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PEOPLE & IDEAS

Terez Shea-Donohue: Optimism helps, and confidence in your work is critical

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Terez Shea-Donohue is the program director of the Division of Digestive Diseases and Nutrition at the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health. As a program director, Terez supports basic and translational research related to neurogastroenterology, gastrointestinal (GI), and GI epithelial barrier function. We spoke to Terez about the transition from active research to a predominantly administrative job, the need for life-long mentorship, and the continued sex/gender bias in health care.

Please tell us a little about yourself and how you first became interested in science.

I was interested in science from a very early age. I grew up in and around the Washington, D.C., area, and so the Smithsonian Institution was in my backyard. People often forget that the institute also has research and educational components, and the museums were among the more popular sites for school field trips as well as visits from out-of-town relatives and friends. My first interest was astronomy, and I was obsessed with the stars and planets. I had a small, mounted telescope and would spend hours looking at the night sky. I memorized everything about the solar system and my parents would embarrassingly quiz me in front of friends and family. The trigger for this interest was regular visits to the Heyden Observatory, which was founded in 1841 and is located on the Georgetown University campus. Father Francis Heyden was a family friend, and the observatory was rededicated to him in 1981 because of his contributions to the school, including a graduate program in astronomy and a program for student researchers from local high schools and colleges. It is the third oldest college observatory in the United States and is a historical building, although sadly no longer in use. My interest in science continued changing several times through marine biology and finally settling on human physiology in graduate school. I started research in the gastrointestinal (GI) tract as a postdoctoral fellow and have remained fascinated with the workings of the gut ever since.

After working as a professor at the University of Maryland, what led to you becoming a program director in the Division of Digestive Diseases and Nutrition at the National Institutes of Health (NIH)? Was the transition away from the bench easy?

There is no greater thrill than discovery research, and the pursuit of innovative science is a powerful motivator to continue to work in a specific research area. The transition from bench to a predominantly administrative position was difficult, but there is probably a point in every research scientist's life when you are ready to consider something outside of the lab. The opportunity to become part of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) program was somewhat serendipitous, sort of the right place at the right time. I really enjoy what I do and whom I work with and, in a sense, I still am involved in discovery research, it is just someone else's work.

Terez Shea-Donohue.

What are some of the qualities or practices that you learned during your time in research that have benefitted you in your current role?

As a research scientist, you need an abundance of patience, strong determination, and a good sense of self-worth. It can take months to years to initiate, conduct, analyze, and publish the results of an experiment, so it is important to recognize that time is a key ingredient in the generation of good science. Scientific research is a marathon, not a sprint, and has its own conventions and idiosyncrasies that exist, in part, because they work. A successful experiment requires considerable effort and attention to detail to ensure rigor and reproducibility and a determination to adhere to the ethics of science, which includes

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honesty, objectivity, and transparency. Any scientist has to be able to accept that you are going to be told "no" more often than "yes," especially in terms of grant applications, publications, and other activities that involve judgment by your peers of the impact of your research on the field. The old saying that if it were easy, anyone could do it applies to medical research, and one cannot take these rejections personally. Optimism helps, and confidence in your work is critical. In science, you really do learn from your mistakes, and sometimes your "mistakes" lead to your best work. One of the most rewarding experiences in research is when the results of a well-designed experiment are totally unexpected. Experimental design is traditionally based on predictable outcomes, and when something unpredictable occurs and can be reproduced, it could be a major advance in the area.

You cover a number of different research areas. What types of projects are you currently most excited about (or are there any you wish to see more of? Although perhaps this isn't something you are able to share)?

My current portfolio includes several areas that I am very excited about. Gut–brain communication is now a vibrant area in GI research, and one area of interest is the mechanisms, both central and peripheral, that underlie disorders of the gut–brain interaction (DGBI) like irritable bowel syndrome. There is a need to identify mechanisms that better coordinate pathology with symptoms and to gain a better understanding of the sensory processes in the gut that coordinate function and that are disrupted in DGBI. Another area of focus is determining the possible role of the gut in the initiation, progression, and pathogenesis of neurodegenerative diseases such as Parkinson's. Starting this fall, the NIDDK is funding a new consortium called the Gut-Brain Parkinson's Disease (PD) Consortium that will take advantage of the combined expertise of neurologists and gastroenterologists. Currently, there are primarily symptomatic treatments for PD and no approved therapies that target the underlying neurodegeneration. The reason for NIDDK's interest in this area is that >50% of patients who develop PD have a history of GI complaints like constipation, gastroesophageal reflux, and nausea, which often precede the onset of motor symptoms (prodromal). This consortium will study PD patients with and without GI symptoms to assess the therapeutic potential of targeting the prodromal phase of PD. The goal is to identify the key gut–brain pathways and biomarkers that can be leveraged to develop mechanism-based diagnostic tools as well as therapies that impact disease progression in PD. The last area of interest is neuroimmune interactions in the gut. The GI tract is an important interface for communication between immune cells and neurons in the enteric nervous, peripheral nervous system, and brain. Dysfunctional neuroimmune communications contribute to the symptoms, severity, and chronicity of GI disorders. Remodeling of neuroimmune interactions may underlie the persistence of symptoms in disease remission in inflammatory bowel disease or in the absence of overt disease pathology in DGBI. These interests coincide with that part of my job to call attention to areas of research that are understudied to increase the number of grant applications in these areas or advocate for a funding opportunity directed to a specific area.

You are also involved in the NIDDK Women's Health Working Group. Sex/gender differences in health and disease is an area that is gaining more research attention. Could you expand a little on your work in this group, and why this oversight is needed?

The NIDDK Women's Health Working Group was formed to promote recognition of the issues related to the health of women across the lifespan, diseases/conditions specific/unique to women, and sex/gender differences in health and disease. The NIDDK Women's Health Working Group is a point of contact for the NIH Office of Research on Women's Health (ORWH), which, in turn, is a point of contact at NIH for the first-ever White House Initiative on Women's Health Research. This initiative was issued by President Biden in November of 2023 and was led by the First Lady, Jill Biden. The stated goals of this initiative are prioritizing investments in women's health research, integrating women's health across the federal research portfolio, and stimulating new research on the midlife health of women. In August of this year, the Biden–Harris Administration announced $27.5 million in funding opportunities to enhance women's behavioral health that will address the unique mental health and substance use treatment needs of women. NIDDK is one of the institutes that cosponsors with ORWH the Specialized Centers of Research Excellence (SCORE) on sex differences. Each SCORE program has three integrated research projects and an administrative core. Importantly, the programs also include a Career Enhancement Core that supports pilot research and trains the next generation of scientists in the study of sex differences. There is still a sex/gender bias in health care, and continuing oversight is needed at the NIH, Health and Human Services, and federal levels to maintain the momentum in addressing these issues head-on.

Do you feel optimistic about the future of women in science in general?

I am cautiously optimistic about the future of women in medical research. When I was in graduate school, there were very few women, and surprisingly, some of the women who were in higher positions did not always go out of their way to support the women coming up. There was an absence of formal outreach or advocacy for women at that time. Luckily that has changed, but while the number of female graduate and medical students as well as post-doctoral and clinical fellows is very equitable to men, the number of women in positions at the top of the academic ladder does not reflect their representation at these early career levels. Academic research is not for the faint of heart as the time and energy needed to run a productive lab is considerable. Work–life balance can be difficult to achieve, and that can be discouraging to graduate students considering a career in academia, especially women. Thus, mentoring is extremely important, and there is a need for women at the top to provide those career-advancing opportunities for early career investigators. A first-time experience in my current position at NIDDK was having a woman as a mentor, and this also emphasizes the importance and need for mentoring across the lifespan. In November 2023, Monica M. Bertagnolli, M.D.,

was sworn in as the 17th director of NIH, and she is the first surgeon and only the second woman to hold that position. It is an exciting time for women in science.

What do you most enjoy about your current role?

My research was always focused on a limited number of topics in the GI tract, and now at NIDDK, I have a real appreciation of the breadth of GI-related research. It is amazing to see the rate at which science advances when one can see everything from a higher vantage point. At the University of Maryland Medical Campus in Baltimore, I led a graduate school track, and my personal goal when I came to NIDDK was to continue outreach to the next generation of scientists, especially women and scientists from underrepresented groups. I enjoy the interaction with the grantees, helping early career investigators navigate the grant review and submission process, trying to stay ahead of the field in terms of anticipating areas that would benefit from targeted funding opportunities.

What kind of approach do you bring to your work, and what motivates you day to day?

I welcome the challenge of acquiring expertise in a different area. Going from the smaller focus of my laboratory research to being exposed to the broader area of research across NIDDK appeals to any scientist's innate need for continuous learning. There is no day that goes by that I am not learning something new, and that is incredibly rewarding.

Is there anything that you miss from the bench (or anything that you were very happy to see the back of)?

I miss more aspects of the lab than I care to admit: reviewing a new set of data, working with students and trainees to solve a problem, and presenting at scientific meetings are just a few of the activities. The one aspect that I am glad to leave behind is the responsibility of funding the lab. It is an all-consuming process, and I am very happy to be in a position that now awards the money.