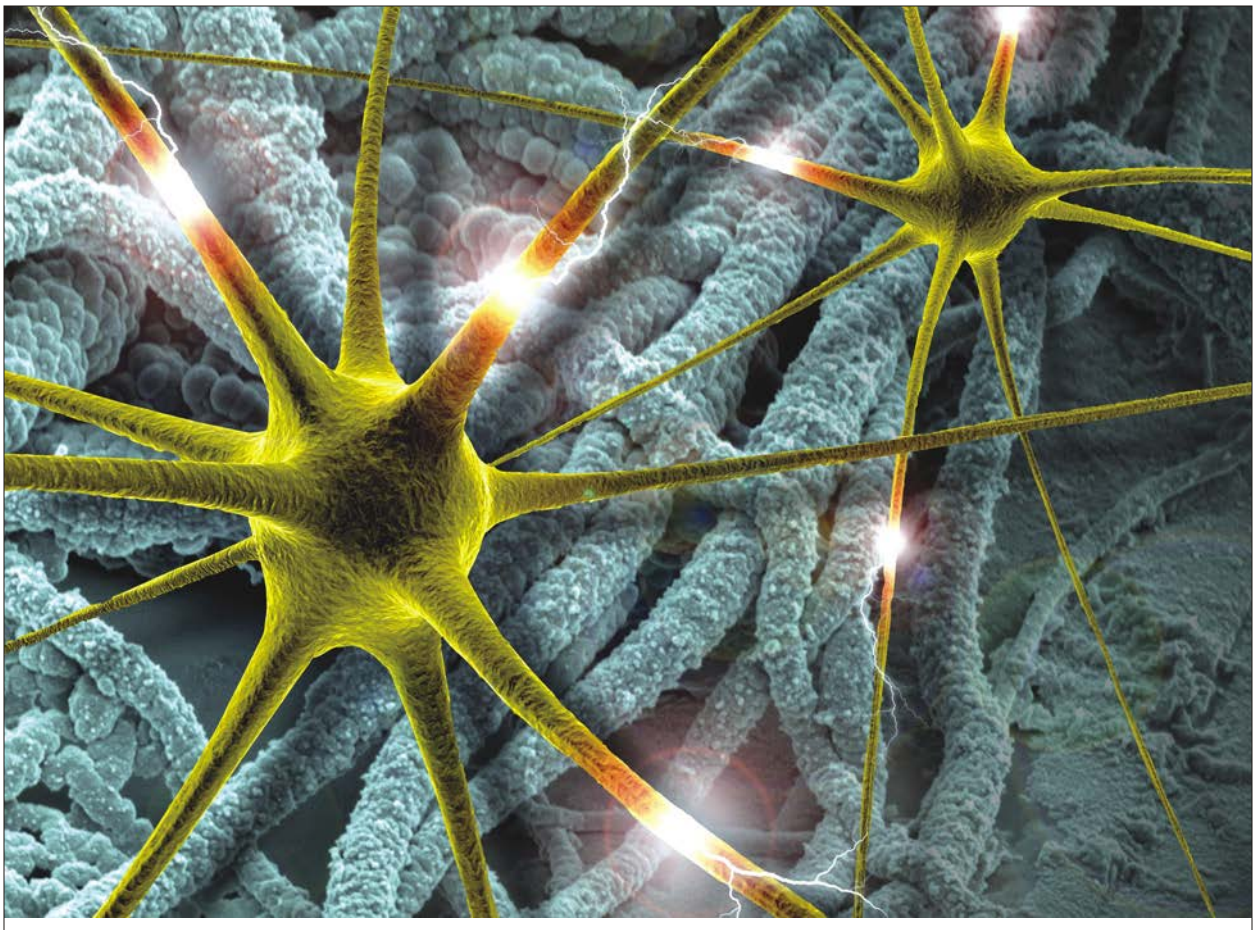

Current Research in **Neuroscience**

ISSN 1996-3408

Academic
Journals Inc.

www.academicjournals.com

What Causes Brain Cell Death in Parkinson's Patients?

Just 5 percent of Parkinson's disease cases can be explained by genetic mutation, while the rest have no known cause. But a new discovery by researchers at The University of Texas Health Science Center may begin to explain why the vast majority of Parkinson's patients develop the progressive neurodegenerative disease.

This week in The Journal of Neuroscience, the researchers demystified a process that leads to the death of brain cells -- or neurons -- in Parkinson's patients. When researchers blocked the process, the neurons survived.

The findings could lead to an effective treatment to slow the progression of Parkinson's disease, rather than simply address symptoms that include tremors, slowed movement, muscle stiffness and impaired balance. Further studies could lead to a diagnostic test that could screen for Parkinson's years before symptoms develop, said Syed Z. Imam, Ph.D., Adjunct Assistant Professor at the UT Health Science Center.

Parkinson's disease, which usually is not diagnosed until age 60 or later, affects an estimated half-million people in the United States.

Dr. Imam joined the U.S. Food and Drug Administration (FDA) after the research was conducted. Co-authors are from the Health Science Center's Barshop Institute for Longevity and Aging Studies; the South Texas Veterans Health Care System; and the Hertie Institute for Clinical Brain Research in Tübingen, Germany.

The mechanism

After analyzing cells and post-mortem brain tissue from animals and humans, researchers noted that oxidative stress -- a known culprit in neuron death -- activated a protein called tyrosine kinase c-Abl in the nigra-striatum area of the brain. Neurons in this part of the brain are particularly vulnerable to Parkinson's injury.

Activation of this protein led to changes in another protein called parkin, which is known to be mutated in hereditary Parkinson's. The altered parkin lacked the capacity to break down other proteins, leading to harmful clumps of unprocessed protein in the neuron. The scientists believe this accumulation leads to progressive neuron death, resulting in Parkinson's symptoms that worsen over time.

Implications

"When we blocked tyrosine kinase c-Abl activation, parkin function was preserved and neurons were spared," Dr. Imam said. "We believe these studies provide sound rationale for moving forward with a preclinical trial of tyrosine kinase c-Abl inhibitors, with the goal of developing a potent therapeutic drug for slowing the progression of Parkinson's."

If preclinical trials in animal models of Parkinson's disease yield positive results, the next step would be clinical trials in human patients, Dr. Imam said.

Tyrosine kinase c-Abl inhibitors are approved by the FDA for treating myeloid leukemia and gastrointestinal tumors. This could speed approval of the drug for Parkinson's and its translation from bench research to clinical practice.

"The race is on to understand the mechanism of the 95 percent of Parkinson's cases with no known cause, and our finding certainly is a building block," Dr. Imam said. "We have found a specific signaling mechanism that is only turned on by oxidative stress and is selective only to Parkinson's-affected neurons of the nigra-striatum, which is the area that sends signals for balance to the cerebellum."

Acknowledgements

Co-authors from the UT Health Science Center San Antonio are Senlin Li, M.D., senior author; Qing Zhou, Ph.D.; Anthony J. Valente, Ph.D.; Mona C. Bains, Ph.D.; Robert A. Clark, M.D.; and James L. Roberts, Ph.D., whose primary appointment is now at Trinity University in San Antonio. Co-authors represent the School of Medicine and the Graduate School of Biomedical Sciences as well as the Barshop Institute.

The National Institutes of Health, Michael J. Fox Foundation, American Parkinson's Disease Association, Parkinson's Disease Foundation, San Antonio Area Foundation and Health Science Center Presidential Research Enhancement Fund supported the research.

Source: The Journal of Neuroscience, January 5, 2011, 31(1) http://www.jneurosci.org/cgi/content/short/31/1/i.