NEWS RELEASE
UC San Diego
University Archives. RSS 6020

Mouse Model Confirms Mutated Protein's Role in Dementia

November 2, 2010

Scott LaFee

A team of scientists from Japan and the University of California, San Diego School of Medicine have created a new mouse model that confirms that mutations of a protein called beta-synuclein promote neurodegeneration. The discovery creates a potential new target for developing treatments of diseases like Parkinson's and Alzheimer's.

The work is published in today's issue of *Nature Communications*. Lead author is Makoto Hashimoto of the Division of Chemistry and Metabolism, Tokyo Metropolitan Institute for Neuroscience, with colleagues including Eliezer Masliah, MD, professor of neurosciences and pathology in the UC San Diego School of Medicine, Edward Rockenstein, a research associate in UCSD's Experimental Neuropath Laboratory and Albert R. La Spada, MD, PhD, professor of cellular and molecular medicine, chief of the Division of Genetics in the Department of Pediatrics and associate director of the Institute for Genomic Medicine at UC San Diego.

In 2004, La Spada discovered mutations in a family afflicted with a neurological disorder known as Dementia with Lewy Bodies. DLB is one of the most common types of progressive dementia, combining features of both Alzheimer's and Parkinson's diseases. Lewy bodies are abnormal aggregates of proteins. There are no known therapies to stop or slow the DLB's progression. There is no cure.

In the 2004 study, La Spada and colleagues found that mutations of the naturally occurring B-synuclein protein in DLB patients "were strong strongly suggestive of being pathogenic." That is, the mutated protein caused or was a cause of the disease. But the findings were not definitive.

The newly published research describes the creation of a transgenic mouse model that expresses the B-synuclein mutation. The mice suffer from neurodegenerative disease, validating La Spada's earlier work.

"Beta-synuclein is interesting because it is closely related to alpha-synuclein, a protein that can cause Parkinson's disease by being mutated or over-expressed," said La Spada. "A-synuclein is viewed as central to Parkinson's disease pathogenesis. The question has been: could B-synuclein also promote neurodegeneration because it's similar in its sequence and expression pattern to A-synuclein? This study shows that the answer is yes."

These findings, said La Spada, establish B-synuclein's links to Parkinson's disease and related disorders, making it a new and, now, proven target for potential therapies.

Co-authors of the study are Masaya Fujita, Shuei Sugama, Kazunari Sekiyama, Akio Sekigawa, Masaaki Nakai, Masaaki Waragai, Yoshiki Takamatsu and Jianshe Wei of the Division of Chemistry and Metabolism, Tokyo Metropolitan Institute for Neuroscience; Tohru Tsukui of the Division of Gene Regulation and Signal Transduction, Research Center for Genomic Medicine, Saitama Medical University; Takato Takenouchi of the Division of Chemistry and Metabolism, Tokyo Metropolitan Institute for Neuroscience and the Transgenic Animal Research Center, National Institute of Agrobiological Sciences in Japan; and Satoshi Inoue of Division of Gene Regulation and Signal Transduction, Research Center for Genomic Medicine, Saitama Medical University and Department of Anti-Aging, Graduate School of Medicine, University of Tokyo.

Funding for this study came in part from grants by Science Research, the Cell Innovation Project; Challenging Exploratory Research, the National Institute of Biomedical Innovation, the Takeda Foundation, the Novartis Foundation for Gerontological Research and the National Institutes of Health.

Media contact: Scott LaFee, 619-543-6163, slafee@ucsd.edu