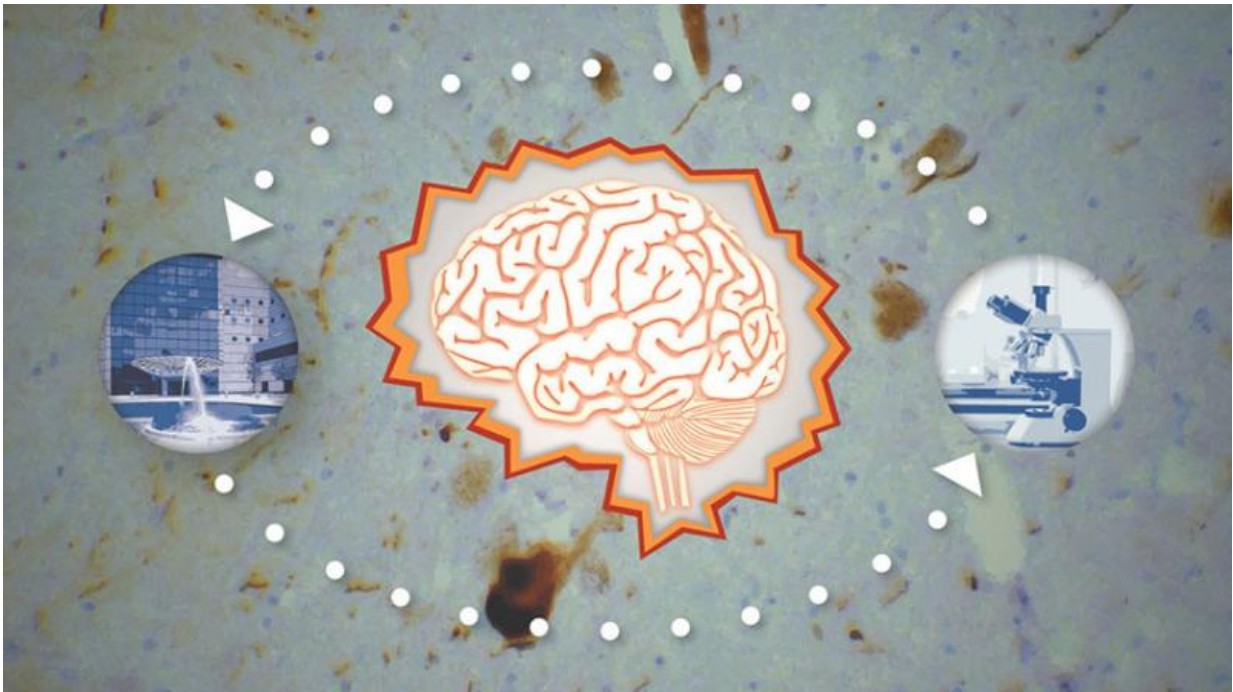


Pursuing links between inflammation and Parkinson's, in lab and clinic

October 16 2015, by Jeff Hansen



A group of UAB researchers have set themselves a two-year target—put an interdisciplinary team in place and have the necessary results in hand that will support the development of a Parkinson's Disease Research Center of Excellence at UAB. Only nine such NIH-supported centers—also known as Morris K. Udall Centers—exist today, none in the Deep South.

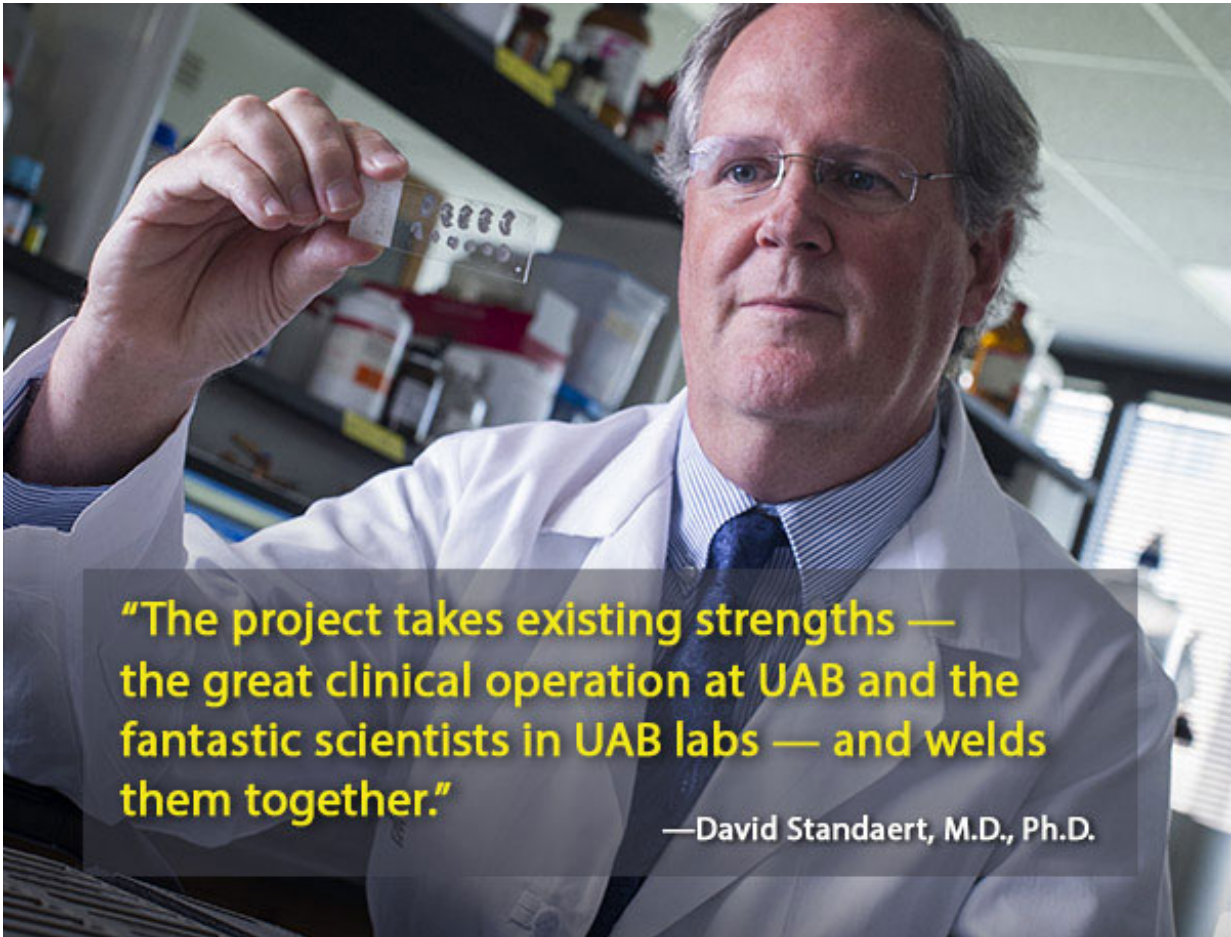
UAB will focus on neuroinflammatory mechanisms in Parkinson's disease, a gap in the research portfolio in the current centers. The team will probe how the body's immune system may contribute to the pathology seen in the brains of Parkinson's disease patients and to the development and progression of the disease.

Only recently have researchers begun to suspect an important role for inflammation in the disease, and that is still largely uncharted territory. Research in this area could lead to therapies that can slow the progression or stop the disease mechanisms of Parkinson's. This is a vital need since no such therapies exist.

The research requires a mix of specialized expertise from both neuroimmunology and neurodegenerative diseases. UAB scientists David Standaert, M.D., Ph.D., Etty "Tika" Benveniste, Ph.D., and Andrew West, Ph.D., are leading that team, bolstered by a two-year exploratory, P20 grant that NIH recently awarded to support preparation for a subsequent Udall P50 grant application.

Seeking synergy

"With centers, the NIH always looks for synergy," said Standaert, who is professor and chair of the UAB Department of Neurology and has deep knowledge of neurodegenerative disease medical care and research, particularly Parkinson's. "The hallmark of a center is the openness and willingness to work together. You have to be willing to share your ideas and frustrations, and share your opinions, in a back and forth manner. Everyone has to give up something, but they will find that the whole is greater than each part taken alone."



Standaert was previously director of the then-Massachusetts General Hospital/MIT Udall Center before coming to UAB. Benveniste, professor and chair of Cell, Developmental and Integrative Biology (CDIB) at UAB, investigates the connections between the immune system and the brain. West, associate professor of neurology at UAB and co-director of the UAB Center for Neurodegeneration and Experimental Therapeutics, focuses on research exploring genetic causes of Parkinson's disease, and he has previously trained at the Mayo Clinic Udall Center for Excellence, the then-UCLA Udall Center for

Excellence and the Johns Hopkins Udall Center for Excellence.

They are adding critical team members from outside the Parkinson's disease research field to the existing core of expertise in the neurology department. These include researchers Hongwei Qin, Ph.D., M.D., an associate professor in CDIB who has studied the immune response in neurological diseases like multiple sclerosis; Chander Raman, Ph.D., an immunologist who is a professor of medicine; and Stephanie Guthrie, CRNP, a nurse practitioner who will be vital in obtaining blood samples from Kirklin Clinic patients who are newly diagnosed with Parkinson's disease. Ashley Harms, Ph.D., an instructor in neurology who trained in neuroimmunology, will be the scientific coordinator for the P20 grant.

Immune residents, or infiltrators?

In addition to solidifying this core collaboration team, the researchers are testing key hypotheses in two pre-clinical model systems. Both of these systems have been engineered to have elevated levels of clumped α -synuclein in their brains to provoke innate immune responses. These model systems can differentiate between the activation of brain-resident immune cells and the infiltration of immune cells from outside the brain. This will lay the groundwork for targeting some of the control systems of these immune responses for therapeutic benefit in the mouse models.

Thirdly, the team will develop a pipeline to human subjects—so researchers can obtain blood from patients newly diagnosed with Parkinson's.

"We see about one to three patients a month with newly diagnosed Parkinson's disease at the Comprehensive Parkinson Disease and Movement Disorder Clinic, which has 11 physicians, four nurses, two nurse practitioners and about 6,000 patient visits a year," Standaert said. "We need to catch them in that window when they are just diagnosed,

before any treatment. This would be difficult to do at a smaller center, but we're big enough to do that."

Fresh blood is needed to isolate monocytes, which are innate [immune system](#) cells that reside outside of the brain. The monocytes will be purified the same day the blood is drawn and immediately tested to see if they have been activated for an immune response. "We get patient blood samples at the clinic, take them to the lab and study them that afternoon," Standaert said. "The number of places that can do that is pretty few."

Standaert has been building collaborations with Benveniste's group for several years, but the appearance of an NIH request for applications for the P20 grant a year ago jump-started a greater push. "That galvanized the effort to bring together a team to ask, what are the critical questions in the field, and how can we build a team to address these problems?"

"This collaboration is what UAB does well," Standaert said. "The project takes existing strengths—the great clinical operation at UAB and the fantastic scientists in UAB labs—and welds them together."

The title of the P20 grant is "Innate and Adaptive Immunity in Parkinson Disease."

The toll of Parkinson's

- As many as 1 million Americans have Parkinson's disease, a chronic and progressive movement disorder. This is more than multiple sclerosis, muscular dystrophy and Lou Gehrig's disease combined.
- About 60,000 new U.S. cases are diagnosed each year, but thousands of others go undetected.
- Worldwide, about 7 million to 10 million have Parkinson's

disease.

Source: Parkinson's Disease Foundation

Provided by University of Alabama at Birmingham

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