



## 2007 Grant - Pahan

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### **Neutral Sphingomyelinase in Beta-Amyloid–Induced Neuronal Death**

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2007 Investigator-Initiated Research Grant

Beta-amyloid is a protein fragment that is deposited in the brains of patients who have Alzheimer's disease. When healthy nerve cells in the brain are exposed to beta-amyloid, they exhibit a number of pathologic changes that are characteristic of Alzheimer pathology, including cell death. Although these fundamental observations have been known for some time, the mechanisms that explain how beta-amyloid causes toxicity are not well understood.

Recently, Kalipada Pahan, Ph.D., and colleagues have found that beta-amyloid may induce a series of events that lead to the activation of an enzyme known as neutral sphingomyelinase (NSMase) in neurons and that such activation leads to characteristic cellular events associated with the death of neurons. The exact process that leads from beta-amyloid to NSMase activation is not clear.

Dr. Pahan and colleagues have proposed to study the cellular mechanisms that mediate the toxic effects of beta-amyloid in neurons and characterize the steps involved in the activation of NSMase. They will also study how this process is modified by other cellular factors and how it can be inhibited. Their studies may help to identify ways of blocking the toxicity of beta-amyloid and subsequently inhibit the progression of Alzheimer's disease.