

The MOG Project- Request for Applications (RFA)

Introduction

Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is a rare autoimmune disease that affects all ages, including children, and is present in both sexes. This disease is a relatively newly characterized inflammatory demyelinating disease of the central nervous system that is distinct from multiple sclerosis (MS) and aquaporin-4 (AQP4)-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG+NMOSD). Although recent investigations have uncovered new information about this disease, more research is urgently needed to further characterize the incidence and etiology, and improve diagnosis and treatment of MOGAD.

Background

The central nervous system (CNS) is encased by myelin, an insulating sheath around nerve cells that allows the efficient transmission of nerve impulses via nerve cell axons. Myelin oligodendrocyte glycoprotein (MOG) is a transmembrane protein found on the outer surface of the myelin and constitutes only a small portion (0.05%) of the myelin. MOG is also a marker of mature oligodendrocytes, which are the myelinating cells of the CNS and produce the insulating sheath of nerve axons. MOG is postulated to play a role in cell adhesion, microtubule stability and receptor function.

MOGAD presents with autoantibodies that target MOG, causing demyelinating diseases, including optic neuritis, transverse myelitis, acute disseminated encephalomyelitis (ADEM), and cerebral cortical encephalitis. Although the clinical features of the MOGAD diseases can overlap with those of multiple sclerosis (MS) and neuromyelitis optica spectrum disease (NMOSD), MOGAD possesses its unique radiologic, pathological, laboratory and clinical features that have now been recognized by the Center for Disease Control in Atlanta, GA, USA. International MOGAD diagnostic criteria have been proposed to the World Health Organization in Geneva, Switzerland. The pathophysiology of MOGAD is recently reviewed by Corbali and Chitnis (*Frontiers in Neurology* 14:1137998, 2023).

Purpose

The purpose of this award is to develop hypotheses and gather preliminary data to support the submission of a future unique proposal of the same subject or portion thereof for major funding from larger organizations such as NIH or the DOD CDMRP. This RFA is not intended for training of personnel or addition of funding to ongoing or existing funded projects. It will not support clinical trials. Research proposed in this RFA should address new, novel research of MOGAD in our stated subjects of interest.

Subjects of Interest

- Biomarkers in MOGAD: better diagnostic testing and biomarkers for relapse prevention.

- Efficacy of treatments (esp. SCIG vs. IVIG) and their mechanisms.
- Data collection to further inform overlaps and differences between MS/MOGAD/NMOSD, including radiological findings.
- Studies addressing optic neuritis mechanisms in MOGAD vs. MS
- Studies to inform the diagnosis of MOGAD via correlation of cerebral spinal fluid (CSF) and serum positivity for MOG antibodies.
- Studies addressing MOGAD and pregnancy.
- Studies addressing MOGAD and aging: pediatrics through puberty as well as adults transitioning to seniors (ages 55-60).
- Studies addressing the etiology of MOGAD.
- Immune mechanisms and triggers of relapse to understand why relapses occur in some patients.

Award Amounts and Number of Awards

A total amount of \$50,000 in awards is available for distribution. A total funding of 2-4 awards is anticipated.

Eligibility

Researchers at academic institutions with a full-time faculty position; research scientists in non-profit institutes; research scientists in the biotechnology sector who are eligible for NIH funding opportunities.

Period of Award

1 year from date of award notification. Extension requests up to an additional 6 months will be entertained and, if approved, will apply to all intended respondents.

Deliverables

The awardee should present the data at The MOG Project Medical Advisory Board Meeting in 2024. Data from the project must be used to apply for a larger grant funding opportunity, either in government, a larger non-profit institution, or a commercial entity such as a biotechnology company.

Important Dates

- RFA release: **April 24, 2023**
- Letter of Intent due **May 15, 2023**
- Question period ends **July 1, 2023** (Answers released within 5 business days of receipt.)
- Proposals due **July 15, 2023**
- Decisions will be communicated on or around **August 15, 2023**

Submission of Application Forms

General Information

- Use English only and avoid jargon and unusual or undefined abbreviations/acronyms. Use Ariel 11 black font; 0.5 inch margins. Although preliminary data is NOT REQUIRED, all graphs and tables submitted must be legible. Although no page limitation is specified for this part of the application, make every attempt to be succinct.
- Email completed applications to Lisa K. Ryan, Ph.D., Lisa.Ryan@mogproject.org on or before **July 15, 2023**. No proposals will be accepted after this date.
- Proposals and preliminary data submissions will remain confidential with The MOG Project and its reviewers. Each reviewer must sign a Non-Disclosure Agreement (NDA).
- Content of this RFA will not be discussed with or reviewed by potential applicants prior to the Release Date.
- The MOG Project will be open to questions up to **July 1, 2023**. Anticipated turn-around-time is five (5) business days. However, to show no preferential treatment, all questions and answers will be published to those with the intent to apply.

Format of the Application

Section 1: Summary and Administrative Information

Completion of all subsections is mandatory.

Subsection 1: Title of Application

Choose a title that is descriptive and specific, rather than general.

Subsection 2: Abstract of Research Plan

Include both a scientific and lay abstract.

Subsection 3: Principal Investigator/Program Director

Name the one or two persons responsible for the conduct of the project. This allows for those circumstances in which a fellow or technician is doing the research under the director of a physician or program director where the fellow is a co-investigator joining the primary investigator in a larger project or program. If the principal investigator / program director has more than one title, indicate the most relevant title to the project.

- Name
- Title
- Organizational Affiliation (e.g., University Department, Division, Section, Laboratory, Institute)
- Mailing Address
- Telephone

Subsection 4: Human Studies

If studies involving human subjects, derived materials, or data which contain personal identifiers, or which can be linked to personal identifiers, are neither planned nor contemplated, state “NO Human Studies Used”. If studies involving human subjects, derived materials, or data are planned or contemplated, state “YES Human Studies Used”. If YES, submit a letter from the institution review board (IRB) stating that the institution or equivalent entity will comply with HHS regulation 45 CFR 46 regarding human subjects in research with the grant application.

Subsection 5: Total Direct Costs Requested for Project Period

Provide the Total Direct Cost of the detailed budget breakdown found in Appendix A. Appendix A will be reviewed in detail.

Subsection 6: Performance Site(s)

List all performance sites where the project will be conducted. The detailed explanation is to be provided in Appendix I: Resources and Environments.

Subsection 7: Legal and Financial Accountability for Funds Awarded

- Name the Organization
- Type of Organization
- Fiscal Officer of Applicant Organization (Person who has fiscal responsibility for the funds and to whom the award checks will be sent).
- Official Signer for Applicant Organization
- Principal Investigator/Program Director Assurance
- Certification and Acceptance

Section 2: Table of Contents

Self-explanatory.

Section 3: Research Plan.

Ensure Subsections 1-4 of the Research Plan answers these questions: What do you intend to do? Why is the work important? What has already been done? How are you going to do the work? How does this support larger related projects (existing or future planned)?

Include all Subsections and if not applicable to the application enter “Not Applicable”.

Subsection 1: Specific Aims (1-page limit)

State concisely and realistically what the research described in this application is intended to accomplish and/or why hypothesis is to be tested.

Subsection 2: Significance (3-page limit)

Write the background of the proposal, evaluate existing knowledge, and specifically identify the gaps which the project is intended to fill. State concisely the importance of

the research described in this application by relating the specific aims to longer term objectives.

Subsection 3: Preliminary Studies (2-page limit)

Provide an account of the principal investigator's/program director's preliminary studies pertinent to the application and/or any other information that will help to establish the experience and competence of the investigator to pursue the proposed project. The titles and complete references to appropriate publications and completed manuscripts may be listed, and four (4) sets of such background materials may be submitted as an Appendix. Supplementary graphs, diagrams, tables, and charts relevant to the studies may also be submitted as Appendix material. Do not exceed two (2) pages for this section, excluding the lists of professional personnel and publications and the Appendix.

Subsection 4: Methods (No page limit)

Discuss in detail the experimental design and the procedures to be used to accomplish the specific aims of the project. Describe the protocols to be used and the tentative sequence of the investigation. Include how the data will be analyzed and interpreted. Describe any new methodology and its advantage over existing methodologies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised.

Subsection 5: Human Subjects, Derived Materials, or Data (2-page limit)

If Section 1, Subsection 4 has been marked "YES Human Studies Included", submit the following information:

1. Identify the sources of potential subjects, derived materials, or data. Describe the characteristics of the subject population such as their anticipated number, age, sex, ethnic background, and state of health. Identify the criteria for inclusion or exclusion. Explain the rationale for the use of special classes of subjects such as fetuses, pregnant women, children, institutionalized mentally disabled, prisoners, or others, especially those whose ability to give voluntary informed consent may be in question.
2. Describe the recruitment and consent procedures to be followed, including the circumstances under which consent will be solicited and obtained, who will seek it, the nature and extent of the information to be provided to prospective subjects, risks to prospective subjects and any mitigation plans (see subsection 4), and the methods of documenting consent.
3. Describe any potential risks (physical, psychological, social, legal, or other) and assess their likelihood, seriousness, and mitigation plans (see subsection 4 for detail) including, but not limited to contingencies and alternative methods, if any. Also, provide potential risks that were considered but not used and why they were not used.
4. Describe the procedures for protecting against or minimizing any potential risks and include an assessment of their likely effectiveness. Include a discussion of confidentiality safeguards, where relevant, and arrangements for medical treatment, if needed.

5. Describe and assess the potential benefits to be gained by the subjects, as well as the benefits that may accrue to society in general because of the planned work.
6. Discuss the risks in relation to the anticipated benefits to the subjects and to society.

Subsection 6: Laboratory Animals (2-page limit)

If laboratory animals have been identified in the Research Plan of the application, state the species, strains, ages, and numbers of the animals involved. If the animals are in short supply, costly, or to be used in large numbers, provide the rationale for their use and their numbers as well as the source of funding if different from this award. Describe the procedures for adequate care of any animals involved. Describe the procedures to avoid unnecessary discomfort, pain, or injury to the animals such as surgical anesthesia, post-trauma analgesia, tranquilizing drugs, and comfortable restraining devices.

Subsection 7: Consultants (1-page limit)

If consultant arrangements have been confirmed in writing, attach appropriate letters from each individual confirming his/her role in the project.

Subsection 8: Consortium Arrangements or Formalized Collaborative Agreements (2-page limit)

Provide a detailed explanation of the programmatic, fiscal, and administrative arrangements made between the applicant organization and the cooperating institutions. Provide a statement that the principal investigators/program directors and the applicant organizations involved in the application have established or are prepared to establish in writing the required inter-institutional agreements. Confirming letters or copies of written agreements may be attached.

Subsection 9: Literature Cited (No page limit)

Do not provide full literature citations throughout the text/document. Number the references in order of appearance and provide the complete citations corresponding to the numbers in a list at the end of the Research Plan. Each citation must include the names of all authors, the name of the book or journal, volume number, page numbers, and year of publication.

Section 4: Appendix

Do not email this material separately.

Appendix material will be made available to the primary reviewers and to any other reviewer. Graphs, diagrams, tables, and charts may also be submitted as Appendix material. Submit separate budgets for each applicant organization involved in consortium arrangements or formalized collaborative agreements.

Appendix A: Detailed Budget

List the direct cost requests for this application in an itemized list. Please note that awards are generally limited to \$25,000 but could be less based on the number of accepted proposals, all at the discretion of The MOG Project. Do not include any items

that are treated by the applicant as indirect costs, except for those associated with contractual or third-party costs. Do not show any cost-sharing contributions of the applicant.

Appendix B: Personnel

List the names and positions of all personnel involved in the project. Attach bio-sketches for all key personnel in Appendix J. Estimate the total percentage of time or effort, or hours per week, spent on the project for personnel. List the dollar amounts separately for each individual for salary (or hourly rate) and fringe benefits. Fringe benefits may be requested to the extent that they are treated consistently by the applicant as a direct cost to all sponsors. For each individual, state the percentage of time or effort, or hours per week, in relation to the total activity commitment of the applicant. In computing estimated salary charges, an individual's base salary represents the total authorized annual compensation that an applicant would be prepared to pay for a specified work period, whether an individual's time is spent on sponsored research, teaching, or other activities. Grant funds may not be used to augment salary.

Appendix C: Consultant(s)

Give the name and institutional affiliate for any consultants who have agreed to serve in that capacity, including consulting physicians in connection with patient care. Briefly describe the services to be performed, including the number of days of consultation, the expected rate of compensation, travel, per diem, and other related costs. Attach bio-sketches and letters of support for all key consultants in Appendix K.

Appendix D: Contractual or Third Parties

Describe and justify all appropriate costs for services purchased for or associated with third parties. No indirect costs will be considered.

Appendix E: Equipment

List separately each item of equipment with a unit acquisition cost of \$400 or more. If funds are requested to purchase items of equipment that appear to duplicate or to be equivalent to items listed on the Resources and Environment page or items used in preliminary studies, justify the reasons for the duplication.

Appendix F: Supplies

Itemize supplies in general categories such as glassware, chemicals, and animals in separate categories. If animals are involved, state how many are to be used, their unit purchase cost, and their unit care cost.

Appendix G: Travel

Describe the purpose of any travel, giving the number of trips involved, the destinations, and the number of individuals for whom funds are requested. Travel is not recommended for on-site personnel.

Appendix H: Other Expenses

Itemize other expenses such as publication costs, page charges, and books by category and unit cost. Itemize and justify such items as patient travel and per diem costs and donor fees. Reimbursement is allowable for personal expenses incurred by human subjects participating in the project, including travel with an escort if required. This reimbursement is applicable to all classes of research subjects, including inpatients, outpatients, donors, and normal volunteers, regardless of employment status.

Appendix I: Resources, and Environment

Self-explanatory. Since awards are generally less than \$25,000, other sources of funds for research are often necessary, and these should be identified.

Appendix J: Bio-Sketches for Key Personnel

Self-explanatory.

Appendix K: Bio-Sketches and Letters of Support for Consultants

Self-explanatory.

Appendix L: Other Supporting Material

Self-explanatory. Include material, description and relevance.