Visualization of BACE1 Protein Trafficking in Living Cells using Fluorescence Microscopy

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Abstract: Alzheimer's disease is a common neurodegenerative disorder among the elderly. The disease's pathology is associated with two lesions of neurofibrillary tangles and senile plaques found in the hippocampus and cortex regions of the brains of patients with Alzheimer's. The senile plaques are made of extracellular peptides known as β-amyloid (39-42 amino acids long). The β-amyloid is cleaved from the amyloid precursor protein (APP), which is a large type-I transmembrane, via a sequential proteolysis using an enzyme β-secretase also known as BACE1. Recently, detergent-based studies in buffer suggest that BACE1 forms a dimer with an enhanced activity in the presence of APP. In this McNair project we genetically encoded BACE1 protein in HEK293 cells with enhanced green fluorescent protein (EGFP). In addition, we used time-lapse confocal microscopy imaging to interrogate the BACE1-EGFP complex in cultured HEK293 cells under both resting conditions and APP-treatment. In addition, we used complementary fluorescence lifetime imaging microscopy (FLIM) to probe changes in both the chemical structure of BACE1 (e.g., dimerization) and its local environment in live cells. Our goal is to assess the dimerization hypothesis of BACE1 in cultured cells under different physiological conditions of APP treatment. These preliminary studies represent a first step towards an understanding of BACE1 and its oligomerization towards an understanding of its role in plaque formation Alzheimer's disease and therefore a better prospect for a cure.