American Thoracic Society

Research News Quarterly

SEPTEMBER 2020

In This Issue

Letter from the Editor

Our feature this month is an interview with the director of the NIH's National Institute on Drug Abuse (NIDA), Nora Volkow, MD. In the interview, Dr. Volkow discusses NIDA's focus on drug abuse, including opioid abuse and the intersections with respiratory health. These include efforts to study the effects of tobacco use, including e-cigarettes, on susceptibility to and severity of COVID-19 disease, new treatments for respiratory complications of opioid overdose, and the effects of opioid overdose on sleep. Dr. Volkow points to these and other areas for collaboration between NIDA and the pulmonary, critical care and sleep community.

The September Quarterly includes several updates from NIH, beginning with recent recommendations by a new Trump Administration ethics advisory board against the use of certain fetal tissue in federally-funded research. The updates include news of the launch of NIH's new MOSAIC program for early career scientists, the announcement of a fall NIH program funding seminar, also intended to assist early career researchers, and a new NCATS's initiative assessing the impact of COVID-19 on individuals with rare diseases.

Next we feature a COVID-19-related commentary series from members of the Research Advocacy Committee (RAC) and other ATS members, on ongoing COVID-19 research, including new animal models and the impact of the pandemic on research careers. The series concludes with an assessment of and call for diversity in the biomedical research workforce.

We round out the Quarterly with a report from our Washington Office on health research funding.

Sincerely,

James K. Brown, MD
Editor
Chair, Research Advocacy Committee

RESEARCH NEWS QUARTERLY FEATURE

Interview with National Institute on Drug Abuse Director
Nora D. Volkow, MD

Nora D. Volkow, MD
Director, NIDA

1. What is your vision for the institute over the next few years?

My vision for NIDA is anchored in its mission to "advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health." At the same time, the specific contours of that vision are being shaped by the dynamic scientific and addiction landscapes, which respectively present us with exciting opportunities and complex challenges.

The resulting research portfolio is wide ranging, but I would like to highlight three key goals outlined below:

- Understanding drug use, behavior, and the developing brain continues to be a major focus of our research agenda. This includes how drug use affects the cells and circuits of the brain, how addiction occurs, and how the brain changes over time with chronic drug use. This also includes understanding the trajectories of drug use in the real world: how drugs are used and by whom, and how different risk and protective factors interact over an individual's lifespan to influence drug-related outcomes.

  The Adolescent Brain Cognitive Development (ABCD) Study is a great example of this category of research. ABCD will determine how childhood experiences (such as family structure, socioeconomics, education, nutrition, sleep patterns, drug exposures, social media among others) interact with each other and with a child's changing biology to affect brain development and their behavioral, academic, health, and other outcomes. ABCD, which is already tracking more than 11,000 children, is the largest longitudinal long-term study of brain development and child health in the United States.

- Developing medications and other treatment interventions for substance use disorders, including opioid use disorders (OUD). NIDA's medication development program and its translation and clinical trial programs have allowed development and testing of new medications such as the FDA-approved intranasal naloxone for overdose reversal and lofexidine for the treatment of opioid withdrawal. Research is also ongoing to identify alternative endpoints other than abstinence for demonstrating medication effectiveness in substance use disorders. These medication development and testing programs have been

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Quarterly Feature: Interview with NIDA Director *(Continued from page 2)*

expanded thanks to the NIH HEAL (Helping to End Addiction Long-term) Initiative, launched in April 2018 to provide scientific solutions to the national opioid overdose crisis, including improved treatment strategies for pain as well as OUD and opioid overdose. In parallel, we continue work to explore innovative interventions that include treatment of stimulant and cannabis use disorders, and adolescent vaping.

- Implementing evidence-based strategies in real-world settings. Our efforts include researching scaled up applications of tested interventions (e.g., screening, harm reduction, collaborative care models), enhancing the integration of prevention, treatment, and recovery support services into general medical care and other settings, including the justice system, and better understanding the impact of racial inequity, cultural differences, social structures, and evolving drug policy on health disparities in accessing and utilizing quality care for substance use disorders.

2. Early evidence suggests that cigarette smoking and vaping each increases susceptibility to and severity of respiratory complications of COVID-19. Is NIDA studying the potential negative effects of these substances on COVID-19's effects in the lung?

NIDA is very concerned about the interactions between COVID-19 and substance use disorders (SUDs) in general, which have a great potential to exacerbate each other's effects. The intersection between smoking/vaping and COVID-19 is particularly relevant because COVID-19 attacks the lungs and could be an especially serious threat to those with histories of smoking tobacco or marijuana or of vaping. Evidence continues to emerge, including a systematic literature review and meta-analysis showing that current smoking is associated with a greater risk for more severe COVID-19 outcomes, and a small survey study that recorded heightened risk of COVID-19 in adolescents who vape. In recognition of this urgent public health need, this past March, NIDA released a Notice of Special Interest to encourage research to investigate COVID-19 in the context of substance use, and we have funded researchers to investigate questions around the intersection of smoking, vaping, and COVID-19.

3. Is NIDA supporting research to find other ways than naloxone to treat respiratory depressant effects of opioid overdose?

Developing new addiction treatments and overdose-reversal tools is one of the major goals NIDA is pursuing right now. While the development of nasal naloxone was a life-saving advance, a wider range of overdose reversal options is needed to combat the extremely potent opioids that are now driving the overdose crisis. These may involve not only new formulations of existing drugs (e.g., longer-acting depot formulations of opioid agonists or longer-acting naloxone formulations that might be more suitable to reverse fentanyl overdoses) but also compounds that stimulate respiration or immunotherapies to prevent opioids from entering the brain. We are also interested in device-based approaches to overdose reversal, including the development of devices capable of detecting respiratory depression associated with overdose and initiating naloxone delivery.

4. Is there interest at NIDA for supporting research on the immunosuppressive effects of opioids and risk for respiratory inflammatory diseases?

Most NIDA-funded studies addressing the impact of opioid use on immune and/or pulmonary function fall within our pathophysiology of HIV portfolio. For example, one study from the University of Miami is investigating the immune deficiency in virally suppressed HIV-infected chronic opioid users that can lead to failure of an effective response to the flu vaccine. Another study from Yale is looking at HIV-1 expression, pro-viral landscape, and genomic architecture in response to different forms of medication treatment for OUD in a group of persons living with HIV. An ongoing study out of Boston University, is using single-cell transcriptomics to investigate the effects of OUD on HIV latent reservoirs and immune dysfunction,

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Quarterly Feature: Interview with NIDA Director *(Continued from page 3)*

while the New England Consortium Node of NIDA's Clinical Trials Network is collecting data from individuals with OUD as well as from emergency departments in four cities to generate time sensitive information about the impact of COVID-19 on individuals with OUD.

5. Is the Institute studying the effects of opioids on sleep?

Healthy sleep is an important aspect of successful treatment of OUD. Natural and synthetic opioid drugs can produce profound sleepiness, but they also can disrupt sleep by increasing transitions between different stages of sleep, and people undergoing withdrawal can experience terrible insomnia. Consequently, this is an active area of research for NIDA scientists. A component of the HEAL Initiative targets sleep dysfunction as a core feature of OUD and recovery. Additionally, researchers in our intramural program are studying how opioid use affects sleep in OUD patients treated with opioid agonist medications and exploring whether and how changing clinic appointment hours could affect the quality of their sleep.

I believe the future of addiction treatment lies in approaches that are more personalized and multidimensional, and this includes using combinations of medications and other interventions that target specific symptoms of the disorder. It could prove very useful to target an individual's sleep problems as one of the dimensions of treatment. For example, investigators in Johns Hopkins are probing the impact of sleep disruption on opioid misuse liability and analgesia in patients with chronic low back pain, the results of which will critically inform clinical decision making related to the prescription of opioids for patients with chronic pain. Also, NIDA is currently funding research to test the efficacy of suvorexant, an FDA-approved insomnia medication that acts as an antagonist at orexin receptors, in people with an OUD.

6. How can ATS and its members most effectively partner with NIDA on areas of priority focus?

There are many overlapping areas of interest that offer natural partnership opportunities between ATS and NIDA. For example, we have recently proposed to organize a session at the 2021 ATS annual meeting about the evolution of the opioid crisis, the public health response to it, and the mechanisms of opioid-induced mortality with a focus on respiratory depression. Our plan is to convene speakers that will address the current understanding of respiratory control, how opioids affect respiration, and recent developments and gaps in research on mechanisms of central and peripheral respiratory control. We want to pay particular attention to mechanisms underlying opioid-induced "wooden chest" syndrome, a phenomenon coming under scrutiny as a potential contributor to opioid-induced mortality. We believe that ATS 2021 will provide a fertile forum for attendees to identify and harness the power of collaborations.

There are certainly many more opportunities for synergistic interactions moving forward. I would like to encourage ATS members to visit our revamped website and take advantage of the extensive knowledge base that can be found there which may be useful to inform clinical care, enhance public health messaging, and craft advocacy campaigns. Our site also offers multiple channels for interacting with us: we always welcome specific concerns, constructive criticism, and topical questions or comments on areas of common interest. ■

RESEARCH POLICY NEWS – FETAL TISSUE RESEARCH

Trump Administration Ethics Advisory Board Rejects Most Fetal Tissue Research Grants

On July 31, 2020, the NIH Human Fetal Tissue Research Ethics Advisory Board convened by the Trump Administration met and reviewed new and competing renewal extramural NIH research grant applications that use human fetal tissue obtained from elective abortions. The 15-member board, chaired by Page Comstock Cunningham, Interim President of Taylor University in Indiana, was charged with making recommendations to the Secretary of Health and Human Services (HHS) on whether extramural NIH research grants utilizing human fetal tissue donated from elective abortions are appropriately justified and should be funded. Ten of the panel's fifteen members have previously publicly opposed abortion or human fetal tissue research. The board was set up as part of the Trump Administration's 2019 policy changes restricting federally-funded human fetal tissue research. These restrictions also specifically include an outright ban on intramural NIH research using human fetal tissue obtained through elective abortions.

During a public open commentary session, ATS Research Advisory Committee Vice Chair Thomas Mariani, PhD, provided comments to the Board on behalf of the ATS. In these, Dr. Mariani pointed out that research studies with human fetal tissues were pivotal to the development of pulmonary surfactant as an intervention to combat the leading cause of death in preterm infants, and are a major resource for vaccine development, including for respiratory viruses similar to SARS-CoV-2. He noted that no alternate exists to replace the use of human fetal tissues for many contemporary research applications. Urging them to refrain from placing any new restrictions upon the use of fetal tissues in research studies, Dr. Mariani said, "Local and regional Institutional Review Boards serve to ensure that research is compliant with the ethical standards and regulations governing human subject research. Any restrictions are best considered at the local and regional level, using the Institutional Review Board process that continues to be fully functional". Despite these challenges, interest in rare diseases research has drastically increased in the past two decades, partly becaus e better communication and data sharing opportunities in the Internet age have allowed patient communities to organize and collaborate with interested researchers. Gene identification and access to genetic testing has improved diagnosis of many rare diseases and provided insight into potential therapeutic targets. As a result, industry has taken a more active interest, recognizing that rare diseases can often serve as natural laboratories for more common conditions.

The grant applications reviewed by this special ethics board had already gone through standard NIH peer and ethics review. On Aug. 18, the Board issued its report recommending that thirteen of the fourteen research grant applications reviewed not be funded. The panel's rationale's for rejecting grant proposals included inadequate justification for the use of human fetal tissue, failure to clarify the amount of tissue to be used, and deficiencies in the informed consent process for individuals who donated fetal tissue. The single research grant that was approved by the board by a nine-to-six vote focused on development of an alternative research model to human fetal tissue, using a comparator previously obtained and available through a biorepository.

The board's recommendations are not binding, and the HHS Secretary will make the final decision on whether the grants will be funded, a decision which has not yet been announced. In accordance with its charter, the board will disband by mid-Sept. 2020. If President Trump is re-elected, a new panel will be convened to review new and competing proposals. The Trump Administration's fetal tissue research restrictions are policy, not law, and can be reversed by future administrations.

NIH NEWS & RESOURCES

NIH Launches New MOSAIC Program for Early Career Researchers

In Aug. 2020, NIH launched the new **Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program**, designed to support career transitions for promising postdoctoral researchers from diverse backgrounds, such as individuals from groups underrepresented in the biomedical research workforce at the faculty level, into independent faculty careers. The program is administered by the NIGMS but is a collaboration across NIH institutes including the NHLBI.

The program has the following two components:

1. MOSAIC Institutionally Focused Research Education Cooperative Agreement to Promote Diversity (UE5). This mechanism supports scientific societies whose members conduct research within the NHLBI mission. Awardees will provide skills development, mentoring, and networking opportunities that prepare cohorts of scholars supported by **MOSAIC K99/R00 awards** to transition into independent faculty careers at research-intensive institutions. For more information see: **PAR-19-342**. **Please note the last application deadline is Nov. 2, 2020.**

2. **MOSAIC Postdoctoral Career Transition Award to Promote Diversity (K99/R00)**. This mechanism assists postdoctoral scientists from diverse backgrounds that are conducting research in areas within the NHLBI mission by providing up to five years of support in two phases. The initial (K99) phase provides support for up to two years of mentored postdoctoral research training and career development. The second (R00) phase provides up to three years of independent research support once the scholar transitions to an independent faculty position. For more information see: PAR-19-343.

For additional information on both funding announcements, please see the MOSAIC website.

Fall NIH Seminar on Program Funding & Grants Administration

NIH plans to hold a virtual seminar Oct. 27 – 30, 2020 on NIH program funding and grants administration for early-career researchers, particularly those new to the NIH grant application process, and grant administrators. The seminar will include live and recorded sessions on grant policies and processes, including live chats with NIH and other Department of Health and Human Services experts. Free registration for the seminar is here.

RARE DISEASES UPDATE

Survey on the Impact of COVID-19 on People Who Live with Rare Diseases and Their Families

As the COVID-19 pandemic reached the United States in early 2020, it became apparent that understanding the impact of COVID-19 on rare disease patients was important because of the high vulnerability of this population. Targeted research was necessary.

In April, a group of Rare Diseases Clinical Research Network (RDCRN) investigators, led by the network's coordinating center at Cincinnati Children's Hospital Medical Center, undertook a survey of rare disease patients living in the United States. The 23 RDCRN research teams are funded by the National Institutes of Health (NIH), led by the National Center for Advancing Translational Sciences, to study how particular rare diseases progress and work to develop improved approaches for diagnosis and treatment. The survey launched in May under the oversight of the Institutional Review Board at Cincinnati Children's.

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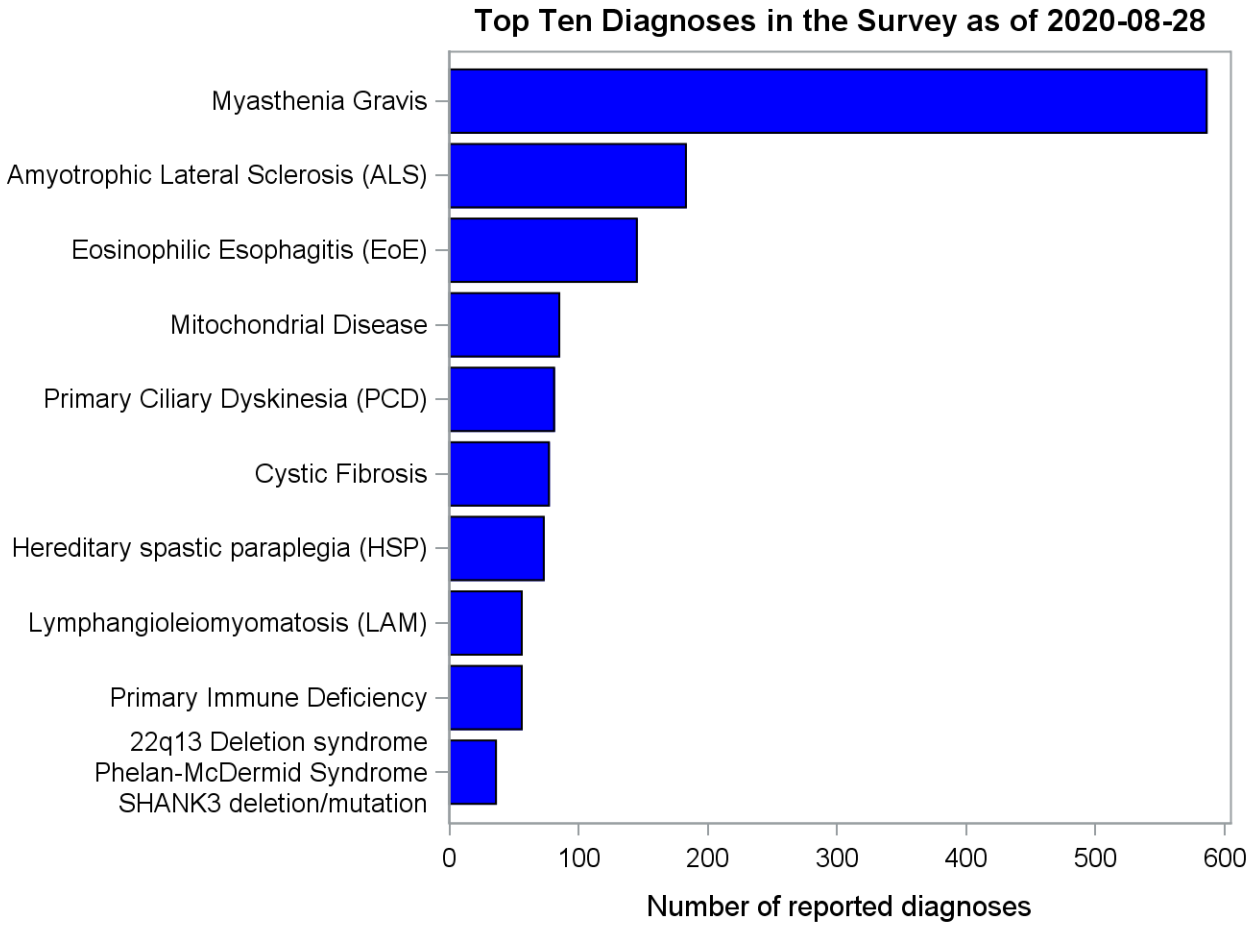
NCATS Rare Disease Program Update *(Continued from page 6)*

The survey is not limited to those with proven COVID-19 infection but collects information on how COVID-19 has affected the lives of all individuals with rare diseases. The investigation has several aims: to estimate the proportion of patients who live with rare diseases who have been diagnosed with COVID-19 infection; to learn about the COVID-19 presentation and the course of the infection (including treatment) among patients with rare diseases; to determine whether certain subgroups of patients have been affected more frequently or have experienced increased severity of the infection; to learn about potential interaction between specific rare disease treatment regimens and COVID-19 infection; to assess the extent to which the COVID-19 pandemic has affected the lives of rare disease patients and their families including their access to medical care and routine medication; and to determine how the RDCRN can respond by providing information and advice through its network of experts, its consortia and in collaboration with patient advocacy groups.

Early Results

As of today, more than 3,500 rare disease patients or their caregivers throughout the nation have completed the survey. The figure below shows the top ten diagnoses reported by survey respondents as of Aug. 28, 2020. Respondents represent nearly 130 rare disease types, including several conditions relevant to American Thoracic Society members, such as cystic fibrosis, lymphangioleiomyomatosis, and primary ciliary dyskinesia. Survey enrollment has been extended through



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the early fall and a first analysis of the data is planned in September. The survey is available in English and Spanish through the RDCRN website (rarediseasesnetwork.org/COVIDsurvey). The site also includes a dashboard with routine updates on select statistics from the survey.

Follow-up surveys may be done in the future to allow a longitudinal assessment of the rare disease population. To learn more, visit rarediseasesnetwork.org/COVIDsurvey or email rd.covid19@cchmc.org.

The RDCRN network, now in its fourth five-year funding cycle, is a partnership with funding and programmatic support provided by Institutes, Centers, and Offices across NIH, including the National Institute of Allergy and Infectious Diseases, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Neurological Disorders and Stroke, the National Heart, Lung, and Blood Institute, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Dental and Craniofacial Research, the National Institute of Mental Health and the Office of Dietary Supplements.

NIH COVID-19 RESOURCES

The following are key NIH COVID-19-related resource websites:

- **NIH COVID-19 resource for applicants and grantees** including guidance for various aspects of research and grant application processes, as well as FAQs and COVID-19 funding opportunities.
- **COVID-19 "Updates History" webpage** that details relevant updates for applicants and grantees by date.
- **FAQ document on COVID-19** flexibilities related to policies and programs affecting the grants process.
- **Funding opportunities specific to COVID-19** lists active and expired funding opportunities across NIH related to SARS-CoV-2/COVID-19 research.

ATS MEMBER RESEARCH PERSPECTIVES

Research to Combat A Pandemic: Considerations for Animal Models of COVID-19

By **Mark D. Ihrie, PhD & Jennifer L. Ingram, Ph.D.,** Div. of Pulmonary, Allergy & Critical Care Medicine, Duke University Medical Center

Animal models of human disease play a critical role in health sciences research by facilitating the study of disease mechanisms and drug and vaccine development. During the coronavirus disease 2019 (COVID-19) pandemic, scientists worldwide are laboring to understand SARS-CoV-2 infection. The result has been rapid research advancements, including the development of potential vaccines, treatments and animal models of COVID-19. While no current animal models fully recapitulate the COVID-19 symptoms seen in humans, important insights have already been gained from these models, and with continued refinement and characterization they may yield information vital to stopping the spread of COVID-19[1,2].

Researchers have used several species of nonhuman primates to study COVID-19. A model in rhesus macaques has been one of the most effective[3,4]. Rhesus macaques, when inoculated with SARS-CoV-2, develop symptoms indicative of acute respiratory distress syndrome (ARDS), and further evidence suggests that the animals develop immunity[3,5]. While nonhuman primates are essential for vaccine development, low animal numbers reduce statistical power, and ethical and logistical concerns prevent widespread use in research. Conversely, the mouse is commonly utilized and readily available for research, but wild-type mice are not a suitable model due to the low affinity of the spike proteins of SARS-CoV-2 for murine ACE2 resulting in low infectivity in mice[6]. However, this problem has been partially circumvented through the

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The COVID-19 Pandemic and Research Careers *(Continued from page 8)*

use of transgenic mice and by adapting clinical isolates of SARS-CoV-2 in the respiratory tracts of mice[1,7]. A mouse expressing human ACE2 under the control of the human cytokeratin promoter was previously developed to study SARS-CoV, and these mice have been shown to be susceptible to SARS-CoV-2 as well[1,8]. Upon inoculation with SARS-CoV-2, these mice develop weight loss and lung inflammation, though no increase in mortality is observed[1].

In addition to this transgenic model, SARS-CoV-2 has been remodeled such that it has a higher affinity for murine ACE2, enabling infection with the recombinant virus[9]. This recombinant virus is able to replicate in the lungs of mice and causes airway inflammation[9]. Though these two mouse models are promising, difficulty in obtaining transgenic mice or recombinant SARS-CoV-2 would make widespread adoption difficult. Additionally, there is some concern about whether transgenic mice expressing human ACE2 properly recapitulate ACE2 expression patterns in humans[4].

Two small animal models of COVID-19, the ferret and Syrian hamster, show promise thanks to their susceptibility to SARS-CoV-2 infection, replication of disease symptoms, and potential general availability. Hamster Ace2 has a high degree of homology to human ACE2, and hamsters inoculated with SARS-CoV-2 develop pathology similar to human clinical symptoms, including altered lung weight, weight loss, airway inflammation (severe ground glass opacity, pulmonary consolidation), and viral N protein expression[2,10]. Additionally, virus transmission can occur between animals through direct contact or aerosols, and hamsters develop extrapulmonary pathology such as intestinal mucosal inflammation and myocardial degeneration[2,11]. Furthermore, hamsters are protected against subsequent challenge with SARS-CoV-2[10]. Ferrets have been commonly used to study viral transmission, and are useful for respiratory research because, unlike mice, they exhibit a cough reflex[4]. Ferrets are highly susceptible to infection with SARS-CoV-2 and exhibit symptoms similar to humans such as cough, reduced activity, and increased body temperature[12]. Viral transmission is also possible between ferrets, and they display histopathology similar to that seen in humans[12,13].

Several other animals have been considered as potential models of COVID-19, including cats, cynomolgus macaques, common marmosets, and Chinese tree shrews[4,14,15]. Though the animal models discussed are potentially useful for studying SARS-CoV-2, they are not without their disadvantages. One major outcome that most of these animals fail to recapitulate is the mortality seen in humans[4]. The single exception to this is cats, but in nearly all other cases, SARS-CoV-2 infections resolve with very low mortality[4,12]. Additionally, the presence or absence of several symptoms have not been adequately addressed in these models, such as gas exchange impairment and systemic changes (e.g. coagulopathy).

With further research, important aspects of these models will likely be refined and prove useful for examining the effects of preexisting conditions, such as age and obesity, on SARS-CoV-2 infection and long-term COVID-19 outcomes. Researchers already are looking at the effects of age on SARS-CoV-2 infection in hamsters, where age differences in susceptibility to disease resemble those of humans[16]. Vaccine development has been enabled through the use of mouse-adapted SARS-CoV-2, and by studying rhesus macaques, we have learned of the potential for immunity[5,17].

As in all research modeling human disease, the value of the model lies in how well the features of human disease are recapitulated, taking into account inherent limitations of the model. Animals have always had some limitations when modeling human respiratory infections, including differences in nasal, lung and airway anatomy and physiological responses (e.g. cough), genetics and immune responses and altered susceptibility or transmissibility of infection. But, these models do offer a valuable tool for performing a variety of viral challenge experiments under specific controlled conditions, in diverse genetic backgrounds and with targeted tissue/cell delivery systems. The use of these models reduces the variability that is necessarily part of human clinical studies and avoids some of the ethical controversy involved in challenging

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human subjects with active SARS-CoV-2. Furthermore, the development of mice with transgenic and adenovirus-delivered human ACE2 overexpression has already provided insights on the role of ACE2 in SARS-CoV-2 infection, immune responses and disease outcomes[18,19]. Also, recent Syrian hamster studies contributed new knowledge on the potential for prophylactic administration of neutralizing antibodies to protect against COVID-19[20,21] and point toward the merit of further human studies.

Although progress with these animal models of COVID-19 to date has been primarily in establishing the infectivity, transmissibility and severity of disease in response to the SARS-CoV-2 challenge, combining these mouse models with other transgenic and complex disease models in mice has the potential to define unique cellular and molecular mechanisms driving active and post-COVID-19 outcomes in patients with specific co-morbidities, including chronic lung diseases. Furthermore, ferrets offer an opportunity for understanding of unique mechanisms of transmissibility of specific SARS-CoV2 mutations[13,22] either before or after these mutations take hold in human populations. Finally, all of these models allow for important pre-clinical testing of vaccines, antivirals and other therapies to show safety and efficacy prior to human studies. In conclusion, animal models of COVID-19 have come a long way in a short time thanks to the work of dedicated researchers during the current pandemic.

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COVID'S IMPACT ON RESEARCH

Great Expectations in Hard Times: The COVID-19 Pandemic and Research Careers

By **Hasina Outtz Reed, M.D. Ph.D., Asst. Professor,** Div. of Pulmonary, Allergy & Critical Care, Weill Cornell Medicine

The COVID-19 pandemic has changed all our lives, both professionally and personally. For many, a feeling of helplessness and a fear of the unknown have combined to make this a truly terrifying time. Professionally, physicians across the country have stepped up to the challenge of an overwhelming clinical burden of incredibly sick patients, often at great personal sacrifice to themselves and their families.

The COVID-19 pandemic has also affected academic research in a variety of ways—in some instances providing new opportunities, but more often, creating roadblocks and setbacks. Because of the unique nature of this moment of crisis, there have been new opportunities for COVID-related research, most notably new funding sources and expansion of existing research programs in ways that may be relevant for the future trajectory of the pandemic. However, the more common experience is that the pandemic has caused most research programs to come to a complete halt. For both bench and clinical researchers, COVID-19 has wrecked havoc on nearly all aspects of their research enterprises. Adapting and expanding existing research programs to focus on COVID-19-related topics is certainly worthwhile when possible and applicable. However, the reality is that obviously not all research can or should be COVID-19-related moving forward. There will be a time when we are on the other side of this pandemic, and we will still need experts in COPD, airway epithelial progenitor cells, health systems delivery, or any one of the myriad research communities that ATS encompasses and supports. We all must get back to the things that we do best. Indeed, the non-COVID-19-related research we do today may well prevent the next global pandemic or health care crisis.

Just as the pandemic has affected all forms of research, so too has it impacted researchers at all stages of their careers. Senior and junior researchers alike have had their research programs come to a standstill and their academic productivity impaired. Senior faculty have faced significantly more challenging conditions for effectively mentoring junior faculty and fulfilling their multifaceted administrative responsibilities. Junior faculty

Source: Getty Images

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are perhaps particularly disadvantaged in this moment, as they are in a sensitive career stage where the tasks of establishing a research program, securing funding, and taking on leadership roles seem even more overwhelming and possibly even out of reach in the current environment.

It is important to acknowledge that among all young investigators, the research careers of physician-scientists have been placed in an especially precarious position. Protected research time, away from clinical responsibilities, is a key element for the success of any junior investigator who aims to have a career that is centered upon research. However, as cases of COVID-19 remain high in many parts of the country, the need for clinicians becomes paramount. Particularly in hard-hit areas, there is a clear sense of collective duty amongst frontline health care workers, especially for those whose training so closely aligns with the current clinical need. As most researchers were, and continue to be, unable to move their research programs forward, being able to contribute to the enormous need for clinical care can in some ways be a relief. There is some solace in being able to help during a time when feeling helpless is the norm.

And yet, as the weeks go by, another panic has set in amongst myself and my colleagues—*when will things get back to normal and stay that way?* As case rates decline and the dust settles, the reality of the demands of a research career will mount once again. Once the COVID-19 crisis is over, how will we assess the damage to the careers of physician-scientists? How will we get back on track? Like all researchers, this crisis has led us to mourn the loss of clinical trials, reagents, mice, and momentum. Like all researchers, we will spend months (years?) trying to claw our way back to productivity. But for the physician-scientist, there will also be a constant concern of continued clinical service needs that will compete with the ability to continue our research productively. In places where the curve has not been bent and COVID-19 cases have flattened to a steady but significant flow, it is possible that a state of increased clinical demands will continue for the foreseeable future. Protected research time is paramount. But how can that be squared with a sense of duty towards our patients, our community, and our colleagues during a health crisis?

This is, in a lot of ways, an illustration of the dichotomy of the career of a physician-scientist in general, that is feeling the pull to clinical service but also the necessity of protected research time. Finding the right balance can be difficult to navigate even in the best of times, let alone during a pandemic. But there will be a time, hopefully soon, when we must attempt to pivot and face the future as best we can. We must get back to our research, hopefully with the support of our academic institutions and funding agencies. Without both protected time and resources, restarting our research will be a tremendous challenge. This support will not only mean a greater chance of future success for researchers but will also signal that even a global pandemic cannot dispense with the mandate for academic institutions to be places where clinical service and research function alongside each other. ■

DIVERSITY IN RESEARCH

Diversity Among Funded Researchers: An Opportunity To Do Better!

By **Jerry S. Zifodya, MD, MPHTM**, Tulane Univ. School of Medicine, Pulmonary, Critical Care, & Env. Medicine Sec. & **Monica Campo, MD, MPH**, University of Washington, Pulmonary, Critical Care & Sleep Medicine

The COVID-19 pandemic has amplified the disparities that exist in the US healthcare system. Concurrently, there have been widespread demonstrations and calls for racial equality after the murder of George Floyd. Academic institutions are not immune to racial and ethnic disparities in faculty, and there have long been wide gaps in racial diversity of faculty in promotions, manuscript publication, funding, and in the scientific review process[1,2,3]. Most recently, there has been a renewed call to arms to address these disparities[4].

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Underrepresented minority (URM) groups are disproportionately represented at a national level in scientific research positions: 4% black, 5% Hispanic or LatinX, 0.2% American Indian or Alaskan Native[5]. This is in contrast to the general US population which is 13% Black, 19% Hispanic or LatinX, and 1.3% American Indian or Alaskan native[6]. Among full-time medical school faculty, only 3.6% are Black and 5.5% are of Hispanic, LatinX, or of Spanish Origin[7]. A lack of diversity in research is pervasive and includes training positions with significant race/ethnicity gaps in those matriculating into graduate medical education positions with only marginal improvements seen over time[8]. From 2002 to 2017, among a representative sample of US medical schools, there was an increase in female matriculants from 49.0% to 50.4%. However, during this time, Black and Hispanic matriculants were only marginally improved from 6.8% to 7.3% and from 5.4% to 8.9%, respectively, remaining disparately low overall[9].

Diversity in the biomedical workforce is urgently needed. Diversity not only increases innovation in approaches but has also business productivity[10,11]. The National Institutes of Health (NIH) has established multiple efforts to increase diversity in the biomedical workforce. However, disparities on R01 applications from the NIH are described in multiple studies[3,12]. In 2009, the NIH introduced an Enhanced Peer Review Process to improve clarity and objectivity for scoring applications[13]. More than 10 years later URMs continue to be under-funded, which translates into less academic positions, less URM representation in academic leadership, and reduced diversity in the biomedical force[14]. These discrepancies in funding are not limited solely to race but also to disability and gender[15,16].

Why do disparities in research funding persist? Bias in the scoring system, a limited pool of applicants, and CVs with less qualifications are some of the factors that explain disparities in research funding. A recent study from Hoppe, et al. found three crucial points that made significant contributions to the funding gap between Black and White applications: 1) reviewer preference for some topics over others, 2) assignment of poorer initial scores and potential triage, and 3) decision to discuss an application[17]. Critically, these decision junctions reflect persistent institutional policies and practices that result in racial inequity, also known as structural racism[18,19].

The intrinsic process of grant review has several limitations. A recent study by Erosheva et al. considered 54,740 R01 applications reviewed by the NIH Center for Scientific Review between 2014 and 2016. After excluding 15% of applications missing PI ethnicity, they found 2.2% applications from Black PIs and 97.8% from white PIs. These authors concluded that preliminary criterion scores fully account for racial disparities. They also found that Black investigators, on average, receive lower preliminary scores on all five criteria, which are Significance, Investigator, Innovation, Approach and Environment, even after controlling for career stage, gender, degree type and area of science[20]. When we examine the pool of applicants, in addition to including fewer Black applicants, Ginther et al. found that disparities are early and pervasive. Black applicants have fewer publications on their biosketches, fewer citations, and publish in lower impact journals[3]. This highlights inequalities in applicant CV and career development. Furthermore, Jeffe and Adriole et al. described in their studies the finding that Blacks are awarded fewer F32 and K career development grants[21,22].

Despite efforts by the NIH, by academic institutions, and by applicants themselves, attempts to solve these disparities are, to date, highly ineffective. As members of academia, each of us must participate at each level to decrease the gap. In addition to participating in the different diversity efforts at our academic centers, we should 1) incorporate and/or hire URMs trainees as early as at the time of high school and college to encourage early career development; 2) radically change the manuscript/grant review system and anonymize this process; 3) ensure that junior trainees, motivated in STEM, join programs and networks and obtain mentorship designed to help them succeed; 4) develop hyper-mentoring programs for URM junior faculty to help

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them navigate academia and develop necessary skills to compete for NIH funding and reach leadership positions; and 5) increase the number of URM researchers in review panels. Commitment from each of us will help transform the structural racism that is still apparent in academia.

Acknowledgment: We thank Dr. Kristina Crothers and Dr. Bessie Young for helpful comments and editorial support.

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WASHINGTON UPDATE – RESEARCH FUNDING

House of Representatives Passes 2021 Health Spending Bill With 13 Percent NIH Funding Increase

Due to the November presidential election and impasses over COVID-19 relief, we do not expect Congress to finalize spending bills for fiscal year (FY) 2021 before the election, particularly as the Senate has not moved any spending bills. Instead, Congress will pass temporary spending measures to provide government funding past the end of the fiscal year deadline of Sept. 30, 2020.

At the end of July, the House of Representatives, on a party-line vote, passed its FY 2021 health spending bill, which proposes a funding increase of about 13 percent for the NIH. Specifically, the bill provides $47.5 billion in total funding for the NIH in FY2021, a $5.5 billion increase over FY2020 NIH funding of $41.5 billion. This bill will serve as the House's negotiating mark with the Senate when the two chambers begin working to finalize FY2021 spending after the election. The House health spending bill includes the following:

- $2.5 billion to offset research costs related to reductions in laboratory productivity resulting from interruptions or shutdowns of research during the COVID-19 pandemic. This is a clarification from last week's Washington Letter, which reported that $5 billion is proposed for research infrastructure.
- A 7 percent funding increase for each NIH institute and center.

For the CDC, the House FY2021 health spending bill proposes $8 billion, an increase of $232 million above the FY 2020 enacted level, and additionally:

- A proposed $9 billion in emergency funding to improve the nation's preparedness for public health emergencies. The emergency funds would include:
- $4 billion for enhanced public health prevention efforts, and
- $2 billion for state and local public health emergency response.
- $240 million for CDC's Office on Smoking and Health, an increase of $10 million above the FY 2020 enacted level.

The ATS Washington Office will continue to monitor the progress of FY2021 spending and alert members when their action is needed.