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iTHRIV Funds Data Driven Efforts to Combat COVID-19

by Keith Jones, iTHRIV Communications Coordinator

The COVID-19 pandemic has greatly affected the lives of millions worldwide. Many have answered the call to help reduce the spread of the virus through social distancing, quarantine, and, in some cases, by providing crucial health data. iTHRIV CTSA partner sites have conducted unique projects seeking to provide researchers with valuable data gathered from Virginia residents.

Natalie Cook, Ph.D., an assistant professor of public health in the Virginia-Maryland College of Veterinary Medicine, and co-investigator Sophie Wenzel, DrPH, MPH, an assistant professor of practice and associate director of the Virginia-Maryland College of Veterinary Medicine’s Center for Public Health Practice and Research, noticed a rise in conflicting information surrounding the pandemic.

“There was so much information at the beginning of COVID-19, a lot of it was misleading, confusing, or outright false,” Cook said.

Contradictory information from multiple sources leads to misunderstanding and confusion. Many Virginians were wondering what to do to protect themselves and their families from the virus, while others may not have been taking the pandemic seriously. The two researchers created an online survey to better understand how Virginians perceive COVID-19 communication and how it affects their actions.

“We were driven by a desire to make sense of it all,” Wenzel said. “We really want to understand what messages or messengers Virginians trust. Where and how are people getting their information? That is very important.”

The goal of this state-wide effort will be to create a better understanding of how to communicate critical messages and reduce harm to Virginians. The team hopes that this research will allow institutions to communicate important health messages more effectively. The survey portion of the study concluded in the summer, and the researchers are now meeting with small focus groups to explore demographic specific responses while they begin analyzing data. The study team includes public health professionals, healthcare providers, educators, and researchers.

I noticed that you put “Dr.” here – if you want to list doctors, then do it consistently for everyone in the newsletter, and put their appropriate credentials after their name (Ph.D., M.D., D.V.M., etc.)

During the early days of the pandemic in Northern Virginia, Inova Health System physician Chris deFilippi, MD initiated a COVID surveillance program to study higher risk healthcare workers. The study enrolled approximately 1,950 participants from Inova Fairfax and Alexandria Hospitals, around 75% of which had regular contact with hospitalized patients with COVID-19. The goals of the longitudinal study were to monitor the prevalence of asymptomatic exposure to COVID, examine the factors that may be associated with exposure, and to evaluate critical scientific questions that could be relevant to the Inova front-line workforce. Using a series of soluble biomarkers, the team will also attempt to determine the effects of COVID related inflammation and end organ
injury in the cardiovascular system, the liver, and the kidneys. The scale of the study has provided additional opportunities to determine not only antibody titers, but the relative efficacy of this immunity with respect to neutralizing antibodies using a live virus functional assay. Inova, in collaboration with George Mason University have found evidence indicating that immunity is sustained over at least 2 months; they have submitted these results for publication.

Meanwhile, at the University of Virginia (UVA), Principal Investigators Don Brown, Ph.D., and Johanna Loomba, ME, CCR, partnered with the Virginia Department of Health (VDH), as well as a cross-state advisory group to create an online tool to collect COVID-19-related health and wellness information from Virginia residents. The “COVID and the Commonwealth: An iTHRIV Health Status Registry” project aims to fill an information gap by collecting self-reported data from individuals who may be healthy or convalescing at home.

“It’s difficult for health researchers to know what’s happening in the state,” Loomba said. “The iTHRIV registry gives us a way to gather all that information in one place, which is more efficient.”

The information collected will pertain to simple demographic identifiers, such as age and gender, social questions regarding job loss and stress, as well as more detailed inquiries surrounding health. The registry is not designed to address one specific question, but rather is an ongoing effort to collect and pool this valuable data.

Together, these projects each represent a commitment from iTHRIV and its partner sites to advance translational research and a desire to serve Virginia residents.
What is iTHRIV?

Resilient Resources for Resilient Researchers

What is iTHRIV?

The integrated Translational Health Research Institute of Virginia, or iTHRIV, is a National Institutes of Health (NIH)-funded Clinical and Translational Science Award (CTSA) Program Hub. In practice, iTHRIV is a cross-Commonwealth collaboration between University of Virginia, Virginia Tech, Carilion Clinic, and the Inova Health System. iTHRIV unites the research infrastructure of these flagship institutions with the latest advances in data science to accelerate innovation in health-related research and foster the next generation of collaborative health research professionals.

What is the CTSA Program?

Recognizing the need for a creative and broadly integrated approach to solve large and complex problems, the NIH created the CTSA Program to support research teams tackling system-wide scientific and operational problems in clinical and translational research.

According to the NIH, the CTSA Program aims to:

- Train and cultivate the translational science workforce;
- Engage patients and communities in every phase of the translational process;
- Promote the integration of special and underserved populations in translational research across the human lifespan;
- Innovate processes to increase the quality and efficiency of translational research, particularly of multisite trials; and
- Advance the use of cutting-edge informatics.

A Community Focus

iTHRIV’s work is not just in the laboratory or clinic. We collaborate with community partners to address meaningful issues that Virginians face every day. Through various projects iTHRIV researchers and community partners have worked to address issues surrounding maternal mental health, foster summer reading programs within vulnerable populations across Virginia, and develop sustainable cancer prevention and detection programs in the New River Valley.

Impactful Discoveries take Time and Expertise

iTHRIV is proud to work closely with the Center for Open Science and the UVA Licensing & Ventures Group to engage health researchers and cultivate emerging ideas into the latest health innovations. These unique relationships align iTHRIV researchers with the thought-leaders of the Open Science Movement while also ensuring access to pivotal industry resources.
iTHRIV AnnouncesIncoming 2020 Scholars Program Cohort

by Keith Jones, iTHRIV Communications Coordinator

The integrated Translational Research Institute of Virginia today announced its fourth class of iTHRIV Scholars. The eight selected researchers, from the University of Virginia and Virginia Tech, will participate in a structured, two-year research training and mentorship program that emphasizes data science training and interdisciplinary research collaboration.

The iTHRIV Scholars program, launched in 2017, helps early career faculty members advance their careers. The program is available to full-time faculty applicants who have a doctoral degree or its equivalent, in a research or health profession. Applicants must seek approval from their supervisors, department chairs or institute directors, allowing them to dedicate roughly 75% of their time to their research project and the training curriculum.

“We appreciate the consideration and encouragement of the department chairs and institute directors by providing protected time for the scholars to pursue these research projects and goals,” Jennifer Kirkham, the iTHRIV Scholars program manager, said.

The 2020-22 cohort includes:

- **Laurie Brenner**, an assistant professor in the Department of Neurology at the UVA School of Medicine. Mentored by Kevin Pelphrey, Jaideep Kapur and Karen Johnston, Brenner will study if “Autism-plus-epilepsy is an autism subtype with a focal neurobiological basis.”
- **Alexandra DiFeliceantonio**, an assistant professor at the Fralin Biomedical Research Institute at Virginia Tech Carilion, and in Virginia Tech’s Department of Human Nutrition, Foods, and Exercise in the College of Agriculture and Life Sciences. Mentored by Warren Bickel, Matthew Hulver and Brooks King-Casas, DiFeliceantonio is an appetitive neuroscientist whose research project will explore the “Neural and metabolic correlates of carbohydrate reward.” Alexandra Hanlon will collaborate with DiFeliceantonio on this study.
- **Brittany Howell**, an assistant professor at the Fralin Biomedical Research Institute at Virginia Tech Carilion, and in Virginia Tech’s Department of Human Development and Family Science in the College of Liberal Arts and Human Sciences. Mentored by Catherine Limperopoulos, Howell is launching a pilot study to examine the “Role of gut dysbiosis in the neurodevelopmental consequences of neonatal abstinence syndrome.” Kim Simcox, Lisa Andruscavage and Cindy Smith will collaborate with Howell on this project.
- **Lisa Letzkus**, an assistant professor in the UVA School of Medicine’s Department of Pediatrics. Mentored by Karen Fairchild, Doug Lake, Jessica Keim-Malpass, Brynne Sullivan and Richard Stevenson, Letzkus will study “Neurodevelopmental infant cardiorespiratory evaluation.” Santina Zanelli, Vince Pulido, Sandeep Pillutla and Randall Moorman will collaborate with Letzkus on this project.
- **Nicole Long**, an assistant professor in the Department of Psychology in UVA’s College of Arts & Sciences. Mentored by Carol Manning, James Morris and Mark Quigg, Long will study “Mnemonic brain states and selective memory deficits in healthy aging.”
- **Kaitlin Love**, a fellow in the Division of Endocrinology and Metabolism in the UVA School of Medicine’s Department of Medicine. Mentored by Zhenqui Liu, Arthur Weltman and Sue Brown, Love will study the “Effect of glucagon-like peptide-1 receptor agonism on microvascular perfusion, cardiorespiratory fitness, and glycemic variability in Type 1 diabetes.” James Patrie will collaborate with Love on this project.
- **Sora Shin**, an assistant professor at the Fralin Biomedical Research Institute at Virginia Tech Carilion, and in Virginia Tech’s Department of Human Nutrition, Foods, and Exercise in the College of Agriculture and Life Sciences. Mentored by Warren Bickel and Robert Trestman, Shin will study “The role of leptin receptor neural circuits in mediating early life trauma-induced binge-eating behavior.” Anthony-Samuel LaMantia will collaborate with Shin on this project.
• **Kara Wiseman**, an assistant professor in the Department of Public Health Sciences at UVA School of Medicine. Mentored by Lee Ritterband, Roger Anderson, Laura Barnes and Robert Klesges, Wiseman will examine the “Effectiveness of publicly available smoking cessation resources: Does rurality matter?"

Due to the COVID-19 pandemic, this year's iTHRIV Scholars Program has transitioned to virtual programming, which starts in July.

“Some of our programming has been postponed or altered to fit our new environment, but we have ultimately harnessed the opportunity to test virtual programs and collaborate with our partner sites,” Kirkham said. “We are grateful to the vast number of instructors who have shared their expertise with our scholars. We thank the mentors for participating in the growth and development of the next generation of clinical and translational research colleagues.”

Funded by a Clinical and Translational Science Award, iTHRIV combines the expertise of biomedical researchers and data scientists to create infrastructure and investigator resources for using data to improve health across Virginia. Partner sites include UVA, Virginia Tech, Carilion Clinic and Inova Health System.

*iTHRIV is supported by the National Center for Advancing Translational Sciences, part of the National Institutes of Health, through award number UL1TR003015/ KL2TR003016.*

The 2020 iTHRIV Scholars are, clockwise from top left: Lisa Letzkus, Alexandra DiFeliceantonio, Kaitlin Love, Kara Wiseman, Sora Shin, Laurie Brenner, Brittany Howell and Nicole Long.
iTHRIV Scholar Spotlight: Tanya Evans, 2019 Cohort

Meet Tanya Evans and discover her motivation to research brain architecture and early childhood development. Click the link below to watch the video.

https://www.youtube.com/watch?v=wMQflWqqrJA
iTHRIV Scholar Spotlight: Sora Shin, 2020 Cohort

by Whitney Slightham, Assistant Director of Communications, Fralin Biomedical Research Institute at VTC

Lousy sleep. A foul mood. Frequent trips to the refrigerator. They’re common signs of stress, but Sora Shin sees something more. Shin’s new laboratory at the Fralin Biomedical Research Institute at VTC examines how stress alters brain circuits, causing lasting changes to mood, behavior, and, in some cases, overall mental health.

“People show a dynamic range of responses to acute and chronic stress. Some people have sleep disturbances, while others feel more tired than usual. Likewise, some people may overeat and others lack an appetite,” said Shin, who is an assistant professor with the Fralin Biomedical Research Institute and Virginia Tech’s Department of Human Nutrition, Foods, and Exercise in the College of Agriculture and Life Sciences.

According to the American Psychological Association, 75 percent of adults in the United States experience stress. But when it comes to treatment, there isn’t a one-size-fits-all solution. By revealing what happens when brain circuits become impaired, Shin hopes her research will one day lead to more precise treatments for psychiatric disease.

“We first look at a functional difference in behavior and trace it to a brain region where the change originated. Then we search for therapeutic targets to correct signaling errors within a defined brain circuit,” Shin said.

Shin’s team uses a combination of in vivo imaging techniques to see what’s happening at a microscopic scale in freely moving mice. The scientists image calcium to reveal neuronal activity and detect cells with impaired calcium signaling. Next, they use a variety of techniques to modulate cell activity in that select group of impaired neurons and trace the behavioral effects.

“We’re investigating specific circuit mechanisms of psychiatric disease and hope that one day we’ll use this knowledge to develop targeted medications that correlate with an individual patient’s unique experience and symptoms,” Shin said.

Not all forms of stress lead to mental illness. As part of the body’s normal reaction to change, stress can be positive, playing an essential role in evolution and adaptation. Stress helps organisms survive by keeping them alert and helping them detect danger.
But chronic stress without relief can come at a cost to mental and physical well-being.

Shin first-authored a 2015 study that sheds light on this phenomenon, studying how chronic stress leads to depression. The study, published in *Nature Neuroscience*, revealed how a chemical signaling flaw in the brain’s nucleus accumbens may be linked to stress-induced depression. When Shin and her colleagues injected a virus carrying genetic instructions to compensate for a missing gene, it increased levels of a key protein involved in regulating reward. The virus did the trick: as levels of the protein increased, the circuit was corrected, and depressive symptoms waned.

Shin and her team revealed how defects in a precise signaling pathway increased the risk of chronic stress-induced depression and then alleviated those symptoms once again using a drug to mimic the virus’s effects and correct the circuit.

Other forms of chronic stress during phases of brain development can also have long-lasting effects on mood, personality, and overall mental health. People who experience early life stress, characterized by abuse or neglect experienced during childhood, are at higher risk of gaining dysfunctional social behaviors as adults.

Shin and her colleagues showed that mice who experienced early life stress and had trouble socializing as adults could gain normal social skills if a specific type of neuron was activated.

First-authored by Shin, the 2018 paper published in *Neuron* showed that mice with social impairments had blunted brain cell activity in response to social interaction in the lateral septum – a brain region that regulates behavioral stress response. When the researchers used a technique called optogenetics to activate specific neurons using light stimulation, the social impairments vanished. The scientists yielded the same results when they used a drug to manipulate the same pathway.

“Many scientists have studied how someone’s genes might predispose them to mental illness, and that is important, but I am interested in how gene expression is altered by our environment,” Shin said.

Prior to moving her laboratory to Virginia Tech, Shin was a postdoctoral fellow at the University of California, San Diego, where she received the Kavli Institute for Brain and Mind innovative research grant award in 2018.

Born and raised in South Korea, Shin completed her bachelor’s degree in biology at Chung-Ang University, master’s degree in physiology at Sungkyunkwan University College of Medicine, and doctoral degree in medical science at Yonsei University College of Medicine.
iTHRIV Under the Microscope, Andrea Bidanset

iTHRIV is relies on its dedicated workforce to ensure operations run smoothly. With cross Commonwealth institutions, it's important to recognize the individuals contributing behind the scenes to iTHRIV’s success.

Andrea Bidanset is the Director of Clinical Trials for Carilion Clinic, a not-for-profit healthcare organization serving western Virginia. Andrea joined Carilion’s Research and Development team in 2016 and has a combined 11 years of experience in clinical research coordination and administration. As part of iTHRIV, she serves on the Clinical Research Access and Workforce Development Committees; which aim to increase clinical research access for underserved communities and provide developmental opportunities for the clinical research workforce at the collaborating iTHRIV sites.

Andrea is from the Roanoke Valley and returned home after completing her undergraduate studies at the College of William and Mary in Williamsburg, VA. She went on to study Healthcare Administration, obtaining an MHA from Radford University Carilion in 2016. In her spare time, she enjoys spending time outdoors and renovating her 100-year-old house with her husband.
iTHRV Portal Highlights

Research Reproducibility 2020 Conference

https://portal.ithriv.org/#/resource/1373

This free conference will bring together experts and novices, researchers and educators, and students and administrators from multiple disciplines and institutions to explore best practices, innovations, policies, and new ideas for education around reproducibility, replicability, and rigor. Individuals with experience or ideas about education on rigor and reproducibility are encouraged to submit an abstract proposal.

Model Selection in R

https://portal.ithriv.org/#/resource/1303

Regression is one of the most commonly used statistical methods – but things can quickly get complicated when you have multiple predictors. In the SAIG Short Course Model Selection in R, we will cover different methods to evaluate different regression models with different sets of predictors.

LEARNING SHOT: Tips for Writing More Readable Consent Forms

https://portal.ithriv.org/#/resource/566

This UVA IRB-HSR Learning Shot offers some tips for simplifying the text in a clinical research consent form.