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# Alzheimer's memory problems originate with protein clumps floating in the brain, not amyloid plaques

April 27 2010

Using a new mouse model of Alzheimer's disease, researchers at Mount Sinai School of Medicine have found that Alzheimer's pathology originates in Amyloid-Beta (Abeta) oligomers in the brain, rather than the amyloid plaques previously thought by many researchers to cause the disease.

The study, which was supported by the "Oligomer Research Consortium" of the Cure Alzheimer Fund and a MERIT Award from the Veterans Administration, appears in the journal *Annals of Neurology*.

"The buildup of amyloid plaques was described over 100 years ago and has received the bulk of the attention in Alzheimer's pathology," said lead author Sam Gandy, MD, PhD, Professor of Neurology and Psychiatry, and Associate Director of the Alzheimer's Disease Research Center, Mount Sinai School of Medicine. "But there has been a longstanding debate over whether plaques are toxic, protective, or inert."

Several research groups had previously proposed that rather than plaques, floating clumps of amyloid (called oligomers) are the key components that impede brain cell function in Alzheimer's patients. To study this, the Mount Sinai team developed a mouse that forms only these oligomers, and never any plaques, throughout their lives.

The researchers found that the mice that never develop plaques were just

as impaired by the disease as mice with both plaques and oligomers. Moreover, when a gene that converted oligomers into plaques was added to the mice, the mice were no more impaired than they had been before.

"These findings may enable the development of neuroimaging agents and drugs that visualize or detoxify oligomers," said Dr. Gandy. "New neuroimaging agents that could monitor changes in Abeta oligomer presence would be a major advance. Innovative neuroimaging agents that will allow visualization of brain oligomer accumulation, in tandem with careful clinical observations, could lead to breakthroughs in managing, slowing, stopping or even preventing Alzheimer's.

"This is especially important in light of research reported in March showing that 70 weeks of infusion of the Abeta immunotherapeutic Bapineuzumab® cleared away 25 percent of the Abeta plaque, yet no clinical benefit was evident."

Provided by The Mount Sinai Hospital