

**EXECUTIVE SUMMARY:** (State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project for California.)

Alzheimer's disease (AD) is the most common form of dementia. It is a progressive neurodegenerative disease that currently affects approximately 4.5 million people in the United States. The proportion of people suffering from AD doubles every 5 years after the age of 65, which ultimately means the total number of elderly will only continue to grow with the increasing lifespan of the population. There are no known cures for AD at this time.

Our goal is to characterize and develop a *Drosophila melanogaster* (fruit fly) model that recapitulates the physiological characteristics of AD. We will construct a novel fly line that expresses the plaque forming amyloid beta peptide and the full-length amyloid precursor protein, in cholinergic neurons which are specifically targeted in AD. Copper, zinc, iron, and manganese are all micronutrients that are critical for biological processes. The imbalance of these metals are implicated in AD. We will use the proposed fly lines to investigate if this imbalance can be recapitulated in a fly model by measuring the total metal ion content in the genetically derived flies and the level of oxidative stress. Our long-term objective is to use these fly as a model system to test potential therapeutics and modifiers of AD.