**Name:** Sterol Carrier Protein 2 is a Novel Link Between Aging and Alzheimer’s Disease  
**Principal Investigator:** Luigi Puglielli, MD, PhD, Assistant Professor  
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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 â-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 â-peptide (Aâ) 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 Aâ 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 Aâ 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.

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

**Met Objectives:** Completed project