

Letter from the Editor

JUNE 2020

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In this special COVID-19 extended edition of the June Quarterly, we are pleased to bring you an interview with the Director of the NIH National Heart, Lung, and Blood Institute (NHLBI), Gary Gibbons, MD. In the interview, Dr. Gibbons gives overviews of the institute’s research strategy to address COVID-19 and current extramural funding opportunities for COVID-related research. He also discusses steps the institute and NIH are taking to support researchers whose studies and laboratories have had to halt operations due to COVID-19. Finally, Dr. Gibbons outlines NHLBI’s initiatives to promote diversity in pulmonary, critical care and sleep medicine.

We are pleased to share a special Quarterly feature with you, our “COVID Collection,” consisting of a series of five articles on the COVID-19 pandemic coordinated by Research Advocacy Committee member, Amali Samarasinghe, PhD. The series discusses some of the first research efforts, clinical and scientific discoveries and questions concerning COVID-19, as well as the impact of the disease on clinical research and training. It also includes an overview of the city of Memphis’ Roadmap for a public and private health system response to COVID-19, including the strategies that were quickly developed to fit the city’s needs. The Quarterly’s “COVID Collection” includes:

- “Encounters of the COVID Kind”, by **Amali Samarasinghe, PhD**
- “Recommendations for Airborne Isolation Precautions Based on Observations of Environmental Contamination of SARS-CoV-2,” by **Joshua Santarpia, PhD**
- “A City’s Response to COVID-19: The Memphis Roadmap,” by **Jonathan McCullers, MD** and **Terri Finkel, MD, PhD**
- “Clinical Research in Era of COVID-19,” by **Patricia Dubin, MD**, and **Nicholas Hysmith, MD**
- “Chronic Lung Disease and COVID-19: A Complicating Duo?” by **Amali Samarasinghe, PhD** and **Charles Dela Cruz, MD, PhD**

Next, we have an update on the opening of the ATS Research Program’s new grant cycle, followed by news and funding opportunity announcements from NIH, beginning with the National Institute on Minority Health Director’s Spotlight blog on COVID-19 and Health Disparities. We have included a listing of NIH and VA Research Program COVID-related resources, including funding opportunities from all of the institutes most relevant to ATS members. The June Quarterly finishes with the latest report from our Washington office on the process and prospects for 2021 health research funding.

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Sincerely,

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Editor
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Gary Gibbons, MD
Director, NHLBI

Quarterly Feature

Interview with NHLBI Director Gary Gibbons, MD

1. Given that many patients with COVID-19 are dying from acute respiratory distress syndrome, is the NHLBI Lung division considering releasing additional respiratory-specific RFAs related to this multi-faceted disease?

NHLBI is pursuing a multipronged research strategy that leverages our existing infrastructure and expertise to fully address the COVID-19 crisis. For example, the Institute was able to quickly activate the Prevention and Early Treatment of Acute Lung Injury (PETAL) Clinical Trials Network to launch the Outcomes Related to COVID-19 treated with Hydroxychloroquine among In-patients with Symptomatic Disease (ORCHID) study. PETAL is also supporting the COVID-19 Observational Study (CORAL), a long-term, natural history study of patients hospitalized with COVID-19 that will collect comprehensive data on severe outcomes including respiratory failure, strokes and heart attacks, as well as risk factors and potential mechanisms of disease.

NHLBI has issued or signed on to multiple Notices of Special Interest (NOSIs) to address COVID-19-related research needs. The first NHLBI NOSI issued in March included new pre-clinical translational research designed to accelerate our understanding of the key determinants of host response to novel coronavirus. The NOSI yielded hundreds of applications, which are undergoing an expedited review process to ensure that the most impactful studies can get underway as quickly as possible. Other NOSIs focus on social and behavioral questions related to COVID-19 and on early phase clinical trials. The Institute also issued a Research Opportunity Announcement (ROA) for an integrated and adaptive “network of networks” that can rapidly and efficiently execute phase IIb and III clinical trials designed to investigate promising host-directed interventions.

We continue to be interested in funding investigator-initiated proposals through standard NHLBI funding opportunity announcements involving other types of clinical research that is (1) patient-oriented, (2) epidemiologic and behavioral, or (3) outcomes research and health services research, as well as basic and translational research, which complements or expands on the high priority objectives approaches above.

The [NHLBI COVID-19 webpage](#) summarizes our research strategy and pushes out funding opportunities as they are developed. The webpage is a one-stop shop for researchers, clinicians, and patients, and is updated frequently.

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Quarterly Feature: Interview with NHLBI Director Gary Gibbons, MD *(Continued from page 2)***2. In what specific ways can the NHLBI support basic science, translational and clinical researchers (as well as trainees and staff) who have had to shut down their labs and studies during the COVID-19 pandemic crisis?**

The NIH is deeply concerned for the health and safety of people involved in NIH research, and about the effects of the COVID-19 public health emergency on the biomedical enterprise. The agency is providing many administrative flexibilities to ensure that the research can continue or resume after the COVID-19 public health crisis is resolved. For example:

- Extramural staff are working remotely and continue to process applications and make awards.
- We are conducting peer review meetings virtually and ensuring that reviewers know [not to penalize applicants for disruptions](#) caused by the pandemic.
- We are working diligently to provide funding opportunities to support COVID-19 research.
- Some FOA expiration dates are being extended.
- If researchers, staff or trainees are unable to work on a grant or training activities, salaries and stipends may be charged to NIH grants, as long as the organization's policy allows such charges from all funding sources.
- Prior approval is not required to divert faculty from research to clinical work related to COVID-19 until the end of the public health emergency period.

The NIH Office of Extramural Research (OER) is fielding all questions about these circumstances via email at grantspolicy@nih.gov. More guidance from OER is available for [applicants and recipients of funding](#), and on the [Q&A page](#). These pages are updated frequently.

3. What is the progress of implementation of the COPD National Action Plan? What is needed to accelerate and fully implement all of its goals and objectives?

The [COPD National Action Plan](#) is the first-ever blueprint for a multi-faceted, unified effort to fight the disease. De-

veloped at the request of Congress with input and contributions from the broad COPD community, the plan provides a comprehensive framework for action by those affected by the disease and who wish to reduce its burden. To that end, all stakeholders who contributed to the Action Plan play a role in implementing it. They should continue to formulate their activities in coordination with the Action Plan's goals and objectives. NHLBI is currently developing a central tracking system that will enable stakeholders to log their activities, and to ensure we can all monitor our progress toward implementation of the plan.

NHLBI is also aware that the COVID-19 pandemic has caused extraordinary challenges in accessing routine health care, and even more so for people with COPD who need pulmonary rehabilitation (PR) services. This crisis highlights the urgent need for innovative ways to deliver much-needed rehab and other health care services, a challenge even in the best of times for populations living in remote or rural environments where traditional PR is not readily available. To address this urgent need, NHLBI is currently supporting a trial that is [testing home-based PR for COPD](#) and a study that is [examining a digitally based PR tool](#).

4. What is the status of current and future big data initiatives supported by NHLBI?

Several NHLBI-supported big data initiatives are underway. For example, the NHLBI [BioData Catalyst](#) is a cloud-based ecosystem providing tools, applications, and workflows that allow investigators to find, access, share, store, and compute with diverse, large-scale datasets. The BioData Catalyst aims to accelerate biomedical research and progress toward novel diagnostic tools, therapeutic options, and prevention strategies for heart, lung, blood, and sleep disorders. Researchers from more than a dozen institutions have received funding from NHLBI to work in the BioData Catalyst ecosystem. In addition, the BioData Catalyst Fellows Program has funded its first cohort of early-career investigators, supporting research on novel and innovative data science and data-focused research problems.

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Quarterly Feature: Interview with NHLBI Director Gary Gibbons, MD *(Continued from page 3)*

The Biodata Catalyst is designed to be nimble and responsive to the ever-changing landscape of biomedical data and the needs of the research community and will be updated and refined continually. Moreover, we will be taking advantage of the Biodata Catalyst platform to make COVID-19 data rapidly available to the research community.

NHLBI also recently launched the [Big Data Analysis Challenge: Creating New Paradigms for Heart Failure Research](#). Through this Challenge competition, NHLBI seeks to foster innovation and address the need for new, open-source disease models to define sub-categories of adult heart failure and support new research hypotheses toward improved management of this disorder. The deadline for submitting ideas is **Aug. 28, 2020**.

In addition, NHLBI's [Trans-Omics for Precision Medicine \(TOPMed\)](#) program continues to collect whole-genome sequencing and other -omics data from clinical study participants with the ultimate aim to improve the prevention and treatment of heart, lung, blood, and sleep disorders. TOPMed currently consists of around 155,000 participants of diverse race and ethnicity from more than 80 different studies based across the United States. TOPMed data are housed within the Biodata Catalyst environment.

5. While the recruitment of women in critical care research has improved recently, are there other specific mechanisms that the institute is exploring to promote diversity in pulmonary, critical care and sleep?

NHLBI is committed to and has invested in programs to build and sustain a diverse workforce. NHLBI has a suite of diversity-focused programs that provide support at the undergraduate level (e.g., [Short-Term Research Education Programs](#)), graduate and fellowship level (e.g., [T32 Training Program for Institutions That Promote Diversity](#)), and early faculty level (e.g., [Mentored Career Development Awards to Promote Faculty Diversity in Biomedical Research](#)). Supplemental awards can also be made to [grantees who diversify their research team](#). These supplements can support individuals at the high school level through early faculty.

Moreover, the NHLBI's [Programs to Increase Diversity Among Individuals Engaged in Health-Related Research \(PRIDE\)](#) prepares junior faculty from underrepresented backgrounds for successful research careers. From 2006 to 2018, graduates from PRIDE's cardiovascular research programs had a 63 percent success rate for NIH grant applications, compared with 19 percent for NIH applications overall.

The NHLBI is also participating in two NOSIs focused on supplements for K awardees and first-time recipients of RPGs who undergo critical life events, such as childbirth, adoption and primary caregiving responsibilities of an ailing spouse, child, partner, or a member of the immediate family during the project period (see [NOT-OD-20-054](#) and [NOT-OD-20-055](#)).

In 2018, NHLBI's Division of Cardiovascular Sciences held a [workshop](#) to examine the Division's current portfolio in diversity training, and to explore future opportunities. The workshop reviewed the Institute's efforts to improve diversity and training across all divisions and reaffirmed the need for continued investments in this area. To that end, NHLBI has appointed Wayne Wang, PhD, as the Institute's New Training Program director. Dr. Wang will provide strategic direction, coordination, and collaborative leadership across NHLBI's extramural training and career development activities, represent the NHLBI in NIH's Training Advisory Committee, and lead the NHLBI's training committee in its efforts to improve trainee diversity.

The NHLBI recognizes that promoting diversity at all levels of the pulmonary and critical care workforce is an ongoing task requiring many different approaches. Currently, the proportion of NHLBI's FY2019 F and K awardees who are female (45 percent and 40 percent, respectively) is above the range for female pulmonary and critical care medicine (PCCM) fellows overall (reported as 29.5-35.2 percent in [ATS Scholar](#)). However, NHLBI's proportion of F and K awardees from underrepresented minority groups does not yet exceed the overall proportions in PCCM fellowship programs reported. NHLBI is committed to doing the work necessary to improving representation. ■

ATS Member COVID-19 Feature

Encounters of the COVID Kind – Too Close for Comfort

Amali E. Samarasinghe, PhD, Member of the ATS Pulmonary Infections-Tuberculosis (PI-TB) Assembly Member and Research Advocacy Committee

Lower respiratory tract infections caused by viruses are a major cause of morbidity and mortality worldwide. Influenza virus, adenovirus, respiratory syncytial virus, and metapneumovirus, have been well recognized as causes of severe lower respiratory infections, especially in groups at the two ends of the age spectrum. Until 2003, circulating coronaviruses mostly caused upper respiratory tract infections. The coronavirus epidemic of 2003, caused by Severe Acute Respiratory Syndrome (SARS) coronavirus (CoV), led to about 8,000 cases in 29 countries and was associated with a mortality rate of 9.5 percent. Since its emergence, infection with SARS-CoV-2 rapidly reached pandemic levels affecting at least 213 countries, associated with a mortality rate of about 6 percent.

Whether this virus will disappear like SARS-CoV-1, or whether it will continue to cause infections for years like Middle Eastern Respiratory Syndrome (MERS)-CoV, and what the long-term consequences of infection will be in both the symptomatic and asymptomatic populations remain to be seen. While the virus fulminates across the world, scientists, clinicians, and science advocates have united against this common enemy so that we will be better prepared for second and subsequent waves, should they arise.

In this COVID collection, we bring you a series of articles based on first efforts, discoveries, and questions as they relate to our members.

First, Joshua Santarpia, PhD, discusses the importance of understanding SARS-CoV-2 airborne dissemination and transmission in the clinical environment based on what was learned from the Diamond Princess cruise ship incident.

As the virus hit cities that are unique in their population demographics, health disparities, and socioeconomic status, countermeasures and health care strategies need to be formulated to fit the city needs. State governmental agencies

(and funding), public and private health care providers, and academic institutions unified efforts to strategically test and mitigate virus spreading. Jon McCullers, MD, and Terri Finkel, MD, PhD, describe one city's response to the first wave of SARS-CoV-2.

All of us in the ATS community are affected by COVID-19; its impact on our lives and careers may be different. Patricia Dubin, MD, a member of the ATS Pediatrics Assembly and Nicholas Hysmith, MD, discuss the impact of this pandemic on clinical research and our fellows in-training.

Finally, my colleague and fellow member of the ATS PI-TB Assembly, Charles Dela Cruz, MD, PhD, ATSF, and I address the importance of understanding the patient with chronic lung disease in order to determine possible ways in which COVID-19 may impact them now and in the future.

Since much remains to be elucidated regarding this novel virus and its disease, numerous agencies have opened calls for applications for a number of funding opportunities focused on COVID-19. We have assembled several of these announcements at the conclusion of this feature for the benefit of our members.

Nobel Laureate, Joshua Lederberg, PhD's statement that "the single biggest threat to man's continued dominance on the planet is the virus" holds new weight as SARS-CoV-2 reminds us of the power these infectious agents hold. At the start of the pandemic, we as a scientific community were perplexed by the infectivity and pathogenesis of this novel virus. It single handedly led to the shut-down of life as we knew it. However, now that daily infections are plateauing and daily deaths are decreasing, perhaps we are in the final stretch of the first wave. Should there be a second wave of this infection, we will be ready – through increased and shared knowledge, and unified efforts. ■

Recommendations for Airborne Isolation Precautions Based on Observations of Environmental Contamination of SARS-CoV-2



Joshua L. Santarpia, PhD
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COVID-19 was declared a pandemic by the World Health Organization in March of 2020. This disease, and its rapid worldwide proliferation, represent the most significant public health emergency in a century. Lack of concrete data on precisely how SARS-CoV-2 is transmitted has led to conflicting direction on isolation guidelines. Understanding the modes of transmission of emerging infectious disease is a key factor in protecting health care workers and implementing effective public health measures. Other emerging coronavirus diseases, such as SARS and MERS, have had indications of potential airborne transmission, particularly in health care settings, but there has been significant resistance in accepting this data. It has also been suggested MERS-CoV may be transmitted by asymptomatic individuals, similar to data from SARS-CoV-2. Surface samples taken in patient care areas for MERS and SARS have shown positive PCR results; however, experts question the possibility of transmission through contact with surfaces that have been contaminated by an infected person, either by the direct contact of the infected person or the settling of virus-laden particles onto the surface. Nonetheless, transmission of coronaviruses via environmental contamination has been implicated in nosocomial outbreaks. Nosocomial transmission of SARS-CoV-2 has been reported, but the role of aerosol transmission and environmental contamination remains unclear.

Emerging data from studies worldwide, add mounting evidence to support the potential of what would classically be described as airborne transmission, beyond what would normally be considered as aerosol generating procedures. In our initial study of 13 individuals from the Diamond Princess cruise ship, that were cared for at the National Quarantine Center and Nebraska Biocontainment Unit, viral contamination was ubiquitous among all samples, which included: air samples, both in and outside of patient rooms; samples of tables and other surfaces in patient rooms; samples of toilet seats; and personal items that were routinely handled by patients, including cell phones, laptops and medical devices. These data clearly indicate the possibility that SARS-CoV-2 may be spread through both direct (droplet and person-to-person) as well as indirect contact (contaminated objects and airborne transmission).

Beyond those initial findings, we continue to look for evidence of infectious virus in size segregated aerosol samples. By determining the size range of virus laden particles, and which particle sizes contain infectious virus we hope to make a more definitive case as to how health care workers should be protected during patient care. Determining the transmission potential of SARS-CoV-2 goes beyond an understanding of the size of infectious virus laden particles produced by individuals infected with this disease. Several other factors impact the ability of a virus to be transmitted via aerosols. First, the stability of the virus as an aerosol is critical to whether or not it can be transmitted as an aerosol. Data on SARS-CoV-2 indicate that at indoor conditions the virus can survive for several hours as a small aerosol particle.

Recent unpublished reports indicate that sunlight, high temperatures and high humidity, more indicative of outdoor conditions, may shorten that period of stability. Finally, an understanding of infectious dose is critical for determining how the potential for airborne infection is interpreted. If the infectious dose is very low, then even a small number of viral particles are of great concern, while a high infectious dose may indicate less potential of infection at a greater distance from an infected individual.

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Based on our ongoing studies, and the mounting evidence around the potential airborne transmission of SARS-CoV-2, I strongly recommend the use of airborne isolation precautions in all aspects of direct patient care of individuals with SARS-CoV-2. Since the first patients from the Diamond Princess cruise ship arrived in Nebraska, we have maintained airborne isolation precautions in patient care, and have used our studies to guide the development and use of isolation protocols around this disease even when this required re-engineering of inpatient units to maintain airborne isolation standards. To date, we have had no observed nosocomial spread of SARS-CoV-2 in the wards used for COVID-19 patient care, which reinforces the value of this approach. ■

A City's Response to COVID-19: The Memphis Roadmap



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As many cities and communities in the United States are dealing with the first wave of the COVID-19 pandemic, much of the current focus is, by necessity, on handling the actual or anticipated surge of cases of severely ill patients in our local hospitals. Memphis is no different – our first case was detected on March 8, 2020. Faculty from the College of Medicine (CoM) at the University of Tennessee Health Science Center (UTHSC) have naturally played integral roles in shaping this response in our affiliated teaching hospitals. However, we have also tried to provide broader strategic leadership in the region's response to the pandemic. This has resulted in the development of the Memphis Roadmap, summarized [here](#). We believe that academic medical centers (AMCs) can contribute in a multitude of areas beyond clinical leadership to help mitigate the overall impact of this pandemic

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on our society, and some of our efforts are summarized in this brief article.

Strategic leadership. As an AMC, UTHSC is uniquely positioned to provide thought leadership and expert opinion to our region as the pandemic evolves. Early in the course of the local outbreak, we constructed a website to provide information, links to resources, and a public-facing “Ask the Expert” service. We held a press conference to announce our intention to provide the region with strategic leadership, and developed a coordinated communications strategy to provide frequent, comprehensive, and consistent information and expert opinion to print, digital, radio, and television media. We engaged with the mayoral offices of our local city and county and began to push an agenda that we thought would best serve the public good.

The initial messaging was that our responses had to be closely coordinated across the entire tri-state, eight county metropolitan Memphis region, not siloed within the City of Memphis or Shelby County offices. We also needed near real-time access and public sharing of data from our local health departments and hospitals to include bed utilization stratified as intensive care (ICU), non-ICU, or emergency department; patient counts of both confirmed COVID-19 cases and persons under investigation (PUIs) overall and within our hospitals; and testing results across the region stratified by age, race/ethnicity, and zip code. As these data became available, evident geographic and racial disparities in access to testing, resources, and outcomes quickly drove changes to our regional processes for handling the mitigation phase of the pandemic.

COVID-19 Testing. One of the early local (and national) storylines was lack of resources to test for COVID-19, accompanied by a narrative that widespread testing was unimportant. As it became clear that the state of Tennessee and commercial laboratories were not going to be able to provide either sites for testing or the capacity to run the actual assays, we pushed back against this narrative and decided to lead this effort ourselves.

Our university physician practice plan partnered with the city of Memphis Police and Fire Departments to rapidly

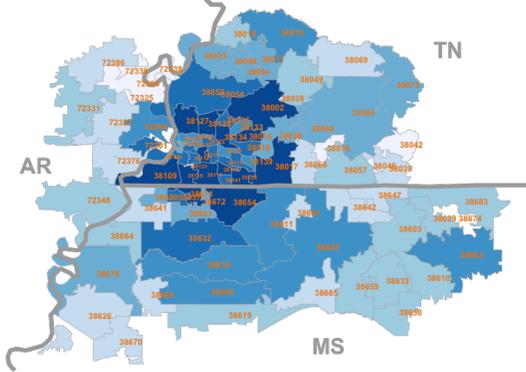
deploy a high-throughput “drive-through” testing site at a local sports stadium – the city provided site infrastructure and security, and we provided marketing, scheduling, operations, and business office support. Within a week of forming the idea, we were providing free testing to the public. The site was initially operated entirely with volunteer faculty, fellows, and medical students before expanding to other sites with community volunteers and students from other Colleges in the UT Health Science Center. We also rapidly assembled a high-throughput laboratory for nucleic acid-based testing for SARS-CoV-2 utilizing equipment scavenged from UTHSC research laboratories and led by volunteer faculty, medical students, and part-time hires from other local laboratories. This was scaled up over a two-week period to process and provide results for more than 1000 tests per day, with a turn-around time under 24 hours.

Preparing for the Second Wave. While the local response remains focused on mitigation of the upcoming surge of cases in our local hospitals, we have begun planning for a series of actions to take after the first wave has passed. The hope is that drastic measures like closing schools and shuttering businesses will not be necessary when the virus returns. Three strategies are being developed. First, we will continue to expand our ability to test for the virus. Our focus will shift to providing education about the need for testing, building broad capacity across the region (with a particular emphasis on underserved communities) and transitioning testing into more traditional outpatient settings, rather than in hospital emergency departments and drive-through sites. We will continue to build capacity locally, so our university and commercial laboratories can collectively process 3,000-4,000 samples per day with a rapid turnaround time. Second, we are urging the local county health department to greatly expand our public health infrastructure to contact persons with newly identified infections, perform contact tracing, and provide realistic options for quarantine or isolation and monitoring of compliance. Pooled test data provided to investigators in the UT Department of Preventive Medicine has supported development of COVID-19 prediction models to direct community, school

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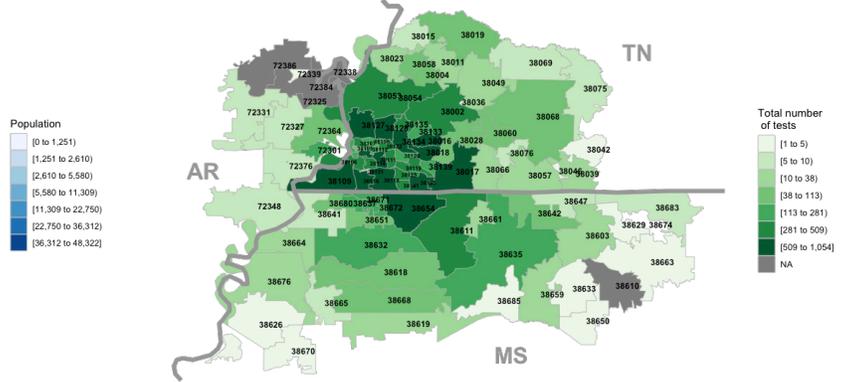
A City's Response to COVID-19: The Memphis Roadmap (Continued from page 8)

Population in the Memphis Metropolitan Area by ZIP-Code
(For comparison of other maps with overall population.)



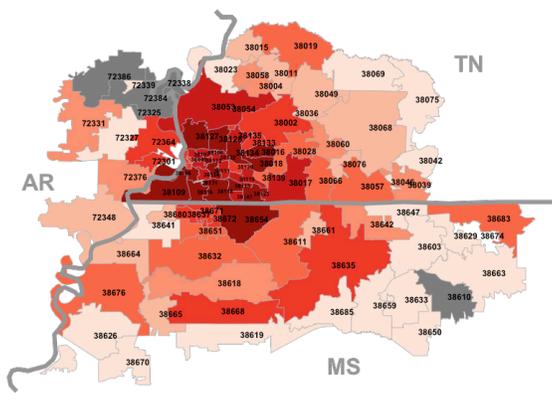
Source: UTHSC College of Medicine | Preventive Medicine | Biostatistics.

SARS-CoV-2 Testing in the Memphis Metropolitan Area
MLH and UTHSC testing as of May 21, 2020 (total of 18,673 tests)



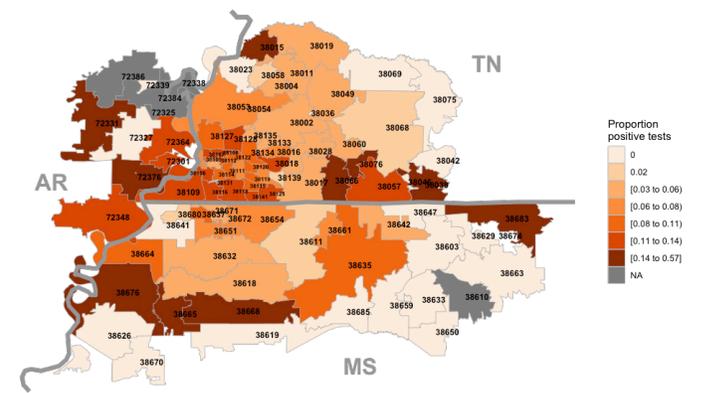
Source: UTHSC College of Medicine | Preventive Medicine | Biostatistics.

Positive Tests in the Memphis Metropolitan Area
MLH and UTHSC SARS-CoV-2 testing as of May 21, 2020 (total of 18,673 tests)



Source: UTHSC College of Medicine | Preventive Medicine | Biostatistics.

Proportion of Positive Tests in the Memphis Metropolitan Area
MLH and UTHSC SARS-CoV-2 testing as of May 21, 2020 (total of 18,673 tests)



Source: UTHSC College of Medicine | Preventive Medicine | Biostatistics.

district, and hospital responses. These prediction models are posted on the UTHSC website at:

<https://www.uthsc.edu/coronavirus/local-data/index.php>. An example of the power of these data is shown here.

While patterns of population density, the number of tests performed and positive tests are highly overlapping, the percentage of positive tests is not. Our ongoing study of validated social determinants of health in these zip codes will inform our understanding of the critical risk factors and challenges we must address if we hope to control the pandemic in these neighborhoods and across all of metropolitan Memphis.

In particular, the serious and disproportionate impact of COVID-19 on our communities of color will be more effectively addressed by targeted education and engagement of our hardest hit neighborhoods. Mitigation of risk for the homeless, and for children and young adults in the juvenile justice system, are areas of focus for implementation of preventive measures for COVID-19. Third, we are currently developing laboratory-based tests at UTHSC (ELISA and micro-neutralization assays) to detect past infection and determine immunity to SARS-CoV-2. We plan to scale these up to a capacity of 3,000 tests per day and begin to assess all health care workers and first responders in the region for immunity. We will follow these front-

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A City's Response to COVID-19: The Memphis Roadmap *(Continued from page 9)*

line groups with more general public testing, prioritizing consumer-facing jobs like grocery store workers, restaurant employees, and critical infrastructure positions. Immune individuals should be able to provide both health care and public services with less concern and a higher degree of safety for the public than occurred in the first wave. This work will also inform our models of community spread through households, schools, and businesses, and, thus, decisions regarding when and how to pace the city's opening.

Research. Le Bonheur Children's Hospital, UTHSC, University of Memphis, St. Jude Children's Research Hospital and Oak Ridge National Laboratory have partnered on high impact initiatives in six critical areas of research which are population health, health worker protection, diagnostics, modeling and simulation, virus/host genetics and pathogenesis, and therapeutics.

With the UTHSC Regional Biosafety Lab, we have obtained rapid IRB approval for prospective and retrospective serum, nasal, and other biological samples for vital pre-clinical validation of diagnostic antigens and assays, and for a biospecimen repository to support ongoing study of viral genetic diversity and disease correlates in humans and novel animal models. In our efforts to protect our health care providers and conserve personal protective equipment, work intended to test efficacy of – and rapidly implement – large-scale decontamination of N95 masks has led to the development and validation of a novel and readily scalable invention.

As we learn more about this new infectious agent, well-curated data will be crucial for tracking disease trends and at-risk populations for study of disease manifestations, viral and host pathogenesis, pathologic and protective immune responses. The Pediatric Infectious Diseases Transplant Network, through its Coordinating Center at St. Jude, has created a survey to capture epidemiologic and clinical information about all cases of pediatric COVID-19 infections in the U.S., including children with underlying health conditions and those of immunosuppressive therapies. Both novel and time-proven ther-

apies will be of critical importance in treating COVID-19, particularly for severe disease, in advance of a safe and effective vaccine.

UTHSC has created a medically compliant process, education, and training, for identification of coronavirus convalescent plasma donors and preparation of convalescent plasma products. We have transfused safely tens of patients with life-threatening COVID-19, with anecdotal benefit. As a new member of the I-ACT (Institute for Advanced Clinical Trials) network, Le Bonheur is exploring an early-phase clinical study of a novel investigational compound for treatment of COVID-19-associated acute respiratory distress syndrome. We are in discussions with a drug company for a pediatric arm of an adult phase IIb-III trial of an anti-inflammatory medication, baricitinib, in severe cases of SARS-CoV-2 infection. Baricitinib, a JAK inhibitor, is FDA-approved for use in rheumatoid arthritis; in addition to its anti-inflammatory effects and a good safety profile, there are preliminary data suggesting that this drug also affects SARS-CoV-2 replication via inhibition of a numb-like kinase, AAK1, a regulator of endocytosis.

Amongst other partnerships nationally and internationally, our longstanding relationship with Oak Ridge National Laboratory has given us access to their world-renowned supercomputing facility and expertise. These assets have facilitated our disease modeling and geo-mapping, analyses of the pan-genome, and identification of promising novel and repurposed drug therapies.

Advocacy. As described above, our efforts to make our UT Community Test Sites accessible and free to all communities in Shelby County have reduced the R0 or "R naught" – the viral reproduction number, defined as how many people one person with the SARS-CoV-2 can infect – from between three and four to less than one, the target number below which the disease will theoretically die out in the population. Supporting these efforts are those of UT's Office of Community Outreach and Engagement, working to build a city of multicultural health, assist jus-

A City's Response to COVID-19: The Memphis Roadmap *(Continued from page 10)*

tice-involved youth, and ensure everyone has a health care provider.

In addition, UT/Le Bonheur has a number of long-standing programs to improve the health and well-being of our underserved populations in the Memphis metropolitan area. The University of Memphis School of Law, Memphis Area Legal Services (MALS) and UT/Le Bonheur have collaborated to create Memphis CHiLD (Children's Health Law Directive), the first medical-legal partnership of its kind in the region, encompassing all of Tennessee, Arkansas and Mississippi. Over the past few months, Memphis CHiLD staff attorneys, medical director, and law students have supported hundreds of patients and families struggling without Social Security benefits, food security, or access to special education services due to state and school closures, facing fears of eviction once the moratorium is lifted June 1, 2020 and exposure risks of public transit, limiting access to medical care.

With the aim of preventing some of the adverse outcomes facing our disadvantaged families, Le Bonheur's Nurse-Family Partnership is an evidence-based home visitation program for first-time pregnant mothers, promoting child development and responsible parenting. The Nurse-Family Partnership has an impressive track-record, with more than 600 mothers and their babies completing the program over the past decade. Of the participants, 89 percent of babies were born full-term, 75 percent of mothers initiated breastfeeding, and 97 percent of toddlers are current with immunizations. Of interest, over the past three months, continuation of this program via telehealth has led to an increased completion rate of weekly or twice weekly in-home virtual visits, with outcomes data as to pregnancy outcomes, child health and development, and families' economic self-sufficiency pending.

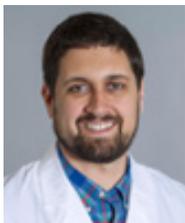
The New Normal. The Memphis Roadmap calls for a series of steps to bring us quickly to a new normal, where rapid and reliable testing is broadly available, positive tests are quickly followed up with standard, proven public health responses, and a growing cadre of immune individuals can play a critical role in returning to normalcy.

This will require a massive and sustained effort which we hope will keep the overall burden of COVID-19 low enough that cancellation of small-to-medium sized gatherings and "shelter in place" measures will not be necessary. Similar measures have been effective in countries that had carefully prepared for this pandemic, such as South Korea and Singapore. Ultimately, either an effective vaccine or development of herd immunity in a substantial proportion of the population will be needed to return to a pre-pandemic state, but as either of these developments is likely to take years, we must be ready to maintain the infrastructure for testing and monitoring over the medium- to long-term. It is also our hope that our national and regional lack of preparation for this pandemic will spur discussions and ultimately drive meaningful change in our health care system, with a renewed emphasis on public health, research, advocacy, prevention, and primary care. ■

Clinical Research in Era of COVID-19



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While the COVID-19 pandemic has impacted every aspect of our lives, the full extent and nature of the impact may not be apparent for years to come. There will be profound effects on our social fabric, workplace environments, educational systems, supply chains, and the economy. We will work to establish a “new normal” which will evaporate and evolve as we develop an understanding of the long-term complications of COVID-19, how long natural immunity may last, and how to develop antivirals and an effective vaccine.

Health care delivery has been convulsed. In the absence of accurate and widely available point-of-care testing, the emergency medicine and critical care complexes have had to learn how to identify and treat COVID-19, all while the disease seemed to evolve before our eyes. Health care workers have cared for the sickest patients while simultaneously field-testing personal protective equipment (PPE). Medical disciplines have grappled with what is “elective” versus “essential” care, and how to deliver that care effectively and safely.

So where does biomedical research fit into this ever-shifting landscape? The shorthand of “elective” versus

“essential” is an oversimplification in research just as it is in clinical care. The initial response of most academic institutions has been to shut down all research except ‘essential’ COVID-19 work. Academic investigators have closed their labs while creating alternative work plans for staff and trainees. Project applications continue to be written and grants awarded. However, research plans are being deferred until labs reopen. While trainees who have research requirements for graduation and certification wonder whether accommodations will be made as their research projects are suspended, institutions wrestle with the ‘how’ and ‘when’ questions with regard to re-opening research laboratories safely. The development of re-opening plans will require tailoring to the type of research, physical plant and university resources. But these considerations will necessarily be superseded by understanding where the community and health care systems are in the arc of this pandemic.

While re-opening basic science labs will not be simple, there will be additional layers of complexity with clinical research due to patient protections as well as the direct impact of COVID-19 on the research itself. There are clear risks of increased exposure to SARS-CoV-2 for all of those involved in research. And, depending on the clinical intervention and patient population, the risks may be quite significant. There is also the risk that acute and late-inflammatory COVID-19 can confound research results.

For studies where data acquisition is almost complete, these increased risks of exposure and confounding from SARS-CoV-2 may be small and inconsequential to the study outcomes; there may also be an ethical obligation to continue the work that so many have already invested so much in. This leaves us to grapple with how to complete the work in this new landscape. For longer-term studies that are midstream or at the start of enrollment, the increased exposure risk to research participants and personnel may be quite significant and harder to justify. The confounding impact of COVID-19 on research outcomes could be quite obvious and profound, or insidious and difficult to detect. How will we understand the impact in the near-term? What will the historical impact be? Will

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Clinical Research in Era of COVID-19 *(Continued from page 12)*

we ultimately need to repeat some of these studies when disease prevalence and burden reach a steady state in the population?

In addition to making qualitative judgements about the risk and reward of the research itself, the supply of PPE also presents logistical and ethical concerns. There is a significant worldwide shortage of N95 respirators and other PPE for health care workers caring for COVID-19 patients. Supply chain issues coupled with the acute increase in demand within individual hospital systems contribute to these shortages. When calculating the ethical obligation to continue clinical studies in the setting of a study that may be near completion, PPE supply should be part of the equation. Is the risk to a health care worker on the frontlines worth the information gathered from the study?

This shortage of PPE has presented research opportunities as well. Clinicians and basic scientists have been working together across the country to test novel methods aimed at reprocessing PPE. From ultraviolet light to industrial ovens; innovation, ingenuity, and collaboration have given rise to unique solutions. The material from which N95 masks are made has been taken into BSL-3 labs and inoculated with SARS-CoV-2 to document the dynamics of viral killing using various methods. As some of the methods require extreme heat and pressure, which may compromise N95 integrity, quantitative measures of mask effectiveness have been repurposed to ensure health care worker safety.

Despite these obstacles, we must also weigh the risks of not engaging in research. We all have examples from our professional experiences of clinical studies that have profoundly improved patient outcomes. How would one- or two-year delays in completion of this work have affected patient morbidity and mortality and the evolution of the field? What duration of delay would be acceptable? How would current delays affect the infrastructure for future research, and training models for our future investigators? What type of investment will it require to get research re-established at full capacity once we have deemed it to be

“safe”? There are no easy answers to these questions. The most effective intervention may be to identify risk mitigation strategies that allow us to continue or resume clinical research as quickly and safely as possible. The FDA and NIH have issued guidelines to address some of these issues.

Society at large has engaged in social distancing, widespread use of facemasks, and the mandated shutdown of workplaces, schools and non-essential activities. Medicine has adapted these concepts to clinical care, utilizing telehealth, facility entry screening, and a moratorium on elective cases. The goal of “flattening the curve” has been to prevent health systems from being overrun and includes decreasing the resulting “avoidable” mortality. But the other key benefit has been to buy us time. Reducing the rate of transmission buys us time to understand viral pathogenesis and identify effective management strategies. It buys us time to develop more sensitive and specific point of care testing, effective antivirals and, ultimately, a vaccine. It buys us time to develop appropriate supply chain and disinfection strategies for PPE. It also buys us time to thoughtfully plan for the resumption of “non-critical” activities like research, utilizing all of these other tools we have had the time to develop.

As of this writing, our institution is re-opening its laboratories but many others around the country remain closed and without a definite opening date as their communities are still on the upswing of their initial COVID-19 wave. So, how are we adapting our COVID-19 mitigation skills to research? Laboratories are re-opening with staggered shifts and adjustments in workspaces, digital platforms are being used to host lab meetings, and conferences are shifting to webinar rather than live formats. Regulatory committees, like the IRB, IACUC, and IBC, have shifted to remote work and large-scale digital meetings. Research protocols have been updated to include televisits for clinical assessment. Industry has established protocols to consolidate and ship study materials less frequently. Investigators are redesigning their work and team assignments to remain productive under the current conditions.

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We are coalescing around solutions, even as the “critical” missions continue to evolve.

Industry, funding agencies, universities, research institutes, professional organizations and government regulatory agencies must also continue to evolve in their approach to support research. In addition to developing strategies to safely resume research, these organizations also need to develop strategies to shore up research infrastructure at both the institutional and the individual level. Dyssynchronous shut-downs and re-openings of research around the country and around the world will result in inconsistencies in research productivity across departments and institutions, but also across laboratories. The impact is likely to be greatest for junior faculty and trainees compared to senior investigators; and, attrition of junior and mid-career investigators will leave an impact on research for decades to come. As a respiratory community, we have the opportunity to alter this course.

As M.F. Weiner wrote in 1976, “don’t waste a crisis.” While he was referring to the individual patient’s health crisis being a teachable moment to change lifestyle behaviors, this phrase has been expanded over the years to recognize the potential for societal change in the face of crisis. In the face of this devastating pandemic, we have an opportunity to re-examine and modify our research infrastructure, supply chain, preparedness planning, educational rubrics and promotion systems and leave a lasting positive impact for years to come. ■

Chronic Lung Disease and COVID-19: A Complicating Duo?



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COVID-19 has emerged to be a major pandemic, resulting in more than 6.2 million infections with SARS-CoV-2 and 372,096 deaths as of May 31, 2020. Pre-COVID-19, it was well known that patients with chronic respiratory conditions such as asthma, COPD, and cystic fibrosis are susceptible to respiratory viruses, and at higher risk of severe disease exacerbations during such infections. Clinical studies thus far on COVID-19 have identified the principal conditions associated with more severe disease and outcomes to include advanced age, hypertension, hyperlipidemia, cardiovascular disease, diabetes, and obesity.

Interestingly, initial reports arising from China showed that patients with chronic lung diseases seemed to be under-represented with prevalence in the one to three percent range. More recent data from the U.S. have identified a prevalence of COPD of only 2.5-5 percent in hospitalized COVID-19 patients. In many of these COVID-19 reports, approximately 20 percent of these patients were either current or former smokers. With more information accumulating during this pandemic, it will be important

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for the pulmonary research community to establish an accurate determination of the reasons behind these observations.

Although the Centers for Disease Control and Prevention lists asthma as a risk factor for severe COVID-19, possibly as a precaution due to the fact that many respiratory viruses cause asthma exacerbations, patients with asthma only make up only a small fraction of hospitalized patients in published reports thus far. SARS-CoV-2 binds to ACE2 receptors on the cell surface, and these receptors are reduced in patients with allergic asthma. Specific subsets of asthmatics may have increased likelihood of developing severe morbidity during COVID-19 as emerging evidence shows that ethnicity, expression levels of ACE2 and TMPRSS2, and other underlying diseases all contribute to altered disease pathogenesis. Eosinopenia at admission has also been noted as a prognostic marker of COVID-19 severity in China which may be a preamble for the discussion on the use of corticosteroids in patients with COVID-19. Since exact inter-disease interactions between asthma and COVID-19 are far from clear, much remains to be elucidated through clinical and basic science research.

Clinicians taking care of patients with chronic lung disease are continuing to help educate these patients about safe practical measures against COVID-19 acquisition as well as the symptoms that require medical attention. Some of these patients with chronic lung disease who develop severe COVID-19-related pneumonia and ARDS will likely have worsening of their underlying lung disease and require follow-up in post-COVID-19 clinics. Research will be needed to follow these recovering patients, including those with no previous lung disease history, to determine the impact of COVID-19 infection on their lung function and overall health outcomes. Many of the ATS community have already begun addressing the chronic lung disease patient population affected by COVID-19 which will likely shed more light on this important topic in the near future. ■

RESEARCH OPPORTUNITIES

ATS Research Program: New Cycle Open!

The ATS Research Program advances the fight against respiratory diseases by providing funding for junior investigators. By partnering with other nonprofit organizations and pharmaceutical companies, the Research Program is able to maximize the number of grants awarded. The ATS reviews all grants and assumes all costs associated with administering the grants. The 2020 Research Program grant cycle opened June 1. [Learn more](#) and [view the 2019 awardees](#).

This year, the ATS is also offering [two GSK-funded COVID-19 specific research grants](#), as well as the [ATS CHEST Foundation Research Grant in Diversity](#). Deadline is June 23, 2020. [Learn more!](#)

NIH COVID-19 News and Funding Opportunities

NIMHD

NIMHD is partnering with other NIH Institutes including the NIEHS to support the funding opportunity announcement (FOA): [NOT-MD-20-023 Community Interventions to Address the Consequences of the COVID-19 Pandemic for Health Disparity and Vulnerable Populations \(R01 - Clinical Trial Optional\)](#).

The FOA is soliciting research to evaluate community interventions testing:

1. The impacts of mitigation strategies to prevent COVID-19 transmission in NIH-designated health disparity populations and other vulnerable groups

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Research Opportunities *(Continued from page 15)*

2. Already implemented, new, or adapted interventions to address the adverse psychosocial, sociocultural, behavioral and socioeconomic consequences of COVID-19 on the health of these groups

Researchers are encouraged to partner with community organizations, health service providers, public health agencies, policymakers, and other stakeholders to prepare and submit applications. **Application deadline: July 22, 2020.**

NIMHD Director's Message on COVID-19 and Health Disparities

On May 26, 2020, the Director of the National Institute on Minority Health and Health Disparities, Eliseo Perez-Stable, MD, released the [NIMHD Director's Spotlight on COVID-19 and Health Disparities](#), entitled [Opportunities to Achieve Better Understanding and Equality for Vulnerable Populations](#). In the blog, Dr. Perez-Stable shares his thoughts on opportunities for the biomedical research community to spotlight and mitigate the COVID-19 burden on minority health and health disparities.

NIH COVID-19 FUNDING/RESOURCES

The following are weblinks to NIH and individual NIH institute grant opportunities and other resources related to COVID-19.

[NIH COVID-19 resource for applicants and grantees](#)

This website is NIH's main COVID-19 resource for current and potential NIH grantees and applicants. It includes guidance for various aspects of research and grant application processes, as well as FAQs and COVID-19 funding opportunities.

NIH Parent Emergency Funding Opportunity Announcement (FOA), [Emergency Competitive Revision](#)

[to Existing NIH Awards \(Emergency Supplement, Clinical Trial Optional\)](#) ([link is external](#)). This FOA includes funding opportunities for NIAID, NIEHS, NIGMS, NCCIH, NCATS and other NIH institutes.

NHLBI COVID-19 related funding opportunities

- [Availability of Emergency Competitive Revisions on Coronavirus Disease 2019 \(COVID-19\) for Currently Active NHLBI Phase I-III Clinical](#) to rapidly initiate and conduct Phase I-Phase I/II (bridging) clinical trials in patients at risk for SARS-CoV-2 infection and/or patients with COVID-19. Expiration is Oct. 6, 2020
- [Notice of Special Interest \(NOT-HL-20-782\), "Availability of Emergency Competitive Revisions on Coronavirus Disease 2019 \(COVID-19\) for Currently Active NHLBI Phase I-III Clinical Trials](#)
- [NHLBI's COVID-19 Guidance for Researchers](#)

NIAID Funding Opportunities

- [Updates on NIAID Funding for SARS-CoV-2 and COVID-2019 Research](#)

NIEHS Resources

- [NIEHS Worker Training Program COVID-19 Resources](#)
- [NIEHS COVID-19 Information & Grants of Interest](#)
- [NIH Public Health Emergency and Disaster Research Response Tools for COVID-19](#)

NCI

- [NCI's COVID-19 Information for Cancer Researchers](#)
- [NCI Funding Notices for COVID-19](#)
- [FAQs for Researchers Looking for COVID Funding](#)

Research Training

NIH issued a May 11 notice extending the application deadline from May 25 to June 30 for institutional T32 and T35 training awards. [Learn more.](#) ■

VETERANS ADMINISTRATION

VA Issues RFP for COVID-19-Related Pulmonary Rehabilitation Research

The VA Office of Research and Development recently issued an RFP (<https://vaww.research.va.gov/funding/docs/RX-20-003-Parent.pdf>) - NOTE – the above link is not available to the public, only to VA researchers. [For more information](#) seeking proposals related to addressing COVID-19-related pulmonary rehabilitation research studies. The RFP has been issued in response to anticipated post-COVID-recovery rehabilitation needs that are likely being experienced by many Veterans. The next deadline for submitting letters of intent for this application is Nov. 1, 2020. ■

CONGRESS BEGINS WORK ON 2021 HEALTH FUNDING

Congress is moving forward with the fiscal year (FY) 2021 spending process. Leading Senate Republicans including the chair of the Senate Appropriations Committee Sen. Richard Shelby (R-AL), have stated that the Senate intends to begin consideration of FY2021 spending bills by late June. However, the health spending bill, known as the Labor-HHS bill, is not expected to move until after the week of July 4.

The House Appropriations Committee Chair Nita Lowey (D-NY) announced this week that her committee intends to begin moving FY 2021 spending bills, including the health spending bill, between July 6 and July 13, 2020, aiming for full House floor votes on the bills before the August congressional recess. But in a presidential election year, it is likely that the FY2021 spending process will be disrupted and passage of temporary spending measure will be necessary. Despite this likelihood, we are cau-

tiously optimistic that NIH and CDC will receive funding increases, due to heightened congressional awareness of the importance of our biomedical and public health infrastructure during the COVID-19 pandemic.

COVID Relief

The House passed a COVID supplemental bill on May 15, 2020 that includes \$4.75 billion in funding for the NIH, including \$3 billion targeted for relief for research labs around the country shuttered due to COVID-19. Senate leaders have indicated that they are working on their own COVID supplemental bill which they do not expect to begin moving until July. ■

