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New therapy for Alzheimer's disease

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Researchers have discovered a molecular mechanism underlying a key regulatory step in the build up of plaques characteristic of Alzheimer's disease. The work published online in Cell Research demonstrates, how the processing of a precursor protein to amyloid-beta by two enzymes is mediated in a mouse model. This could lead to improved therapeutic strategies for Alzheimer's with fewer side effects than existing treatments.

Alzheimer's disease, the most common neurodegenerative disorder in the world, affects more than 20 million people. It causes progressive memory loss and cognitive dysfunction, and is a major cause of dementia. Current treatment options are limited and only manage the symptoms. A disease-modifying therapy that is able to prevent and reverse the disease is not currently available. Gang Pei and colleagues find that a member of the G protein-coupled receptor superfamily known as delta-opioid receptor (DOR) forms a complex with two enzymes, beta- and gamma-secretase. This promotes the processing of amyloid precursor protein without affecting the processing of their other substrates. Until now, therapeutic strategies involving inhibition of these enzymes are difficult because the enzymes mediate the processing of many other proteins and therefore their inhibition can lead to undesired side effects. This study reveals how blockage of DOR specifically reduced activities for amyloid-beta production in a mouse model of the disease without affecting the enzymes' appetite for other substrates. DOR forms a complex with the secretases and thus defines a special population of the enzymes for the amyloid-beta precursor protein.

The findings suggest that intervention in the formation or trafficking of the DOR/secretases complex could lead to a new strategy against Alzheimer's disease without affecting the normal function of these enzymes.

Author contacts:
Gang Pei (Shanghai Institute of Biochemistry and Cell Biology, China)
Tel: +86 21 54921373; E-mail: gpei@sibs.ac.cn

Jian Zhao (Shanghai Institute of Biochemistry and Cell Biology, China)
Tel: +86 21 54921373; E-mail: jzhao@sibs.ac.cn

Editorial contact:
Dangsheng Li (Cell Research, Shanghai, China)
Tel: +86 21 5492 2951; E-mail: dsli@sibs.ac.cn