

**Project Title: Dissecting mechanisms of endocytic trafficking (de)regulation in neuronal aging and Alzheimer's disease**

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**Summary: (1000 characters)**

Alzheimer's disease (AD) that affects more than 95% of AD patients lacks treatment. In neurons of AD there is an aberrant accumulation of beta-amyloid (A $\beta$ ), the primary trigger of neurodegeneration. The deregulation of intracellular endocytic trafficking contributes to increased A $\beta$  generation. However, the cellular and molecular mechanisms that regulate A $\beta$  generation in neurons remain unclear. This project consists in studying regulators of endocytic trafficking that are AD risk factors or implicated in neuronal aging. The work plan aims to understand the mechanisms, develop new models that better recapitulate late-onset AD and identify new therapeutic strategies. In this project primary mouse neurons, human induced neurons in 2 or 3D cultures will be used. Endocytic trafficking will be studied using live-cell imaging, super-resolution microscopy, and quantitative single cell analysis, in addition to synapse biology and biochemistry techniques. We expect to contribute to find a cure for AD.

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