



Summary of Community Conference Call on
Cognitive Deficits and Mood Disorders in Parkinson's Disease 2008

Tuesday, January 22, 2008
12:00 noon U.S. Eastern Time

Part 1: Program Scope

Q: What is the Cognition Deficits and Mood Disorders in Parkinson's Disease program and why did MJFF decide to launch it?

A: Parkinson's disease has traditionally been considered a disorder affecting the motor system. However, more attention is being paid to the non-motor facets of PD including cognitive and psychiatric disturbances. Cognitive dysfunction and emotional or behavioral disorders are often the most disabling features of PD for patients and caregivers, and their development is closely associated with poor prognosis. While the importance of these conditions and their impact on patients' quality of life is recognized by patients and clinicians alike, research in this area, including the development of effective therapies, has been hindered by lack of a fundamental understanding of the phenomenology and pathophysiology of these symptoms, and a lack of validated clinical tools to assess these aspects of PD.

MJFF launched the DOPA Non-Responsive program in 2006 and was pleased with the response from the RFA, supporting proposals focused on gait and balance, apathy, and MJFF would now like to specifically request proposals on cognitive and behavioral disorders in Parkinson's disease. These symptoms are a large unmet need to patients and effective treatments do not exist.

Q: What types of studies can be done under the Cognitive Deficits and Mood Disorders 2008 program?

A: In the interest of facilitating development of treatments for the cognitive deficits and psychiatric disorders in Parkinson's disease patients, The Michael J. Fox Foundation for Parkinson's Research (MJFF) is seeking investigator-initiated applications designed to support pre-clinical and clinical research to understand the biological basis of, and facilitate the development of treatments for, the cognitive deficits and psychiatric disturbances associated with PD.

Topics appropriate for this RFA include but are not limited to:

- Novel approaches to understanding the pathophysiology of cognitive dysfunction and psychiatric disorders in PD - Studies to explore the neuropathological/neurochemical substrates of these symptoms. Studies examining non-dopaminergic lesions and non-nigrostriatal pathways in Parkinson's disease are of interest.
- Development and characterization of animal models for these symptoms.

- Examination of the role of cognitive dysfunction and psychiatric disorders in disease onset, progression and prognosis.
- Development and/or validation of clinical tools (screening tests, scales, or clinical markers) to predict or assess early development of cognitive dysfunction and psychiatric disorders in PD, or to predict or assess PD dementia.
- Detailed evaluation of the impact of existing PD treatments on these symptoms.
- Pre-clinical and clinical testing of available and/or experimental treatments for cognitive dysfunction and psychiatric disturbances in PD patients.

Q: Can I apply to Cognitive Deficits & Mood Disorders 2008 with clinical projects (those involving human subjects)?

A: Yes, MJFF is accepting both preclinical and clinical project proposals.

Q: Who can apply to Cognitive Deficits & Mood Disorders 2008?

A: Applications may be submitted by U.S. and non-U.S. entities, public and private non-profit entities, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the federal government, and for-profit entities. Post-doctoral students or fellows are not eligible to apply as principal investigators for this RFA. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the principal investigator.

Q: What animal models are appropriate for this program?

A: MJFF does not make any recommendation for specific animal models, as there is no clear single model that adequately mimics these non-motor symptoms PD in humans. Applicants are encouraged to contact experts to identify the most appropriate animal model for the study being proposed. Applicants should clearly justify the choice of animal model in the proposal and why the model is relevant to Parkinson's disease. Evidence of an applicant's (or collaborator's) expertise with the proposed animal model(s) is also a major criterion for review.

Q: What will the reviewers look for in an ideal proposal?

A: Applications will be reviewed against multiple criteria as listed in the RFA. These include overall clarity and rationale, the potential impact of the proposed work, the strength of the study design, investigator and environment, as well as the justification of the proposed budget. It is also critical that applicants consider and point out possible limitations of their approaches and how these might be addressed. Many applications fail because they do not provide a clear plan of attack, attempt to 'over propose', or provide insufficient methodological details to allow a proper evaluation of the research plan. Quality grantsmanship is key to improving your chances of receiving a favorable review.

Part 2: Administrative Questions

Q: Can multiple investigators be involved on a project?

A: While MJFF requires that one Principal Investigator lead and manage the proposed project, it is acceptable and encouraged for Principal Investigators to seek out collaborations with other experts. Project teams may involve Co-Principal Investigators from multiple institutions as long as the collaborative involvement is justified for the project and within the budget. Given the interdisciplinary nature of this program, MJFF encourages collaborations that extend across disciplines between PD researchers and those with expertise in cognition and mood alterations. While it is not a requirement, these collaborations will be viewed favorably.

MJFF funds can go directly to multiple institutions if necessary; however, total indirect costs for the project may never exceed 25% of the direct costs.

Q: If I already have some funding covering this work, can I still apply?

A: For those applicants invited to submit full proposals, MJFF requires that any overlap in the proposal aims with work supported by other funding sources be clearly stated. If the submitted proposal is the 'next step' of a currently funded project, the applicant should explain this within the project narrative.

Q: Can previous MJFF awardees apply to this program?

A: Yes. Applicants may be past or current MJFF awardees, as well as those investigators who have never before submitted an application for or received MJFF funding.

Q: How much money is being committed to Cognitive Deficits and Mood Disorders 2008?

A: Thanks to generous leadership funding from Merck Serono (EMD Serono in North America), MJFF is committing up to \$2M for this program.

Q: How long can my proposed project be?

A: Proposed projects may be for up to three years, although we are open to funding projects that are less than three years.

Q: How much funding can I seek for my project?

A: MJFF has not specified a maximum project amount for this program. Applicants will be asked to clearly justify their budgets in the full application. While there is no limit for total project costs, indirect costs may not exceed 25% of the direct costs.

Q: What is MJFF's policy regarding direct and indirect costs? If I am collaborating with an investigator whose institution has a higher indirect rate, can I charge some of the extra indirect cost as direct cost to my institution?

A: Indirect costs for this program can be no more than 25% of total direct costs. If multiple institutions are collaborating, indirect costs are only paid once – either to the PI's institution as 25% percent of total direct costs or to each PI's institution as 25% percent

of each institution's total direct costs. Indirect costs higher than 25% can not be listed as direct costs for an institution.

Q: How do I submit a pre-proposal and what should I include in it?

A: We only accept pre-proposals submitted through the on-line system, which can be accessed at https://www.grantrequest.com/SID_592/?SA=SNA&FID=35039. Pre-proposals should be clear, succinct and provide sufficient details to allow a clear understanding of the proposed project and its aim(s). Further information can be found on our Pre-Proposal Instructions form located on http://www.michaeljfox.org/funding_programs/Cognitive%20and%20Mood%20Disorders%202008%20-%20Pre-prop%20InstrFinal.pdf

Q: When are pre-proposals due and are they required?

A: Pre-proposals are due February 13, 2008, no later than 6PM U.S. Eastern Time. They are required for all applicants and will be evaluated by MJFF staff and select members of the review committee. Those that are not felt to adequately fit the scope and intent of this program will not be invited to the full proposal stage. Applicants will be informed whether they are invited submit full proposals no later than March 3, 2008.

Q: If I'm successful in being invited to the full proposal stage, when will these be evaluated and ultimately awarded?

A: All invited full proposals will be due April 15, 2008, and reviewed by members of the review committee in May 2008. Review decisions will be made in June 2008.

Q: Who will evaluate my proposal?

A: Reviewers will be chosen from appropriate experts in the field who meet eligibility criteria as defined by MJFF policies (e.g., are not themselves paid applicants on any reviewed application and will not be involved in the review of applications from their own institution). Reviewers may include members of the MJFF Scientific Advisory Board, but also include external experts from the community. All reviewers sign confidentiality disclosure agreements with MJFF.

Q: What documentation does MJFF require for animal work done as part of a Cognitive Deficits and Mood Disorders 2008 project?

A: Investigators whose projects involve *in vivo* animal work will need to demonstrate to MJFF that they have received IACUC or other relevant ethical approval for the animal studies.

Q: What is MJFF's policy on making the results of the awards public?

A: MJFF maintains the right to publish a general summary of results from awardee projects within 3 months of the project end date. MJFF also encourages all awardees to publish their results in the peer-reviewed literature as quickly as possible.

Q: Are there guidelines regarding how an awardee can communicate its decision to apply to MJFF for funding?

A: Upon being selected as an awardee, MJFF will work with the awardee and his/her organization(s) to coordinate the press announcement regarding the awarded funding. Prior to the selection of awardees, MJFF requests that applicants do not issue press releases if they have submitted a pre-proposal or have been invited to submit a full proposal. Failure to follow these guidelines could result in an investigator's application being removed from review.

Q: If I am selected as an awardee, is funding contingent on milestones?

A: If invited to submit a full proposal, full proposal submission instructions will stress that applicants should outline milestones and deliverables for the proposed project. Upon selection as an awardee, MJFF will interact with awardees throughout the course of the project to determine progress toward achievement of milestones and deliverables. Depending on the project's progress, MJFF has the right to alter the payment schedule.

Part 3: MJFF General Philosophy and Approach

Q: What is MJFF's overall philosophy?

A: MJFF is solely focused on developing improved treatments and ultimately a cure for PD. We do this through aggressive and strategic allocation of funds toward research and development efforts that are in line with these goals. Although we tackle the problem in a variety of ways, we ground our efforts in two fundamental beliefs:

1. ***Promoting movement along the therapeutic pipeline is essential for success.***
This concept drives almost everything we do: basic research uncovers new 'targets' which once validated in preclinical translational studies lead to the development of new treatments that can be tested in people. However, in the current absence of any one clear 'path to the cure', we take a portfolio approach and invest along the entire therapeutic pipeline to ensure that discoveries are continuously followed and tested. By identifying gaps and barriers where resources—funds, research tools, expertise, community consensus—are lacking, we can play a key role in helping to accelerate movement of promising ideas in an efficient, data-driven and goal-oriented fashion.
2. ***Appropriate therapeutic decision-making requires clear and definitive data.***
We see therapy development as a step-wise critical pathway, with the ultimate end goal (the treatment) requiring top-down planning and consideration of the studies and activities needed to reach that goal. (For example, we do not support work to study alpha-synuclein out of interest in the protein *per se*; rather, we support work on alpha-synuclein out of a desire to see it ultimately validated or invalidated as a therapeutic target.) To 'de-risk' promising targets involves the collection of critical and definitive positive and/or negative data to support whether a particular therapeutic option should be further pursued. This is essential to increase confidence of later stage industry players who have the resources to develop and ultimately test new treatments in the clinic.

Q: How does MJFF apply its beliefs and philosophy in practice?

A: MJFF has developed an overall portfolio approach to funding across the entire spectrum of the therapeutic development pipeline. We also use a critical pathway mindset, with all of our programs ultimately focusing around the general concept of the therapeutic ‘target’ and the steps needed to translate it into clinically meaningful therapies. This idea can be conceptualized in the following manner:

- **Define the target:** This involves supporting basic disease-focused research that can uncover promising new targets (e.g., our Rapid Response Innovation Awards program).
- **Validate the target:** This involves supporting studies that seek to determine whether a particular target has potential therapeutic relevance for PD (e.g., our Target Validation annual program).
- **Translate the target:** This involves developing and optimizing therapeutic strategies that can modulate a particular target (e.g., our Therapeutics Development Initiative program).
- **Test in patients:** These include early safety and efficacy trials in PD patients (e.g., our Clinical Discovery Awards annual program).

In addition to target-focused efforts, we also seek to promote the development of tools and resources that can impact the overall pipeline. For example, the development of biomarkers can greatly improve our ability to identify people with PD and more definitively test therapies. Development of animal models of PD can provide systems in which to test a variety of promising therapies.

Q: How does MJFF raise and manage its money?

A: It is important to realize that MJFF does not maintain an endowment or large pool of capital and must raise its money from scratch each year. Indeed, because of our desire to move quickly, we often commit to a program or effort before we have raised the money to do so! This requires that we continuously evaluate the impact of each dollar spent and strategize how best to allocate our funding and other committed resources. Ask any past or current MJFF awardee and you will know that we take a real interest in the work that we support. This includes telephone updates with awardees, as well as in-person assessment meetings at midpoint and/or final stages of the award. Continued funding is by necessity dependent on continued progress of the grant and delivering on key milestones and project goals as promised. Good progress with promising findings can also lead to the potential for supplemental funding opportunities. With this philosophy in mind, we strive to do more than just act as a bank, but to be an integral partner in the PD research endeavor.

Q: My laboratory does research in PD. Will MJFF be interested in what I do?

A: Yes (maybe). It is important to remember that MJFF does not support PD science simply because it is PD science. Rather, we strive to identify and support work that can clearly answer the question: Is it worth taking this idea/therapeutic strategy to the next stage? Researchers interested in seeking support from MJFF should carefully examine the work they are doing and how it fits within the therapeutic pipeline. Can it be realistically

translated into a potential therapy? Does the proposed work address the most essential and critical next step for moving a therapeutic option forward? MJFF is particularly interested in supporting areas where our investment and involvement can have real impact. If you feel you share our goals and have work relevant to the cause, we invite you to examine the various open funding programs on our website, or to contact our research staff at research@michaeljfox.org.

Q: My laboratory really needs funding, but my work does not exactly fit your open programs. Can I apply anyway?

A: No. Please understand that we spend a good deal of effort and time strategizing about specific programs and RFAs that we feel could have significant impact on the field. This involves speaking with external experts and performing our own internal due diligence to define and refine priority areas that fit within the philosophy and goals of the Foundation. We appreciate that we may not always have a program that fits your funding needs, especially when other funders' paylines may be low, but we feel that our best impact comes through targeted effort in key critical areas rather than as a general pool of additional funding for PD science as a whole.