

Research identifies new therapeutic target for Alzheimer's disease

November 1 2012

Research led by Chu Chen, PhD, Associate Professor of Neuroscience at LSU Health Sciences Center New Orleans, has identified an enzyme called Monoacylglycerol lipase (MAGL) as a new therapeutic target to treat or prevent Alzheimer's disease. The study was published online November 1, 2012 in the Online Now section of the journal *Cell Reports*.

The research team found that inactivation of MAGL, best known for its role in degrading a cannabinoid produced in the brain, reduced the production and accumulation of beta [amyloid plaques](#), a pathological hallmark of Alzheimer's disease. Inhibition of this enzyme also decreased neuroinflammation and neurodegeneration, and improved plasticity of the brain, learning and memory.

"Our results suggest that MAGL contributes to the cause and development of Alzheimer's disease and that blocking MAGL represents a promising [therapeutic target](#)," notes Dr. Chu Chen, who is also a member of the Department of Otolaryngology at LSU Health Sciences Center New Orleans.

The researchers blocked MAGL with a highly selective and potent inhibitor in mice using different dosing regimens and found that inactivation of MAGL for eight weeks was sufficient to decrease production and deposition of beta amyloid plaques and the function of a gene involved in making beta amyloid toxic to [brain cells](#). They also measured indicators of neuroinflammation and neurodegeneration and found them suppressed when MAGL was inhibited. The team discovered

that not only did the integrity of the structure and function of synapses associated with cognition remain intact in treated mice, but MAGL inactivation appeared to promote spatial [learning and memory](#), measured with behavioral testing.

Alzheimer's disease is a [neurodegenerative disorder](#) characterized by accumulation and deposition of amyloid plaques and neurofibrillary tangles, neuroinflammation, synaptic dysfunction, [progressive deterioration](#) of cognitive function and [loss of memory](#) in association with widespread nerve cell death. The most common cause of dementia among older people, more than 5.4 million people in the United States and 36 million people worldwide suffer with Alzheimer's disease in its various stages. Unfortunately, the few drugs that are currently approved by the Food and Drug Administration have demonstrated only modest effects in modifying the clinical symptoms for relatively short periods, and none has shown a clear effect on disease progression or prevention.

"There is a great public health need to discover new therapies to prevent and treat this devastating disorder," Dr. Chen concludes. The research was supported by grants from the National Institutes of Health. In addition to scientists from LSU Health Sciences Center New Orleans, the research team also included investigators from the Massachusetts Institute of Technology.

Provided by Louisiana State University

Citation: Research identifies new therapeutic target for Alzheimer's disease (2012, November 1) retrieved 19 April 2024 from

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