Lorraine Iacovitti, PhD

Conquering a Medical Frontier

PHOTOGRAPHY BY KAREN KIRCHHOFF

Lorraine Iacovitti, PhD, helped pioneer stem cell research in Parkinson's disease 15 years ago. Today, she remains in the forefront of discovering how the brain works and how to help it heal.

Her groundbreaking research offers the hope of preventing the debilitating deterioration of Parkinson's patients while also mitigating the devastating effects of stroke. Her discoveries come at an opportune moment in history: With the graying of America, neurological disease and stroke have become the major causes of disability and death in the United States.

Iacovitti, a researcher in Jefferson's Vickie and Jack Farber Institute for Neuroscience, became interested in science at her Philadelphia high school and majored in biology in college, eventually earning a doctorate in neurobiology from Cornell University Medical College and undertaking her postdoctoral work at Washington University School of Medicine in St. Louis.

"I became intrigued by the brain," she says. "It really is the last frontier. All of us are interested in where thoughts come from, what controls our decision-making, our emotions."

Much of her focus has been on dopamine neurons. By the time Parkinson's patients exhibit symptoms, more than 70 percent of the dopamine neurons in their brains have died, and nothing can stop the onslaught. Iacovitti believes induced pluripotent stem cells—those derived from bone marrow, skin, blood or the brain instead of embryos—hold the key to treatment.

Iacovitti's lab stands as one of the top labs in the world undertaking the extremely difficult and expensive process of developing pluripotent cells and using a technique that the lab developed to turn the majority of cells into disease-targeting neurons. While her lab focuses on dopamine, the establishment of the Stem Cell Center in December, through the generosity of benefactor Kimberly Strauss, gives researchers studying other neurodegenerative diseases at Jefferson and throughout the region a resource for pluripotent cells.

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The ability to coax a patient's own cells into reverting to stem cells and to guide the majority to differentiate into dopamine neurons gave Iacovitti a rich canvas to study individual aspects of a patient's disease. It also moved her one step closer to developing a cell replacement therapy for Parkinson's patients.

The lab also focuses on "neuroprotective" strategies to prevent damage from Parkinson's in the first place. Instead of taking the route of other researchers, Iacovitti turned to an unstudied region of the brain unaffected by Parkinson's and discovered a protein with the capability to protect and even rescue vulnerable dopamine neurons. The lab has begun identifying the cellular mechanisms behind the protective effect in the hope of eventually introducing the protein into the susceptible region to reverse the damage Parkinson's wreaks.

Iacovitti expanded her research to include stroke about eight years ago. She solved one mystery by determining that stem cells live in many pockets in the brain, not just in two as commonly thought, and that these cells proliferate greatly after a stroke. The discovery offered insight into how the brain tries to repair itself. To help the repair process, the lab turned to the potent antioxidant dimethyl fumarate, also known as DMF, and found that it helps stroke-damaged nerve cells heal, resulting in fewer long-term neurological problems in lab rats that had suffered strokes.

With many stem cell treatments, a critical step involves getting the differentiated cells to the areas needing repair, and a barrier surrounding the brain makes the challenge particularly daunting in neurological cases. Iacovitti's lab, for the first time anywhere, accomplished this seemingly impossible task recently by coaxing the barrier open wide enough to allow a stem cell to pass and then closing it with no permanent damage. The ramifications for treatment are profound.

Those mysteries that drew Iacovitti to the brain as a young researcher? She has earned an international reputation for helping solve them.

WHAT BROUGHT YOU TO JEFFERSON?

In 1998, I followed Elliot Mancall (MD), my chairman at Hahnemann University (now Drexel), and research colleague Jay Schneider (PhD). At the time, Jefferson had wonderful pockets of neuroscience and promised to bring them together. The university established the Farber Institute for Neuroscience two years later. Neuroscience has gotten nothing but better since. We have cutting-edge research. The university has made a lot of investment in neuroscience, increasing our numbers greatly; we're even recruiting now. Collaboration is encouraged and appreciated. The environment is cozy and nurturing.

WHEN YOU ENTERED SCIENCE IN THE '70S, FEW FEMALE RESEARCHERS EXISTED. WHAT CHALLENGES DID YOU ENCOUNTER?

Do I think people were prejudiced, that they didn't take me seriously because I was a woman? No. The discrimination had more to do with the amount of time needed to compete. When I started, few women were married, let alone mothers. But I very much wanted a family. I remember painfully being forced to move back to Pennsylvania while nursing a 1-month-old baby so my mother could help while I wrote my first NIH grant. My competitors were men with wives at home looking after the children. I could do good work, publish and get grants, but I didn't have time to promote myself at every opportunity while raising a family. Women often make that choice.

WHAT WOULD YOU TELL WOMEN WHO WANT TO ENTER SCIENCE TODAY?

Much more support exists for women today than when I started. But you still need a passion for research; you really have to love it. It's harder today for everyone, not just women, because funding is so scarce. With just one two-year postdoc I got hired as an assistant professor at Cornell. Today you might not get your first grant until you're 40 years old. It isn't easy, but it is incredibly gratifying. I love the level of variety and creativity. I learn something new every single day. How many people can say that?

To learn more about Dr. Iacovitti or to support her work, contact Martina Grunwald, Assistant Vice President, Neuroscience, at 215-955-6426 or martina.grunwald@jefferson.edu.

HOW SOON DO YOU EXPECT TO SEE YOUR WORK TRANSLATED INTO CLINICAL TREATMENTS?

If we received funding, we could conduct clinical trials right now on the ability of DMF to help heal stroke-damaged cells. We see great potential to mitigate the devastating neurological effects of stroke, and we can move quickly because the government has approved DMF for other disorders. With the other developments, I don't want to put a timeline on them. But I do hope that before I leave the lab we will see treatments based on our stem-cell research.

WHAT HAS BEEN THE MOST THRILLING MOMENT IN YOUR WORK?

I've been fortunate to experience many thrilling moments. It was exciting to make a stem cell into a dopamine neuron for the first time and then see an animal get better after injecting the neurons into its brain. I was thrilled to discover that stem cells exist in many areas throughout the brain; it was a really important finding that sheds light on how the brain heals itself after injury such as stroke. The day a lab colleague coaxed open the blood-brain barrier and got a stem cell across was incredible, amazing.

If I don't have an exciting moment in a project, that project usually goes away. You have to have "eureka" moments or you won't get that next grant.

—J. LEE SUTHERLAND