Mouse Models Developed by UCSD Researchers Provide Insights into Multiple System Atrophy

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Researchers at the University of California, San Diego (UCSD) School of Medicine have developed a series of transgenic mouse models of multiple system atrophy, a progressive, fatal neurological disorder. The work is reported in the November 16 issue of the Journal of Neuroscience by Eliezer Masliah, M.D., Professor of Neuroscience and Pathology at UCSD and Cliff Shults, M.D. Professor of Neuroscience at UCSD and Neurologist at the VA San Diego Healthcare System.

The mouse models are important, not only in providing new insights into the processes that cause degeneration of the nervous system in patients with multiple system atrophy, but also as models in which to study treatments for the disease.

"The models will help researchers develop therapies for this degenerative disease by enabling us to study potential treatments that might interfere with the aggregation of alpha-synuclein and slow the progression of multiple system atrophy," said Shults.

Masliah added, "Development of these models may also prove relevant to our understanding other neurological disorders, enabling us to test new drugs for Parkinson's and other diseases."

UCSD School of Medicine is one of the world's leading centers for research in alpha-synuclein, the major component of inclusions or clusters found in the brains of patients with multiple system atrophy, Parkinson's disease and other neurological disorders. Patients with multiple system atrophy suffer from progressive, worsening symptoms of Parkinson's disease, impaired coordination, and dysfunction in control of blood pressure and bladder function. The disease is characterized by aggregates of alpha-synuclein in oligodendrocytes, a type of cell in the brain that provides insulation for the nerve processes in the brain. The presence of alpha-synuclein was first identified in the human brain by researchers at UCSD.

Mice were genetically engineered in Masliah's laboratory to express high amounts of alpha-synuclein in oligodendrocytes. The mice exhibited symptoms, including problems with movement and injury to nerve cells, found in patients with multiple system atrophy. The models' brains

demonstrated abnormal clusters of alpha-synuclein, similar to those seen in the brains of patients with the disease.

The work was carried out as part of a multi-institutional effort at 12 of the leading centers in research in neurological disorders in the United States, coordinated from UCSD, to understand the causes of multiple system atrophy and to eventually develop treatments to slow the progression of the disease. Masliah and Shults have already begun to use the mice models to screen drugs that might benefit patients with multiple system atrophy, another example of leading translational research being conducted at UCSD.

Shults led the work at UCSD, which was funded by the National Institutes of Health, the Michael J. Fox Foundation, and the William M. Spencer Jr. Research Fund.

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