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Abnormal APP Processing in Living Cortical Neurons from Alzheimer Brains

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In the brain, amyloid precursor protein (APP) is cut into pieces, one of which is beta-amyloid. Under some conditions, beta-amyloid aggregates to form amyloid plaque, a hallmark feature of Alzheimer pathology. Because of the central role of APP in the development and progression of disease, the production, processing and cutting of this protein are of great interest. Indeed, these processes are potential targets for therapies to slow or halt disease progression.

Yong Shen, M.D., Ph.D. and colleagues are studying the processing of APP in nerve cells affected by Alzheimer's disease. They have developed the ability to maintain living brain cells from individuals who recently died of Alzheimer's disease. Using these cells, Dr. Shen and colleagues plan to examine the factors affecting the production of beta-amyloid.

The researchers plan to first examine the activity of the Alzheimer nerve cells, using imaging methods and methods to record electrical activity. They expect to see abnormally high activity of these cells compared to cells unaffected by Alzheimer's disease. Next, the researchers will examine whether cellular activity causes increases in the production of beta-amyloid. Finally, they will determine if activity affects the expression of enzymes involved in cutting APP, especially an enzyme known as BACE1 (beta-site amyloid precursor protein-cleaving enzyme-1). These studies will directly examine the cellular effects of Alzheimer's disease in the brain, and they may help to explain the mechanisms of beta-amyloid production and disease progression.