Duke Institute for Brain Sciences

Oct. 28, 2020

## DIBS Announces 2020 Seed-grant Funding Recipients

### *Programs fund innovative, interdisciplinary science*

Five interdisciplinary teams have received 2020 Research Incubator or Germinator Awards from the Duke Institute for Brain Sciences (DIBS). The awards are designed to promote high-risk/high-return neuroscience research that is collaborative, crosses disciplinary boundaries, and is likely to draw external funding.

The research teams will address health issues affecting millions, including spinal-cord injuries, the relationship between tobacco use and chronic pain, how changes in the gut are communicated to the brain, the use of novel technologies to understand the neural mechanisms of Parkinson's disease, and the effects of toxins on the developing brain. They represent multiple departments and schools, including the Duke School of Medicine, the Pratt School of Engineering, Trinity College of Arts & Sciences, and the Nicholas School of the Environment.

Three of the Incubator Award teams will receive $75,000; a fourth will be funded at $100,000 through the generosity of the DIBS External Advisory Board. Previous awards have brought in significant external grants after the initial seed funding, resulting in a seven-to-one return on investment over the past six years. The follow-on grants typically come from the National Institutes of Health, the National Science Foundation, and private foundations. The fifth is a Germinator Award of $25,000 that will support a study led by a graduate student with support of faculty mentors.

"We are pleased to be able to make these awards and highlight the value of interdisciplinary research," said DIBS Director Geraldine Dawson, PhD, in announcing the award recipients. Even during these financially challenging times, Dawson noted, "we remain strongly committed to supporting collaboration and innovation in the neurosciences at Duke. We were especially pleased to see the breadth of departments and schools that received funding."

Dawson also expressed gratitude for the generosity of the External Advisory Board. "Our board members are very enthusiastic and generous supporters of the Incubator program, and we thank them for making a fourth Incubator Award possible for 2020-2021."

Following is information about all award recipients and their research projects:

## DIBS External Advisory Board Incubator Recipient, $100,000

| | |
|---|---|
| ***Timothy Dunn, PhD***<br>Neurosurgery<br>School of Medicine<br><br>*Michael Tadross, PhD,*<br>*Biomedical Engineering,*<br>*Pratt School of Engineering* | **Parkinson's Advance with DART and DANNCE**<br><br>Parkinson's disease is caused by a degeneration of brain areas controlling movement. However, while we know which area of the brain degenerates, we have not yet understood exactly how this degeneration leads to movement defects such as tremors and slowing/stiffening of body motions. If we understand this mechanism in animal models, we will be one step closer to next-generation therapies that mitigate the disease without debilitating side effects and without a loss in effectiveness over time. Two fundamental obstacles to this goal have been (1) that relevant brain areas contain intermingled neuron types that have been hard to individually manipulate with clinical drugs, and (2) |

| | |
|---|---|
| | movement impairments are complex and diverse, so we have not yet been able to measure these defects quantitatively. Our collaboration unites two different technologies, creating a novel framework for understanding Parkinson's. The first, Drugs Acutely Restricted by Tethering (DART), enables delivery of any clinical drug to a specific brain-cell type in an animal. DART has already shown a novel causal link between the neurotransmitter glutamate signaling onto one neuron type and Parkinson's disease. The second technology, 3-Dimensional Aligned Neural Network for Computational Ethology (DANNCE), uses deep learning to track the fine details of body movement in 3D. This technology allows us to more precisely identify the movement defects in Parkinson's. With DIBS Incubator funding, we will pair DART with DANNCE to discover new relationships between neurons and movement defects and identify potential therapies. |

## Incubator Recipients, $75,000 each

| | |
|---|---|
| ***Timothy Faw, PhD***<br>Orthopaedic Surgery<br>School of Medicine<br><br>*Daniel T. Laskowitz, MD, MHS, Neurology; Muhammad Abd-El-Barr, MD, PhD, Neurosurgery; Haichen Wang, MD, Neurology, School of Medicine* | **A Novel Apolipoprotein E (apoE)-mimetic Pentapeptide to Improve Recovery in Acute Spinal Cord Injury**<br><br>Novel therapies that improve mobility after spinal cord injury (SCI) could lead to better quality of life and save billions of dollars in lifetime costs. Targeting the early inflammatory response to SCI is appealing, as it is the main cause of tissue damage after the initial injury. Apolipoprotein E (apoE) plays a critical role in mediating this neuroinflammation after nervous system damage. However, systemic delivery of the intact protein is ineffective as a therapeutic because it fails to cross the blood-brain barrier. As such, we have developed small, apoE-based peptides that mimic the function of the intact protein, cross the blood-brain barrier, and have few side effects. Here, we will test the hypothesis that early treatment with an apoE-mimetic peptide, CN-105, reduces inflammation, tissue damage, and improves recovery in a clinically relevant animal model of SCI. This peptide, developed at Duke, has received Investigational New Drug and Orphan Drug designations from the Food and Drug Administration, which will facilitate translation to early clinical trials. |
| ***Maggie Sweitzer, PhD***<br>Psychiatry & Behavioral Sciences, School of Medicine<br><br>*Katherine Martucci, PhD, Anesthesiology; F. Joseph McClernon, PhD, and Alison Adcock, MD, PhD, Psychiatry & Behavioral Sciences, School of Medicine* | **Neural Mechanisms Underlying Tobacco Withdrawal-Induced Hyperalgesia**<br><br>Chronic pain and cigarette smoking influence one another, in that smokers are more likely to have pain, and individuals with pain are more likely to smoke. People with chronic pain have more difficulty quitting smoking, in part, because temporarily going without smoking (early withdrawal) leads to increased pain sensitivity. The goal of this study is to examine the brain's response to heat pain stimuli among smokers in early withdrawal, to better understand the reasons for increased |

| | |
|---|---|
| | pain sensitivity. Daily smokers will complete two fMRI sessions, one after smoking as usual, and one after not smoking for 24 hours. During the scans, participants will experience heat pain delivered through an electrode and will provide ratings of their pain response. It is expected that participants' ratings of pain in response to heat stimuli will be greater during the withdrawal session, and that this increased pain will be associated with greater activation throughout a network of brain regions involved in perceiving pain. This approach will allow us to determine which brain regions are most involved in pain sensitivity during withdrawal, which will help to identify targets for treatment. In addition, these processes might differ among smokers who also have chronic pain, compared to those who do not. As such, half of the participants will be those diagnosed with chronic pain, while the other half will be pain-free. We anticipate that the effects of smoking withdrawal on pain-related brain function will be more pronounced among those with chronic pain. |
| ***Eva Naumann, PhD***<br>Neurobiology<br>School of Medicine<br><br>*John F. Rawls, PhD, Molecular Genetics and Microbiology, School of Medicine* | **Gut-to-Brain Sensory Conduction in Zebrafish**<br><br>Debilitating neuropsychiatric conditions such as autism, obesity, depression, and epilepsy can all be improved by changing diet and microbiome in the gut. Yet, it is largely unknown how these changes originating in the gut are communicated to the brain. Recent studies have revealed that gut-to-brain communication begins with a special cell type in the lining of the gut called enteroendocrine cells (EECs). For decades we have known there are different types of EECs that sense and respond to chemicals from diet and microbes by releasing hormones and neurotransmitters to influence the brain and other organs. Recent studies at Duke have revealed that some EECs also directly contact the vagal nerve, which serves as a key entry point to the rest of the brain. What we don't know is whether EECs are able to communicate with deeper regions of the brain in general, and whether distinct chemical stimuli and distinct EEC types in the gut evoke distinct patterns of brain activity. Here, we propose to address these gaps in knowledge by combining the skills of a gut specialist, Dr. Rawls, and an expert in brain imaging and anatomy, Dr. Naumann, to establish a powerful vertebrate system to examine this gut-to-brain communication. |

## Germinator Recipient

| | |
|---|---|
| ***Carina Fowler***, Graduate Student, Psychology & Neuroscience, Trinity College of Arts & Sciences<br><br>*Michael Gaffrey, PhD, and Aaron Reuben, PhD, Psychology & Neuroscience* | **Neural Correlates of Multi-toxicant Exposure in Preschool-age Children**<br><br>Animal studies show that certain chemicals, called toxicants, may change our brains. Exposure to flame retardants, pesticides, air pollutants, and second-hand smoke appears to harm parts of the brain involved in learning, memory, coordination, emotion regulation, and long-term planning. Children are particularly vulnerable to these types of changes |

| | |
|---|---|
| *Heather Stapleton, PhD, Environmental Ethics and Sustainable Environmental Management, Nicholas School of the Environment* | because they have greater exposure and fewer biological defenses than adults. This is particularly problematic because early childhood is a period of major neurobiological growth, and changes that occur during this critical developmental period can become permanent. However, many of the toxicants that could harm children's brain development have yet to be studied in children directly, and no research to date has tested whether exposure to multiple toxicants produces greater harm—even though children are routinely exposed to multiple toxicants at once. Our study will help us understand the association between children's brain structure and (1) exposure to individual toxicants and (2) combined exposure to multiple different toxicants at once. We believe that this work can help parents, pediatricians, and policymakers protect the developing brain. |