

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

### PRE-PROPOSAL TEMPLATE

Please upload the pre-proposal template below (as a PDF) to your online application in the Grant Portal. Use a minimum 11-pt font, with a **2-page max length**. You may use bullet points and delete instructional text, but **keep headings in the left column**. Images, graphs, and references are optional to include and do not count toward the page limit.

**Principal Investigator:**

**Institution/Company:**

**Project Title:**

**T2T TARGET:**  **GLOD4**

**VALIDATION GAP:** Select target validation gap(s) this project aims to address.

- Independent Validation and characterization of GLOD4
- Validation of GLOD4 in PD-relevant systems

**T2T TARGET:**  **DYRK1A**

**VALIDATION GAP:** Select target validation gap(s) this project aims to address.

- Validation of DYRK1A as the effector gene at the locus
- Resolve the apparent paradox of DYRK1A roles in PD
- Is DYRK1A activity a tractable therapeutic strategy?

**T2T TARGET:**  **TG2**

**VALIDATION GAP:** Select target validation gap(s) this project aims to address.

- Is TG2 biology convincingly anchored in human PD?
- Is there a PD relevant splice variant and does it matter biologically?
- What is the disease mechanism and therapeutic strategy?

<b>VALIDATION GAP(S)</b>	Clearly define the target validation gap(s) this project aims to address.
<b>EXPERIMENTAL PLAN</b>	<p>Provide a detailed validation plan, including a brief description of:</p> <ul style="list-style-type: none"> <li>• the models to be used (e.g., <i>in vitro</i>, <i>in vivo</i>, or <i>ex vivo</i> models, including patient-derived samples, add RRID# where known)</li> <li>• 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.</li> <li>• the approach for data analysis, specifying statistical models (e.g., ANOVA, regression, Bayesian inference)</li> <li>• the use of controls and replicates to ensure data robustness and reproducibility.</li> </ul>

<b>OUTCOME</b>	<ul style="list-style-type: none"> <li>Define the key milestone or inflection point this project aims to achieve and its impact on filling the validation gap(s).</li> <li>Describe any resources that will be leveraged or generated along with their availability status.</li> </ul>
<b>PROGRAM SUPPORT</b>	Identify areas where MJFF can provide support (e.g., expertise, model advice, generation of tools & reagents, or PD patient samples).
<b>RISKS</b>	Highlight the primary risks associated with the project and potential mitigation strategies.
<b>TIMELINE</b>	Provide an estimated timeline for project completion, including key milestones.
<b>INTELLECTUAL PROPERTY</b>	Describe any intellectual property considerations or restrictions (e.g., freedom-to-operate) that may impact data or resource sharing with the broader PD community.
<b>BUDGET</b>	Present a high-level budget estimate, including anticipated costs.