

MAY 2019 REQUEST FOR APPLICATIONS

PILOT RESEARCH AWARDS – EFFECTS OF AGING ON MULTIPLE SCLEROSIS

Introduction

The National Multiple Sclerosis Society is pleased to announce a new Pilot Research Award to study the effects of aging on multiple sclerosis (MS). This request for applications (RfA) is being supported by a collaboration with EMD Serono, through its MS-Leadership and Innovation Network (MS-LINK™). MS-LINK™ is an initiative that brings together a community of multiple sclerosis (MS) stakeholders, including industry, academia and advocacy groups, to form a top-tier scientific research network for sustainable transformation of MS care, with the shared goal of improving patient outcomes.

Background

The prevalence and age of people with MS have increased during the last two decades. The introduction of disease-modifying therapies and a better understanding of comorbidities in people with MS are likely contributing to these phenomena. Age is one of the factors most strongly influencing the course of progression in MS. Aging is often accompanied by a transition from an inflammatory to a neurodegenerative phenotype and explains, at least in part, reduced effectiveness of disease modifying therapy and disability progression.

Immunosenescence might be partly responsible for this transition. Age related reduction in the numbers and altered function of lymphocytes, including changes to cytokine production may have a role in reducing cell-mediated immunity and CNS inflammation. There is also a notable decline in the total number of phagocytes and an intrinsic reduction in their function that likely also contributes to changes in the immune response associated with aging.

There is also evidence that senescent cells accumulate in the nervous system with aging and neurodegenerative diseases like MS and may aggravate its course. Recent advances in senescence markers and the development of animal models have accelerated our understanding of the role of cellular senescence in neurodegenerative diseases. The aim now is to fully elucidate its role in neurodegeneration in order to efficiently and safely exploit cellular senescence as a therapeutic target.

With advancing age, repair, remyelination, and other physiological functions become less robust. Animal studies indicate that, while oligodendrocyte precursor cell (OPC) recruitment to lesions remains intact, differentiation into myelinating oligodendrocytes decreases with age. Aged rats demonstrate a slower and less effective remyelination process compared to young rats. Similarly, elderly humans also show reduced remyelinating capabilities. Understanding the intrinsic and extrinsic factors, along with epigenetic changes that are known to occur during aging will lead to new targets that promote myelin repair.

Goals

The goal of this RfA is to advance the understanding of how aging contributes to the pathogenesis and natural history of MS progression and to use this knowledge to reveal potential targets and develop strategies that slow down or stop disability progression.

Areas of high impact for this program include but are not limited to:

- Approaches directed at removing barriers to OPC maturation to improve remyelination and/or neuroprotection (including stimulation of endogenous repair and cell-based approaches)
- Therapeutic regulation of senescence to enhance regenerative capacity of neural progenitor cells
- Determining impact of senescence on microglial/macrophage functions such as clearance of myelin debris
- Evaluating T and B cell senescence and its contribution to the transition of MS from an inflammatory to neurodegenerative condition
- Assessing astrocyte-endothelial integrity and maintenance of the blood-brain barrier
- Determining the contribution of senescent neurons/glia cells to neurodegenerative processes that lead to brain atrophy and disability progression
- Understanding mechanisms whereby juvenile MS patients experience secondary progressive MS sooner than adult patients, potentially indicating an accelerated aging process and premature biological aging.
- Elucidating the effectiveness of disease modifying therapy in MS during aging

Mechanisms of support:

The Society funds high-risk Pilot Research Awards to quickly test novel ideas. Funding is provided for one year to eligible researchers to test innovative, cutting-edge ideas or untested methods to understand the impact of aging on MS, and to gather enough preliminary data to apply for longer-term funding. We welcome applications for studies related to MS that may serve to advance our mission of stopping MS progression, restoring function and improving quality of life, and preventing MS. The Society supports fundamental as well as applied studies, non-clinical or clinical in nature, including projects in patient management, care and rehabilitation.

Funding: \$50,000 will be awarded based on the scientific merit of the study concept and must be justified based on the scientific research work plan. Facilities and administrative (indirect) expenses not to exceed 10% of the direct research expenses are allowable.

Eligibility: Researchers who have completed their post-graduate training, and who are considered eligible by their institutions to apply for a research grant, are invited to apply. Individuals who are currently postdoctoral fellows or the equivalent, or who are graduate/medical students or residents, are not eligible for support under this program. Applicants are not eligible to apply if they have an existing National MS Society pilot research award that expires later than the application deadline.

Submission guidelines and process: Important dates:

- Pre-applications will be accepted beginning **July 3rd, 2019**
- Final date for acceptance of pre-applications: **September 9th, 2019**
- Final date for receipt of completed full applications: **September 11th, 2019**

A brief pre-application is required to determine if a proposal is aligned with the objectives of the RfA. Inquiries with Society staff are strongly encouraged (see contact information below). Proposals 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 at [this link](#). Pre-applications should indicate that they are responsive to this MS-LINK RfA.

Applicants invited into full review will have until September 11th, 2019 to complete the application and submit all required documents. Proposals will undergo evaluation by the Society's Pilot Research Award review committee. Application information and reviews from projects determined to be meritorious for funding will be shared with EMD Serono scientific staff for final funding decision.

Inquiries:

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

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