

Degenerating Neurons Respond to Gene Therapy Treatment for Alzheimer's Disease

Postmortem brain studies suggest nerve growth factor safely triggered functional cell growth

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Degenerating neurons in patients with Alzheimer's disease (AD) measurably responded to an experimental gene therapy in which nerve growth factor (NGF) was injected into their brains, report researchers at University of California, San Diego School of Medicine in the current issue of *JAMA Neurology*.

The affected neurons displayed heightened growth, axonal sprouting and activation of functional markers, said lead author Mark H. Tuszynski, MD, PhD, professor in the Department of Neurosciences, director of the UC San Diego Translational Neuroscience Institute and a neurologist at VA Medical Center, San Diego.

The findings are derived from postmortem analyses of 10 patients who participated in phase I clinical trials launched in 2001 to assess whether injected NGF – a protein essential to cellular growth, maintenance and survival – might safely slow or prevent neuronal degeneration in patients with AD.

Administering NGF directly into the brain – a first for treating of an adult neurodegenerative disorder – was done for two reasons. The NGF protein is too large pass through the blood-brain barrier, making it impossible to inject elsewhere. And freely circulating NGF causes adverse effects, such as pain and weight loss. By precisely injecting NGF into targeted regions of the brain, researchers could introduce the protein only to surrounding degenerating neurons.

The gene therapy approach has since progressed to phase II trials at multiple test sites. Results have not yet been released. The published findings come from AD patients who participated in safety trials from March 2001 to October 2012 at UC San Diego Medical Center. The participants lived one to 10 years after treatment.

"All of the Alzheimer's disease brains showed anatomical evidence of a growth response to the growth factor," said Tuszynski, who has been principal investigator for the trials from the

beginning. "This means that growth factors as a class consistently result in activation of dying cells in human neurodegenerative disorders."

Tuszynski said the findings indicate NGF is safe over extended periods and that it merits continued testing as a potential AD treatment. Currently, there is no effective treatment or cure for AD.

Co-authors include Jennifer H. Yang, Mary M. Pay, Eliezer Masliah, David Barba, Hoi-Sang U, James M. Conner, Peter Kobalka, Subhojit Roy, and Alan H. Nagahara, all at UC San Diego; and Roy A. E. Bakay, Rush University Medical Center.

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Disclosure: Mark Tuszynski is scientific founder of Ceregene, Inc., but has no present financial interest in the company.

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