



Medical Education and Research Grant Outcome Report

Name: Sterol Carrier Protein 2 is a Novel Link Between Aging and Alzheimer's Disease

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Department: Medicine, Geriatrics

Program: New Investigator Program

Grant Duration: 08-01-05 to 07-31-07 (24 months)

Expenditures: \$100,000 (100%)

Use of Funds (Taxonomy): Basic Science

Research Keywords: SCP-2; aging; Alzheimer's disease; gene regulation; cholesterol

► **Description:** This project seeks to identify new molecular links between aging, Alzheimer's disease and cholesterol metabolism. Sterol carrier protein-2 is a small protein that is highly expressed in the brain, can function as a cholesterol carrier and is activated in an age-dependent fashion. Since intracellular cholesterol metabolism and distribution can regulate the rate of amyloid β -peptide generation, the first molecular step in the development of Alzheimer's disease, understanding more about sterol carrier protein 2 may shed new light on the pathogenesis of Alzheimer's disease.

► **Contributions/Results:** : The study produced unexpected and extremely novel results that will have wide implications for basic biomedical research in the pathogenesis of Alzheimer's disease.

The abnormal accumulation of amyloid β -peptide (A β) in the form of senile (or amyloid) plaques is the first molecular event involved in the pathogenesis of Alzheimer's disease (AD). Both the generation and accumulation of A β are affected by cholesterol metabolism and distribution in the brain. The investigator identified sterol carrier protein 2 (SCP-2) as a major regulator of both cholesterol metabolism and A β generation, providing a possible molecular mechanism to explain why the risk of AD increases during aging. These results can potentially help to identify pharmacological approaches to prevent this form of dementia.

► **Met Objectives:** Completed project

► **Timeline for Application of Results:** Unknown

► **New partnerships or collaborations:** None noted

► **Contributions to the Transformation:** None noted

► **Matched Dollars (cash or in-kind):** \$0

► **Dissemination:** Abstract: Ko MH, and Puglielli L., Society for Neuroscience 2006 (Atlanta, GA), The transcriptional activity of the sterol carrier protein (SCP-x/pro-SCP-2) gene regulates cleavage of the amyloid precursor protein and requires post-translational competition of its own products

Article: Ko MH, and Puglielli L., The sterol carrier protein SCP-x/pro-SCP-2 gene has transcriptional activity and regulates the Alzheimer disease gamma-secretase. J Biol Chem. 2007;282(27):19742-52

► **Additional Funding:** None reported (currently funded for an unrelated NIH RO1)