the information that might be contained in such databases.
3. Development of new tools that might be used for "mining" the information contained in such databases.

G. 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 understanding complex systems at the cellular and organism level.
5. Improved methods for the simulation and prediction of the dynamics of biological macromolecules.

H. 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 libraries, cloning techniques, probes).

D. Development of probes for detection of human genetic polymorphisms, including disease genes.

E. Development of improved procedures for cytogenetics.

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 new tools and models for study of the genetic architecture of complex phenotypes.

K. Development of improved technology to scale up the growth of approved human embryonic stem cells in culture and to regulate their differentiation state.

L. Development of markers, reagents and tools to characterize the unique properties of approved human embryonic stem cell lines and to distinguish them from adult stem cells and more differentiated cells.

M. Development of human embryonic stem cell lines as a primary cell type to be used as a model system for drug discovery.

N. 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.

O. Development of methods for chemical modifications that improve the properties of nucleic acids for gene silencing.

P. Improvement in procedures (statistical, computational, laboratory) for the high- and medium-throughput analysis of gene expression patterns and regulatory networks.

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 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 interindividual differences in drug responses.

1. Identification of human polymorphisms in drug receptor and drug metabolizing enzymes.
2. Methods for pharmacogenetic and pharmacogenomic analyses and their application to phenotypic and genotypic characterization of populations.
3. Development of proteomic and metabolomic methodologies to support research in this area.
4. Development 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 for quantitating protein and lipid glycoconjugates and for determining their structures. Development of generally applicable methods for the synthesis of branched chain oligosaccharides.

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 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. Applications that develop carbohydrate specific databases and informatics tools to mine carbohydrate data bases, as well as development of high through put assays for assessing carbohydrate binding protein specificity and or disease biomarkers.

Z. 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.

Center for Bioinformatics and Computational Biology

A. Development and enhancement of databases for activities that fall within the mission of NIGMS.

B. Development of methods for data mining and providing integration and interoperability of different databases and varying modalities of data.

C. Development of tools to model complex biological systems that fall within the mission of NIGMS.

D. 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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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, 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:

Directed Stem Cell Differentiation for Cell Based Therapies for Heart, Lung, Blood, and Aging Diseases. See: http://grants.nih.gov/grants/guide/pa-files/PA-06-124.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-125 (STTR)

Bioengineering Approaches to Energy Balance and Obesity. See: http://grants.nih.gov/grants/guide/pa-files/PA-06-055.html (SBIR) and http://grants.nih.gov/grants/guide/pa-files/PA-06-056.html (STTR)

Phase II Competing Renewal Awards

The NHLBI will accept Phase II 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) acceptance or approval of the Phase II product in the form of an Investigational New Drug (IND), Investigational Device Exemption (IDE), 510K, Pre-market Approval (PMA) or a Humanitarian Device Exemption (HDE). 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, vaccines, medical implants, etc. 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 II Competing Renewal funding must submit an application no later than the first six receipt dates following expiration of the previous Phase II project budget period.

Budgets up to $1,000,000 total costs per year and time periods up to 3 years may be requested for this Phase II Competing Renewal opportunity. An applicant must provide evidence that their research plan and objectives follow FDA guidance for the development of a drug, biologic, or medical device. Examples of acceptable FDA guidance includes, but is not limited to, published guidelines and direct letters of communication from FDA personnel for an investigational new drug (IND) application, investigational device exemption (IDE), 510K, Pre-Market Approval (PMA), or Humanitarian Device Exemption (HDE). The applicant should also provide the status of their project in a timeline related to Federal regulatory approval processes. An updated commercialization plan is also required.

Prospective applicants are strongly encouraged to contact NHLBI program staff prior to submission of an SBIR Phase II 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
- 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 or Pre-market Approval (PMA).
- FDA-required biocompatibility studies of surface materials of putative medical implants or other studies needed for 510k approval.
- FDA-required assessments of novel imaging systems.

Direct questions about scientific/research issues to:

Cardiovascular Diseases

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Lung

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Sleep

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Blood

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Cardiovascular Diseases

The NHLBI Division of Cardiovascular Diseases (DCVD) plans and directs research grant, contract, and training programs in heart and vascular diseases. These programs encompass institute- and investigator-initiated basic research, targeted research, specialized centers and clinical trials. The DCVD 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 DCVD 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.

The Division has five branches: the Advanced Technologies and Surgery Branch, the Atherothrombosis and Coronary Artery Disease Branch, the Development and Structural Heart Disease Branch, the Heart Failure and Arrhythmias Branch, and the Vascular Biology and Hypertension Branch, in addition to a Research Training and Special Programs Group.

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.

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.

Development and Structural Heart Disease Branch. Supports basic, applied, and clinical research in normal and abnormal cardiovascular development as well as the etiology, pathogenesis, prevention, diagnosis, and treatment of pediatric and adult structural heart disease.

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.

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.

Research topics of interest to the Division of Cardiovascular Diseases include but are not limited to the following:

A. Materials and Devices.
    1. Angioscopes with increased flexibility and enhanced resolution
    2. Medical implants (heart valves, vascular grafts, stents, pacemakers, defibrillators, 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
    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. Biological, chemical, and mechanical sensors
    6. Diagnostic instrumentation for the mouse and rat
    7. Point-of-care (POC) devices for monitoring and diagnostics

B. Computing and Informatics.
    1. 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
        c. Optimization of implantable defibrillator algorithms for arrhythmia prediction, efficient intervention, device fault detection or early failure detection
    2. Informatics:
        a. Novel use of information technology to enhance adherence to medical regimens or promote translational research
        b. Approaches to integrating diverse types of data from cardiovascular research

C. 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, arrhythmia.

D. 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.

E. Preventive Approaches.

1. Nutrition and dietary interventions and products.
2. Technologies to assess energy balance and control weight.

F. Transplantation.

1. Methods to increase success of cardiac zeno-transplants.
2. Methods to induce tolerance to cardiac allografts.
3. Non-invasive methods to diagnose cardiac allograft vasculopathy.
4. Preservation methods for cardiovascular tissues or organs for use in transplantation and in research studies.
5. Pediatric heart transplantation.

G. Training and Education.

1. Instructional, research, and clinical computer programs for the normal and abnormal cardiovascular system.
2. Educational materials and approaches targeting self-directed or supervised exercise therapy for treatment and management of peripheral arterial disease.

H. Diagnostic and Theraputic Approaches.

1. Device-Related:
    a. Resuscitation-enabling technologies
    b. Robotics in treatment of cardiovascular disease. For example: treatment of congenital heart disease
    c. Computer-assisted surgery for treating cardiovascular diseases
    d. Point-of-care (POC) approaches and techniques
    e. Technologies targeting self-directed or supervised exercise therapy for treatment and management of peripheral arterial disease
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. Development of viral and non-viral vectors for gene therapy for cardiovascular diseases
    f. Pro- and anti-angiogenic and vasculogenic genes, proteins and drugs
3. Research:
    a. Approaches and technologies to measure lipid content in the blood
    b. Non-invasive methods of detecting cardiac rejection, particularly in infants and young children
    c. Non-toxic and selective molecular cages for delivering short-lived vasoactive agents to the vasculature

d. High-throughput assays or screening for cardiovascular research and disease detection

e. Non-invasive diagnostic tests. For example: salt sensitivity; vascular and renal tubular fluid dynamics

f. Heart failure, early detection and treatment strategies

g. Anti-hypertensive drugs from natural and synthetic sources

h. Vaccines for the prevention or treatment of atherosclerosis or other cardiovascular diseases

I. 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.
3. New medical imaging systems, enhancements 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. Specific agents for high resolution 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.

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 diseases, asthma, cystic fibrosis, control of breathing, bronchiolitis, respiratory neurobiology, sleep, and other adult airway diseases.

Lung Biology and Disease Branch. Supports research, education, and training programs in lung cell and vascular biology; lung growth and development and pediatric lung disease; acute lung injury and critical care medicine; interstitial lung diseases, including pulmonary fibrosis and sarcoidosis; and AIDS and tuberculosis.

National Center for Sleep Disorders Research. Focuses on basic research using state-of-the-art approaches to elucidate the functions of sleep and the fundamental molecular and cellular processes underlying sleep; 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.

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. Imaging techniques to monitor lung cell functions in vivo.
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. Use of ambulatory monitoring techniques to diagnose and manage respiratory disorders of sleep.
10. Computerized tomography to quantify and monitor pulmonary disease processes.
11. Novel methods for bioassays.
12. Methodologies that provide an objective and semi-quantitative assessment of sleepiness in children.
13. Non-invasive imaging technologies to assess neurophysiological and regional brain blood flow changes associated with sleep disorders and other causes of excessive daytime sleepiness.

B. Information and Health Education Tools.

1. Computer 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 in infants and children.
6. Use of interactive and computer technology to teach self management to asthma and chronic obstructive lung disease patients.
7. Health education interventions on the recognition, management, or prevention of problem sleepiness and sleep disorders for the public, physicians, and other health care professionals.
8. Educational interventions to improve worksite productivity and school performance through the prevention and management of insufficient sleep and poor sleep environment conditions.
9. Methods to improve patient compliance with sleep disordered breathing treatments.
10. 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.
11. Develop and test novel and effective approaches to increase patient and/or provider adherence to clinical practice guidelines for management of lung diseases and sleep disorders.
12. 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.
4. Improved devices for continuous oxygen administration, including airline travel.
5. Improved extracorporeal or implantable devices for blood gas exchange (artificial lung).
6. 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.
7. Personal exposure monitors for aeroallergens and other environmental pollutants.
8. Personal exposure monitors for measures of environmental exposures.
9. Thrombo-resistant materials for extracorporeal or implantable devices for blood gas exchange and for indwelling catheters.

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 lung stem cell types.
8. Identify species and strain differences of Pneumocystis carinii.
9. Isolate, identify, and characterize cells found in pulmonary granulomas.
10. Methods to monitor levels of alertness or sleepiness continuously over extended periods of time.
11. Three-dimensional static, mathematical, cell culture models of airways and alveoli to define parameters determining aeropollutant absorption, deposition, and effects.
12. Develop technologies and tools for use in genomic or proteomic investigations of pulmonary diseases.
13. New technologies and instrumentation scaled for high-throughput phenotypic characterization of sleep in animal models.
14. High volume, inexpensive assays to assess variations in gene expression related to circadian and behavioral state (sleep and wakefulness).
15. Methodologies that are practical for the objective measurement of both physical activity and sleep duration for epidemiological research.

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, alpha1antitrypsin 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. Novel pharmacologic approaches for treatment of sleep apnea.
6. Pharmacological means of stimulating growth and repair of alveoli and reparative or restorative elastogenesis in lungs suffering emphysematous changes.
7. Countermeasures for excessive daytime sleepiness, including methods that alter the output of the circadian clock to optimize sleep and wakefulness.
8. New pharmacological agents for the treatment of sleep disorders, especially sleep disordered breathing.

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 immunde 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 Hemostatis 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, and clinical cellular medicine.

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, thalassemia, Fanconi anemia, Diamond Blackfan anemia, and other anemias.
   2. Bleeding disorders including: hemophilia, von Willebrand disease, and thrombocytopenia.
   3. Platelet diseases.
   4. Thrombosis and thrombolysis.
   5. Hereditary hemorrhagic telangiectasia.
   6. Paroxysmal nocturnal hemoglobinuria.
   7. Hemochromatosis.
   8. Myelodysplastic syndrome (MDS) and myeloproliferative disorders (MPD).
   9. Hematologic malignancies.

B. Animal models for complications associated with transfusion of blood products or cell-based therapies.
   1. Transfusion Related Acute Lung Injury (TRALI).
   2. Alloimmunization.
   3. Transfusion-transmitted infections such as Transmissible Spongiform Encephalopathy (TSE).
   4. Idiopathic Pulmonary Syndrome.
   5. Graft versus Host Disease.

C. Animal models for the demonstration of safety and efficacy of novel cellular therapies.

D. Tools, reagents, and assays for hematologic translational research.
   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. Iron overload.
   8. Blood-borne infectious agents transmitted by blood transfusion, including agents of transmissible spongiform encephalopathies such as variant Creutzfeldt-Jakob Disease (vCJD).
   9. Diagnosis of inherited blood disorders.
   10. Prolonging the in storage of transfusable blood components for therapeutic uses.
   11. In vitro inactivation or removal of microorganisms and other infectious moieties from blood, blood components, and plasma derivatives.
   12. Platelet storage methods that preserve biological efficacy.
   13. Synthesizing, screening, and evaluating the safety and efficacy of therapeutic oxygen carriers.
   14. Synthesizing or purifying plasma proteins for therapeutic use.
   15. Measuring iron non-invasively.
   16. Non-invasive measurement of blood cell counts or other blood components.
   17. MHC haplotype determination by methods such as DNA fingerprinting techniques and single nucleotide polymorphisms.
   18. Tracking of engrafted cells using imaging and/or other techniques.

F. Drugs to Treat Hematologic Diseases and Cytopenic States.
   1. Anti-coagulants.

2. Anti-thrombotic agents.
3. Anti-sickling agents or other pharmacologic approaches to sickle cell disease.
4. Fetal hemoglobin enhancing agents.
5. Fibrinolytic and anti-fibrinolytic agents.
6. Iron chelators.
7. Replacement agents for hematologic factor deficiencies.

G. Cellular Therapies.

1. Expansion of cell populations.
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.

H. Gene therapy vectors and delivery systems for the treatment of hematologic genetic diseases.

I. Prothrombotic and hemorrhagic biomarkers and risk factors.

J. Computational models for blood diseases and complications associated with transfusion of blood products and cellular therapies.

K. Bioinformatics to store and analyze genes, proteins, and biomarkers for hemostasis.

L. Equipment and procedures for the collection, separation, processing, preservation, storage, and distribution of blood and blood components and other cell therapies.

M. Patient and physician health education programs to improve patient management and to prevent or reduce the impact of blood diseases.

N. 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.

O. Newborn Screening.

1. Genetic counseling programs for families of infants with hemoglobinopathies or trait.
2. Innovative data or surveillance systems to track follow-up and patient outcomes.

Prevention and Population Sciences

The NHLBI Division of Prevention and Population Sciences (DPPS) supports and provides leadership for population- and clinic-based research on the causes, prevention, and clinical care of cardiovascular, lung, and blood diseases and sleep disorders. Research 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 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 also supports training and career development for these areas of research. The Division has three branches: the Epidemiology Branch, the Clinical Applications and Prevention Branch, and the Women's Health Initiative Branch.

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.

Research topics of interest to the Division of Prevention and Population 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 reducing clinical inertia in implementation of evidence-based guidelines for control of cardiovascular risk factors, including hypertension.
3. Approaches to improving care of cardiovascular patients transitioning from hospital to ambulatory or home care.
4. 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. Clinical trial methodologies.

C. Community education and demonstration research studies.

D. Studies of cardiovascular disease information, education, prevention, and treatment systems for use in primary medical care and home care, including care by family caregivers.

E. Interactive databases.

F. Measures of patient adherence/compliance.

G. Assessment of polypharmacy, particularly for the elderly.

H. Methods.

1. Lifestyle intervention, including matching patients to lifestyle, intervention, or treatment.
2. Health-care systems and outcomes research, including development of new quality measures for evidence-based cardiovascular health care.
3. Quantitative measurement systems for behavioral and lifestyle variables, e.g., diet and physical activity.

I. Models of behavior modification and other approaches to behavior change.

J. Interventions in patients to promote healthy lifestyles, adherence to medications, and cardiac rehabilitation, including stress and exercise.

K. Preventative Approaches.

1. Nutrition and dietary interventions and products.
2. Technologies to control weight.

L. Treatment agents or strategies, including medications and devices.

M. Assay systems/techniques to measure patient responses to behavioral or medical interventions.

N. Materials, equipment and software for enhanced medical Imaging systems.

O. Methods for communication of research results.

P. Methods for collection, transmission, management and analysis of clinical data.

Q. Nutrition, physical activity, obesity, stress reduction and smoking cessation interventions.

R. Nutrition and physical activity measurement methods and devices.

S. Population tracking mechanisms.

T. Psychosocial measurement instruments, especially in minority populations, including chronic social stress, depression, and discrimination.

U. Communication techniques for minority and low-income populations.

V. Prognostic assays.

W. Quality of life measurement and analytic methods.

X. Software.

1. Clinical trials.
2. Epidemiology studies.
3. Literature abstracting.
4. Meta-analysis
5. Statistical analysis.
6. Shared clinical decision-making.
7. Monitoring and providing feedback to patients and providers in clinical care settings.
8. Analysis of context-dependent genetic effects.
9. Longitudinal data analysis
10. Microarray data analysis.
11. Automated systems for genotyping quality control and error checking.

Y. Screening, assessment, and tracking tools including biomarkers for hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases.

Z. Survey questionnaires.

AA. Training techniques and modules.

BB. Interactive web-based programs for health promotion.

CC. Computerized systems to support evidence-based clinical practice in prevention and treatment of hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases.

DD. Biomarkers for long term exposure to environmental factors including diet, physical activity, smoking, alcohol, and contaminants.

EE. Measures of gene expression in individuals.

FF. Cell immortalization, storage and distribution service.

GG. Standardized assays of glycosolated hemoglobin.

HH. Better measures of impaired glucose tolerance.

II. Simplified measures of sleep useful for population based studies.

JJ. Better measures of heart failure, including diastolic heart failure.

KK. Measures of small vessel disease.

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

For additional information on research topics, contact:

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NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)

The scientific community now has available to it an extensive and large data set of genome resources and tools. The finished genomic sequences of many model organisms, the draft genomic sequences of

human, mouse and rat, and the finished genomic sequences of a number of human chromosomes have been published. In addition, many other tools and technologies that allow these resources to be exploited are available, including microarray technologies and thousands of sequenced full-length cDNAs generated by the Mammalian Gene Collection. These resources can be used in creative and powerful ways to facilitate our understanding of human biology.

With the completion of many of the original goals of the Human Genome Program, the NHGRI unveiled its vision for the future of genomics in April 2003 (http://www.genome.gov/11007524). The vision has three major themes- (1) genomics to biology; (2) genomics to health; and (3) genomics to society. There are also six cross-cutting areas which support the vision: technology development, computational biology, resources, training, education, and ethical, legal and social issues.

The success of the Human Genome Project has been due in large part to the development of improved technologies, strategies and methods that can be applied on a genome-wide scale in a cost-effective manner. As the vision of genomics expands, the development of new and improved technologies will be even more important in helping to accomplish the NHGRI's new research goals. Therefore, the NHGRI solicits SBIR/STTR grant applications in the areas listed below. Innovative and new approaches in other areas not listed in the major topics below, but that are relevant to genomics, will also be seriously considered.

DNA Sequencing

The ultimate goal of the DNA sequencing technology program is to develop technologies that can generate accurate DNA sequence from whole genomes in a short time and at a very low cost (e.g., $1000 for a mammalian-sized genome). To achieve that, more near-term goals include the development of innovative, cost-effective technologies and strategies to (1) reduce the cost, increase the throughput, or improve the accuracy of large-scale DNA sequencing of complex genomes; (2) obtain DNA sequence in the gaps that are left by current sequencing methods or improve the efficiency of sequencing in genomic regions that have proved difficult to sequence due to limitations in available cloning and sequencing technology; (3) determine sequence in regions of difference between closely-related organisms; (4) determine the sequence of any particular region of a genome and its syntenic regions from genomes of several other species; (5) rapidly and cost-effectively determine the sequence of one or more large (megabase) genomic regions from many individuals of a single species (e.g., human) for mutation detection; and (6) rapidly and cost-effectively resequence entire genomes to detect polymorphism. Instrumentation and methods development from feasibility through prototype development and introduction into production are supported. Any applicable technology approach is welcomed; micro- and nanotechnology approaches are particularly encouraged.

Human Genome Sequence Variation

Development of new or improved methods and analytic tools for: (1) the large-scale identification, scoring, and interpretation of DNA sequence variants; (2) the identification of haplotypes and generation of haplotype maps; and (3) facilitation of studies relating genetic variation to association with disease, to gene mapping, and to an understanding of chromosomal and population processes.

Comparative Genomics

Improvement in the technology for generating clone libraries useful for genomic analysis with DNA inserts that are stable, free of artifacts, and faithfully representative of genomic DNA from complex organisms. Also of high priority is the development of technology to generate physical maps efficiently and rapidly.

Functional Genomics

Development of new or improved technologies for large-scale or genome-wide approaches relating to: (1) gene discovery, full-length cDNA synthesis, or gene expression analysis; (2) improved or new technologies that are more efficient for isolating cDNAs for mRNAs that are rare or long (>4kb), or both; (3) analysis of the products of gene expression (e.g., proteins, metabolites), their identification in biological samples, their modifications, their interactions; (4) functional analyses of non-coding sequences; (5) generation and detection of mutations; and (6) innovative instrumentation used in screening for chemical modifiers of function, i.e., chemical genomics. Micro- and nanotechnology approaches are particularly encouraged.

Bioinformatics and Computational Biology

Development of new or improved tools for: (1) obtaining, representing, analyzing and archiving data; (2) assembling sequence data; (3) extracting information from comparative genomic sequences; (4) improving databases, in the areas of DNA sequence, gene mapping, complex trait analysis, genetic variation and homology, and functional genomics; (5) editing and implementing controlled vocabularies for genomic and phenotypic information; and (6) integrating genomic and genetic data for the purpose of identifying and modeling genetic pathways and networks.

Bioinformatics Education

Development of new educational curricula and tools to facilitate the teaching of (1) bioinformatics to high school and college students and (2) genomics, genetics, and bioinformatics approaches to understanding human biology and disease to physicians.

Ethical, Legal and Social Implications (ELSI) of Genomics and Genetics Research

Examination of issues surrounding the commercialization of genetic technologies, including issues relating to patenting, licensing, and other intellectual property concerns.

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:

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NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

The mission of the National Institute of Mental Health (NIMH) is to diminish the burden of mental illness through research. To achieve this goal, the NIMH funds basic research, translational research, clinical studies, and services delivery research concerning any aspect of behavioral and mental disorders (including HIV prevention and neuro-AIDS research). Ultimately, this research will lead to greater understanding, better treatment and rehabilitation or prevention of mental disorders. The NIMH is also concerned with the speedy dissemination and use of this knowledge through scientific communications and public education, and in its more effective implementation in practice and service delivery systems. There is a general need to develop reliable and inexpensive products, that can serve these needs.

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:

1. Innovations in Biomedical Computational Science and Technology: SBIR/STTR Initiative
   http://grants.nih.gov/grants/guide/pa-files/PAR-06-535.html (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PAR-06-534.html (STTR)
2. Development of PET and SPECT ligands for brain imaging
   http://grants.nih.gov/grants/guide/pa-files/PA-06-017.html (SBIR)
   http://grants.nih.gov/grants/guide/pa-files/PA-06-018.html (STTR)
3. Pharmacologic Agents and Drugs for Mental Disorders
   http://grants.nih.gov/grants/guide/pa-files/PA-06-027.html (SBIR)

http://grants.nih.gov/grants/guide/pa-files/PA-06-028.html (STTR).

4. Development of Biomarkers for Mental Health Research and Clinical Utilities
http://grants.nih.gov/grants/guide/pa-files/PA-06-016.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-015.html (STTR)

5. Probes for Microimaging the Nervous System
http://grants.nih.gov/grants/guide/pa-files/PA-06-021.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-022.html (STTR).

6. Integration of Heterogeneous Data Sources
http://grants.nih.gov/grants/guide/pa-files/PA-06-011.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-010.html (STTR).

7. High Throughput Tools for Brain and Behavior
http://grants.nih.gov/grants/guide/pa-files/PA-06-023.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-024.html (STTR).

8. Bioengineering Nanotechnology Initiative
http://grants.nih.gov/grants/guide/pa-files/PA-06-008.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-009.html (STTR).

9. Novel Tools for Investigating Brain-derived GPCRs in Mental Health Research
http://grants.nih.gov/grants/guide/pa-files/PA-06-375.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-374.html (STTR)

10. Tools to Mitigate and Understand the Mental Health Effects of National Disasters
http://grants.nih.gov/grants/guide/pa-files/PA-06-335.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-336.html (STTR)

11. Small Business Innovation Research to Improve the Chemistry and Targeted Delivery of RNAi Molecules
http://grants.nih.gov/grants/guide/pa-files/PA-06-003.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-004.html (STTR)

12. Molecular Libraries Screening Instrumentation
http://grants.nih.gov/grants/guide/pa-files/PA-06-019.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-020.html (STTR)

13. Manufacturing Processes of Medical, Dental, and Biological Technologies
http://grants.nih.gov/grants/guide/pa-files/PA-06-013.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-012.html (STTR)

14. Therapeutics Development for HIV/AIDS-Associated Neuropsychological Disorders
http://grants.nih.gov/grants/guide/pa-files/PA-06-432.html (SBIR)
http://grants.nih.gov/grants/guide/pa-files/PA-06-433.html (STTR)

Phase II Competing Renewal Awards

(See http://grants.nih.gov/grants/guide/pa-files/PA-06-079.html.)

The NIMH will accept Phase II SBIR Competing Renewal grant applications to continue the process of developing technologies that ultimately require federal regulatory approval. Such technologies include, but are not limited to, pharmacologic agents and drugs, biological products, devices, vaccines, etc., related to the mission of the NIMH. This renewal grant should allow small businesses to get to a stage where interest and investment by third parties is more likely. Budgets up to $800,000 total costs per year and time periods up to 3 years may be requested for this Phase II Competing Renewal opportunity.

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-07-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 Competing Renewal grant.

The following examples would make appropriate topics for proposed NIMH SBIR Phase II 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.

Direct your questions about scientific/research issues to:

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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 transgenic 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 simulations of parts of neurons, neurons, circuits or even organisms to observe the manner in which these components interact. For example, simulations of individual organisms with constellations of particular traits that vary across individuals would allow analysis of their interactions and their impact on the population as a whole.
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). Improved techniques for path analysis when examining functional imaging datasets would also 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.
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.
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*. Both recording techniques and analysis techniques.
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.
7. *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. Due to its greatly increased use in recent years, technologies specifically focused on improving the utility of fMRI techniques are of particular interest.

1. Innovative agents and/or technologies to visualize brain connectivity and/or activity 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 quantitation 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 quantitation 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 MRI 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, etc).
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.

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 quantitating the low levels of bound ligands for quantitating 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. New approaches to study the multiple functions of particular proteins.
13. Tools to study post-translational changes in proteins (expression levels, post-translational modifications, etc.) in specified tissue compartments and subcellular domains.
14. Technologies to study functional entities within cells (e.g., green fluorescent protein approaches) and subcellular compartments.
15. Tools and approaches to study coordinate changes in genes and their functional relationship to phenotypes, including phenotypes associated with specific brain disorders.
16. Develop novel markers for elucidating how signaling cascades impact DNA transcription.
17. 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).
18. 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.
19. Develop novel techniques for isolating and identifying the structure of brain-derived membrane proteins.
20. 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.
21. New approaches to facilitate faster and more reliable screening of novel genes and gene products that may be up or down regulated due to the administration of pharmacological therapies for mental disorders (e.g.: antipsychotics and antidepressants).
22. Development of new and optimization of the existing methods for non-invasive quantitative detection of hormones in awake behaving 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 in generating behavioral models of 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 standardized behavioral tests 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 new technologies to study gene function and expression, including approaches to studying gene and protein expression at single cell resolution.
8. Development of embryonic stem (ES) cell lines from rodent strains (rats and mice) of relevance to behavioral research.
9. Development of technologies and approaches to facilitate the collection and distribution of ES cell lines containing mutations of potential relevance to behavioral research.
10. Develop methods for long-term storage of transgenic germ cell lines.
11. Develop technologies and approaches to aid in the renewal of founder colonies of transgenic mice from repositories of transgenic germ cell lines.
12. 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.
13. 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.
14. Develop methods to analyze and manipulate DNA structure to study epigenetic modifications and chromatin remodeling in brain tissue and neuronal populations.

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 special 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 (other than the usual screening for "markers").
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 neurimaging 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. Relevant 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 novel drug delivery systems.
9. Tools for Drug Development including neuroimaging (e.g., radiolabeled compounds) and development of animal models.
10. Pharmacological profiling (in vitro and in vivo) for potential therapeutic drugs.
11. 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 Pediatric Translational Research (DPTR) or the Division of Adult Translation Research (DATR) at NIMH.
12. Improving existing, and developing new, vectors for delivery of genes to the brain.
13. Development of novel therapeutic approaches based on drug-induced changes in gene promoter activity.
14. 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 behavioral assays.
15. 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 connections and the connections of structures not easily accessed in vivo.

J. ***Basic Behavioral Science.*** 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 are also needed to increase the accessibility and reliability of information made available to the research community.

1. *Methodological Research and Development*. There is a need to devise new ways of data collection, analysis, management and dissemination. The goal is to encourage research that will improve the quality and scientific power of data collected in the behavioral and social sciences, relevant to the mission of NIMH. Research that addresses methodology and measurement issues in diverse populations, issues in studying sensitive behaviors, issues of ethics in research, issues related to confidential data and the protection of research subjects, and issues in developing multidisciplinary, multimethod, and multilevel approaches to behavioral and social science research is particularly encouraged.
    a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.
    b. Computer software to ease analysis of behavior monitored by video or telemetry systems.
    c. Innovative computer-based observation techniques, and computer software and hardware that allow on-line methods for characterization of a person's behavioral or physiological responses to group 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. There is a need for the development of hardware for time-stamped diary collecting instruments for use in actigraph studies of circadian rhythms in adults, children, and adolescents. Diaries are critical for the evaluation of activity data, and time-stamped diary collecting instruments can ensure investigators of receiving reliable information.

h. Web-based software tools for designing, updating, sharing, linking, and searching databases containing detailed information about the methodology and results of behavioral science studies.

2. Diagnosis and assessment of emotional and psychological states such as automated methods to detect specific emotional states using behavioral and autonomic indicators.

a. *Physiological Monitoring*. Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for behavioral clinical research would include developing:

i. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.

ii. New techniques for electrophysiological images from the level of the single cell and surface EEG recording on the scalp.

iii. Small, portable automated systems to monitor eye function (e.g., pupil size, accommodation) and eye movements.

iv. Better portable sleep monitoring devices to enhance studies of sleep in human subjects, for use in basic research and/or clinical labs.

v. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real-time.

b. *Measurements of Infant Development Using Physiological and Behavioral Measures*.

i. Psychophysiological measures to evaluate infants during the first six months of life.

ii. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).

iii. Telemetry capability for non-invasive devices so that infants can be monitored for prolonged periods without interfering with their behavior.

iv. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.

c. *Behavior Monitoring and Analysis*.

K. ***Educational Tools.*** Neuroscience and basic behavioral science 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.

L. ***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 Pediatric Translational Research and Treatment Development

The Division of Pediatric Translational Research and Treatment Development 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 Tools:* 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. Biochemical, genetic, physiological and psychological tool development is welcomed.

a. Technologies to assess CNS effects of psychosocial or pharmacological 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. Measures that quickly, and reliably assess mental disorders that are co-morbid with other mental disorders or with substance abuse disorders.

e. New technologies to assess and validate occurrence of and injuries resulting from child abuse and neglect.

f. Behavioral and laboratory measures to define and assess specific impairment-related components of psychiatric disorders, e.g., cognitive dysfunctions in schizophrenia.

g. Biologically based technologies that will aid medical doctors in determining how a particular individual may respond to a particular 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.

h. 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. 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. *Methodological Research and Development*. There is a need to devise new ways of data collection, analysis, management and dissemination. Examples include:

   a. Instrumentation and equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions 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. Video-based instruction for prevention of mental disorders, to be used by parents or in school settings.

   f. 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.

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). Examples of the research support include: trials to establish the short- and long-term efficacy of interventions and off-label or innovative applications of established interventions.

1. *Pharmacologic Treatment Intervention.* Areas include clinical psychopharmacology, new/innovative applications for established treatments (off-label use), and somatic treatments. Also included are studies to determine the safety of interventions that have not been shown to be efficacious. It is expected that compounds have received IND approval and will be tested clinically in this program.

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.

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 in schools and community settings are also encouraged.

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, sleep and 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, research training and resource development in the etiology and pathophysiology of mental disorders of late life as well as the treatment and rehabilitation of persons with these disorders. Disorders studied include Alzheimer's disease and related dementias, psychotic disorders and schizophrenia, mood, anxiety and personality disorders, suicide, sleep disorders and eating disorders. Selected areas of emphasis include: development of more reliable and valid phenotypes, assessments and behavioral markers for late-life mental disorders,

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. Programs exist to develop new treatments for psychotic disorders and also for mood and anxiety disorders.

Traumatic Stress Disorders Research Program. This program is the DATR/NIMH point of contact for disaster/terrorism/biodefense-related research. The program supports research on biopsychosocial risk/protective factors for psychopathology after traumatic events and the development of interventions for PTSD in adults; and research spanning and integrating basic science, clinical practice, and health care system factors regarding mass trauma and violence (e.g. war, terrorism, natural and technological disaster), including interventions and service delivery targeting an array of relevant mental health concerns (distress, disorder, functional sequelae) in children, adolescents, and adults.

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.*** Modern equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.

   1. *Physiological Monitoring*. Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for clinical research would include developing:

      a. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.

      b. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real time.

   2. *Development of Adult Physiological and Behavioral Measures*.

      a. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and motor behavior).

      b. Telemetry capability for non-invasive devices so that adults can be monitored for prolonged periods without interfering with their behavior.

      c. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psycho-physiological measure(s) of interest.

      d. Automated methods to detect specific emotional states using behavioral and autonomic indicators in adults.

   3. *Behavior Monitoring and Analysis*.

a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.

b. Computer software to ease analysis of behavior monitored by video or telemetry systems.

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 are also needed to increase the accessibility and reliability of information made available to the research community.

1. *Assessment Tools*.

a. New technologies to assess and validate occurrence of and injuries resulting from physical and sexual abuse or from trauma as a result of terrorism or natural disaster

b. Technologies to assess CNS effects of psychosocial variables and interventions.

c. Innovative approaches to assessing mental disorders using new statistical and psychometric techniques such as Item Response Theory.

d. Computerized methodologies for assessing various mental disorders suitable for use in primary care settings.

e. Inexpensive methodologies or techniques for assessing adherence to medication regimens.

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 trails.

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. Studies to validate new biomarkers or predictors of therapeutic response to pharmacological interventions.
3. Development of novel somatic treatments or medical devices for the treatment of mental illness.
4. Development of biomarkers or predictors of treatment response or side effects of therapeutics.
5. Development of new approaches to understand and predict the types, rates and pathophysiology of adverse effects of psychotropic medications.
6. New approaches to understand age-related changes on the emergence of adverse effects from psychotropic medications.
7. 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.
8. New methods to predict and assess the effects of psychotropic medication on cerebrovascular and cardiovascular function.
9. 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 and Health and Behavior Research (DAHBR)

The DAHBR supports research and research training to develop and disseminate behavioral interventions that prevent HIV/AIDS transmission, understand and alleviate the neuropsychiatric consequences to HIV/AIDS infection and, using a public health model, supports studies to reduce the burden of mental illness from medical co-morbidities, non-adherence to treatment, stigma and health disparities, including but not limited to research associated with HIV/AIDS. Two main research components make up this division: The Center for Mental Health Research on AIDS and the Health and Behavior Research Branch. Specific topics related to these two research areas are listed below. Inquiries are encouraged.

THE CENTER FOR MENTAL HEALTH RESEARCH ON AIDS:

A. ***Behavior Change and Prevention Strategies.***
To reduce HIV transmission especially among minority populations and hard to reach subsets of those populations.

1. Training
   a. Use of technology to develop and/or disseminate curricula for training clinicians and other health care practitioners in the prevention and treatment of HIV-related mental disorders.
   b. Innovative approaches to the development and/or dissemination of curricula for training in multicultural issues and development of cultural competence in HIV risk assessment, counseling and prevention.
   c. Development of low cost strategies to assist community-based organizations in using computers to educate hard to

reach populations about HIV risk and prevention.

d. Curricula, computer software and virtual reality programs that provide communication skills, training and role-play exercises for HIV risk reduction.

2. Community-based

a. Development of school-based curricula to promote HIV prevention by educators and teachers.

b. Dissemination of HIV prevention materials to be used in community based outreach programs for special populations (school dropouts, homeless, street youth, incarcerated youth).

c. Development of strategies or application of technology to assist organizations in identifying and implementing proven HIV prevention strategies and in addressing health disparities.

d. Development of innovative approaches to reduce stigma often expressed toward individuals with HIV/AIDS

e. Novel systems for distributing, dispensing, or administering antiretroviral drugs that are designed to enhance patient adherence to these regimens

f. Systems that improve adherence to medical care among HIV patients by enhancing patient management of medical appointments, prescription refills, and medication dosage requirement.

3. Primary care

a. Development of print and/or computer based materials to assist primary care practitioners in informing their patients about HIV risk and prevention.

b. Development of materials and other programs to assist health care practitioners in improving patient adherence to medical and lifestyle regimens.

c. Computational systems that physicians and researchers can use to model the development of drug resistance based on rates of patient adherence to antiretroviral medications.

d. Informatics that screen patients for medication adherence and risk behavior and integrate these reports into the provision of routine medical care.

e. New tools and methods that physicians and researchers could use to monitor patient adherence to prescribed antiretroviral medication regimen in real time.

4. Risk Reduction

a. Development of methods to reduce, prevent and/or change HIV-associated and STD risk behaviors.

b. Novel approaches to address the issue of relapse prevention of HIV-associated risk behaviors.

c. Methods to increase use of HIV testing and facilitate effective test result obtainment, confirmation and counseling.

d. Development of new behavioral strategies to reduce high risk behavior among persons recently infected.

e. Web-based networks and software for the dissemination, identification, and tailoring of effective behavioral interventions targeting at-risk populations.

f. Electronic systems that will facilitate participant scheduling, tracking, and retention in clinical trials and longitudinal studies.

g. Innovative approaches for assessing HIV sexual risk behavior among research study participants and at-risk populations, including biomarkers.

B. ***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: 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. 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.

C. ***AIDS Mental Health Services Delivery.***

1. Video and computer-assisted methods to train health and mental health care providers in the psychosocial and neuropsychiatric aspects of HIV infection and AIDS.
2. Development of methods to assess functioning in families in which there is an HIV infection in order to develop improved treatment modalities.
3. Development of novel programs to train people infected with HIV in self-care management and identification of stress and development of improved coping strategies in order to improve quality of life.
4. Development of novel programs to help people recognize and seek treatment of mental health problems arising from living with HIV/AIDS as a long-term chronic condition.
5. Development of information, instruments or methodologies to improve and/or track adherence to complex HIV/AIDS drug therapies for Hispanic and African American populations.
6. Development of innovative approaches to link researchers with community providers in the implementation of research-based HIV prevention efforts at the community level.
7. Develop rehabilitative approaches to alleviate HIV-associated neurodevelopmental abnormalities that may restrict children's academic achievements and quality of life.

HEALTH AND BEHAVIOR RESEARCH:

The Health and Behavior Research Branch supports research on a range of health behaviors in people with mental disorders. Research is supported on identifying potent, modifiable risk and protective factors for mental disorders that may guide the development and initial testing of theory-driven interventions. Interventions may be prevention, treatment, or rehabilitation and include biological, pharmacological, behavioral, psychosocial, or environmental components. Research is supported on co-morbid mental and other physical disorders, adherence to interventions for mental disorders, ethics in mental disorders research, mental disorders stigma and discrimination, mental health disparities, health behavior change in people with mental disorders, and functional assessment in people with mental disorders. Areas of emphasis include:

- Identifying the potent, modifiable mechanisms and processes linking mental and medical illnesses (comorbidity) and developing early stage interventions.
- Translating findings from basic behavioral research into processes to improve adherence to treatment, discourage harmful behaviors associated with mental disorders and physical disorders, and promote

therapeutic alliances and help-seeking behaviors.

- Identifying effective strategies for reducing mental illness stigma and discrimination, and examining the mechanisms through which they work.
- Studying cognitive processes, decision-making, and other basic behavioral and social processes to clarify factors that influence the choice of treatment or mental health services, acceptance or denial of illness, and coping response to stigma.
- Developing behavioral strategies for assessing mental health functioning and disability.
- Using findings from basic behavioral and social sciences research to elucidate factors involved in mental health disparities.

A. ***Adherence Research Program.*** This program supports studies of factors that influence decisions and behaviors related to adopting and adhering to treatment and preventive interventions (including person related, disease related, and treatment related factors and treatment alliance issues). The program also supports empirical studies of informed consent, research ethics, the development and testing of measures of adherence and behavior change, and epidemiological studies of risk factors for good or poor adherence.

B. ***Behavior Change Research Program.*** This program supports research on basic behavioral processes (such as cognition, emotion, decision-making, and motivation) to improve our understanding of the etiology and course of health behaviors among people with mental disorders. It also facilitates the development of behavioral and psychosocial interventions aimed at changing health behaviors among people with mental disorders to improve functional outcome and to reduce morbidity and mortality associated with mental disorders.

C. ***Comorbidity Research Program.*** This program supports research on mental disorders and their relationship to other physical disorders and behavior. Emphasized are: (1) the development of reliable and valid assessment approaches to identify comorbid disorders accurately; (2) epidemiology to elucidate the potent, modifiable mechanisms and processes linking mental and other physical disorders; and (3) the development and early testing of innovative interventions — prevention and treatment — targeting these potent, modifiable mechanisms and processes.

D. ***Functional Assessment and Mental Disorders Program.*** This program supports research on the translation of findings from basic behavioral and social science research to improve the definition and assessment of functioning and disability in people with mental disorders. The goal of the program is to encourage the further translation of knowledge gained from assessment approaches into innovative interventions for both prevention and treatment in order to improve function and reduce disability in people with mental disorders.

E. ***Stigma and Health Disparities Program.*** This program is concerned with mental illness stigma and discrimination and mental health disparities. It supports research to understand better the processes underlying stigma and discrimination; to develop effective strategies and approaches for reducing stigma and discrimination; and to examine media influences on attitudes about mental illness and its treatment. In the area of health disparities, the program supports research to examine the influence of social, cultural, and environmental factors on diagnosis, help-seeking decisions and preferences, and the helping relationship. It also supports examinations of the mechanisms through which social, cultural, interpersonal, and environmental factors affect disparities in risk for and course of mental disorders.

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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 comprised of three branches: Services Research and Clinical Epidemiology Branch, Adult and Geriatric 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 2007 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"* (http://www.nimh.nih.gov/council/TheRoadAhead.pdf). 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.

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).

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: (a) 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.

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.

For further information on Services and Intervention Research contact:

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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 killers and disablers such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, stroke, epilepsy, and autism are well known. Other disorders we study may be known only to the patients and families affected, their doctors, and scientists who look to rare disorders for help in understanding the brain as well as treating more common diseases.

Phase II Competing Renewal Awards

NINDS will accept Phase II 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 $750,000 per year in direct costs or $1,000,000 per year in total costs.

The following examples would make appropriate topics for proposed SBIR or STTR Phase II 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 (but are not limited to): pharmacology studies aimed at evaluating the potential therapeutic activity and side effect profile of drug candidates, and their efficacy following chronic dosage; 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 Dr. Randall Stewart (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-07-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 II Competing Renewal applications that do not propose to develop products that require regulatory approval, or that exceed the direct or total cost budget caps, will be withdrawn from consideration prior to peer review.

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Examples of research topics within the mission of the NINDS that may be of interest to small businesses are shown below. For additional information about areas of interest to the NINDS, please visit our home page at http://www.ninds.nih.gov.

Extramural research is organized in the following programmatic areas within NINDS: clinical trials, neurogenetics and neurodevelopment, repair and plasticity, systems and cognitive neuroscience, channels, synapses and circuits, neurodegeneration, neural environment, and technology development. Specific areas of interest are listed below:

Clinical Trials

The NINDS is committed to identifying effective treatments for neurological disorders by supporting well-executed clinical trials. SBIR applicants are strongly encouraged to contact Dr. Scott Janis (contact information provided below) within NINDS Clinical Trials Group for advice about potential clinical trial proposals *prior* to submission in order to determine the relevance of the proposed research to the NINDS and its potential for translating discoveries to clinical interventions for neurological disorders.

Pediatric Brain Imaging

1. Development of computer software to permit reconstruction of magnetic resonance imaging (MRI) from unrestrained patients or animals that may change position within the MRI magnetic field.

2. Development of technology to assess fetal neurological integrity such as fetal MEG.
3. Non-invasive monitoring of brain function such as improvements in PET imaging, MRI imaging and spectroscopy, and methods of optical imaging such as development of near infrared spectroscopy (NIRS) for monitoring of changes in cerebral oxygen saturation, cerebral blood flow and volume, and oxygen utilization in the brain, and for functional imaging utilizing scattering and absorption characteristics of brain tissue.
4. Non-invasive techniques for structural imaging, such as near infrared imaging.
5. Development of computerized histological tomographic brain atlas graphics, which can be stored and manipulated on a personal computer for teaching, research data modeling and display, and correlation with clinical neuroimaging.
6. Development of practical imaging modalities in extremely ill very low birth weight infants.
7. Non-invasive techniques for assessment and continuous bedside monitoring of cerebral function in the neonate, such as, but not limited to, functional near infrared spectroscopy and amplitude-integrated EEG.
8. Development of improved technology for MRI imaging of infants and small children, for example, specially designed pediatric sized head coils, or devices to minimize movement artifact in unsedated infants.

Neurogenetics and Neurodevelopment

A. *Cell lineages in the nervous system*

1. Analysis of central nervous system cell lineages for treatment of development and degenerative disorders.
2. Development of embryonic stem cell models of nervous system development and function.
3. Development of methods for identification of specific neural cell lineages.

B. *Brain tumors*

1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of CNS tumors.
2. Advancement of molecular analysis of DNA, RNA and protein in CNS tumors.
3. Surrogate markers for cerebrovascular, immune, and infectious diseases and CNS tumors.
4. Techniques for brain specific antisense, gene and protein transfer into cerebrovascular, neurons, or glial cells in brain tumors.
5. Methods to deliver brain specific proteins and genes through the blood-brain and blood-CSF barriers for targeting CNS tumors.
6. Mass spectrometry for the analysis of protein in the CNS and in brain tumors.
7. Highly specific radiolabeled markers for different types of brain tumors that can be used under histopathological or brain imaging conditions.
8. Refinement of functional, structural and metabolic imaging techniques for brain tumors.
9. Methods and devices for high throughput genomic and proteomic expression and data analysis in brain tumor.

C. *Gene Expression/Proteomics*

1. Development of technology for the production of high quality cDNA libraries from small tissue samples of the brain during development and in response to disease, injury or pharmacological agents.
2. Identification of optimal DNA vector systems to standardize and expedite the sequencing of cDNA libraries derived from micro dissected brain tissues.
3. Development of technology for micro dissection of brain tissue for single cell analysis of gene expression.
4. Development of informatics systems to expedite the analysis and use of sequence data that will be derived from projects to identify novel genes and to map temporal and spatial dimensions of gene expression in the brain.
5. Development of proteomics technologies to quantitatively detect levels of expression, post-translational modifications, and subcellular distribution of proteins in the nervous system.

6. Development of technology to detect and quantify metabolite (carbohydrates, lipids, peptides) changes in the nervous system.
7. Development of in vitro methods to either fractionate membrane proteins or express recombinant membrane proteins at sufficient levels for proteomics analyses.
8. Development of technology for single-cell analysis of neurons and glia to detect dynamic changes in the transcriptome, proteome, and metabolome.

D. *Other*

1. Development of methodologies to deliver therapeutics (gene vector, drugs, enzymes) across the blood-brain-barrier.
2. Improved methodologies for creating transgenic animal models for diseases in the nervous system.
3. Development of an intracranial pressure monitor.
4. Improved methods to deliver neurotrophic factors and other small proteins or peptides normally found in the brain.

Repair and Plasticity

A. *Neural Prostheses and Deep Brain Stimulation*

1. Design, development, and evaluation of neural recording and stimulating microelectrodes for neural prostheses and deep brain stimulation.
2. Development of thin, insulating coatings to make implanted electronic packages impervious to the corrosive action of body fluids and tissues.
3. Development of transducers of position, touch, and force for use in functional electrical stimulation systems.
4. Development of addressable arrays of sub-micron or nano-scale dimension electrodes for use in the CNS.
5. Non-invasive methods to focally stimulate small populations of neurons within the body.
6. Development of communication aids for individuals with “locked-in syndrome.”
7. Development of a complete system utilizing existing microelectrodes, lead wires and telemetry to transfer neural signals outside the body.
8. Develop new high charge density electrode materials.
9. Development of a method to repeatedly inhibit neuronal electrical activity in a safe and effective manner.
10. Development of a non-invasive method of selectively stimulating and/or inhibiting small groups of nerve fibers within a nerve trunk.
11. Development of materials to minimize scarring following surgery in the central nervous system.
12. Development of techniques for precise functional placement of microelectrodes within the central nervous system.
13. Development of neural controllers to restore micturition and defecation for individuals with spinal cord lesions.
14. Development and implementation of automated signal processing algorithms in hardware or software capable of neural signal analysis for neural prosthetics applications.
15. Development of novel nerve cuff electrode or nerve interface technologies capable of selective stimulation and/or recording from intact afferent and efferent nerve bundles.

B. *CNS Trauma and Rehabilitation*

1. Means of assisting or achieving restitution of function after injury to the nervous system.
2. Develop transgenic, knockout and inducible knockout animal models for stroke and CNS trauma research.
3. Develop technology for data gathering and analysis for assessment of multiple parameters of ICU recording in brain trauma.
4. Develop instruments or techniques to enhance monitoring of nervous system activity during surgical procedures, aimed at improving the safety, targeting or efficacy of those procedures.
5. Develop new preclinical testing for promising therapies for acute and chronic central nervous system injury.

6. Establishment of networks to test pharmaceutical agents in animal models of CNS trauma.
7. Development of monitors for such modalities as intracranial pressure, brain temperature, and cerebral blood flow.
8. Develop drugs or other agents to reduce scarring after spinal cord injury.
9. Develop and test novel biological assays for use as diagnostics in acute stroke (ischemic vs. hemorrhagic), traumatic brain injury, and spinal cord injury.
10. Development of high- or middle-throughput screening systems, and their validation as useful to efficiently assess libraries of potential therapeutics for brain, spinal cord or peripheral nervous system injury.
11. Develop portable hand-held technology for the diagnostic assessment of brain injury.

C. *Neuroimaging*

1. Development of ultrasound imaging methods for the central nervous system.
2. Develop methods and reagents that allow tracking of grafted cells in the living host animal using non-invasive imaging methodologies.
3. Development of imaging techniques to track the course of injury and repair following spinal cord injury.

D. *Stem Cell Biology*

1. Development of a website and database for posting and discussion of protocols and best practices used in harvesting, maintaining in culture, and inducing differentiation of stem cells.
2. Development of a stem cell repository for the storage of stem cells from different sources and immortalized cell lines, and for making these reagents readily available to the research community.
3. Develop efficient and reproducible methods for harvesting and storing stem cells for research use.
4. Develop markers, reagents, and new methodology for the identification and/or harvesting of stem and progenitor cells in the nervous system and in other tissues.
5. Develop methods for phenotyping stem and progenitor cells in the nervous system.
6. Use of mutant and transgenic mice or rats to study the effect of identified genetic alterations on neurogenesis in the adult central nervous system.

E. *Axonal Regeneration/Guidance and Synapse Formation*

1. Develop biomaterials to serve as paths for supporting or guiding axonal growth across a site of injury.
2. Develop methods to deliver neurotrophic factors, cells or genes to injured brain sites to enhance regeneration or restoration of function.
3. Develop biomaterials to promote sprouting and directed growth of axons toward specific sites in the central nervous system.
4. Develop biomaterials to promote dendritic growth and stability, and synapse formation in localized areas.

Systems and Cognitive Neuroscience

A. *Cognitive and Behavioral Neuroscience*

1. Development of computerized neuropsychological assessment tools to facilitate testing of neurologically impaired subjects.
2. Development of techniques and devices for imaging of small animals such as transgenic and knockout animal models of complex behaviors.
3. Design, development, and evaluation of automated systems for assessment of behavioral parameters.
4. Development of computer software that integrates imaging and physiological measures of brain activation.
5. Development of technologies to facilitate high-throughput analysis of behavior.

B. *Sleep Neuroscience*

1. New therapies for sleep disorders.
2. New methods to categorize sleep stages on line – especially in human infants and patients with EEG-distorting brain dysfunction.

3. New methods for quantifying optimal alertness.
4. Models of neurological sleep disorders.
5. Novel applications of evoked potentials to sleep neuroscience.
6. Further development of portable devices that facilitate cost-effective screening for potential sleep disorders, and can be used to monitor the progress of already diagnosed sleep disorders.
7. Applications of proteomic and/or metabalomic methods to detect sleep deprivation.

C. *Pain*

1. Development of objective methods for quantitative assessment of pain, including development of a quantitative sensory testing battery for pain patients.
2. Development of novel pain model systems, particularly more accurate pre-clinical experimental models.
3. Development of tools to elucidate potential analgesic targets, and models for testing and validating these for efficacy in patients.
4. Development of new diagnostic tools for different pain mechanisms and objective measures of analgesic drug action.

D. *Sensory-Motor Systems, Integration, and Rehabilitation*

1. Development of methodologies and tools for real-time analysis of sensorimotor neurophysiological events in vivo.
2. Development of innovative techniques for collecting large and multiple scales of neural signals from cortical and subcortical sensory and motor structures.
3. Development of innovative approaches for evoking sensory response of specific modalities by discrete stimulation of brain structures or pathways.
4. Development of reliable tools for quantitative assessment of sensorimotor performance in human and experimental animals.
5. Development of tools for therapeutic electrical stimulation for rehabilitation following stroke, or other disorders that disrupt normal sensory-motor functions.
6. Development of effective and practical approaches or strategies for transcranial magnetic or electrical stimulation of sensorimotor structures to facilitate post-injury reorganization.
7. Development of innovative approaches of facilitating sensorimotor functional recovery through robotic assisted motor learning.
8. Development of effective rehabilitation approaches for enhancing cognitive and sensorimotor performance through enriched virtual reality environment.

E. *Systems Neuroscience and Neuroimaging*

1. Development of tools to enhance visualization of specific brain markers.
2. Development of devices for artifact-free monitoring of vital neurological parameters during MRI procedures involving very high static and dynamic magnetic fields (greater than 2 Tesla) and high-energy microwave radiation typical of the MRI environment.
3. Development of functional imaging techniques.
4. Development of combined imaging strategies, i.e., fMRI and PET.
5. Development of radioligands for functional imaging of targeted molecules implicated in normal brain function and brain disorders.
6. Development of non-invasive optical imaging approaches
7. Development of software for improving interoperability of neuroimaging data.

Channels, Synapses and Circuits

A. *Epilepsy*

1. Devices for automated detection and quantification of seizures.
2. New therapies both for the control of seizures and for the prevention of the development of epilepsy.
3. New formulations and delivery systems for antiepileptic drugs.
4. New models of seizures and epilepsy useful for screening therapies.
5. Improved methods of monitoring compliance/medication dispensing.

B. *Muscular Dystrophy*

1. Development of minimally invasive diagnostic techniques for the muscular dystrophies.
2. Development and validation of the role of muscle imaging in diagnostic evaluation or as an endpoint measure for clinical trials in muscular dystrophy.
3. Evaluation of the efficacy of existing anti-inflammatory drugs for treatment of muscular dystrophy.
4. Therapeutic drug discovery for the range of muscular dystrophies.
5. Development of assistive devices for individuals with muscular dystrophy.
6. Development of standardized instruments to measure quality of life, cognitive, and central nervous system function for individuals with muscular dystrophy.
7. Development of optimized models for mechanistic studies of specific muscular dystrophies, including models appropriate for therapeutic development screens.
8. Development of cell-based assays that target aspects of pathogenesis and pathophysiology in the muscular dystrophies, to enable high throughput drug screening.
9. Development of high-throughput, small molecule screening efforts for promising therapeutic targets and identify novel targets for drug development
10. Determine the benefits and risks of varied exercise approaches in muscular dystrophies and develop scientifically based recommendations concerning optimal exercise, physical activity, and recreation.
11. Development of strategies to improve vocational outcomes and reduce social isolation of patients with muscular dystrophy.

C. *Channels and Synapses*

1. Medium to high throughput techniques for studying channels, transporters, receptors and synapses.
2. Development of tools, assays, and strategies to facilitate ion channel, receptor and transporter-related research.

Neurodegeneration

1. Development and preliminary testing of instruments, devices, or drugs that enhance diagnostic, treatment, or monitoring capabilities.
2. Identification or development of animal models for research on neurodegenerative disorders.
3. Development of early or presymptomatic diagnostic procedures for neurodegenerative disorders.
4. Epidemiology of neurodegenerative disorders.
5. New delivery methods of medications for degenerative neurological disorders.
6. Development of cell lines for in vitro modeling of neurodegenerative disorders.
7. Therapeutic drug discovery targeted to neurodegenerative disorders.
8. Development of drug screening assays, including biochemical, cellular or model organism assays for high-throughput screening approaches.

Neural Environment

A. *Infectious and Immune Disorders*

1. Development of therapies to prevent, arrest or reverse autoimmune neurological disorders such as multiple sclerosis.
2. Development of methods that aid the diagnosis of infectious and immune disorders.
3. Development of methods or vectors for the delivery of biologics (e.g., cytokines, DNA), drugs, and other agents to the nervous system.
4. Development and studies of drugs with high blood brain barrier permeability intended for treatment of CNS infections including HIV-related opportunistic infections.
5. Development of animal models for infectious and immune disorders (e.g., k.o. or transgenic mice, viral systems) that allow

the study and identification of the effect and contribution of genes to disease.

6. Development of techniques such as microarray, gene expression analysis or immunological techniques that allow the study and identification of the effect and contribution of genes to disease or the effect of therapies.
7. Development of techniques such as microarray, gene expression analysis or immunological techniques that allow studies on the mechanisms and effect of therapies.
8. Development of functional and other imaging techniques and tools, and of combinations thereof.
9. Development and evaluation of biomarkers for infectious and immune disorders.

B. *Stroke*

1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis, treatment, rehabilitation and recovery of stroke patients.
2. Develop methods or devices for the removal of blood clots in the ischemic CNS.
3. Develop and validate large and small animal models, including transgenic, knockout, and inducible knockout animals that reflect the complexity and diversity of the human brain and its responses during ischemia.
4. Develop brain specific gene and protein transfer methods that target cerebral vessels, neurons, and/or glia in the ischemic or hemorrhagic brain.
5. Develop instruments, devices or drugs that control inflammation in the prevention, diagnosis, treatment, and recovery of stroke.
6. Develop preclinical strategies to address the translational barriers in stroke research.
7. Expand brain imaging capabilities to include refinement of functional, structural and metabolic imaging techniques in the ischemic brain.
8. Develop bioinformatic databases for stroke to include sharing of clinical, genomic, and/or proteomic data.
9. Identify biomarkers for vascular, inflammatory, and immune diseases of the brain.
10. Develop and test combination therapies for stroke.
11. Develop instruments, devices, and methods to enhance drug delivery through the blood-brain or blood-CSF barrier.

C. *Prion Diseases*

1. Development of a rapid and sensitive assay for the detection of normal and variant prions as well as the detection and isolation of various prion strains.
2. Transgenic, knockout and inducible knockout animal resources for Transmissible Spongiform Encephalopathy research.

Technology Development

1. Neuroinformatics, including research, development and application of informatics tools to acquire, store, organize, archive, analyze, or visualize neuroscience and neurological data, particularly large quantities of complex and dynamic data, including clinical data.
2. Computational neuroscience, including the research, development and application of computational data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to studies of the nervous system.

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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

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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, 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 program, NCRR supports primary research to create and develop critical resources, models, and technologies.

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

Research and Development in Instrumentation and Specialized Technologies for Biomedical Research

A. 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, fluorescent or kinetic or laser spectroscopies, X-ray absorption/diffraction, electron or confocal microscopies, and flow cytometry.

B. Development of computer science/technology to study biomedical or behavioral research problems, e.g., computer visualization, computer modeling/simulation, structure-based drug design. Development of new bioinformatics technology infrastructure such as data management and analysis tools, networking infrastructure and collaborative tool development.

C. Development of novel technologies for proteomics and glycomics discovery, e.g., sample handing, separations, mass spectrometry, and computational tools for protein identification, data curation and mining.

Electron Microscopy, X-ray Diffraction, Other Topics
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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 embryonic stem cells (ESC), as well as fetal and adult stem cells from laboratory animals. Improved methods for causing ESC and other types of animal stem cells to differentiate along specific pathways in vitro and in vivo.

C. Development of improved reagents, techniques, and equipment for isolating, propagating and characterizing specific gene sequences cloned in bacterial artificial chromosome (BAC) vectors and for preparing and characterizing BAC libraries made from laboratory animals.

D. Development of improved reagents, techniques and equipment for preparing and analyzing full-length cDNA libraries made from tissues or cells of laboratory animals.

E. Development of new technologies to rapidly phenotype large number of mutant animals.

F. 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 Herpesvirus B in nonhuman primates.

G. Development of commercially valuable reagents for lower organisms or established cell cultures.

H. Development of cost-effective methods for culture and/or preservation of commercially

valuable organisms, including specific types of bacteria and other microorganisms.

I. 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.

J. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control.

K. 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.

L. Development and refinement of new technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.

M. Development of improved reproductive biology techniques (e.g., cloning techniques; embryo splitting) to produce genetically identical laboratory animals.

N. 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.

O. Development of improved reagents, techniques, and equipment for performing and analyzing the results of microarray experiments.

P. Development and refinement of technologies for the analysis of regulation of gene expression in a wide range of model organisms, including non-mammalian species. This could be accomplished by genetic means (e.g., transgenesis, conditional knock-out or knock-in) or epigenetic means (e.g., morphilinos, RNAi).

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Clinical Technology Applications

A. Development of patient-centered research technologies. This includes therapies, diagnostics, education, disease prevention techniques, sensors, and imaging technologies used for patient management, diagnosis, monitoring, safety, and treatment.

B. Diversification and development of methods used for clinical and translational clinical research, such as clinical tools, monitoring processes, evaluation tools, health literacy assessment and education implementation tools, patient safety risk assessment and mitigation tools, health care quality assessment tools, micro-analytical sensors, or imaging devices. Ultimate end users of the developed technology would include any of the following: researchers, physicians, other clinic providers, medical institutions, hospitals, urgent care or health care centers, clinics, laboratories, radiology centers, health care administrators, or patients.

C. Development of medical and health care informatics technology in clinical research: (1) information architecture and technologies that support health care information systems; (2) software, hardware, or web-based databases, information systems, protocol systems, health care data quality, security systems, and information tracking; (3) communication technologies; (4) wireless systems and infrastructure; (5) accessible and usable computing, and (6) decision-support systems.

D. Development of clinical research informatics: (1) collection, collation, and archiving of databases; (2) assuring compatibility with other databases; (3) protected storage and transmission of confidential medical data; and (4) software which facilitates the review or implementation of clinical and translational research protocols; (5) software and hardware to handle processing data from multiple and simultaneous clinical and translational research protocols across multiple clinical sites; and (6) methods and instrumentation to support clinical imaging data.

E. Miniaturization of existing biomedical technologies for adaptation to pediatric use.

F. Development of vehicles for drug delivery, including for patient groups with a potential for altered pharmacology or adherence, such as

children, the elderly, or persons with disabilities.

G. 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. This extends to the development of techniques, instruments, reagents and vector systems for use in clinical gene therapy protocols.

H. Development of high throughput technologies, methods, and techniques for studies of human diseases.

I. Development of techniques, instruments and reagents to optimize the recovery and quality of cells obtained from vertebrate and human organs for subsequent use in either basic research or clinical protocols.

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Development of Discovery-Oriented Software and Tools for Science Education

Development of new discovery-oriented educational software and the application of educational technology and tools for education on health science topics that targets K through 12 students and undergraduate students are sought. Topics can range from basic molecular and cellular biology to human diseases. Development of this software may be directed toward the adaptation of existing or recently developed educational programs for interactive learning. This effort is intended to yield efficient and user-friendly educational units for K-12 and undergraduate students that can be extended to enhance the health science literacy of the general public. A broad dissemination is strongly encouraged.

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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 practices 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 practices that are not currently an integral part of conventional medicine. The list of practices that are considered CAM changes continually as CAM practices and therapies that are proven safe and effective become accepted as "mainstream" healthcare practices. NCCAM groups these practices within four major domains of mind-body medicine (for example, meditation), biologically based practices (for example, herbal therapies, special diets), manipulative and body-based practices (for example, chiropractic, massage), and energy medicine (for example, Reiki, Qi gong). In addition, NCCAM also studies whole medical systems (for example, Traditional Chinese Medicine, Ayurveda). 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 encouraged to contact the NCCAM representatives prior to submitting an application.

Technology Development and Research

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 methods for standardization and characterization of active ingredients in natural products;
- Development and validation of methods for standardization and characterization of active components of mind-body interventions;
- Development and validation of devices for measurements of putative healing energies;
- Development and validation of innovative biomarkers for measurement of stress for studying efficacy of mind-body therapies;
- Development and validation of standardized, reliable and economical surrogate markers of brain states that correlate with brain imaging;
- Development and validation of technical imaging tools or instruments for studying manual therapies;
- Development of tools for pain management that are not conventionally accepted;
- Development and validation of innovative devices for CAM diagnosis and treatment; and
- Development of standardized complex botanical reference materials that will allow for comparison of research study products and validation of methodologies. Applicants should pay particular attention to the NCCAM Policy on biologically active agents http://nccam.nih.gov/research/policies/bioactive.htm.

Topics That Are of Little or No Interest to NCCAM

The NCCAM Office of Communications is responsible for disseminating CAM information to the public. Therefore applications addressing database creation or maintenance, software development, or educational materials and courses (including CME courses or CD's) in general 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.

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

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NATIONAL CENTER ON MINORITY HEALTH AND HEALTH DISPARITIES (NCMHD)

The mission of the National Center on Minority Health and Health Disparities (NCMHD) 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 NCMHD 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.

NCMHD 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 NCMHD programmatic interests. NCMHD'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

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 NCMHD, please visit our home page at http://www.ncmhd.nih.gov.

Broad Area of Research that we Support

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.

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NATIONAL LIBRARY OF MEDICINE (NLM)

The NLM supports research and development projects in biomedical informatics and bioinformatics. NLM defines biomedical informatics as the intersection of basic informational and computing sciences with a wide range of application domains in biomedicine and public health. Bioinformatics is the intersection of basic informational and computing sciences with the biological sciences.

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

Biomedical Informatics

There are broad needs for informatics concepts, tools and systems to manage the information of health care delivery, reduce medical errors, provide decision support for clinicians, extract outcome and public health information from large datasets, and predict health events.

To support such projects, NLM is interested in:

A. Disaster information management research, including management and delivery of information in disaster settings, and for syndromic surveillance.

B. Mechanisms to capture and integrate new information into existing knowledge bases, including integration of heterogeneous data sets.

C. Approaches for retrieving, extracting and analyzing data from large health-related and heterogeneous databases, such as patient data, population health data, or image databases.

D. Systems, devices, or programs that facilitate utilization of electronic medical record systems in clinical practice, for such functions as order entry, decision support, reduction of errors.

E. Systems, devices, or programs that facilitate utilization of electronic record systems and tools in public health, for such functions as disease monitoring and trend analysis.

F. Projects exploring human-machine interaction, including interface design, use and understanding of health related-information, intelligent agents, information needs and uses.

G. Projects in high-performance computing and communications relating to biomedical applications, including efficient machine-machine interfaces, transmission and storage, real-time decision support.

Bioinformatics

High through-put scientific research has greatly increased the volume of research data and has magnified the problem of information management and interpretation.

To help manage and utilize such data, NLM is interested in:

A. Software algorithms and database query methods capable of capturing scientific data from published knowledge sources or multiple related factual databases.

B. Tools for data management and analysis for genetic linkage mapping, physical mapping, DNA sequencing, and proteomics.

C. Tools and systems for bringing "bench to bedside," applying research data to clinical problems.

D. Algorithms capable of predicting structure and/or function in model biological systems.

E. Algorithms capable of enhanced computational modeling of biological, biomedical and behavioral sciences data at multiple scales of research, ranging from molecular to population.

Other Research Topic(s) Within the Mission of NLM by pre-arrangement with NLM Program Staff

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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, 2007 submission dates.

The CDC serves as the national focus for developing and applying disease prevention and control, environmental health and health promotion and health education activities designed to improve the health of the people of the United States. To accomplish its mission, CDC identifies and defines preventable health problems and maintains active surveillance of diseases through epidemiologic and laboratory investigations and data collection, analysis, and distribution; serves as the PHS lead agency in developing and implementing operational research aimed at developing and testing effective disease prevention, control and health promotion programs; administers a national program to develop recommended occupational safety and health standards and to conduct research, training, and technical assistance to assure safe and healthful working conditions for every working person; develops and implements a program to sustain a strong national workforce in disease prevention and control; conducts a national program for improving the performance of clinical laboratories; and develops programs to prevent premature death and avoidable illness and disability caused by noninfectious, non-occupational environmental and related factors.

CDC is responsible for controlling the induction and spread of infectious diseases, and provides consultation and assistance to other nations and international agencies to assist in improving their disease prevention and control, environmental health, and health promotion activities.

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

NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

The National Center for Injury Prevention and Control plans, directs, and coordinates a national program to maintain and improve the health of the American people by preventing premature death and disability and reducing human suffering and medical costs caused by nonoccupational injury, addressing both intentional injuries that result from violent and abusive behavior and unintentional injuries. The national program encompasses the prevention of nonoccupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons. The Center will address injury prevention and control through an orderly sequence of activities beginning with research on causes, circumstances, and risk factors; progressing through research on interventions and their impact on defined populations. These activities then lead to the broad,

systematic applications of interventions that are soundly based scientifically.

CDC is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. CDC encourages applicants to submit grant applications with relevance to the specific objectives of this initiative. Potential applicants may obtain a copy of "Healthy People 2010"; (Full Report: Stock No. 017-001-00537-1): through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325, (202) 512-1800.

More recently, the Centers for Disease Control has published its *CDC Injury Research Agenda*, June 2002, Atlanta Georgia, which identifies 95 research themes in various areas of injury research, including preventing injuries at home and in the community and in sports, recreation and exercise, preventing transportation injuries, preventing intimate partner violence, sexual violence, child maltreatment, youth violence and suicidal behavior and acute care, disability and rehabilitation. The full report is available at http://www.cdc.gov/ncipc.

The focus of the research topics for SBIR should reflect the themes represented in the research agenda designed to control injury morbidity, mortality, disability, and costs. These projects may be categorized by the three phases of injury prevention and control. Research topics of interest include, but are not limited to:

A. ***Prevention.*** There is interest in the development, application, and evaluation of innovative interventions applicable to intentional and unintentional injury. The focus should reflect target populations at high risk for injury and injury consequences, including minorities, children, the elderly, rural residents, and farm families. SBIR projects that have relevance for reducing injury or increasing dissemination and adoption of effective injury prevention interventions are sought. The following are examples:

   1. Develop technology to improve technology transfer on effective interventions to prevent unintentional injuries and violence.
   2. Develop a practical, valid tool to measure the adequacy of supervisory practices to prevent childhood injuries, such as drownings and falls.
   3. Develop technology-based methods to obtain exposure and injury incidence data for injuries in sports and recreational activities.
   4. Develop new improved and practical alcohol breath testing devices that can be used in multiple settings (by enforcement personnel, bar patrons, and the public).
   5. Develop environmental and behavioral devices that can assist in the prevention of pedestrian injuries, including technology-based strategies that provide feedback to drivers and walkers about impending hazards.
   6. Design, develop, and evaluate educational materials to train public health personnel in injury prevention that could be adapted for medicine, nursing and allied health.
   7. Develop and evaluate injury and violence prevention materials uniquely targeted to and disseminated in medical care and managed care settings, such as in-house kiosks, computer-based self-assessments, and clinical preventive services based interventions or through the use of distance-based learning technology. These materials can address topics such as falls, helmets, supervision and prevention of youth violence or intimate partner violence.
   8. Develop and test a passive alcohol sensor device to passively measure the blood alcohol level of injured patients arriving at the emergency department.
   9. Develop products to improve monitoring and control of exposure to violent media.
   10. Develop innovative educational products to teach non violent resolution of conflicts in partner or family situations.
   11. Develop and evaluate video/computer technology to improve staff training and program fidelity monitoring of efficacious parent training programs for the prevention of child maltreatment.

B. ***Acute Care.***

   1. Develop developmentally appropriate devices, instruments, methods, models, tests, and computer software related to the full spectrum of acute care of the trauma patient, beginning with the establishment of access to emergency care, response at the

injury scene, transportation of the critically injury, to management of postoperative complications such as multiple organ failure syndrome.

2. There is a need to improve diagnostic modalities in several areas, particularly in those related to perfusion and oxygenation at the tissue level. Further, among those patients whose bleeding has been controlled and who will survive the acute phase of injury, the major causes of death are irreversible cerebral damage or uncontrollable cerebral swelling and multiple organ failure. There is an urgent need for research into methods of reducing secondary cerebral injury and of controlling brain swelling and preventing multiple organ failure.
3. Design, develop and evaluate Emergency Department-based prevention services for the identification and referral of persons at risk for violence or alcohol-related injury.

C. ***Rehabilitation.***

1. Develop developmentally appropriate adaptive equipment, assistive devices, and instructional materials directed toward preventing or minimizing the secondary complications of individuals with traumatic brain or spinal cord injuries including cognitive learning problems, pressure ulcers, contractures, muscular atrophy, skeletal deformity and other definable conditions.
2. Design, develop and evaluate educational materials for persons with traumatic brain or traumatic spinal cord injury, their families and/or caregivers that are directed toward preventing or minimizing the secondary complications associated with these injuries.
3. Develop training materials to assist persons with disabilities and their care givers to safely and efficiently evacuate various buildings, (e.g., multi-storied structures) in emergencies.
4. Develop products to improve monitoring and control of exposure to violent media.
5. Develop innovative educational products to teach non violent resolution of conflicts in partner or family situations.

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

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NATIONAL CENTER FOR HEALTH STATISTICS (NCHS)

The NCHS conducts and supports statistical and epidemiological activities for the purpose of improving the effectiveness, efficiency, and quality of health services in the United States. This includes collecting statistics on the extent and nature of illness and disability of the population, as well as life expectancy, incidence of various acute and chronic illnesses, and infant and maternal morbidity and mortality; impact of illness and disability of the population on the economy of the U.S. and on other aspects of the well-being of its population; environmental, social, and other health hazards; determinants of health; health resources, including physicians, dentists, nurses, and other health professionals, by specialty and type of practice and

the supply of services by hospitals, extended care facilities, home health agencies, and other health institutions; utilization of health care, both ambulatory health services and services of hospitals, extended care facilities, home health agencies, and other institutions; health care costs and financing, including trends in health care prices and cost, sources of payments for health care services, and Federal, State, and local governmental expenditures for health care services; family formation, growth, and dissolution. It also undertakes and supports research, demonstrations, and evaluations of new or improved methods for obtaining current data on matters pertaining to its mission.

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

1) The development and refinement of innovative techniques for measurement of biomarkers in survey research conducted in households or other non-clinical settings including the collection of biological specimens such as urine or blood, measuring heart rate, or measuring senses;

2) The development of kits for collecting biomarkers that can be used in survey research conducted in households or other non-clinical settings;

3) The validation of biomarkers collected via nontraditional measures, such as filter paper and saliva, with those collected using traditional measurement techniques;

4) The development and refinement of summary measures of health including measurement of functioning and disability;

5) The development and improvement of sampling strategies for subpopulations of interest including minority populations, people with specific rare diseases or conditions, specific socioeconomic statuses, or people with only cell phones;

6) The development and improvement of techniques to avoid disclosure of confidential data in public use data including tabular data, microdata, web-based query and regression servers, and secure distributed statistical analysis;

7) The development and validation of improved diary methods to record data such as short term contraceptive use, intercourse, pregnancy outcomes, cohabitation and other health-related behaviors;

8) The development of improved training techniques and programs for collection of birth certificate data in hospitals;

9) In conjunction with state registrars, the development of a process for evaluating Electronic Birth Registration System (EBRS) Software and associated work sheets;

10) The evaluation of current methods and development of improved measures and methods of data collection for “date of last normal menses” (LMP), and other factors associated with preterm birth and low birth weight, especially as collected on birth certificates;

11) The development and evaluation of a process and procedures for validating data from birth certificates using the 2003 revision:

12) A feasibility study of the “bridging” of data from the 1989 and 2003 revisions of the birth certificate.

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NATIONAL CENTER ON BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES (NCBDDD)

The National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention seeks to promote optimal fetal, infant, and child development; prevent birth defects and childhood developmental disabilities; and enhance the quality of life and prevent secondary conditions among children, adolescents, and adults who are living with a disability.

The NCBDDD areas of interest focus on:

A. Develop, produce and evaluate the effectiveness of educational modules for birth defects prevention.

B. Develop, produce and evaluate the effectiveness of educational modules with the goal of preventing developmental disabilities.

C. Develop and evaluate assistive technology for promoting and maintaining health and reducing secondary conditions.

D. Develop and evaluate tools, modules or materials to identify children with developmental problems including developmental and early hearing screening.

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

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NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP)

The NCCDPHP plans, directs, and coordinates programs in health promotion, chronic disease prevention, and reproductive health to enhance quality of life, improve reproductive health, and reduce the incidence of heart disease, stroke, cancer, diabetes, arthritis, obesity, oral disease, infant and maternal morbidity and mortality, unintended pregnancy, and emerging chronic diseases. NCCDPHP uses two essential criteria to prioritize its research portfolio, societal burden and disproportionate burden. NCCDPHP places high priority on chronic diseases and conditions and reproductive health outcomes that have the greatest total impact on health, longevity, and quality of life. NCCDPHP places high priority on eliminating disproportionate burden related to sex, age, race, ethnicity, geography, sexual orientation, socioeconomic status, disability, and special needs. NCCDPHP supports three primary types of applied research, research on cause (determinant research), research on effect (intervention research), and research on application and benefit (dissemination research). NCCDPHP emphasizes cross-cutting research that is participatory, accounts for social and ecological factors, and is implemented at multiple levels.

NCCDPHP has identified ten priority research areas: (1) develop new measures and research designs to strengthen the quality of research; (2) identify the underlying determinants of racial and ethnic health disparities; (3) develop and evaluate interventions to eliminate health disparities; (4) examine established and emerging risk factors for chronic disease and investigate their potential for public health interventions; (5) assess the effectiveness of policy and environmental interventions to promote health; (6) improve the processes and outcomes of health care systems; (7) develop effective communication strategies to promote health; (8) examine methods for helping people manage their own health; (9) develop and evaluate the effectiveness of population-based health promotion and disease prevention policies and programs at the local, state, national, and international levels; (10) examine approaches for effectively translating successful community interventions into widespread practice. For examples of specific research questions in each of the ten priority areas, see the publication *Setting the Agenda: CDC Research in Chronic Disease Prevention and Health Promotion*.

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Division of Adult and Community Health

The mission of the Division of Adult and Community Health (DACH) has four major components:

1. ***Aging.*** CDC has established national, state-based programs targeting cardiovascular disease, diabetes, cancer, arthritis, injuries, and immunization. CDC's unique expertise can be readily applied to target the health needs of older Americans by providing public health leadership and coordination, by enhancing surveillance, and by putting research to work for older Americans.
2. ***BRFSS.*** The Behavioral Risk Factor Surveillance System (BRFSS), the world's largest on-going telephone survey, tracks health and behavioral risk factors in the United States, including all 50 states, the District of Columbia, Puerto Rico, Guam, and the Virgin Islands. BRFSS is one of the leading innovators of survey research methods and approaches, including the uses of mixed-mode surveys, addressing changes in telecommunications technology such as cell phones, and surveying hard-to-reach racial and ethnic groups.
3. ***Health-Related Quality of Life Surveillance.*** In public health and medicine, the concept of health-related quality of life refers to a person's or group's perceived physical and mental health over time. Tracking health-related quality of life in different populations can identify subgroups with poor physical or mental health and can help guide policies or interventions to improve their health.
4. ***Prevention Research Centers.*** The PRC Program is a network of academic centers, public health agencies, nonprofit organizations, and community partners that strives to improve health promotion and disease prevention efforts. The centers, which focus on high-priority public health issues, work to bridge gaps between scientific knowledge and public health practice. The network translates promising research findings into practical and effective programs and policies for use in communities throughout the nation.

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Division of Cancer Prevention and Control

The Division of Cancer Prevention and Control (DCPC) supports comprehensive cancer surveillance, epidemiologic, health and behavioral science research, communications and program services to reduce the illness and death associated with cancer. The mission of DCPC is:

- To plan, direct, and support cancer control efforts through collaborations with prevention partners in state health agencies, federal agencies, academic institutions, and national, voluntary, and private sector organizations.
- To direct, monitor, and report on activities associated with the implementation of the Breast and Cervical Cancer Mortality Prevention Act of 1990, Public Law 101-354 (1998 Code PDF-56KB), and the Cancer

Registries Amendment Act, Public Law 102-515 (1998 Code PDF-36KB).

- To plan and conduct epidemiological studies and evaluations to identify the feasibility and effectiveness of cancer prevention and control strategies. DCPC provides state and local public health agencies and other health care provider organizations with technical consultation and assistance to improve education, training, and skills in the prevention, detection, and control of selected cancers.

- To identify problems, needs, and opportunities related to modifiable behavioral and other risk factors. The division also recommends priorities for health promotion, health education, and cancer risk reduction activities both for professionals and the public. DCPC pursues the building of local coalitions and community networks and the implementation of grassroots activities to reach the target populations of persons at increased risk for developing cancer.

Future Directions

- Enhance its relationships with partners and policy makers to increase the effectiveness of cancer prevention and control activities nationwide.

- Expand the use of information technology in cancer surveillance, particularly in cancer registries.

- Improve the cost-effectiveness of the National Breast and Cervical Cancer Early Detection Program.

- Expand CDC's focus to include malignancies not previously addressed, such as lung cancer and malignancies of the head and neck.

- Define the proper role for management of chronic diseases, including cancer, in the case of catastrophic disaster.

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Division of Nutrition and Physical Activity

The Division of Nutrition and Physical Activity (DNPA) partners with fruit and vegetable stakeholders such as the National Cancer Institute (NCI), the United States Department of Agriculture (USDA), the Produce for Better Health Foundation (PBH), the American Cancer Society (ACS), American Diabetes Association (ADA) and others to work towards increasing American's intake of fruit and vegetables. High intake of fruit and vegetables has been associated with reduced risk of cardiovascular disease, many cancers, as well as other chronic diseases and conditions. Further, over consumption of food combined with lack of physical activity is creating an epidemic of overweight and obesity in the United States. Opportunities exist to prevent or reduce the burden of many chronic diseases by increasing knowledge of nutrition, increasing availability of and access to healthy foods, and changing policies to promote healthful choices.

Chronic Disease Nutrition

There is interest in the development, dissemination, and evaluation of innovative methods to increase knowledge of healthful nutrition practices including increased fruit and vegetable intake, decreased fat intake, and decreased caloric consumption among persons of many different backgrounds and at different stages of life. Although effective strategies for nutrition education exist, few have been disseminated to a larger audience than the original research population. The focus of proposed projects should reflect target populations at high risk of developing nutrition related chronic diseases. There is also interest in the development of nutrition intervention programs that are targeted toward changing the environment or policies that affect people's food choices. Most nutrition interventions provide nutrition education for individual dietary change but do not change the environment or policies that affect a population's access to healthful foods. Some limited research has examined how the availability of and access to fruit and vegetables impacts consumption. Environmental and policy interventions to increase availability and reduce prices of fruit and vegetables have been effective in

the short-term. Few of the interventions have lasted long enough to determine whether increased consumption could be sustained over the long-term.

Use of innovative or new strategies to promote health:

1. Design and develop an innovative series of educational tools (i.e. audiovisuals, series of lunch and learns) for a worksite health promotion program that incorporates both the volumetrics/energy density principles as well as the promotion of fruits and vegetables. The educational series should clearly define the benefits of eating fruits and vegetables and explain the volumetrics/energy density eating concept. In addition, it should be emphasized that replacing high-energy dense foods for low-energy dense foods can help a person eat fewer calories. Some examples of educational tools include a video/DVD on shopping for and preparing food; a video on the principles of Volumetrics with specific examples of varying levels of energy density in foods; a supermarket tour guide (with an emphasis on fruits and vegetables); a video or booklet on how recipes can be modified to incorporate fruits, vegetables and low-energy dense foods; a series of lunch and learns with handouts. A successful intervention should target the specific population – working adults who have little time to think about, prepare and cook meals. In addition, the tools should reach different ethnic and socioeconomic groups. This program should be supported at work but also translatable into the employee's everyday life both at home and away from home. Coordination on this project with CDC's Fruit and Vegetable Program is strongly encouraged for a successful outcome.

2. Design, develop, and evaluate innovative food methods to increase the appeal and availability of fruits and vegetables as healthy snacks for use at worksites, schools or other locations. This project must include the marketing expertise of the food industry and employ a promotional component. The promotional component may be computer-based or driven by the media. Some examples include mobile salad bars, burrito or pasta bars that include fruit and vegetables, vending machine alternatives, or other similar options. Several of these food service alternatives have been tried in school systems and worksites across the country. Examples to follow include the Santa Monica Farmer's Market Salad Bar Program, innovative changes in food service in the Los Angeles County School System, Chefs in schools and worksites, and successful research interventions that changed availability and pricing in school, workplace, or community cafeterias and vending machines. Coordination on this project with CDC's Fruit and Vegetable Program is strongly encouraged for a successful outcome.

3. Design, develop, test, and evaluate a culinary intervention in the supermarket that encourages increased consumption and purchase of fruit and vegetables. This intervention should involve local chefs and supermarkets to provide hands-on demonstrations that include culinary skills such as storing, preparing, and purchasing vegetables. This project should evaluate the effectiveness of an intervention that should include opportunities for participants to learn menu planning with simple, accessible, low-cost fruit and vegetables. The target population for this intervention must include low-income households. The recruitment of participants should include collaboration with community-based organizations such as the Food Stamp Office, Head Start, and WIC. The intervention should consider building the culinary skills of individuals with low incomes so that the individuals feel confident in making healthy food choices for their family. Coordination on this project with CDC's Fruit and Vegetable Program is strongly encouraged for a successful outcome.

4. Design, develop, and evaluate a user friendly, web-based system for tracking local, state, and national level changes that support increased fruit and vegetable consumption. The web-based system should include technical assistance for stakeholders on ways to include policy and environmental change strategies that positively impact fruit and vegetable consumption into strategic and program planning. This system should also include the technology to aggregate and dis-aggregate data at the local, state, and national levels. The web-based system may include capacity to connect policy and environmental changes. This web-based system should also employ methods for connecting policy and environmental changes to behavior changes in targeted populations thus providing local, state, and national stakeholders the ability to monitor

their efforts. To assure the web-based system meets the needs of fruit and vegetable stakeholders at the local, state, and national levels, it is strongly encouraged that the web-based system is pilot-tested with those stakeholders. Coordination on this project with CDC's Fruit and Vegetable Program is strongly encouraged for a successful outcome.

5. Design, develop, and evaluate (pilot test) a comprehensive educational strategy/program with school aged children and young adults (preschool to college) that focuses on increased vegetable and fruit consumption. This comprehensive educational strategy/program may be school or community based. It should be interdisciplinary, have a multi-dimensional approach, be theory based and generalizable. Partnering is encouraged with those entities interested in improving community health. Innovations may include interventions in other youth organizations or programs such as Boy and Girl Scouts, 4-H Boys and Girls Clubs, YMCA, and college groups. Coordination on this project with CDC's Fruit and Vegetable Program is strongly encouraged for a successful outcome.

6. Environmental change interventions can be an effective way to support a community effort to increase community vegetable and fruit intake. Design, implement, and evaluate an environmental change intervention incorporating 5 A Day. This intervention should be an educational and ecological effort emphasizing such factors as access to vegetables and fruits, cost/pricing of vegetables and fruits, and point-of-purchase education. Behavior-specific ecological models should be used to guide this intervention. This intervention may use innovative methodology and partnering to facilitate consumption of vegetables and fruits (examples include: strategies for edible trails, Jr. Master Gardener projects, Senior and/or farmers markets and/or school and community gardens). Coordination on this project with CDC's Fruit and Vegetable Program is strongly encouraged for a successful outcome.

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Office on Smoking and Health

The Office on Smoking and Health (OSH) is responsible for leading and coordinating strategic efforts aimed at preventing tobacco use among youth, promoting smoking cessation among youth and adults, protecting nonsmokers from environmental tobacco smoke (ETS), and eliminating tobacco-related health disparities.

OSH has identified two research areas for which proposals are requested:

Linking GIS Technology with Essential Public Health Services

We predict that, by the year 2010, GIS applications in public health practice will no longer consist of the ad hoc approaches we have seen in the 1990s. By the year 2010, we expect to see GIS technology customized for public health applications. This GIS health software will offer applications that "know" which data systems are needed and where they are located. After loading the appropriate data and performing relevant analyses, the system will offer alternative courses of action ranging from informing other people in the public health system to issuing health advisories.

Following is an example of GIS technology applied in tobacco-related research:

Inform, educate, and empower people about health issues. One of a community's identified priorities is to develop an anti-smoking campaign. An anti-smoking coalition uses GIS technology and commercial lifestyle segmentation profiles (or a public health analogue developed by CDC by 2010) to identify subgroups that are most likely to include active smokers, the Census blocks where active smokers are most likely to reside, and the most effective communication media and times of day to deliver anti-smoking messages to these subgroups.

Tools to Enhance the Utilization of Tobacco Cessation Quitlines

While tobacco cessation services are available in every state through the 1-800-Quit Now national portal number quitlines are underutilized. A significant barrier to the utilization of quitlines has been lack of knowledge about the specific services that will be provided to the tobacco user who calls

the quitline. Additional information on what is provided through quitlines is needed for health care providers who are a major source of referrals to quitlines. Also, referrals and the exchange of information both to and from the quitlines to health care providers need to be enhanced to maximize the number of referrals that quitlines are receiving.

Applications are invited for small business collaboration with a quitline vendor, state health department, or other agency that supports or operates a tobacco cessation quitline to develop tools/strategies that will increase the number of tobacco users who utilize effective tobacco cessation treatments in their quit attempts and increase the numbers of successful quitters.

1. Develop tools that will educate the public and health care providers about the services that are provided to quitline callers. These educational tools could be produced in many different formats including but not limited to CD's, instructional videos, pamphlets, and web-based information. An assessment should be made on what format(s) will reach the largest number of potential quitline users and health care providers. Special emphasis should be given to developing tools that can be used to educate high risk or underserved populations.
2. Develop tools that will enhance referrals to tobacco cessation quitlines and the exchange of information to and from quitlines. These tools could be in many potential formats including but not limited to web-based interfaces, automatic messaging, and text messaging. An assessment should be made on format(s) that will achieve the largest increase in the number of patients referred and the number of patients ultimately counseled by the quitline.
3. Propose strategies for effective utilization of the tools among the public and practitioners.
4. Propose a plan for distribution of final product(s) to the public and to practitioners.

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Division of Oral Health

The Division of Oral Health seeks to improve the oral health of the nation by extending the use of proven strategies to prevent oral diseases, enhancing surveillance of oral diseases, strengthening the nation's oral health infrastructure, and guiding infection control in dentistry. At the core of the DOH mission is the critical relationship between oral health and general health and well-being. DOH programs focus on educating the public, public health and clinical professionals, and policy makers on steps that individuals and communities can take to improve oral health at different ages throughout the lifespan, and serving as a resource for these efforts.

Providing Safe Dental Care

Infection control in the dental care environment remains essential to ensuring the public's safety and retaining its confidence. In the 15 years since CDC published its first guidelines for infection control in dentistry, infection control practices have dramatically improved. Nevertheless, the potential for disease transmission during visits to the dentist continues to arouse intense public interest and media scrutiny. To minimize this potential, CDC assesses the risks of infectious disease transmission, updates guidelines to minimize those risks, investigates disease outbreaks and environmental hazards in dental settings, and identifies emerging problems. Infection control activities address the "Healthy People 2010" priority areas in Occupational Safety and Health, Immunization and Infectious Diseases, and HIV Infection.

1. Develop surveillance system(s) and outcome measures for adverse events related to exposure to pathogens and other hazardous agents during dental treatment.
2. Develop and evaluate tools and models for screening dental patients for infectious and chronic diseases.
3. Develop methods or models for evaluating the effectiveness and cost-effectiveness of infection control interventions.
4. Develop dental devices with passive safety features that meet or exceed performance criteria identified by CDC (www.cdc.gov/oralhealth/infectioncontrol/forms.htm).

5. Develop devices, both accurate and passive, to measure biofilm or bacterial contamination in dental waterlines.
6. Develop educational/training materials and demonstrate their effectiveness in on-the-job training of dental assistants in dental office infection control and quality assurance.
7. Develop and evaluate training and educational materials for using the oral rapid HIV screening test in dental facilities to identify cases of HIV infection that may otherwise go undetected.

Oral Health

In collaboration with several partners, the DOH develops national plans and supports programs in specific areas of oral health including appropriate use of fluorides and sealants to prevent dental caries (tooth decay); activities that address the oral health needs of an aging population; and implementation of strategies to reduce disparities in oral health status. This includes expanding the capacity and ability of state health departments to implement community water fluoridation and school-based/-linked dental sealant programs. The following are topics of interest in oral health.

1. Develop methods/technologies to assist in the collection and analysis of data to estimate the effectiveness and cost effectiveness of community/school programs delivering interventions to prevent dental caries.
2. Identify biomarkers or develop methods or devices to measure total fluoride exposure.
3. Develop oral hygiene products or devices for adults with motor difficulties.
4. Develop innovative fluoride delivery systems for home use among persons at increased risk for dental caries (tooth decay).
5. Develop innovative methods to defluoridate water with high natural fluoride concentrations.
6. Develop innovative sealant materials, supplies or equipment for use by sealant programs in non-traditional dental settings.

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Division of Reproductive Health

The mission of the Division of Reproductive Health (DRH) is to promote optimal reproductive and infant health and quality of life by influencing public policy, health care practice, community practices, and individual behaviors through scientific and programmatic expertise, leadership, and support.

The Division accomplishes its mission by working with partners throughout the nation and world to

- Conduct epidemiologic, behavioral, demographic, and health services research.
- Support national and state-based surveillance systems to monitor trends and investigate health issues.
- Support scientific and programmatic development within states and other jurisdictions.
- Provide technical assistance, consultation, and training worldwide.
- Translate research findings into health care practice, public health policy, and health promotion strategies.

Goals

- **Outcomes** – Improve and promote infant health and reproductive health, and well being of men and women globally.
- **Leadership** – Provide global leadership to optimize reproductive and infant health.
- **Research** – Define, conduct, and promote public health research in reproductive and infant health.
- **Translation** – Translate science and technology into strategies and interventions that promote reproductive and infant health.
- **Infrastructure** – Maintain a healthy, productive environment, which supports achievement of the mission.
- **Capacity Building** – Enhance the ability of others to identify and address reproductive and infant health issues.

Priorities

- Women's Reproductive Health
- Unintended Pregnancy Prevention
- Maternal Health
- Infant Health
- Global Reproductive Health

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Division for Heart Disease and Stroke Prevention

Heart disease and stroke are the first and third leading killers of Americans and are leading causes of disability in the US. The Division for Heart Disease and Stroke Prevention (DHDSP) currently funds health departments in 32 states and the District of Columbia to develop, implement, and evaluate programs that promote heart–healthy and stroke–free communities; prevent and control heart disease, stroke, and their risk factors; and eliminate disparities among populations. These programs emphasize the use of education, policies, environmental strategies, and systems changes to address heart disease and stroke in various settings and to ensure quality of care.

The DHDSP houses CDC's WISEWOMAN program. With 15 projects in 14 states, WISEWOMAN helps women with little or no health insurance gain access to screening and lifestyle interventions that can reduce their risk of heart disease, stroke, and other chronic diseases.

Program priorities of DHDSP focus on high blood pressure control; high cholesterol control; knowing the signs and symptoms of heart attack and stroke and need to call 911; improving emergency response; improving quality of care; and eliminating gender, racial/ethnic, and geographic health disparities.

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NATIONAL CENTER FOR ENVIRONMENTAL HEALTH (NCEH)

The National Center for Environmental Health (NCEH) plans, directs, and coordinates a national program to maintain and improve the health of the American people by promoting a healthy environment and by preventing premature death and avoidable illness and disability caused by non-infectious, non-occupational environmental and related factors. The main activities of NCEH is to provide national leadership, through science and service in prevention programs, global health, and the use of human genetic knowledge, and tests.

Research topics within the mission of the NCEH can include, but would not be limited to, those identified below:

A. ***Environmental Health/Anti-Chemical Terrorism—Rapid Field Tests for Human Exposure.*** There is a need to develop rapid, reliable, field rugged methods for detection and quantitative estimation of human exposure to environmental contaminants and toxic chemical-based weapons of mass destruction or terrorism. Such methods must be able to sense the presence or absence of such substances quickly and reliably, and provide estimations of concentration in human urine, saliva, breath, blood, or transpired through the skin. Minimums of false positives and false negatives are important for such technology to avoid wasting resources and missing actual exposures.

B. ***Detection of Human Exposure to Aflatoxins and Other Mycotoxins from Food or as Chemical Warfare or Terrorism Agents.*** Aflatoxins and other mycotoxins are products that naturally occur from fungi on grains and other food materials. They are produced at harmful levels under certain weather conditions or during improper storage. They have the

potential to be weaponized as chemical warfare or terrorism agents. There is a need to develop analytical methods for detection of these compounds in urine, saliva, or blood in the field to support epidemiologic investigations or under battlefield conditions. Methods/ instruments must reliably detect and quantify human exposure to these agents, with limits of detection consistent with background levels in populations as well as levels in exposed persons.

C. ***Rapid Field Tests or Continuous Monitors for Arsenic in Drinking Water.*** Drinking water with toxic levels of naturally occurring arsenic obtained from shallow wells is a serious problem in many parts of the world. Recently, this problem has become especially acute in rural areas of the under-developed world because of efforts to improve drinking water sources that unfortunately did not fully consider natural sources of arsenic. The solution requires deep wells, or water treatment at the point of use. However, because of uncertainty about the level of arsenic in water from these improved sources, and because of the need to give attention to the most heavily contaminated existing shallow wells first, there is a need to develop rapid, reliable, and cost effective tests or monitors for water arsenic.

D. ***Rapid Field Tests for Iodine Levels in Urine and Salt.*** Iodine deficiency is a global problem affecting millions of people, leading to reduced population IQ, cretinism, goiter, and contributing to thyroid cancer. To facilitate efforts to eliminate this problem, rapid, simple, and inexpensive tests are needed that can determine the concentration of iodine in urine for population screening work, and that can determine the concentration of iodine in salt samples for quality control purposes in iodized salt production. While field tests for iodized salt have been developed in recent years, they have proven to be inaccurate and unreliable. Tests for urinary iodine typically have required complicated laboratory procedures. Simple, reliable measures for field use would be a great help.

E. ***Coronary Heart Disease.*** The development of a laboratory technology to standardize and improve the quality and reliability of laboratory tests for cholesterol and other metabolically related lipids and lipoproteins that are known risk factors associated with coronary heart disease is an area that needs improvement of diagnostic techniques. Specifically, the contractor should develop and characterize improved serum reference materials that can be used by NCEH to standardize laboratories which conduct epidemiological and lipid research and clinical trials into the causes and prevention of coronary heart disease.

F. ***Rapid Field Tests for Vitamin A Status.*** There is a need for the development of rapid, rugged field portable, and economical techniques for determining vitamin A status in finger stick or earlobe blood samples collected by microcapillary techniques or on filter paper. Methods may be based on fluorescence, optical density, or any other technique which reliably estimates vitamin A status in humans, but it should correlate to widely accepted "reference" methods such as high performance liquid chromatography (HPLC). Such methods would be highly valuable in global efforts to eliminate vitamin A deficiency, a high priority for WHO, UNICEF, USAID, and many other international agencies. Vitamin A deficiency is a devastating problem especially in developing countries where it contributes significantly to childhood morbidity and mortality, and is a leading cause of blindness in many parts of the world.

G. ***Rapid and Reliable Field Tests for Serum Ferritin and Transferrin Receptor.*** Iron deficiency and iron deficiency anemia are serious problems throughout the developing world and in many high-risk groups in developed countries, including the United States. These problems negatively impact societies by reducing work capacity, impairing mental development and learning, and increasing morbidity and mortality, especially in women of child bearing age and young children. There is a need to develop reliable, easy to operate, and cost effective devices for screening for serum ferritin, and if possible for serum transferring receptor in populations and for managing individuals receiving iron intervention treatments. These devices would have to operate properly in climatic conditions that are not always regulated. Portable devices would be desirable. The use of blood collected through a minimally invasive technique would be preferred.

H. ***Development of Stable Isotope Labeled Proteins for Quantitation of Protein Biomarkers.*** Improving the accuracy of measurements of protein levels in humans is

an important step toward a better understanding of many diseases. The choice of standards is usually the key for the precision, reproducibility and accuracy of measurements of different compounds. Isotope dilution mass spectrometry is widely used for the quantitation of small molecules in biological specimens. It improves the measurements of low concentrations of chemicals and biomarkers in such samples so that concentrations can be correlated to internal dose. The use of isotope dilution mass spectrometry for the analysis of proteins is less developed due to the difficulties associated with the synthesis of the isotopically labeled proteins used as internal standards in this technique. In order to fulfill this gap, high purity proteins (>95% purity) are needed in which stable isotopes are incorporated into the protein. 13C and 15N are to be incorporated as labeling isotopes instead of 2H or 18O because the later can sometimes be exchanged during sample processing. Enough number of labels should be introduced in the protein so they can be analyzed with a triple quadrupole mass spectrometer and produce meaningful results. We would like to develop a new project for producing high purity labeled hemoglobin, albumin and insulin, which will be used as standards for the quantitation of protein biomarkers.

I. ***Improved Tests for Zinc Status and Zinc Body Stores in Humans.*** The essential element zinc has been shown to be extremely important in human health. Recently it has been especially important as a cofactor in efforts to combat iron deficiency and vitamin A deficiency in the developing world. There is a need to develop simple, reliable, easy to operate, and cost effective methods or instruments for screening for zinc deficiency in populations and for managing individuals receiving intervention treatments. There is also a need for improved approaches to assessing zinc body stores.

J. ***Improving Assessment of Children's Exposure to Toxic Substances.*** Children tend to be more susceptible to toxic substances than adults because of a variety of differences related to physical and functional characteristics. It is imperative that exposure of children to toxic substances be minimized or eliminated since exposures could result in subtle effects upon children's growth, maturation, and health. Children are generally at greater risk than adults for exposure to environmental pollutants from inhalation because they have a higher respiratory rate; from dermal exposure because they have more exposed surface area; and from ingestion because they have a tendency to play in and eat dirt. In order to address children's exposures, the following rapid response technology is needed:

1. Development of an "environmental sensor" that would detect concentration levels of volatile organic compounds (VOCs) and particulates at threshold levels that would be harmful to small children.
2. Development of a "soil tester" that would determine the concentration level of various trace metals and other environmental pollutants that might concentrate in soil, where children are likely to play.

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NATIONAL CENTER FOR INFECTIOUS DISEASES (NCID)

National Center for Zoonotic, Vector-Borne, and Enteric Diseases

The National Center for Zoonotic, Vector-Borne, and Enteric Diseases (NCZVED) is composed of four divisions, that maximize public health and safety both nationally and internationally through the prevention and control of disease, disability, and death caused by zoonotic, vector-borne, foodborne, waterborne, mycotic, and related infections. In carrying out its mission, NCZVED, provides leadership, expertise, and service in laboratory and epidemiological science, bioterrorism preparedness, applied research, disease surveillance, outbreak response, policy development, health communication, education and training, and program implementation and evaluation. (CDC website, 2006 http://www.cdc.gov/ncidod).

Division of Foodborne, Bacterial and Mycotic Diseases

The Division of Foodborne, Bacterial and Mycotic Diseases (DFBMD) develops research and health initiatives which align with the mission of improving public health nationally and internationally through the prevention of disease, disability and death caused by zoonotic, bacterial enteric infections and fungal infections.

One area of interest within DFBMD focuses on the need to:

a.) Develop field-expedient testing technology (including clinical laboratory tests and accompanying instrumentation) to detect and genotype pathogenic *Vibrio spp*. in patient specimens, environmental samples and/or to determine drug resistance of *V. cholerae* . The

technology should be readily usable by staff in clinical and public health laboratories.

b) Build capacity to rapidly identify emerging pathogens of *Vibrio spp*., including members of the O141 serogroup, and simultaneously identify virulence factors that may contribute to severe *Vibrio* infection and disease in a single assay.

c) Design, development and evaluation of procedures and instrumentation to facilitate nucleic acid amplification testing methods for *Vibrio spp*. and optimize the ease-of-use and cost-efficiency of nucleic acid amplification testing.

d) Design and development of automated and integrated test kits for sample preparation, amplification and genotyping of *Vibrio spp*.

e) The development of rapid cost-efficient methods and accompanying instrumentation to determine drug resistance of *Vibrio cholerae* suitable for use in clinical laboratories.

f) Translate and optimize the designed assays and analytical methods within microfluidic prototypes to achieve clinically relevant sample-to-answer detection limits; validate the assay and microfluidic device performance on a large panel of *Vibrio* isolates relative to (gold-standard) DNA sequence analysis; and establish standard operating procedures for cartridge manufacture, storage, and use.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)

The NIOSH plans, directs and coordinates the national program effort to develop and establish recommended occupational safety and health standards and to conduct research, training, and related activities to assure safe and healthful working conditions for every working man and woman. NIOSH has both a regular grant program and an SBIR grant program; the purpose of both is to develop knowledge that can be used in preventing occupational diseases and injuries. In the regular NIOSH grant program, the following types of applied research projects are supported: causal research to identify and investigate the relationships between hazardous working conditions and associated occupational diseases and injuries; methods research to develop more sensitive means of evaluating hazards at work sites, as well as methods for measuring early markers of adverse health effects and injuries; control research to develop new protective equipment, engineering control technology, and work practices to reduce the risks of occupational hazards; and demonstrations to evaluate the technical feasibility or application of a new or improved occupational safety and health procedure, method, technique, or system.

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.

F. Develop alternatives to pesticide application and hazardous waste remediation.

G. Develop micro sensing devices to notify workers before chemicals break through protective clothing and identify failures in containment systems for hazardous materials.

H. Develop new materials for clothing to protect against chemical and physical hazards.

I. Develop information dissemination methods to help businesses learn about and implement occupational safety and health programs.

J. Develop training materials to teach hazards and risks, demonstrate solutions, measure changes in behavior and practices, and improve injury and illness rates.

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.

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.

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.

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 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.

Construction

Each day, construction workers face trench cave-ins, falls, machinery accidents, electrocutions, and motor vehicle incidents. NIOSH researchers identify causes of and develop programs to prevent injuries and fatalities in construction.

A. Commercialization of new designs or controls to reduce dust emissions from tools such as jackhammers.

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) on job sites.

Agriculture

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.

Mining

The mining industry is one of the more challenging occupational sectors having to deal with adverse natural conditions such as cramped work space, poor visibility, handling of large volumes of bulky and heavy materials, and in many cases, a variety of unknowns including the physical characteristics of the materials being mined and the surrounding materials with little knowledge of the conditions ahead of mining and difficulties in predicting and measuring the environmental conditions of the mine workings. These environmental conditions include dust concentrations, gas concentrations, noise levels, diesel particulate matter levels and noise levels. Advancements in technology and knowledge which would address any of the above concerns

would be beneficial to improving worker health and safety in the mining industry. The advancements could be achieved through the development of new and innovation technologies, enhanced understanding of the conditions and improved approaches and strategies for dealing with the issues.

A. Develop new approaches for measurement or identification of conditions in the vicinity surrounding current underground mining operations.

B. Develop technology that has application for measuring or predicting the exposure of mine workers to any of the factors present in surface and underground mines. The factors include noise levels, diesel particulate matter and dust concentrations.

C. Determine the effectiveness of and/or develop improved approaches for training used to protect the health and safety of mine works.

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.

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FOOD AND DRUG ADMINISTRATION (FDA)

FDA will accept SBIR grant applications on the April 5, August 5, and December 5, 2007 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, postmarketing 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, postmarketing drug safety, evaluation of effectiveness of regulatory actions, patterns of drug use, including off-label, signal detection methodologies (e.g., datamining 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 practioners 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 Center for Food Safety and Applied Nutrition conducts research and develops standards on the composition, quality, nutrition, and safety of food, food additives, colors, and cosmetics. The Center also 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 additives and food additives; collects and interprets data on nutrition, food additives, and environmental

factors affecting the total chemical result posed by food additives; and maintains a nutritional data bank.

CFSAN regulates all foods **except** meat, poultry and processed egg products. CFSAN seeks research designed to complement and accelerate efforts for the detection, prevention, and control of contamination that may be responsible for illness or injury conveyed by foods, colors, and cosmetics.

The priorities of FDA's food defense research program are based on determining the food/agent combinations of highest concern. Mission-critical knowledge gaps are addressed through translational research concerning the need to anticipate, prevent, detect, respond, and recover from terrorists' assaults on the food supply. This requires research activities in five areas: (1) knowledge of the behavior of microbiological, chemical, radiological, and biologically-derived toxic agents in priority vulnerable foods during the stages of production, distribution, marketing, and preparation; (2) enhanced information on the susceptibility of the population to microbiological, chemical, radiological, and biologically-derived toxic agents via priority vulnerable foods; (3) identification and/or development of new techniques for "shielding" priority vulnerable foods through the development of new prevention and/or security technologies; (4) development of enhanced sampling and detection methods for priority agents in vulnerable foods including field deployable and in-line sensor-based screening, analytical, and investigational (forensic) technologies; and (5) development of effective methods for ensuring that critical food production and manufacturing infrastructure can be rapidly and effectively decontaminated in event of a terrorist attack. In accord with section 3402(d) of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, FDA's food defense research is particularly focused on tests and sampling methodologies to detect intentional adulteration and tests that are suitable for inspections of food at ports of entry to the U.S. The mission-critical needs require that the research not stop at the generation of new knowledge and technologies, but also include the validation of those approaches under realistic conditions that reflect the diversity of the food industry, and the transfer of that technology to the 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 and effectiveness standards and good manufacturing practices regulations, operates postmarket 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 to 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. The overall research program may be categorized into four areas, as follows:

1. Characterization of the constituents or components of products.
2. Measurement of product performance.
3. Bioeffects that derive from human exposure to radiation or medical devices.
4. Radiation metrology in support of Agency regulation of radiation-emitting products.

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 an optical non-destructive method for rapid microtopographic evaluation and measurement of wear of articulating surfaces of implant prostheses.

B. Develop a system, including CDROM database of human chemical physiological, electrical and mechanical service environment test parameters, for use to design test protocols for

implant device performance and for accelerated reliability testing.

C. Develop a system, including database and radiation dosimetry badges, for monitoring and registering radiation exposure (dose) of health care providers during interventional radiologic procedures (e.g., angioplasty, percutaneous renal stone removal).

D. Develop a context-sensitive audio and video user assistance or training system that can be temporarily attached or permanently integrated with a moderately complex medical device such as an IV pump, defibrillator, or ventilator. Its ability to address the use of these devices in the home environment is advantageous.

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.

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 pediatric formulations for already approved products for the specific purpose of submitting data to the FDA to include pediatric labeling to the current label of the approved product.

B. 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.

C. 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.

D. 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

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