Introduction

Preclinical models are important tools for investigating the pathogenesis and potential therapeutic strategies for diseases like Parkinson’s disease (PD). As the precise etiology of PD is currently unknown and appears to vary among individuals, numerous preclinical models are available to study this disease. To ensure the research community has access to well-validated models of PD, The Michael J. Fox Foundation (MJFF) has taken an active role in designing, validating, and distributing various models of PD that rely on different genetic or intervention measures that can be used to investigate mechanisms of PD neurodegeneration or strategies for slowing, stopping, or halting disease progression. Ultimately, MJFF’s investment in providing the research community with robust, well-characterized animal models and information on choosing an appropriate model will hopefully lead to advancements in PD research.

**Alpha-Synuclein Pre-formed Fibrils**

The use of alpha-synuclein pre-formed fibrils (αSyn PFFs) to generate an in vitro or in vivo model of PD is gaining traction in PD research. Investigators may opt to use the αSyn PFF model as it is an inducible model that allows spatiotemporal control of αSyn pathology and nigrostriatal degeneration resulting from pathological alterations in endogenous αSyn after introduction of the recombinant αSyn PFFs. Although many groups have successfully adopted the αSyn PFF model, issues with generating complex pathology have been reported. To improve the replicability of this model and minimize these issues, MJFF is providing the research community with guidelines and practical tips for generating and using αSyn PFFs. A summary of common pitfalls and solutions can be found below, along with information on the αSyn PFF generation protocol in Figure 1, recommended validation experiments in Figure 2, and a list of αSyn PFF species made available by MJFF through Proteins in the table below.

![Figure 1. Schematic depiction of the protocol for generating αSyn PFFs.](image)

**Key Messages for Avoiding Common Pitfalls in the Generation of αSyn PFFs for a Preclinical Model of PD**

- **Preparation of αSyn Monomers**
  - Use a well-characterized source of αSyn
  - Formulate αSyn monomers using 300mM NaCl, 30mM NaHCO3, pH 8.5

- **Preparation of αSyn Pre-formed Fibrils**
  - Monitor the morphology and purity of αSyn fibrils using dynamic light scattering (DLS) and transmission electron microscopy (TEM)
  - Sanitize the αSyn fibrils in αSyn monomer solution before use
  - Use lyophilized αSyn PFFs for in vivo studies

- **Preparation of αSyn PFFs for Use**
  - αSyn PFFs can be used in transfected HEK293 cells in panels A and B. The mouse SNCA miR

**MJFF Preclinical Model Resources**

In 2017, MJFF added a new webpage to provide investigators with information on various preclinical models used in PD research. In addition to highlighting common preclinical models of PD, this webpage hosts a variety of resources aimed at helping investigators choose an appropriate model for their research. These resources include links to the PD research models page on the Alzheimer’s Disease page, results of MJFF-led efforts to characterize a variety of transgenic rodent models of PD, and information on our preclinical biospecimen repository.

**Summary and More Information**

MJFF is invested in providing the PD research community with high-quality tools and models to support rapid new discoveries and encourage replicable, reproducible data. The tools described in this poster provide the research community with collaborative efforts aimed at generating molecular tools for αSyn-related research in particular.