Fighting Alzheimer's on LI

Clinical trials based on findings of Manhasset lab

BY DELTHIA RICKS
delthia.ricks@newsday.com

MICHAEL OWENS

Alzheimer's researcher Peter Davies at the Feinstein Institute for Medical Research in Manhasset.

Despite billions of dollars and decades spent on Alzheimer's research, medical scientists still haven't found a cure, but a designer molecule developed on Long Island may pave the way to a new form of treatment.

Medical scientists at the Feinstein Institute for Medical Research in Manhasset have developed a protein antibody that is the basis of an experimental medication now under study.

The drug developed from it is so new, said renowned Alzheimer's researcher Dr. Peter Davies, it's known only by letters and numbers: LY3303560. It is being tested in a clinical trial sponsored by pharmaceutical giant Eli Lilly, which is producing it.

"I am very excited. This is one of the monoclonal antibodies made in my lab," said Davies, who has researched Alzheimer's for decades with the hope of discovering how the disease unravels the mind.

A monoclonal antibody is a protein designed in the laboratory to perform a specific task. The one Davies and his colleagues developed zeroes in on a protein called tau, which insidiously damages brain cells from the inside out.

Imagine a healthy brain cell as a tree abundant with branches and leaves. Then picture a brain cell damaged by tau — a dead, withered tree with broken and missing limbs.

"It's possible that if you can block tau with an antibody you might block progression of the disease," Davies said. "We're at a very interesting time for Alzheimer's right now. There are other new clinical trials getting underway as we speak."

Davies is a global expert on the protein tau, which has long been considered a key suspect in the theft of human minds by Alzheimer's disease. Tau also plays a role in other forms of dementia, such as the rare Alzheimer's-like disorder called Pick's disease, Davies said.

The hope, he added, is that the experimental medication will help stop tau's progression and preserve brain cells. LY3303560 is administered by infusion. No results have yet been reported from the clinical trial, he said.

Other researchers are also investigating tau.

In July, Dr. Marc Diamond and colleagues at the O'Donnell Brain Institute, a division of the University of Texas Southwestern Medical Center, described tau as a shape-shifting molecule that underlies the Big Bang of Alzheimer's disease.

Diamond and his team said they discovered how the protein goes rogue and becomes toxic to brain cells. That knowledge alone, they said, can help point the way toward a cure.

But Dr. Allison B. Reiss, an Alzheimer's researcher at NYU Winthrop Hospital in Mineola, said the disease is one of the biggest conundrums in medicine.

Even after spending billions and holding hundreds of clinical trials, no one has closed in on the key question: What sets off the series of biological events that cause Alzheimer's in the first place? No one can explain why brain cells die, she said.

"I think that tau is emerging now as a more prominent area of research because of so many other failures," Reiss said. "What we really need to do now is get to the nitty-gritty of Alzheimer's disease."

In the past several years, all Alzheimer's medications in clinical trials have failed, a pattern that has occurred throughout much of the 21st century.

Between 2002 and 2012, more than 400 trials were initiated for Alzheimer's medications, but only one — a drug called Namenda — was approved.

Over the past 22 years, there have been only five drugs, including Namenda, that have been approved for a disease that affects 5.7 million people in the United States alone.

Reiss described Alzheimer's as a relentless neurodegenerative disorder for which there is no cure. The condition is the sixth leading cause of death in the United States, and the only one in the top 10 without a cure or reversible treatment.

More than 400,000 people in New York, including 50,000 on Long Island, are living with the disorder, according to the Alzheimer's Foundation of America.

Reiss said she's worried because some of the drug failures involved monoclonal antibodies that were aimed not at tau, but another Alzheimer's molecule called beta amyloid protein, sometimes referred to as BAP.

Autopsy results of people with Alzheimer's show that their brain tissue is riddled with "plaques and tangles." Gummy plaques form between brain cells are made up of BAP. Tangles, also called neurofibrillary tangles, are mostly composed of tau.

Davies argued that some Alzheimer's researchers had been so swayed by one protein or the other as Alzheimer's cause that he refers to them as BAPtists and TAUists.

"I have spent 25 years, much of my life working on tau and being a big critic of the amyloid hypothesis. I am a vigorous anti-BAPtist. But I am not strictly a TAUist. I am agnostic," he said.

Reiss declared that it is time to get beyond BAP and tau. "These are the two biggest proteins in Alzheimer's and the balance seems to get tipped one way or the other.

"For a while it was tipped in a way that beta amyloid was the cause. Now, the scale is tipping toward tau," she said. "If you're going to fix Alzheimer's, you have to stop neurons [brain cells] from dying."