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ACAT1/SOAT1 as a therapeutic target for Alzheimer's disease

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Alzheimer's disease (AD) is the most common cause of dementia with no cure at present. Cholesterol metabolism is closely associated with AD at several stages. While brain only accounts for 2-3% of the body weight, it occupies 25% of the total body cholesterol.Cholesterol ester (CE) is the storage form of cholesterol. In normal brains, CE levels are less than 1% of free, unesterified cholesterol. However, in the vulnerable regions of brain samples from late-onset AD patients, CE levels were 80% higher; in the brains of three AD mouse models, the CE levels rose to values 3 to 11 fold higher than those in control mice. In addition, when fed with a high-cholesterol diet, the brain CE content in human ApoE4 knock-in mice was 3-fold higher than that in human ApoE3 knock-in mice. These observations suggest a causal relationship between AD and increased CE content in the brain. Acyl-CoA:cholesterol acyltransferase 1 (ACAT1) converts free cholesterol to cholesteryl esters, and plays important roles in cellular cholesterol homeostasisin various tissues including the brain. Recent studies show that in a mouse model, blocking ACAT1 provides multiple beneficial effects on AD. Here I review the current evidence that implicates ACAT1 as a therapeutic target for AD. I also discuss the potential usage of various ACAT inhibitors currently available to treat AD.

Biography

Chang is internationally known for his research work in the cholesterol metabolism field. His laboratory did ground breaking work on the key cholesterol storage enzyme acyl-CoA:cholesterol acyltransferase 1 (ACAT1/SOAT1). He and his colleagues identified the Acat1/Soat1 gene, performed functional analysis of the enzyme, and demonstrated Acat1/Soat1 as a target for treating several human diseases including Alzheimer's disease. Dr. Changhas served as an editorial board member of several major scientific journals, and as a review panel member for NIH. He received an NIH Merit Award in 1994, and was elected AAAS Fellow in 2011.

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