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iTHRIV Funds Data Driven Efforts to Combat COVID-19

by Keith Jones, iTHRIV Communications Coordinator

“These cells aren’t in the brain at the first stages of development, they move up and migrate to the brain...they’re like me, an immigrant” muses Dr. Ukpong Eyo, PhD. Speaking about microglia, immune cells that reside in the brain, he states “I feel a connection to this research, I want to find out what role microglia play in brain function”. Dr. Eyo is seeking to understand how the microglia help manage brain function through vascular regulation as well as in seizure disorders.

Based on the strength of his initial findings Dr. Eyo has received qualifying scores on two new NIH R01 grant applications to study microglia in depth. The combined grants will total $5M over five years.

The brain accounts for only about 2% of our body’s weight, however it utilizes up to 20% of the body’s energy which is mostly delivered through the blood circulation of oxygen and nutrients. The brain, therefore needs a constant and consistent supply of blood and well-functioning blood vessels. Neurological pathologies, such as Alzheimer’s disease have a connection with impaired blood vessel function. Dr. Eyo’s research seeks to determine what, if any, effect microglia have on blood flow in the brain. “If you’re looking for microglia in the brain, there is a good chance you will find them on a blood vessel”, says Dr. Eyo. His previous research indicates that about a third of the brain’s microglia are concentrated around blood vessels, and Dr. Eyo intuits that “they most likely play an important role in neurovascular function”.

To test his hypothesis, Dr. Eyo used pharmaceuticals to eliminate microglia in the brain. This approach targeted both vessel-associated and non-vessel-associated microglia. The study yielded remarkable results; the size of the blood vessel changed and this corresponded to a change in the amount of blood flowing into the brain. Dr. Eyo’s study seems to suggest that microglia can be manipulated to regulate blood flow. The findings are important, as this indicates the possibility for a new approach to resolve impaired blood flow function in diseases such as Alzheimer’s disease.

Dr. Eyo has designed a three step study for the first project. He and his investigative team will seek to determine whether all the microglia mediate the blood vessel/blood flow changes, or if it is specifically the vessel-associated microglia that control this function. In the second stage, the researchers will determine whether microglia perform this function directly or indirectly by instructing an intermediate cell type, the astrocyte. Finally the team will determine whether these findings are relevant for blood vessel flow regulation in a mouse model of Alzheimer’s disease.
His second project has a deeply personal connection. Dr. Eyo relates that his son endured several febrile seizure events before he reached three years of age. Febrile seizures are the most common form of childhood seizures. They affect 2-5% of children from age six months up to five years. The underlying mechanisms are not fully understood, but febrile seizures occur with a rise in body temperature that is often associated with a fever. Though the seizures are benign, physical effects of the seizure can lead to ancillary injury. In preliminary studies, the team developed a mouse model of febrile seizures. The researchers noted that with increased temperatures, the test mice showed seizures. Mice whose microglia were eliminated experienced more severe seizures, suggesting that microglia may play a mitigating protective role against seizures.

Like his other project, this study will include a three step process. Dr. Eyo explains, for “the first part we will use more specific approaches to eliminate microglia and determine whether this would actually worsen the seizures.” Dr. Eyo clarifies that “previously, we could only remove cells that look like microglia without sufficient specificity”. The second part of the study is designed to identify whether or not there is a specific microglial protein that regulates the beneficial role of microglia in seizures. If this protein is identified, it could lay the groundwork for future studies to target this protein to modulate seizures in patients. The final part will be to determine whether targeting microglia and this protein receptor could prevent the incidence epilepsy in adulthood following temperature-induced seizures.

When not in the lab, Dr. Eyo serves as one of a select group of Scholar mentors leading the mentor training program with the integrated Translational Health Institute of Virginia (iTHRIV). The iTHRIV Scholars Program combines structured mentoring sessions, career development, and a core curriculum. Additionally, Scholars and mentors are connected to researchers and resources from across the iTHRIV partner sites. “It is truly amazing to have a program dedicated to fostering career development for early career researchers. This program seeks out talented researchers and connects them to the resources they need to succeed”. Dr. Eyo is paired with current iTHRIV Scholar Dr. Kaitlin Love and is looking forward to lending his perspective as an accomplished basic scientist. “Far too often in research we are silo-ed. We should break those barriers, when the clinical side communicates with the basic science side everyone benefits”.
iTHRIV Awards $80,000 to Community-Focused Research Projects in Charlottesville

The integrated Translational Health Research Institute of Virginia, or iTHRIV, a National Institutes of Health-funded Clinical and Translational Science Award hub, has awarded almost $80,000 in seed funding across two community-focused projects.

The seed grant program is part of iTHRIV’s goal to promote translational science that bridges the gap between community and health researchers. The projects also reflect iTHRIV’s commitment to advancing social equity by funding research that will benefit underserved groups across Virginia.

“iTHRIV seeks opportunities to partner with the community to address health problems which are important to the people who live in Virginia,” said Kristin Miller, iTHRIV partnership manager.

The 2021 projects will study:

**The Benefits of Greenspace Activities for Seniors**

Noting that the pandemic has had a uniquely detrimental impact on seniors, Marta Keane, chief executive officer of the Jefferson Area Board for Aging, has partnered with Jenny Roe, director of the UVA School of Architecture’s Center for Design and Health, and Christopher Neale to study whether various nature-based activities can lead to improvements in emotional, physical and cognitive health in seniors.

“Isolation [for] any amount of time can negatively impact emotional, physical and cognitive health. The extreme social isolation created by COVID could exacerbate these risks,” Keane said. “Due to the heightened isolation from the pandemic, it is more important than ever to investigate the impact that purposeful nature experiences could have on seniors’ well-being.”

Preliminary research indicates that there are many benefits of green space activities in older adults; use of outdoor space is a way to increase social interactions in a COVID-safe manner.

Roe agrees: “We know that interacting with nature – in gardens, in parks, in wilder settings – builds emotional, cognitive, physical and social wellbeing. At a time when so many older people are suffering from lack of mobility and social isolation, our research will help identify what type of nature intervention works best for health and for whom. That is, comparing a physical approach – walking in nature – versus a cerebral approach – engaging in environmental citizen science – versus a nurturing approach – gardening and growing plants.”

Study participants will engage in activities including walking, planting and various “citizen science” projects. The researchers will then evaluate metrics related to contemplative, physical and cognitive health. Keane
hopes that the team’s work will have positive effects not only for the Jefferson Area Board for Aging service users, but also for seniors nationwide.

**Improving Access to Medicaid for Noncitizen Children**

Michaela Lieberman, a staff attorney and the Health Justice Legal Fellow at the Legal Aid Justice Center in Charlottesville, noticed that while many noncitizen children are legally eligible for Medicaid, they remain uninsured. Lieberman has partnered with Dr. Dianne Pappas, a pediatrician at UVA Health, to study this issue. Their community-based team aims to identify and reduce common barriers to Medicaid enrollment for noncitizen children, as well as collect information on primary care and emergency room use.

“Honestly, we don’t really know how many of these children and families there are in our community, or what the challenges and barriers are that keep them from accessing health care,” Pappas said. “The first step to improving access and health is to understand the community and the barriers that prevent them from successfully accessing the health care system.”

Lieberman is delighted their proposal was funded: “It was designed and implemented in partnership with directly affected community members. This grant will ultimately ensure more Medicaid-eligible kids in Virginia get access to the critical health care services they may otherwise not be able to afford. We see this funding opportunity as an important tool in capturing and reducing a source of health inequity in the commonwealth.”

The researchers will also measure if participants report an increase in self-perceived overall wellbeing. The team plans to develop a set of best practices to reach and enroll this historically underserved and overlooked population.

iTHRIV is supported by the NIH through National Center for Advancing Translational Sciences (award number UL1TR003015). A cross-commonwealth collaboration of the University of Virginia, Virginia Tech, Carilion Clinic and the Inova Health System, iTHRIV unites the research infrastructure of these flagship institutions to accelerate innovation in health-related research with the latest advances in data science. iTHRIV is committed to engaging with community voices to understand what is important to them regarding their health and their needs.

*To learn more, visit [www.iTHRIV.org](http://www.iTHRIV.org).*
Community Engagement Studios: Connecting Researchers and Community

by Emily Wells, Research Program Manager, University of Virginia Wise

Community engagement is critical in all phases of clinical and translational research from proposal development to dissemination of research results. To increase opportunities for community input and feedback iTHRIV offers Community Engagement Studios (CES), a facilitated discussion between researchers and the community. In a CES the community participants are individuals who have knowledge about the particular research topic (i.e., breast cancer, substance abuse etc.), through an individual lived experience, as a caregiver, job or other understanding.

A CES provides an opportunity for the researchers to learn from the community members who are the experts on the topic. Community experts are compensated for their time in the studio and provides experts the opportunity to learn about research that could impact their community, provides information they can share back and creates opportunities for communities to have their voices heard. A CES begins with the researcher providing an overview of their proposed research, the facilitator then asks a set of preidentified questions to the community experts and the researcher becomes the student. The CES is one-way iTHRIV is creating opportunities to bridge the gap between academic institutions and communities, assess feasibility of proposals and improve research quality.

Currently Community Engagement Studios are being held virtually through Zoom and can be used at different stages in the research process. Please contact Kris Miller, iTHRIV Partnership Manager, to learn more.
THRIVing Communities: Check-in with a 2019 iTHRIV Community Seed Grant Project

by Kris Miller, iTHRIV Partnership Manager

The iTHRIV Community and Collaboration Core’s pilot grants encourage, facilitate and fund partnerships between community organizations and iTHRIV researchers.

KJ Holbrook, LCSW, Chief Clinical Officer for Mount Rogers Community Services Board (MRCS), partnered with Virginia Tech’s Department of Psychology Professor Angela Scarpa, PhD, LCP, on a research project, entitled, Providing Mobile Diagnostic Evaluations and Psychoeducation for Autism Spectrum Disorder in Rural Southwest Virginia. The aim of the project was ‘to reduce disparities in access-to-care for parents and their children affected by Autism Spectrum Disorder (ASD) in rural, under-resourced communities by providing geographically easier-to-access assessments and psychoeducation for the parents of ASD diagnosed children (chosen based on input from focus groups in the MRCS catchment area). Funded by one of the iTHRIV pilot grants, these collaborators were able to conduct their research project amid the COVID-19 shutdown and completed their final report in early 2021.

Jennifer Scott, Rural Outreach Coordinator for the VT Mobile Autism Clinic, states how thankful the team is, “Virginia Tech Autism Clinic and Center for Autism Research (VTCAR) is grateful to have had funding that allowed us to establish a collaborative relationship with MRCS. Both novel ASD assessment and mobile and telehealth psychoeducation delivery formats proved feasible and helped rural families overcome barriers to access, including distance and cost”.

In addition, says Ms. Scott, “the parent’s knowledge of autism was improved and they felt empowered with the diagnosis, which enables them to advocate for appropriate services throughout their child’s lifetime within their local community service boards and with other providers.”

The results also ‘suggest that the Mount Rogers staff and the screening measure are successful in identifying children of concern. Several unanticipated challenges presented themselves, during the 2019-2020 time period, fortunately the team developed new strategies that they will utilize moving forward.
VTCAR is building on a larger statewide pilot project. In addition to MRCS, many other community service boards will be included. The project explores barriers to care for those with ASD and co-occurring mental health challenges. The team has qualified for follow-on funding and looks forward to continuing their work with the community.

If you are a researcher at an iTHRIV institution and would like to learn more about community partnership opportunities, please contact Kris Miller.
iTHRIV Under the Microscope: Tina Nunez

Tina Nunez is the iTHRIV Program Assistant coordinating outreach to the LatinX community. She works closely with Dr. Max Luna at the Latino Health Initiative at the University of Virginia School of Medicine. Tina is able to draw on her vibrant history of service with the Charlottesville community. She is passionate about helping others and has volunteered with numerous nonprofits and government agencies such as the Legal Aid Justice Center, Sin Barreras, and the Shelter for Help in Emergency. Immediately prior to joining iTHRIV, Tina worked as a Lead COVID-19 Case Investigator with the Blue Ridge Health District. She is now serving as a point of contact for the Latino community in the COVID vaccine promotion efforts, and has been instrumental in scheduling over 1,700 community members for their COVID vaccine in recent weeks! In her iTHRIV role Tina will seek to better understand and help address the healthcare barriers facing the LatinX community.

Tina is driven by a steadfast commitment to service and uses her experience as an immigrant to help foster an open and inclusive community. In her free time, Tina enjoys reading, gardening and playing with her dogs.
Clarifying the NIH Genomic Data Sharing policy

by Medard Ng, iTHRIV Research Quality Manager

Dr. John designed a research study involving specimen banking (keeping specimens for future research). He did not include the genomic data sharing language in the informed consent form because he considered it unlikely that the specimens will be used for genetic research. Three years later, Dr. Jane proposed an exciting research project to Dr. John involving large-scale genomic research on the banked specimens. To conduct this research with Dr. Jane, Dr. John has to re-consent the participants regarding sharing of the genomic data – a labor intensive task that could have been avoided if the consent form was worded differently.

If your investigator initiated research project involves genetic research or specimen banking, you may want to include the genomic data sharing language in the consent form from the beginning. This will avoid the possibility of re-consenting subjects in the future.

The genomic data sharing language in the consent is one of the requirements of the NIH Genomic Data Sharing (GDS) Policy. Even though your current research project may be outside the purview of the GDS policy, the policy may still impact your research, for examples:

1. The small-scale genetic data obtained in a pilot grant application may be included in future grant application that falls under the purview of the GDS policy.

2. The banked specimens may be used for large-scale genomic research in the future - even if it seems unlikely now.

3. Genetic data may need to be deposited in a NIH repository. The use of such data repository usually requires participants be informed of the sharing of their genomic data.

The NIH Genomic Data Sharing (GDS) Policy

The GDS Policy set forth expectations that ensure the broad and responsible sharing of genomic research data. The policy became effective for competing grant applications submitted for the January 25, 2015, receipt date; contract proposals submitted to NIH on or after January 25, 2015; and for intramural projects generating genomic data on or after August 31, 2015. The NIH GDS Policy applies to NIH-funded research (e.g., certain grants, contracts, and intramural research) that generates large-scale human or non-human genomic data, regardless of the funding level, as well as the use of these data for subsequent research. Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data.

According to the GDS Policy, investigators who intend to use research or clinical specimens collected or cell lines created after January 25, 2015, to generate genomic data may only do so when informed consent processes explicitly discuss future research use and broad data sharing, even if the data are generated from specimens that are de-identified. NIH-designated data repositories will not accept genomic data derived from specimens or cell lines collected or created after January 25, 2015, without this type of consent. NIH strongly encourages the broadest appropriate future use and sharing of genomic and phenotypic data.
NOT-OD-14-111: The GDS Policy has no direct cost threshold associated with it and applies only to grant activities requesting support for research, such as:

- Research project grants (R);
- Program projects (P) and SCORs (S);
- Cooperative agreements for research (U);
- Individual career development awards (K) that include a research component;
- S activities that include a research component; and
- All other activities that include a research component.

The GDS Policy does not apply to:

- Institutional training grants (T32s, T34s, T35s, and TL2s);
- K12 career development awards (KL2s);
- Individual fellowships (F);
- Resource grants and contracts (S);
- Linked awards derived from previously reviewed applications (KL1, KL2, RL1, RL2, RL5, RL9, TL1, UL1);
- Facilities or coordinating centers funded through related initiatives to provide genotyping, sequencing, or other core services in support of GDS.

Additional information about the GDS policy can be viewed in the iTHRIV portal.