#### **Unraveling the Impact of α-Synuclein Mutations in Parkinson's Disease**

A diagram of a structure

Description automatically generated

**Figure 1.** Overview of project aims.

**Aim 1. Determine the structures of α-synuclein filaments with missense mutations and *SNCA* duplication from human brains.**

**Aim 2. Characterize the structural impact of *SNCA* missense mutations in iPSC-derived neurons.**



**Figure 2.** Cryo-EM 2D class averages from brains with mutations. The yellow arrows indicate the width and distinct features of each class.

Preliminary data suggest that some mutant amyloids share structural characteristics with wild-type (WT) forms, while others adopt distinct conformations (Fig. 2).