Immune Signals in Parkinson's Disease

The Jefferson Comprehensive Parkinson's Disease Center is one of the Parkinson's Foundation's 33 Centers of Excellence in the United States. Its director, **Richard Smeyne, PhD**, professor of neuroscience, and his research group are examining the cell signaling and cascade of events that leads to initiation of Parkinson's disease (PD), seeking important clues about ways to arrest the condition's progression. Mutation within the Leucine-rich Repeat Kinase 2 (LRRK2) gene is thought to underlie about 20 percent of all PD cases. Two of the group's recent studies suggest that immune signaling from T-cells and B-cells in the blood plays an unexpected and important role in development of LRRK2-related PD.

The first of these studies explores neuro-inflammation—one of the most common pathologies seen in PD—where specialized brain cells release chemicals that lead to neuron death. To understand how this process starts and is regulated, researchers led by senior postdoctoral fellow **Elena Kozina, PhD**, looked at the way that LRRK2 gene mutations affect inflammation in mice. When they administered a compound that mimics bacterial infections, they found that only mice with LRRK2 mutations showed PD-like effects in the brain. These effects included an exacerbated brain inflammation that appeared to arise from signals initiated in T- and B-cells in the blood. This finding has the potential to provide new targets for interfering with the onset and progression of PD; it could also lead to identification of blood-based biomarkers that could be used as an "early warning" of PD.

In the second study, the researchers explored the impact of substituting a normal mouse immune system for one that has LRRK2 mutations. Would it "rescue" the mice from PD-like pathologies? They pursued this question in a creative way: generating a new strain of mice that contained LRRK2 mutations in all cells, but lacked an immune system; then using bone marrow transplantation to give the mice a normal immune system. Thus, the mice had normal LRRK2 in their T- and B-cells, but LRRK2 mutations in other cells, including all their brain cells. These chimeric mice could then be used to directly test the notion that signals from the peripheral immune system (the T- and B-cells) prompted inflammation in the brain—and that not having LRRK2-mutated immune cells would prevent PD-like symptoms.

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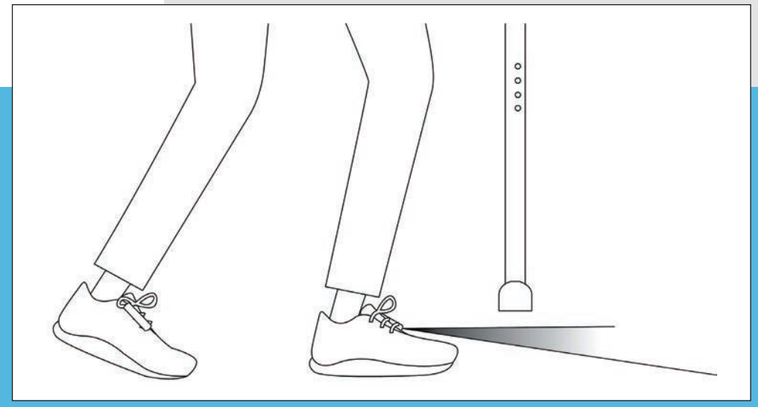
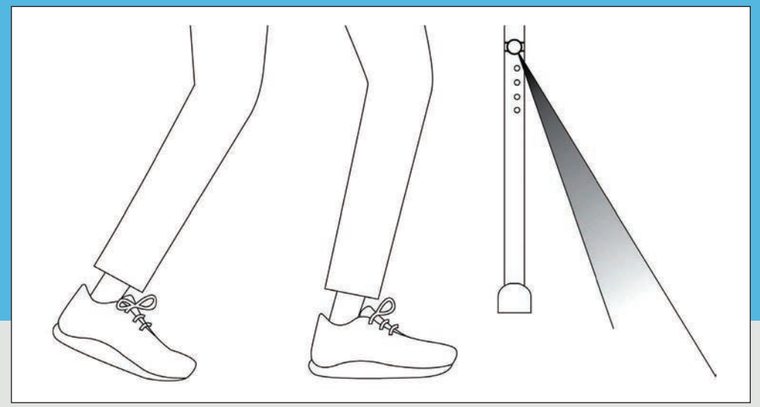
"Our hypothesis proved correct," Dr. Smeyne says. "Much of the mice's brain-immune response was normal; no neuron death was observed. This important finding points to a new way to think about how PD starts, and we are examining if this 'crosstalk' between the peripheral immune system and the brain is at work in other forms of PD." ■



One of the unique aspects of Thomas Jefferson University is that students from the Kanbar College of Design, Engineering and Commerce have the opportunity to interact and work with neurologist **Tsao-Wei Liang, MD**, to develop novel and practical devices to help patients with PD.

Through a summer work-study program, design students have been invited to the Movement Disorders clinic to evaluate the daily struggles of patients, return to the studio and then brainstorm to create and develop prototypes that have the potential to improve the quality of life of persons with Parkinson's.



Applying New Knowledge for Parkinson's Patients

Beyond its leading program of basic and translational research into the biological mechanisms underlying Parkinson's disease, the Jefferson Comprehensive Parkinson's Disease Center leverages the University's broad range of capacities in clinical and applied research. For example, the Center's active clinical research and experimental therapeutics program runs clinical trials that range from evaluating novel delivery systems for levodopa and testing adjunct medications for motor complications to assessing new systems for deep brain stimulation therapy and gauging the impact of nutritional support for PD patients.

On the applied end of the research spectrum, Jefferson design students work with **Tsao-Wei Liang, MD**, associate professor of neurology, to develop novel and practical devices to help patients. The students observe and learn about the daily struggles of patients in the Center's Movement Disorders clinic; then they return to the design studio to conceive and develop prototypes of products with real potential to improve quality of life of those patients.