Keynote with Dr. Michael Lauer

>> Mike Lauer: Hello. I'm Mike Lauer. I'm the NIH deputy director for extramural research. I'd like to take this opportunity to welcome you to our first-ever virtual regional seminar. We usually do the regional seminar in-person. The last one we did was in Phoenix. We welcome you now to our virtual seminar. What I'd like to do in this keynote is talk about extramural research, and I'm going to do that by talking about three aspects of it that should be familiar to all of you: money, people and science. So let me start by telling you a story. This goes back to 2014, 2015 when we saw this article that was published in "PNAS." It was written by two people from Penn State University, and they wrote an opinion piece entitled "Celebrating Research and Development Expenditures Badly Misses the Point." Now, what these authors suggested is that universities sometimes describe their research programs in terms of how many grants or how much money they are getting. They might say that we have a $200 million program or a $50 million program or that we have a program with 100 grants or 50 grants. These authors suggested that that would be kind of like saying that an airline spends more money than any other airline moving passengers or burns more gas than any other airline in moving their airplanes. There should be a different way of telling the story about research and development. So how do we tell the story about research? What should our story be? The authors argued that we should have a different finish line than what we currently have. This is a figure that was taken out of their paper. You might think of it as a highly simplified view of biomedical research. On the left, it starts with the application, which then leads to a grant award. You hope, of course, that the grant will get funded. After the grant is funded, research gets done. The results of that research will get published, and we hope then that those publications will lead to citations. They argue that the finish line right now is the checkered flag on the left, which is that the award has been given. They argue for a different finish line, which is the one on the right. Now, maybe that's not the correct finish line. We can talk about that later. But the key point here is that telling a story about grants and a research program goes way beyond how many grants or how much money is actually being spent. So if we think about this, we can think about our story in terms of three major components: money, people and science. So let's go ahead and explore that. Now, before talking about these in detail, I'd like to take you on a quick, very high-level tour of how the NIH works. For many of you, this is going to be old hat. For some of you, this may be relatively new. NIH gets its money from Congress. All of the money that we spend is taxpayer money. That money then may be used to support grants. A very large proportion of our money is used for grant support. So scientists who work at research institutions come up with ideas, or they respond to requests for applications from the NIH. They then put together a grant proposal. The grant proposal gets submitted through an electronic system and then goes to a scientific review panel. Now, here is a picture of a scientific review panel sitting around a table. These days, we don't do that anymore. These days, we do everything virtually, but the basic idea is the same, which is that you've got a group of people, a group of experts who look at a number of applications and make judgments about them, come up with an assessment of the scientific merit of those applications. So the scientific review panel, or sometimes it's referred to as a study section or review group, they will look at the applications and then come up with a score and a critique of that application, which they send on then to a program officer. That program officer will then use that information, along with other kinds of input, to think about whether or not that application should be funded, and if so, in what way and to what degree. Those applications that potentially might be funded are then brought forward to a second level of review. We call that our advisory council. Each institute of the NIH ... There are 27 institutes of the NIH, so each institute has an advisory council. That advisory council will then look at the applications a second time. Certain kinds of applications will undergo additional scrutiny, such as those applications which cost more than a certain amount of money, and then they will then make further recommendations regarding which applications might be appropriate for funding. So the results now of the first peer review, the peer review that occurs at the scientific review panel and then the assessment of the program staff and the assessment of council then get brought to the institute or center director. Each of our ICs, institute or centers, has a director. That director will then be responsible for making the final funding decisions, and that director will determine which grants get funded and to what degree and in what way, and then that money then and award will then go back to the research institute. So that is the cycle here. Money is allocated by Congress. Scientists at research institutes and research-institute staff submit applications that then undergo peer review. Peer review then goes to program. Program makes assessments that then go to council. Council then takes care of the second level of review, and ultimately then, the IC director will decide which applications get funded. All right. So now, having given you that very high-level tour of how NIH works, let's talk about money, people and science, and we'll start by talking about money. Well, of course, one of the most common questions that people ask about NIH is, "What's our budget?" So here is a figure showing what our budget has been over the last 20 years or so. On the left is 1998. On the right is 2019, and the y-axis shows our budget in millions of dollars, so you'll see back in 1998, we spent about $11 billion. Then there was a period of time from 1998 to 2003 when our budget increased dramatically. That is referred to as the NIH doubling. Now, you'll see there are two lines. The top line, which is black, that represents our budget in nominal dollars, what the amount of money that Congress said was going to be allocated to NIH. The line on the bottom, which is blue and dashed, that describes the budget in inflation-adjusted dollars, so what one sees is that number is lower. You can think of it as representing, what was our purchasing power compared to where we were at the beginning of this in 1998? All right. Well, no matter how you look at it, between 1998 and 2003, there was a dramatic increase in our budget. But then between 2003 and 2014 or so, our budget remained flat. Some people might use the word stagnant. In terms of nominal dollars, the numbers didn't change very much. In terms of inflation-adjusted dollars, our purchasing power decreased. Now, beginning of 2014, 2015, we see a clear reversal. Our budgets have increased substantially. This is something for which we are grateful. There is strong bipartisan support for the biomedical research that NIH does. You can see that in 2020, our budget had increased to $41 billion. That's compared to $29 billion back in 2013, a substantial increase. Then if you look at the line on the bottom, you'll see that our purchasing power has increased, as well, although it is not quite as high as it was at the end of the doubling in 2003. That's a very high-level look at money. Now we're going to talk about people. Now, if we think about the people who are involved in biomedical research, they come in many different types, but I'd like to start by calling out people who work in research administration, so this would include grants offices, compliance offices, offices of sponsored research. We are very appreciative for the work that you do. You are a critical part of the success of this operation. This is taken from a website of one institution, and the reason why I pulled this one down is, I really like the tagline. The tagline says, "Handling the business of research so faculty can perform the research," and I think it's incredibly important to understand that the conduct of extramural research goes way beyond the science itself. There's much more to it, which, of course, is the reason why many of you have come here to the regional seminar. Now, scientists are under a great deal of stress. This is a series of articles that appeared in "Nature" in 2016. That was 4 years ago. It was a long time ago, and yet what's written here is very much apropos of what's happening today. Scientists, and particularly scientists who are in early stages of their career, complain about a desperate pursuit of grants, long hours without time for science, extreme competition ... We'll talk about that in a bit, about the fact that we exist in what's been termed a hypercompetitive state ... dependence on senior scientists and a state of administrative overload. And so the question is, what's behind all this? By the way, when I do this talk in person, I will often ask people, do these ideas resonate? Do you, either as scientists or people who work closely with scientists, do you get the sense that you're under a lot of stress? And invariably, 95 percent or more of the hands in the room go up. So what's behind all this? Here is a paper that came from a workshop that was done at the University of Wisconsin. It was led by Dr. Judith Kimble. She brought together experts from all around the country to think about the stress that biomedical research is under, and they identified two core problems. One is that there are too many researchers vying for too few dollars and that there are too many postdocs who are competing for too few faculty positions, and essentially, everything else, all the other stress points, such as concerns about peer review, are manifestations of these two core problems. So is this really true? Do we really have too many researchers who are vying for too few dollars? Well, one way we can look at this is shown here. We can look at the numbers of researchers who are receiving support from NIH, and then we can also look at the number of researchers who are seeking support from NIH. So this shows data since the end of the doubling. Remember, the doubling ending in 2003. The line on the bottom, which is a red line with circles, that shows the number of unique people who could say that they were a principal investigator on a research-project grant at NIH, and that number starts around 25,000 back in 2003. It remained relatively flat through about 2014, 2015 and since then has begun to increase. We'll take a look at that in a little bit more detail. The line on the top, which is a green line with green triangles, that line represents the number of unique people who sought to be funded in that particular year. Now, remember, a grant typically lasts for 4 or 5 years, so somebody who applied for a grant in 2002 or 2001, they were hoping to be funded in 2003. So we take that into account, and what we see is that between 2003 and about 2014, there was a dramatic increase in the number of people who wanted to be funded. It went from about 60,000 to close to 90,000. If you think about that, that's a 50 percent, a 5-0 percent increase in the number of people who are seeking funding, whereas the number of people who actually received funding, that number went up by a much lower amount. And then there's a blue line, which we call that the cumulative investigator rate, and that is simply the ratio between the red line and the green line. In other words, it's the number of people who were funded divided by the number of people who actually wanted to be funded. So let's look at this in a little bit more detail. What I'm showing you here is the exact same data that I showed you before, but I'm focusing on the number of unique people who could say that they were serving as a PI on at least one NIH research-project grant. Back in 2003, a little over 25,000. The number increases a little bit over the years, and then with the recent budget increase starting around 2015, there's a dramatic increase. Now it's up to about 33,000, so we've seen a substantial increase in the number of scientists who we're able to fund. And this is that ratio of the number of unique awardees divided by the number of unique applicants, and what one sees is that beginning ... From 2003 to 2014, that number decreased dramatically, and then starting 2014, 2015, the curve changes direction and now is going up. I think to a large extent, we can thank the budget increases that we have received for that, but there also have been a number of policy decisions, as well, and interest on the part of the agency to fund as many scientists as we possibly can, and I would view this as good news. Now, I think it is important to recognize that we are not where we were in 2003. We are still in an environment that is much more competitive than it was back then. Now, the stress is particularly faced by early career investigators. This is something which Congress has noticed. In 2016, the Congress passed by overwhelming bipartisan majorities the 21st Century Cures Act, and in there, there is a provision that states that the director of the NIH shall take steps to make it easier for early career investigators to receive funding and to also take steps to enhance workforce diversity. There's been a lot of interest in the fate of researchers who are at early stages of their career. We had an advisory committee to the director that put together a report on the next generation of researchers. There was a report from the National Academy of Sciences, and as a result of these reports and other input, NIH has taken a number of steps to enhance our ability to fund career researchers who are earlier on in their career. And here is some data that shows the results. The x-axis shows time from 1995 through ... This is 2019, and the y-axis shows the number of unique early career investigators who received support on at least one RO1 or RO1 equivalent. You can see from 1995 to 2010 that that number was relatively flat. We actually did have some improvement with some early stage investigator policies that were put into place in the late 2000s. 2013 was a really bad year, and some of you may remember. 2013 was the year of sequester. That was a time when our nominal budget decreased, and early stage investigators were hurt by this. The number of early stage investigators that we supported well to below 600. Now, look what's been happening over the last few years. The number of early stage investigators has increased dramatically, up to about 1,300 a year. Our goal is to fund at least 1,100 a year, so this is an example of where a combination of budget increases and policy has led to a desired result. All right. So I've talked about money, talked about the trajectory of the NIH budget. We went through a period of doubling from 1998 to 2003. We then went through a period of stagnation from 2003 through 2014 or so. Since that time, we've seen a substantial increase in our budget, and that has had positive effects on people, in that a hypercompetitive system is now slightly less hypercompetitive, and we're now able to fund more researchers and more early stage investigators. Nonetheless, I think it is important to recognize and appreciate that we continue to exist in a hypercompetitive environment, much more so than we did in times past. All right. So let's talk about science. How do we talk about science? Well, one way we can talk about science is by using a framework which is described as Pasteur's Quadrant. This came from a book that was written by Professor Stokes in 1997. It was published by the Brookings Institution, and he argued that one can think about science in terms of two axes. One is relevance, so relevance to applied problems. That's on the x-axis, so as you go from left to right, we're going to more science which is more applied and more, quote-unquote "relevant." The y-axis is knowledge. Are we trying to take something that we already know about and make it more applicable to the community, or are we trying to discover something new that we didn't know about before? And so in that way, we can divide science into four quadrants. The quadrant in the upper left is where what we're really after is knowledge, and we're not really worried about whether or not that knowledge is relevant, so we can call that Pure Basic Research. An example of that would be Niels Bohr, who was one of the early pioneers in physic's quantum theory. Now, the lower right-hand corner would be where what you're primarily interested in is taking known technology or known science and converting that into something which can be used in real life. And so we call that Pure Applied Research, and an example of that would be Thomas Edison, who invented the light bulb and the movies and other types of technologies which are applied. And then the upper right-hand corner is what Stokes referred to as Use-Inspired Basic Research. The example he gives of that is Pasteur. Here, what we're doing is, we're trying to enhance knowledge, but we're enhancing knowledge because of a problem, and there's a problem that we're trying to solve, so I think one way we can think about research and tell a story about research is, we can think about this as Pure Basic Research, trying to enhance knowledge without really think about there's an application. We can think about Pure Applied Research. What we're trying to do is leverage the technology and science that we have to make it more applicable and relevant to the public, and the upper right-hand corner, what some people might think of as the sweet spot where we're trying to enhance knowledge but we're doing that in order to solve a problem. So let's think about COVID-19, which, of course, is what we're in the middle of right now. Maybe Pure Basic Research is where we're trying to learn more about viral biology and viral biology in general, maybe how the human systems or the immune system responds to viruses and other insults. That would be Basic Research. The lower right-hand corner is Pure Applied Research. Here, for example, we have a drug that we already know has antiviral capabilities, like remdesivir, and we put it through a clinical trial to see whether or not it works for COVID-19. It turns out remdesivir actually does. Or we take a drug that we know may have usefulness in inflammatory states, like dexamethasone, and we see whether or not it might work in the inflammatory condition of severe COVID-19. That was a trial that was done in the UK called the Recovery Trial, and shows that it works. Implementation science, where we know that a particular treatment works, but we're trying to figure out how do we make it actually available and accessible and used within clinical practice or within communities? And then Use-Inspired Basic Research would be upper right-hand corner. Here we're thinking about drug development and vaccine development specifically to deal with the COVID-19 pandemic. NIH has a number of programs that are addressing COVID-19 that we might think of as sitting in these various quadrants that Professor Stokes talked about. One of them is the ACTIV Program, A-C-T-I-V, which stands for Accelerating COVID-19 Therapeutic Interventions and Vaccines. This is a public-private partnership. It is truly unprecedented. This was developed in a extremely short period of time. This effort divided itself into four categories. One was preclinical. You can think of that as a mix of Basic Research and Use-Inspired Basic Research. Therapeutics clinic, this was developing therapeutic agents or identifying therapeutic agents that might be worthy of further study. Clinical trial capacity: This is now moving closer to Pure Applied Research, which is coming up with ways in which we could conduct clinical trials rapidly, efficiently on a very large scale much more so than we can in times past. And then on the right group, the fourth group was vaccines, and this group helped to develop the various vaccine trials, some of which are currently underway. Now another aspect of COVID-19 work is what's called the RADx Program. This is rapid diagnosis. Congress allocated a large sum of money for this program. The program has four components. One is what we call RADx Tech. This is where we're looking at technologies that have some degree of maturity and trying to identify those that might get to a point where we could potentially develop tests that would work very well and could reach the point where they would be scalable fairly soon. The second is what we call RADx ATP, so this is advanced technology. In other words, these are technologies that are already quite mature, and issue is, how do we scale it? How do we get to a point where we can use these technologies in thousands, tens of thousands, hundreds of thousands, millions of people in a user-friendly, efficient way. Then we have a third component, which we call RADx RAD. These are for technologies that are more immature, that require quite a bit of work. They may be of value later on down the line but not just yet, and then finally, a very important part of the program is what we calendar RADx UP. UP stands for underserved populations. Now, we know that COVID-19 has particularly serious effects in underrepresented populations, where the rates of illness are higher. The severity of illness are higher, and so these are communities and populations that we really want to make sure we have adequate testing that works and that works well. The goal here is that we will be able to dramatically increase our testing capabilities by the end of summer or fall of 2020. All right. So I've gone over with you a story of science focusing on COVID-19 and using the Pasteur's Quadrant framework to help understand that. Here is another way we can think about the science that we fund. We have Big Science. Now, Big Science means that we're spending a fairly sizable sum of money to support a very large grant proposal of researchers who work together on various large-scale efforts. One example of this is the All of Us study. This is a study that is aiming to enroll a million people. I believe they've already enrolled over 300,000, a large scale cohort so that we can learn more potentially about precision medicine and the nature of health and illness in the community and in various clinical settings. The BRAIN Initiative is a large program that is focusing on better understanding the anatomy and physiology structure of the central nervous system. Then we also fund what is sometimes referred to as Small Science, and I don't like that term, Small Science, because it isn't small. It's just that the budgets are smaller, and what we're talking about is funding a very large number of projects, but each project gets a relatively small sum of money compared to Big Science, so a typical research-project grant, for example, will get about $500,000 a year, whereas some of the larger scale studies may get millions or even tens of millions or dollars per year, and the purpose of this slide, it demonstrates that we fund research in a very wide diversity of fields: diet, genetics, biotechnology, basic science. There is absolutely no way we can possibly do justice to the diversity of the NIH portfolio. We fund about 60,000 projects every year. Okay. So I've talked about money. I've talked about people. I've talked about the kind of science that we fund. Now what I want to talk to you about are some of the concerns that we have, and these concerns affect all three of these. These affect money. It affects people, and it affects science. So, of course, one concern is COVID-19 and dealing with COVID-19, coping with COVID-19 in an environment where laboratories have been shut down or their operations have been dramatically affected because of public-health mitigation efforts. This is our web page. Please come and visit it if you haven't visited already. There was a period of time where we implemented a large number of combinations and flexibilities. Someone of them are still present because these are things that NIH can do. Some of them less so, and this has to do with how we work across the government. Another issue is illustrated in this letter. This was a research letter that was published in "JAMA" by Dr. Reshma Jagsi. She did a study in which she conducted a survey of people who had received a K Award, a career award, and she asked them whether or not they had ever experienced sexual harassment during the time that they were receiving their award, and what she found was that 30 percent of women experienced harassment. These findings, of course, are very concerning. The government commissioned the National Academy of Sciences to conduct a study on sexual harassment of women. The results of that study were released in 2018. The study showed that there ... That sexual harassment, unfortunately, is extremely common, so the results that Dr. Jagsi found in her study of NIH K awardees were absolutely in line with what's been observed elsewhere. The study identified certain characteristics that go along with sexual harassment. This includes male-dominated fields as well as an organizational climate. And they say here that the "Organizational climate is, by far, the greatest predictor" of problems. A bad organizational climate would be one where people are afraid to complain, where there's a lack of sanctions. There's a lack of accountability, a sense that complaints are not being taken seriously. There's a really worry that NIH may be part of the problem by virtue of supporting researchers with large sums of money who then feel that they can do whatever they want or engage in inappropriate behaviors and their institutions will have their back because of the money that they're getting. In 2019, we had a working group to the advisory committee that put together this report. The report was issued last December of 2019. If you haven't seen this report, I would strongly encourage you to take a look at it. The report is entitled "Changing the Culture to End Sexual Harassment," and I think this points out here that this is a cultural phenomenon, that a lot has to happen for sexual harassment to come to an end. Now, NIH has long expected, and this is something which is in our grants policy statement, NIH has long expected that recipients will provide an environment which is safe and healthful, and that this will be an environment that will be conducive to high-quality research. The advisory committee to the director pointed out to us that an environment in which there is harassment is not safe, and therefore, we should use the leverage of our existing policies to address this. One problem that we're particularly concerned about and was also brought up in a number of venues is the phenomenon of what we call passing the rogue. What does that mean? So we have a scientist who is at an institution who engages in some form of professional misconduct, and that misconduct could include harassment, bullying, intimidation, discrimination, retaliation. That scientist is then subject to an internal investigation but then will leave the institution before formal findings are made and go to another institution under the cover of a nondisclosure agreement, and in this way, the new institution has no idea of what's been going on, and neither does the NIH. The NIH just finds out that a scientist is moving from one institution to another, and the institutions would like to move the grant. So effectively then, a person is being protected by virtue of this system. We put out a guide notice, which if you haven't seen, I would strongly encourage you to look at, just a few months ago in June of 2020, in which we said that if a scientist is moving from one institution to another or a scientist has been put on leave or there's been some kind of change in that scientist's employment status that affects their ability to oversee an NIH grant at the institution where the grant was given that the NIH needs to know if the reason for that is because of a safety problem, a problem with a difficult or challenging work environment. We've engaged in a number of other outreach efforts. This includes our web page. This is our web page. There's a lot of resources there, and I would strongly encourage you to take a look at it. We have a web form where people can - anyone, you don't have to be an administrator or an PI- anyone can let us know that there may be problems in a particular laboratory, and if you want to, you can submit this anonymously so that we don't know who you are. Okay. Now another way of thinking about this, you may remember that the National Academy's report identified two problems. One was a problematic organizational climate. The second problem that they identified were male-dominated fields. These are data from the Association of American Medical Colleges. They look at 179,000 faculty who were appointed in 2019 in medical schools around the country. Forty-two percent of the faculty were women. That sounds pretty good. It's not parity, but it doesn't sound that bad until you look at their ranks. So here, what they show is as you go from instructor to assistant professor to associate professor to full professor, the percentage who are women goes down dramatically. So instructors, 59 percent are women, and then as you get to full professor, only 26 percent are women. Well, we see this reflected in our grants, so what this shows are different kinds of grants and the percentage of PIs on those grants who are women. The x-axis shows time from 1998 to 2019, and the y-axis is a percent. The yellow line on the top are career grants, or K grants. Back in 1998, maybe 35 percent of K awardees were women. We are now well over 50 percent. We're approaching 55 percent, but now look at, you might say, more advanced grants or grants that would correspond to higher ranks in the academic sphere, and what we see here is that the percentage of women goes down. So RPGs, research project grants, only about 33 or 34 percent are women. There has been an improvement since 1998, but we are still way below parity. Research centers, like CTSAs or cancer centers, the percentage is below 30 percent, and small business grants, the percentages are lower still. Okay. Another concern has to do with inappropriate interference or influence from foreign actors, and this can manifest itself in undisclosed conflicts of interest or undisclosed disclosure of foreign employment or foreign research grants. We've even seen cases where NIH was unwittingly funding a grant that was identical to a grant being funded by a foreign country. These are two documents that if you haven't seen, I would suggest you do look at. The one on the left, "Threats to the US Research Enterprise" from China's talent-recruitment programs, this was a bipartisan report that was put out by a Senate committee. The item on the right is a presentation that was put together by OSTP, the Office of Science Technology and Policy. The link is on this slide. I would strongly encourage you to look at this because these two reports will give you a sense of the kind of concerns that we have. All right. Another concern that we have is peer review. Now, you may remember at the very beginning when I took you through that high-level tour of NIH, I said that applications go to peer-review panels. What I didn't mention at the time is that that's confidential process. Peer reviewers are supposed to be looking at those applications in strictest confidence. They're not supposed to be sharing their applications with anybody else, and there's not supposed to be any kind of discussion except outside the process between peer reviewers and applicants who are peer reviewers and each other. Unfortunately, we have discovered a number of breaches of peer-review integrity. We have identified a number of these, and some of these, we've published on our blog. I would encourage you to take a look at this. The most important point of all is that as an applicant, you shouldn't be talking to reviewers, and as reviewers, you should keep things to yourself. We have a lot of detailed rules, but generally, they follow this particular framework. So I hope you found this interesting. I've talked to you about general frameworks about how we think of extramural research, that we shouldn't just think about the number of grants or number of dollars, but rather, we're telling stories. We're telling stories about ... We are telling stories about money, but we're also telling stories about people and telling stories about science. I walked you through various ways we can think about the stories. Are we talking about applied research or basic research or something in between, like Use-Inspired Basic research? We talked about big science and small science, and then I also shared with you a number of the concerns that we have. Now, for those of you who are listening to this as part of the regional seminar, again, I want to take this opportunity to welcome you to our virtual seminar. We have a tremendous amount to offer. We'll be talking about fundamentals and resources. We'll talk about preparation of applications, human-subjects research, inventions, patents and contracts. We'll have an open mic session where we can discuss anything that happens to be on your mind. We have sessions about policy compliance, conflict of interest, and we will also have a session, a dedicated session, on sexual harassment, and there is much more. So thank you very much for being part of this. Thank you for your attention, and I wish you well.