RESEARCH FUNDING OPPORTUNITY

Evaluation of STX6 silencing on the novel AAV-based PSP mouse model

Using recombinant virus-mediated gene transfer technology, Professor Ikezu and his team will undertake the first study using the syntaxin-6 gene, newly associated with PSP, to develop a new PSP mouse model for further testing.

Budget: $112,000 for 2 years

Professor Tsuneya Ikezu
Boston University School of Medicine

Budget:

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404 5th Avenue
3rd Floor
New York, NY 10018
347-294-2873 (CURE)
Canada: 844-287-3777
www.curepsp.org
Facebook.com/curepsp.foundation

For further information, please contact:
David Kemp
President
kemp@curepsp.org
802-734-1185

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PRINCIPAL INVESTIGATOR

Tsuneya Ikezu, MD, PhD

Dr. Ikezu is a professor in the Departments of Pharmacology and Experimental Therapeutics and Neurology and a member of Alzheimer’s Disease Center at Boston University School of Medicine. Dr. Ikezu has extensive expertise in on Alzheimer’s disease and frontotemporal dementia with over 68 first-rated peer-reviewed publications, including Nat Neurosci, Nat Commun, J Neurosci, Ann Neurol, Brain, Sci Transl Med, Brain, PNAS, and EMBOJ.

He has developed a systematic approach to characterize disease mouse models using virus-mediated gene transfer systems, including animal behavior, neuropathology and electrophysiology. He will be directly involved in the planning and implementation of the experiments cited in the application, coordinate collaborators and necessary reagents and supervise a postdoctoral fellow.

RECOGNITION OPPORTUNITIES

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PROGRESSIVE SUPRANUCLEAR PALSY (PSP) is a fatal neurodegenerative disorder that affects approximately 20,000 people in the U.S., though it is likely underdiagnosed because of lack of experience with the disease by many physicians. Therefore, it is extremely important to find the pathophysiological basis and a treatment of this devastating disease. Although we have gained significant knowledge in pathology and human genetics of PSP in the last several years, the progress of understanding the disease mechanism is significantly hampered by the lack of testable animal models of PSP.

Professor Ikezu's laboratory has been successfully developing animal models of neurodegenerative disorders using recombinant virus-mediated gene transfer technology. In this study, he proposes to express a frontotemporal dementia (FTD)-associated point mutation of tau protein (proline 301 to leucine), which forms tau protein aggregation as seen in PSP brains, in the specific brain region commonly affected in PSP.

Professor Ikezu and his team will perform histological and behavioral examination to assess if this approach develops an animal model consistent with PSP. They will also target a gene called syntaxin-6, which has been newly associated with PSP. Syntaxin-6 regulates protein transport in the cells, and its dysfunction may be toxic to neurons. Professor Ikezu's lab will examine if suppression of syntaxin-6 expression accelerates aggregation of tau protein or degeneration of neurons in the virus-mediated gene transfer to PSP mouse model. These molecules have never been tested to develop a PSP animal model.

If the study is successful, it will be highly significant because a new PSP mouse model will be available for testing, and it will serve as the first study to assess the effect of syntaxin-6 gene reduction in the progression of PSP-like pathology development in the mouse brain, potentially leading to new gene targets, drugs and therapies.

### PROJECT BUDGET

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<tr>
<th>Category</th>
<th>Expense Year 1</th>
<th>Expense Year 2</th>
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<td>Immunohistochemical/biological reagents</td>
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<td>Publication cost</td>
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<td>Grant administration @12% (CurePSP)</td>
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**Total budget per year**

$56,000          $56,000