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New Theory of Cell Death Proposed in UCSB Alzheimer's Research

Alzheimer's disease, the most common form of dementia, currently affects four million Americans -- a number expected to increase to 14 million by the year 2050. Not surprisingly, researchers are racing to understand the disease so that effective therapies can be developed.

To develop a drug that could arrest or prevent Alzheimer's disease, scientists must first understand what is causing the death of brain cells known as neurons. Brain tissue samples of Alzheimer's victims reveal extensive neuronal cell death, as well as two abnormal pathological structures known as "neurofibrillary tangles" and "amyloid plaques."

A new way of looking at the disease is described by University of California, Santa Barbara scientists and reported in the July 28 online issue of the Proceedings of the National Academy of Sciences. The work is a collaboration between the labs of Professors Leslie Wilson, director of the UCSB Alzheimer's Disease Research Center, and Stuart Feinstein, director of the UCSB Neuroscience Research Institute. Both are also faculty members of the Department of Molecular, Cellular and Developmental Biology.

Wilson has done extensive work on understanding microtubules, long thin filaments that serve as a "cyto-skeleton" in all cells, similar in many ways to our own bones. However, unlike our bones, microtubules are dynamic structures, constantly growing

and shortening. Proper control of the growing and shortening dynamics of microtubules is essential for cells to perform their many tasks and remain alive. In neuronal cells, a protein known as tau is a major regulator of microtubule dynamics. This protein, extensively studied in Feinstein's lab, is also the major component of the neurofibrillary tangles of Alzheimer's disease.

The new model proposes that loss of normal tau function leads to abnormal microtubule dynamics, resulting in cell death. This is in contrast to a widely held model in which the neurofibrillary tangles themselves cause cell death. "The neurofibrillary tangles may not be involved in causing cell death in any way," said Feinstein. "They may simply be a downstream consequence of tau dysfunction." The exact mechanism of neuronal cell death "is enormously important because to develop effective drugs, we need to know precisely what molecular steps need to be affected."

Although progressive mental deterioration has been recognized and described throughout history, Alzheimers disease was first described by Dr. Alois Alzheimer in 1906 -- following his work with his patient "August D." and a subsequent autopsy that revealed the now familiar neuritic plaque and neurofibrillary tangles that mark the disease.

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