Phosphodiesterase Inhibitors for the Treatment of Alzheimer's Disease

Technology #2439

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Preventing the Decline of Cognitive Function in Alzheimer’s Patients Alzheimer’s disease, as the leading cause of dementia, represents a significant health burden. Post-mortem diagnosis of Alzheimer’s patients has established amyloid beta (A-beta) as playing a significant role in disease progression. A-beta is a small protein fragment that accumulates in plaques in the brain. A-beta is created through enzymatic processing by secretase. The decline in cognitive function in patients with Alzheimer’s is a result of inflammation and damage to neuronal function. Ideal strategies for treatment of Alzheimer’s could prevent disruption of synaptic dysfunction and memory loss by reducing A-beta and increasing neuronal survival.

Compounds Capable of Inhibiting PDE5 Activity This invention is a class of compounds capable of inhibiting the activity of phosphodiesterase type 5 (PDE5) for the treatment of Alzheimer’s. PDEs are a large family of proteins that catalyze the hydrolysis of 3',5'-cyclic nucleotides to monophosphates. Cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate are both key messengers that regulate a wide variety of biological processes. PDE 5 inhibitors specifically prevent the degradation of cGMP by PDE5. In a mouse model for Alzheimer’s, APP/PS1, the PDE5 inhibitor sildenafil has been shown to modulate secretase activity and reduce levels of A-beta. In addition, sildenafil was shown to improve cognitive function in mice as measured by tests of spatial memory, contextual fear conditioning, long-term potentiation, and others. This invention also includes computational and structural information for finding and screening for PDE5 inhibitors.

Applications:
• Treatment of Alzheimer’s disease
• Treatment of dementia

Advantages:
• Existing PDE5 inhibiting compounds are currently used as drugs against erectile dysfunction and pulmonary hypertension
• Compounds have been shown to cross the blood brain barrier
• PDE5 has been shown in mice to reduce Ab and improve cognitive function


Licensing Status: Available for Licensing and Sponsored Research Support

Publications: Daniela Puzzo, Salvatore Sapienza, Ottavio Arancio, and Agostino Palmeri. Role of phosphodiesterase 5 in synaptic plasticity and memory. 
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