Abstract:

The mechanism by which neurons die in Alzheimer’s disease is not known. Despite the fact that a multitude of hypotheses have been proposed, none has been proven. We have identified a neuronal signal transduction pathway initiated by the Alzheimer’s amyloid precursor protein that is disrupted in a model of Alzheimer’s disease. Activation of this pathway causes enlargement of endosomes and neuronal cell cycle entry, both of which are among the earliest known pathological features of Alzheimer’s disease. The details of this pathway, which lead eventually to neuronal death, will be described.