National Multiple Sclerosis Society

SPRING 2021 FUNDING OPPORTUNITY

Detecting Multiple Sclerosis before the onset of neurological deficits

Background

The mission of the National Multiple Sclerosis Society is to cure multiple sclerosis (MS) while empowering individuals affected by MS to live their best lives. To achieve this mission, the Society has developed the Pathways to Cures Research Roadmap (pdf). The Roadmap was developed in consultation with global scientific experts and people affected by MS and outlines a vision of the most promising research that will ultimately lead to cures for MS. A high priority objective of the Roadmap is the early detection of MS prior to the accumulation of neurological deficits. This request for applications (RFA) is designed to solicit research to advance this objective. This RFA is open to applicants working in academic or industrial institutions from around the world.

There has been a gradual recognition that MS, like many other autoimmune and neurological diseases, has preclinical and prodromal phases. As defined in this RFA, preclinical MS occurs after pathological initiation of the disease, and before any clinical signs or symptoms manifest themselves in an individual patient. An example of the preclinical phase of MS is radiologically isolated syndrome (RIS), an asymptomatic period that indicates a higher risk of developing MS. The prodrome is defined as a period marked by appearance of non-specific, early clinical signs and symptoms suggestive of underlying pathology.

While we cannot currently identify people at risk for MS, recent advances made in other chronic autoimmune conditions like type 1 diabetes and rheumatoid arthritis and other neurological conditions like Parkinson's and Alzheimer's disease suggest that this might be possible. Recent studies in MS have also begun to uncover insights about the pre-clinical and prodromal stages of MS that could eventually be used for risk assessment or disease staging.

In MS, work has been done to better understand the RIS population and the potential for early treatment. Retrospective reviews of medical records and health utilization have uncovered prodromal signs five to ten years before a first demyelinating event or MS diagnosis. In addition, some evidence suggests that age, sex, and disease course may impact the prodromal period. Little is known about how race or ethnicity may impact the course of the prodromal period. Finally, evidence of neuronal damage in the period well before clinically definite MS is emerging through studies of biomarkers such as blood neurofilament light chain.

Earlier identification of individuals who will go on to develop definite MS will require advances in several research areas including: understanding the biological pathways driving the MS preclinical and prodromal periods, further development of biomarkers, and improved understanding of environmental and genetic risk factors and their interactions that lead to pathological initiation of disease. Advances in these areas will ultimately lead to earlier diagnosis, treatment, and perhaps even prevention of MS.

Purpose of this RFA

This RFA is intended to support knowledge generation that will eventually lead to early detection of MS at the individual level. The RFA does not include funds to start new MS cohorts, applicants are encouraged to utilize existing cohorts and associated datasets and biological samples. Applications should address critical knowledge gaps in our understanding of preclinical and prodromal phases of MS. These knowledge gaps include but are not limited to:

- A better understanding of the risk factors that play a role in initiating MS and the interactions between them
- Biomarkers (fluid, tissue, imaging, behavioral) with potential utility to identify those who will develop MS
- An improved definition of the period prior to clinically definite MS with biological and behavioral markers, health data and sociological features
- A mechanistic understanding of the pathophysiology of preclinical and prodromal MS
- A better understanding of the heterogeneity of preclinical and prodromal phases of MS in different populations

This list is not meant to be exhaustive and applicants are encouraged to identify and address other gaps that stand in the way of earlier detection of MS.

Areas of high interest include studies:

- That utilize robust/well characterized biomarkers (fluid, tissue, imaging, behavioral)
- To evaluate combinations of risk factors, biomarkers, and health data in stratifying risk
- In underserved and understudied ethnic and racial MS populations
- To better understand the mechanism of specifically identified MS risk factors using animal models, cellular models, or MS tissues

Areas not supported include:

- Early treatment (prevention) studies using animal models
- Studies that require the establishment and long-term support of a new cohort
- Research/Development of a disease modifying therapy

Qualified Institutions:

This RFA is open to not-for-profit research institutions and commercial organizations from around the world. The evaluation of proposals from all types of organizations will be done by a single peer review committee, however, commercial proposals will also be expected to address the commercial viability of the approach – including intellectual property strategy and commercialization strategy.

Funding: A total expense of up to a total of $300,000 USD (direct cost) for two years of support will be provided and must be justified based on the scientific and development work plan.

Submission guidelines and process: Important dates:

- Pre-applications will be accepted beginning: **March 1st, 2021**
- Final date for acceptance of pre-applications: **5 pm ET**, **April 23rd, 2021**
- Final date for receipt of full applications: **5 pm ET**, **April 30th, 2021**

A brief pre-application is required to determine if a proposal is aligned with the objectives of the RFA. Potential applicants are strongly encouraged to consult with Society scientific staff prior to submitting a proposal (see contact information below). Applications are to be submitted through the National MS Society's online grant submission portal - MSGrants. All proposal information, including instructions for accessing MSGrants, can be found on this web page. Upon review of pre-applications by staff, applicants proposing work that is aligned with the RFA objectives will be invited to submit full applications.

The reviewers will evaluate proposals based on the following criteria:

- **Rationale**: Does the proposal address an important gap or barrier in our understanding of subclinical/prodromal MS?
- **Preliminary Data:** Has the applicant provided sufficient preliminary data to demonstrate they have the skills and expertise to carry-out the proposed studies? Does the data provide reasonable preliminary support for the project?
- **Research Team**: Are the lead investigator and collaborators qualified and well-suited to carry out the proposed research?
- **Scientific Plan:** Is the research plan sufficiently developed and appropriate to the project? Are the specific aims clearly defined? Has the investigator considered alternative outcomes and the impact on the plan? Is the analysis plan and statistical methodology appropriate for the project?
- **Environment**: Is the research environment appropriate and likely to contribute to the success of the proposed research? Does the environment foster collaborative arrangements that may support the proposed research activities? Is the research environment compliant with appropriate rules and regulations for study conduct?
- **Budget**: Is the proposed budget reasonable and justified relative to the proposed research?

For Commercial proposals also:

- **Commercial Feasibility:** Does the proposal define a potential path to the marketplace? What are key milestones or barriers to achieve commercialization?
- **Intellectual Property Strategy:** Has the applicant secured intellectual property for the technology? If not, is it in the process of doing so? What protections are considered critical to advance the technology?

Applicants will be notified of the results of the review process by September of 2021.

Inquiries:

Applicants are encouraged to contact Society scientific staff for clarification of any issues or questions regarding this RFA.

Walt Kostich	Director, Commercial Research	walter.kostich@nmss.org 212-476-0428
Mark Allegretta	Vice President, Research	mark.allegretta@nmss.org 212-476-0459