UC San Diego Health

A Vaccine Approach to Treating Parkinson's Disease

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San Diego, Calif. – Researchers at the University of California, San Diego (UCSD) School of Medicine working with scientists at Elan Pharmaceuticals, have reported promising results in mice of a vaccine approach to treating Parkinson's and similar diseases. These results appear in the June edition of the journal *Neuron.*

Eliezer Masliah, M.D., Professor of Neurosciences and Pathology at UCSD, and colleagues at UCSD and Elan Pharmaceuticals in San Francisco, vaccinated mice using a a combination of the protein that abnormally accumulates in the brains of Parkinson's (called human alpha-synuclein) and an adjuvant. This approach resulted in the generation of anti-alpha synuclein antibodies in mice that are specially bred by Masliah's team to simulate Parkinson's disease, resulting in reduced build-up of abnormal alpha-synuclein. The accumulation of abnormal alpha-synuclein is associated with degeneration of nerve cells and interference with normal inter-cellular communication, leading to Parkinson's disease and dementia.

The work marks the first time a vaccine for this family of diseases has been found effective in animal studies. Scientists at Elan Pharmaceuticals have been working for the past few years in a vaccine for Alzheimer's Disease.

The researchers focused on a spectrum of neurological disorders called Lewy body disease, which include Parkinson's and Alzheimer's. These disorders are marked by the presence of Lewy bodies -- abnormal clumps of alpha-synuclein – in the brain. Normally, alpha-synuclein proteins support communications between brain cells, or neurons. However, when abnormal proteins clump together in the neurons, a build-up of synuclein can cut off neuron activity, blocking normal signaling between brain cells and ultimately choking the cells to death.

"We found that the antibodies produced by the vaccinated mice recognized and reduced only the abnormal form of alpha-synuclein, since the protein's normal form is in a cellular compartment where antibodies can't reach it," said Masliah. "Abnormal alpha-synuclein finds its way to the cell membrane, where antibodies can recognize it."

Masliah stressed that the team's experimental active immunization, while effective in mice, may not be as useful in humans. "We would not want to actively immunize humans in this way by

triggering antibody development, because one could create harmful inflammation," he cautioned. "However, it might be feasible to inject antibodies directly, as if the patient were creating his or her own."

The team, the first to identify the presence of these proteins in the human brain, originally thought the protein played an important role in the development of Alzheimer's disease. Then, an explosion of research linked Lewy bodies and their constituent proteins to both Alzheimer's and Parkinson's. The team spent four years clarifying alpha-synuclein's role in Parkinson's, developing a mouse model that contained the faulty and normal genes for alpha-synuclein, and conducting the experiments that led to their current findings.

With evidence that this approach could be effective in treating Lewy Body disease, the UCSD researchers are now working with Elan Pharmaceuticals to develop alternative ways to produce alpha-synuclein antibodies, with the goal of making a vaccine that is safe and effective in humans. While this research could take many years and holds no promise of prevention or cure, the researchers are hopeful that the mouse studies are a step in the right direction.

"This shows the first demonstration of a vaccine for this family of disease," Masliah said.

Co-authors of the paper are Edward Rockenstein, B.S., Anthony Adame, B.S. , Michael Alford, B.A., Leslie Crews B.S. and Makoto Hashimoto, Ph.D. at UCSD, and Peter Seubert, Ph.D., Michael Lee, Ph.D., Jason Goldstein, Ph.D., Tamie Chilcote, Ph.D., Dora Games, Ph.D. and Dale Schenk, Ph.D. at Elan.

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