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Therapeutic Protection Against Synapse-Targeting Abeta Oligomers

Candidate for 2009 Zenith Fellows Award

The protein fragment beta-amyloid is suspected of causing brain damage in Alzheimer's disease. Beta-amyloid tends to accumulate into clumps within the Alzheimer brain, and many scientists believe the most toxic forms of beta-amyloid are clumps that occur early in the accumulation process. These clumps, called oligomers, consist of only a few beta-amyloid molecules.

William L. Klein, Ph.D., and colleagues were among the first researchers to recognize the role of beta-amyloid oligomers in the Alzheimer brain. They discovered that oligomers kill particular types of brain cells and inhibit long-term potentiation (LTP). LTP is a kind of "increased sensitivity" that develops when brain cells repeatedly send and receive messages across tiny channels called synapses. Oligomer-related damage to LTP inhibits a person's long-term memory. Recently, Dr. Klein's team has identified areas of certain synapses to which oligomers bind and begin to damage brain function.

For this grant, the researchers will test the ability of several compounds to block the attachment of oligomers to these synaptic binding sites. They will also test whether such compounds produce harmful side effects, including the disruption of important synaptic activity. The team's efforts could suggest novel ways for preventing oligomer-related damage in the earliest stages of Alzheimer's.