SOUTHWESTERN NEWS

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Gene vaccine for Alzheimer's disease shows promising results

DALLAS – Dec. 13, 2004 – UT Southwestern Medical Center at Dallas researchers have found a way of stimulating the immune systems of mice to fight against amyloid proteins that cause the devastating plaques that are characteristic of Alzheimer's disease.

For years scientists have examined the possibility of using a protein-based vaccine to slow the progression of the disease in its early stages. UT Southwestern researchers have created a gene-based vaccine aimed at stimulating the immune systems of mice to potentially fight off plaque-causing amyloid protein in the brain.

Their findings appear in today's issue of the *Archives of Neurology.*

"Previous Alzheimer's vaccines were protein-based," said Dr. Baoxi Qu, the study's lead author and assistant professor in the Center for Biomedical Inventions and internal medicine. "We wanted to try a DNA-based genetic vaccine instead to see if we could enhance the immune response."

Although prior studies of amyloid protein vaccination had shown some slowing in the plaque buildup, negative side effects also occurred in a handful of patients. Some had autoimmune responses that caused encephalitis.

The key in the UT Southwestern study was finding another way to vaccinate patients without stimulating the body's own immune cytotoxic T cells, said Dr. Roger Rosenberg, a study author and director of the Alzheimer's Disease Center.

"This dilemma was discussed with my colleagues, and we decided to try vaccination with an amyloid gene, rather than the amyloid protein vaccine," said Dr. Rosenberg.

The UT Southwestern researchers vaccinated mice with a "gene gun." The gene gun and gene-vaccination technologies were invented by Dr. Stephen Albert Johnston, director of the Center for Biomedical Inventions and senior author of the latest study.

"We have been developing ways to use gene-immunization to manipulate the immune response," Dr. Johnston said. "This study was the first step to see if we can apply these techniques to create a safe and effective Alzheimer's vaccine."

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Said Dr. Rosenberg: "When we vaccinated the mice with the mouse form of the amyloid gene, they made lots of antibodies without stimulating cytotoxic T cells. When we get to human studies, we hope to show that humans can make human antibodies against the amyloid as well."

Current treatments for Alzheimer's disease focus on the symptoms since no therapies have been clinically proven to slow or prevent progression of the disease. Amyloid protein deposits are present in the early phase of the disease – a fact that suggests a gene vaccination would be a step forward in slowing the progression of dementia.

From the mouse studies and in previous clinical trials of patients with Alzheimer's disease, immunization with amyloids slowed the buildup of plaque on the brain and appeared to slow cognitive loss.

"Although human clinical trials are still at least two years out, theoretically, we are on the right track," he said.

Other UT Southwestern authors involved in the study were Dr. Liping Li, a research fellow in the Center for Biomedical Inventions; and Dr. Philip Boyer, assistant professor of pathology.

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