



Cornell University
**Center for Technology Enterprise
and Commercialization**

395 Pine Tree Road, Suite 310
Ithaca, New York 14850
p. 607-254-4698
f. 607-254-5454
www.cctec.cornell.edu

Technology Brief
Inhibition of A β Production: Alzheimer's Disease Therapeutics
D-3799

INVENTION SUMMARY: Currently, there are no disease-modifying drugs available to treat Alzheimer's disease. This invention introduces a novel approach to discover and develop new treatments for Alzheimer's disease.

Aggregation of amyloid beta peptide (A β) in the brain is associated with Alzheimer's disease. Unlike other treatments such as inhibitors of A β aggregation and intravenous immunoglobulin to eliminate misfolded proteins, this invention offers a method to decrease the production of A β by controlling the conformation of amyloid precursor protein (APP). The novel pathway can be used to screen for biological molecules that may prevent the production of A β . The invention also offers small molecules that are designed to inhibit APP processing.

POTENTIAL COMMERCIAL APPLICATIONS:

- Alzheimer's disease therapeutics.

ADVANTAGES:

This invention provides a new pathway to target the treatment of Alzheimer's disease. This method, together with other approaches if necessary, may result in disease-modifying drugs.

TECHNICAL MERITS:

- A β are derived from amyloid precursor protein (APP). The phosphorylated Ser/Thr-Pro motifs in APP can exist in either *cis* or *trans* conformations. Pin1 is an isomerase that binds this site when it is phosphorylated and catalyzes their conversion.
- Isomerization inhibits amyloidogenic APP processing that leads to A β production. Pin1 overexpression reduces A β production and knockout mutations of Pin1 increase A β production.
- Pin1 is found with APP at the plasma membrane and in clathrin-coated vesicles close to the plasma membrane. Unlike amyloidogenic processing, which occurs in endosomes, non-amyloidogenic processing of APP occurs at the plasma membrane.
- Under proper conditions, a compound that mimics the pSer/Thr-Pro motif in APP will potentially inhibit amyloidogenic APP processing and A β production.

INVENTORS: Linda Kay Nicholson <<http://www.mbg.cornell.edu/cals/mbg/faculty-staff/faculty/nicholson.cfm>>, Kun Ping Lu, Lucia Pastorino, Xiao Zhen Zhou, Soumya De

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PATENT STATUS: U.S. Patent Application Serial Number 11/623,672

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For more information, CONTACT:

Alice Li, Ph.D.

Technology Commercialization and Liaison Officer

Phone: (607) 254-4487; Email: XL11@cornell.edu