THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

# TARGETS TO THERAPIES (T2T) PROGRAM: T2T VALIDATION CORE

## PRE-PROPOSAL TEMPLATE

1) Please use the template below to create an executive summary of your experimental plan and upload a single PDF copy with your online submission.
2) Text should be no smaller than 11-pt font and not exceed **2 pages, including optional references.** You may delete any instructional text to save space.
3) Review the RFA pre-proposal Instructions linked here.

**Principal Investigator:**
**Institution/Company:**
**Project Title:**

Select the **target** and validation **gap(s)** your proposal will address.

### T2T TARGET: STING1
**Validation Gaps:**
- ❑ Confirm STING1 activation in *in vitro* PD models and elucidate activation mechanisms.
- ❑ Demonstrate direct STING activation in PD patient samples, beyond IFNβ production.

### T2T TARGET: TREM2
**Validation Gaps:**
- ❑ Generate TREM2 clinical evidence in PD Patient Samples.
- ❑ Conduct TREM2 mechanistic studies in *in vitro* PD models.

### T2T TARGET: TLR2
**Validation Gaps:**
- ❑ Define therapeutic intervention window for TLR2.
- ❑ Evaluate sTLR2 as a biomarker for patient stratification and disease progression.
- ❑ Support development and scaling of TLR2 occupancy assay.

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| **EXPERIMENTAL PLAN** | Provide a detailed validation plan, including a brief description of:<br>• the models to be used (e.g., *in vitro*, *in vivo*, or *ex vivo* models, including patient-derived samples, add RRID# where known)<br>• the key assays and techniques (e.g., biochemical, imaging, molecular, and functional assays) that will be employed to evaluate critical target endpoints such as target expression, function, and engagement.<br>• the approach for data analysis, specifying statistical models (e.g., ANOVA, regression, Bayesian inference) |

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| | • the use of controls and replicates to ensure data robustness and reproducibility. |
| **OUTCOME** | • Define the key milestone or inflection point this project aims to achieve and its impact on filling the validation gap(s).<br>• Describe any resources that will be leveraged or generated along with their availability status. |
| **PROGRAM SUPPORT** | Identify areas where MJFF can provide support (e.g., expertise, model advice, generation of tools & reagents, or PD patient samples). |
| **RISKS** | Highlight the primary risks associated with the project and potential mitigation strategies. |
| **TIMELINE** | Provide an estimated timeline for project completion, including key milestones. |
| **INTELLECTUAL PROPERTY** | Describe any intellectual property considerations or restrictions (e.g., freedom-to-operate) that may impact data or resource sharing with the broader PD community. |
| **BUDGET** | Present a high-level budget estimate, including anticipated costs. |