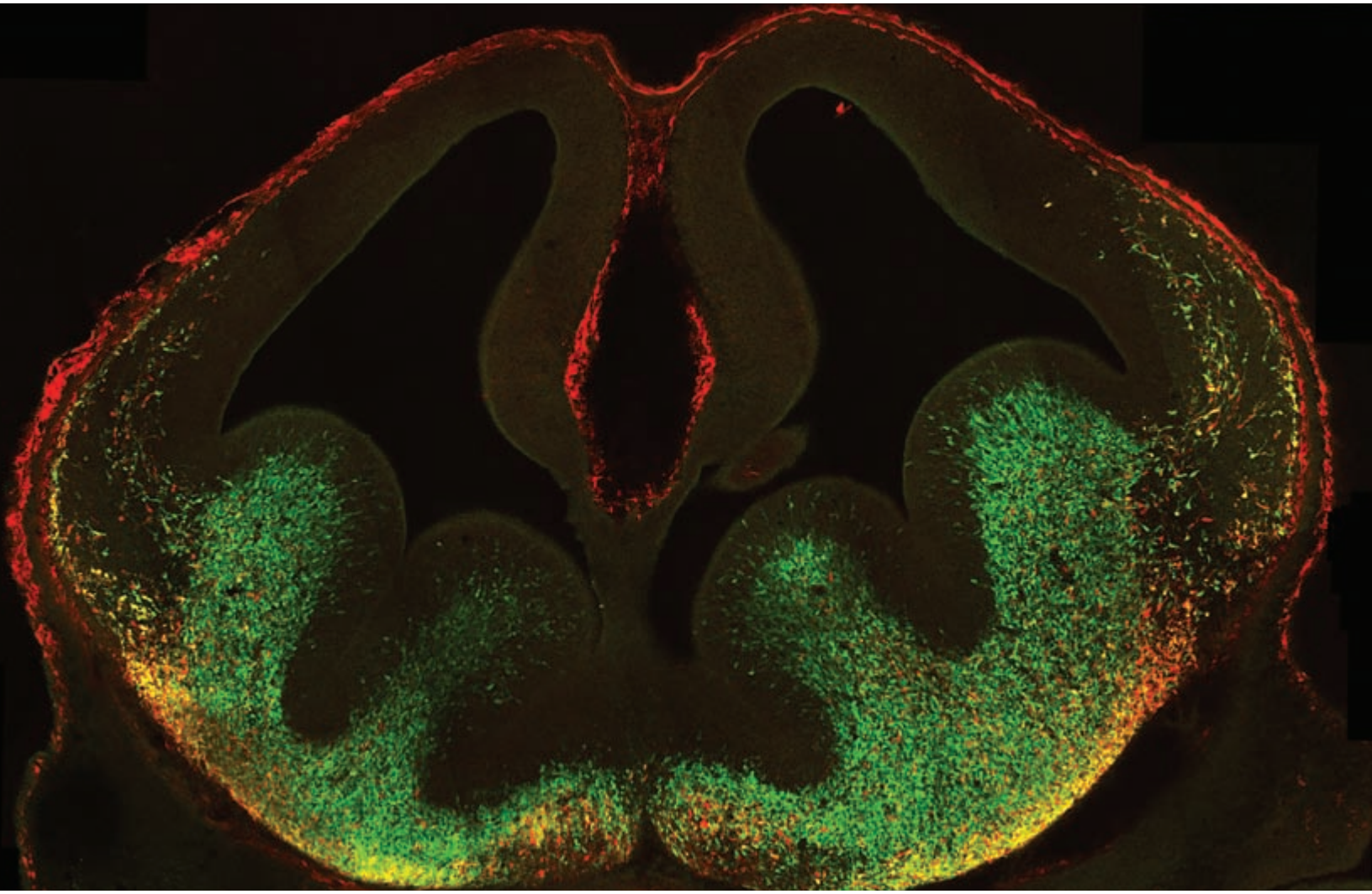

Illuminating the Mind

Scientists with GW's new Institute for Neuroscience are exploring how the human brain is built, and how to fix it when the process goes awry. BY KATHLEEN KOCKS

When the university announced last year the establishment of an Institute for Neuroscience, founding director Anthony-Samuel LaMantia saw an opportunity to foster a community of neuroscientists and boost the caliber of neuroscience research on campus.

Within two months, the institute had hit the ground running and began racking up successes, including a study published in March in the journal *Neuron*.

Contributor Kathleen Kocks caught up with Dr. LaMantia to discuss the institute's work on a topic that, as Dr. LaMantia notes, is at once scientific and philosophical. "We are trying to understand the organ that makes us who we are," he says.

Q: What are the two biggest challenges in neuroscience today?

The first challenge is to understand how brains are built—how individual cells develop and wire up properly. The second challenge is how to repair a brain that's broken.

These challenges exist because neuroscience is still in its infancy. We now have the entire sequence of the human genome, so we have a set of instructions but we still have to figure out how to read them. We need to discover how brains

are made, how brain development can be disrupted, how brains degenerate, and how to fix brains when something goes wrong. This is the research focus at the GW Institute for Neuroscience.

Q: Perhaps this is the Holy Grail of neuroscience—what's being done to map the human brain and determine what is "normal?"

That's a good question. Neuroscientists have mapped all brain connections in only one organism: a flatworm having 300 nerve cells out of 900 cells in the whole worm.

Human brains have more than 100 billion nerve cells. When you consider how many connections are possible, you see how complex the problem is. We have to determine the baseline for a normal brain and then determine what is far enough from the baseline to be considered abnormal.

Some neuroscientists are using structural MRIs to map the human brain's physical features and functional MRIs to map electrical activity. But it is still very hard to determine which connections are "significant" and what might change in the connections to cause disorders.

Q: What has been happening at the institute since opening its doors last August?

We have established our labs and our Biomarkers Analysis and Discovery Core facility. We've formed a team of 26 investigators from around GW, including the School of Medicine and Health Sciences and the departments of psychology, biology, anthropology, and speech and hearing sciences. Some of our investigators also work at Children's National Medical Center, giving the institute a tie-in to its expertise and equipment.

Besides doing research, we want the institute to be a major forum for the overall neuroscience community. A key part of this is our Neuroscience Seminar Series, a weekly presentation by prominent neuroscientists. It's an opportunity for them to see what we are doing, and for us to hear what they are doing.

We also created an eight-week course, Neural Development and Neurodevelopmental Disorders, for graduate students and postdoctoral fellows.

And we held our first annual symposium on April 27, focusing on relationships among neural development, stem cells, and cancer.

The institute is also applying for multi-investigator research grants—one of them to study the relationship between brain and face development. That research would look at how genes and foreign agents, like alcohol, disrupt physical traits and behaviors.

Q: What research is the institute currently doing?

Most of us are using the mouse, examining basic issues of how the brain is made and modeling genetic disruptions that cause disease in human patients. Some investigators are studying brain stem cells and how they develop into mature neurons, and others are exploring how nerve cells in the developing brain form circuits and what happens when things go awry.

Due to recent discoveries in human genetics, we and others have identified many genes that, if disrupted, correlate with disorders in neural development and behavior. What we don't know is how disrupted genes cause the disorders. Some investigators are studying mouse models of genetic disorders that cause autism-like and ADHD symptoms. Others are using mice to mutate major genes that have been identified in humans, to determine what breaks when the genes don't work.

For example, my laboratory focuses on the genes that are lost in DiGeorge Syndrome, or 22q11.2 deletion disorder. The loss results in improper brain development and severe physical deformities, including serious disruptions of face and heart development and their function. Using the mouse, we are finding that these genes regulate how nerve cells are made and move around to form appropriate circuits as the brain develops.

Another research area, pursued by Sarah Shomstein in GW's Department of Psychology, uses MRI imaging to study behavioral changes in attention and perception of the world around us when a stroke damages the brain. Judy Liu and her colleagues at Children's National Medical Center are studying how the mutation of a single gene that causes severe epilepsy in children influences how nerve cells move molecules around so that the right proteins are in the right places to ensure proper cell function.

Several investigators have recently published key findings. Vittorio Gallo and his colleagues at Children's National discovered an interaction between two signaling pathways in the brain that maintains a balance of cells needed for brain development, maintenance, and repair.

Josh Corbin and Molly Huntsman, also at Children's National, have shown that the gene that causes fragile X syndrome disrupts the way some neurons "communicate" with other neurons in the cerebral cortex. And collaborative work from my lab with Christopher Walsh and colleagues at Children's Hospital Boston discovered that fluid in the developing brain—cerebrospinal fluid—contains signaling modules that are critical for driving the generation of neurons during early brain development.

All this may seem like incremental progress, but science is the art of discovering and understanding very small parts of a much larger and complex whole. It's like the tiled mosaic art in St. Mark's Basilica in Venice; each tile contributes to the image that, over time, is seen only when you step back.

DANIEL MEECHAN

In this image from Dr. LaMantia's lab, young cells (labeled in green and red) are seen migrating across a developing mouse brain from the two bumps at the bottom of the image, where they originate. The road to becoming mature nerve cells, however, is a "perilous journey," says Dr. LaMantia; along the way, cells can get lost or not mature properly. The cells are thought to play an important role in an array of brain diseases, including schizophrenia, autism, and epilepsy.