2022 Lupus Mechanisms and Targets Award (LMTA)
Request for Applications (RFA)

Release Date: December 7, 2021

Letter of Intent Due Date: March 1, 2022

Full Application Due Date: August 1, 2022

Earliest Start Date: March 2023

Purpose

The Lupus Mechanisms and Targets Award (LMTA) provides up to $200,000/year total costs for up to three years to support highly meritorious research focused on the identification and/or investigation of molecular pathways or targets with the potential to lead to new or improved therapies for patients with lupus.

Background

The Lupus Research Alliance (LRA) is the world's leading private funder of lupus research. The organization's mission is to improve treatments while advancing lupus towards a cure and prevention. At present, therapy for lupus is empiric and involves a variety of mostly nonspecific anti-inflammatory and immunosuppressive agents. While these treatments are frequently beneficial, many patients do not respond adequately and suffer significant side effects. Importantly, even patients with low disease activity accrue organ damage over time. There are many unanswered questions regarding the pathogenesis of lupus. Thus, new conceptual and therapeutic approaches are urgently needed. To enable the development of more effective and safer lupus therapies, and to address major barriers in lupus research and translation, the LRA has established the LMTA grant mechanism.

Note: the same research project may **not** be submitted for consideration to multiple LRA grant mechanisms in the same year. Such submissions will be triaged without review.

Award Goals

The goals of the LMTA are to: (1) characterize key steps in the pathogenesis of lupus that will allow for the development of new therapeutic agents; (2) promote basic and clinical research studies to identify and/or better characterize molecular pathways and cellular mechanisms that suggest promising approaches for lupus treatment; and (3) support research that facilitates the clinical evaluation of innovative approaches to the prevention, management or treatment of lupus and its complications.

LMTA grants are intended to be highly focused on lupus and, as such, should lead directly to knowledge that will facilitate drug discovery and/or testing of new treatments that may be used to treat systemic or organ-specific manifestations of the disease. As the goal of this program is to **advance the treatment of lupus and the outcomes for lupus patients**, projects must be based on **realizable goals for** ultimate **translation into therapeutic discovery programs**. LMTA research can lay the groundwork for development of therapeutics that include small molecules, biologic agents, vaccines, gene therapy, as well as predictive biomarkers and novel approaches in public health and risk reduction.

The LRA encourages applications proposing research that will apply knowledge gained in other disease areas (e.g., other autoimmune and inflammatory conditions, cancer, metabolic diseases) to mechanisms relevant to lupus. These studies can be initiated or conducted in either humans or animals, although any work on animals must include a plan for extension and verification in patient populations. Studies working towards the identification or validation of lead therapeutic compounds for lupus must provide a clear scientific rationale for the compound(s) under investigation, and a research plan that would enable a decision regarding the viability of the compound(s) as a therapeutic approach in lupus. Clinical studies to improve the ability to evaluate innovative therapies in lupus may focus on mechanistic studies and/or the development of systems or processes that enhance the ability to obtain reliable and timely answers to therapeutic questions in lupus. The LRA encourages the use of previously collected longitudinal and/or cross-sectional patient samples and/or data.

Research Priority Areas

In keeping with the strategic research objectives of the LRA, priority consideration will be given to projects that address understanding of lupus heterogeneity or enable patient stratification by active disease mechanism and ideally employ emerging technologies to address these priority areas.

Areas of interest include but are not limited to:

- Defining pathogenic cell types in human lupus using state-of-the-art approaches;
- Defining the drivers of the type I interferon signature in lupus;
- Developing and applying *ex-vivo* human models of immune cell interactions for disease modeling
- Defining the role of the microbiome in disease pathogenesis and treatment in human lupus
- Identifying ancestral differences in the presence and importance of disease pathways in lupus, such as those underlying lupus nephritis;
- Correlating clinical features of SLE with peripheral biomarkers;
- Characterizing the immunologic and molecular factors that differentiate responders from non-responders in each class of biologic therapeutics currently being used or tested in SLE.

Eligibility

Individuals with a doctoral degree (MD, PhD, DO or equivalent), holding a faculty, or equivalent, position and leading an independent research team at an academic, nonprofit, or government research institution are eligible to apply. There are no citizenship requirements. Collaborations between academia and industry can be appropriately supported. Federal government research laboratories are not eligible for this award.

Application Guidelines

Applications must be submitted electronically, via ProposalCENTRAL by 11:59 pm ET on the stated deadline. All resubmissions of formerly declined Target Identification in Lupus (TIL) applications must be submitted under the LMTA grant mechanism and must follow the general resubmission guidelines below.

A two-stage application process will be employed. A 2-page Letter of Intent (LOI) will be used to evaluate the novelty, significance, and alignment of the proposed project concept with the LMTA funding mechanism. Applicants whose LOIs have successfully passed this first peer-review stage will be invited to submit full applications.

I. *Letter of Intent*

A 2-page LOI, inclusive of text, figures, tables, legends but excluding references, must be submitted electronically, via ProposalCENTRAL, by 11:59 pm ET on the stated deadline. It should contain the following information:

1. *Brief background*: Provide a succinct contextual framework for the proposed project. This section may be particularly valuable to applicants new to lupus and applying knowledge from other scientific areas—that need to be introduced—to bear on lupus.

2. *Objective and Specific Aims*: State the overall objective and outline the specific aims.

3. *Project plan*: Describe the innovation, significance, and approach for the proposed project.

4. *Resource assessment*: Assess your ability to carry out this project and outline resources you may need to accomplish it, such as access to proprietary reagents or technologies and key collaborators. If the applicant's primary scientific expertise is outside of lupus, please describe how you intend to apply your unique knowledge to address a critical issue in the pathogenesis and/or treatment of lupus.

In addition to the 2-page LOI, applicants should submit NIH-style Biosketch for all key personnel working on the project. This should also include a description of other financial support available to the applicant(s) for their research endeavors. International applicants may submit a copy of their curriculum vitae listing all funding sources.

Only one LOI may be submitted by the principal investigator per grant cycle.

II. *Full Application*

Full applications may be submitted only by applicants whose LOI has been approved and who have been invited by the LRA to advance to the next stage of the review process. Applications must be submitted via ProposalCENTRAL by 11:59 pm ET on the stated deadline. Submissions must be completed using 12-pt Times New Roman font or equivalent and must contain the below-listed components:

1. *Lay Abstract:* A summary of the proposed research and its potential significance to the fundamental causes of lupus, not exceeding 3,000 characters and written in lay language geared to a sixth-grade reading level and suitable for use in publications. Please do not submit a scientific abstract in this section.

2. *Scientific Abstract:* A technical summary of the proposed research, written in scientific terms and not exceeding 3,000 characters. Investigators should highlight the relevance of the work to lupus.

3. *Research Plan*: A description of the proposed research, not exceeding 12-pages excluding references, should be clearly formulated under the following subheadings:

    A. Background
    B. Significance and Innovation: highlight the significance and novelty of the work, describe the relevance of the project to the cause, cure, treatment or prevention of lupus and/or its secondary complications as well as emphasize the relevance of the project to the goals of the LMTA program.
    C. Hypothesis and Specific Aims
    D. Preliminary Data
    E. Experimental Design and Methods including feasibility, anticipated outcomes, and alternative strategies
    F. Milestones: List the expected status of the project at various time points for the duration of the grant. The list of milestones, ideally presented in a table format, should reflect the specific aims of the proposal. These milestones will be used to evaluate progress and to facilitate communication between the principal investigators and the LRA.

4. *Biosketch:* A standard NIH Biosketch for all key personnel working on the project should be provided. International applicants may submit a copy of their curriculum vitae.

5. *Detailed Budget and Summary:* A budget for the project should be prepared in U.S. dollars. The budget should be for up to three years and should not exceed $200,000 per year, including 10% indirect costs. The LMTA does not provide funds for major pieces of laboratory equipment.

6. *Budget Justification:* A detailed justification for the budgetary requests must be provided. The information in this section should be divided into two sections. The first section should include the following line items: personnel, consultant costs; equipment and supplies (both office and medical or laboratory). The second section should include all other line items including but not limited to: travel to annual investigator's meeting, patient care, other expenses, consortium and

contractual costs. Funds cannot be used to pay for tuition or education expenses. Each section should not exceed 2,000 characters. Any additional information should be included as an appendix to the application.

7. *Other Support:* A description of other financial support available to the applicant(s) for his/her research endeavors should be provided. Applicants must list current and pending grant applications, their specific aims, funding amounts, percent effort, funding period and the extent of scientific overlap with the proposed research, if any. If overlap exists, a statement regarding intended dispositions of funds in the event of dual granting is required. International applicants must include all funding sources and clearly explain scientific overlap with the proposed work, if any.

8. *Facilities & Equipment Description:* A succinct description of the facilities and equipment available to support the project.

9. *Assurances:* Appropriate institutional assurances regarding human subjects and animals as applicable.

10. *Consent Forms:* If relevant, copies or drafts of all informed consent forms, to be distributed to participants for signature in this study (or their legal guardians), should be provided.

11. *Consultant/Co-Investigator/Collaborator Letters:* Optional, only submit if relevant to the application.

12. *Signed Cover Page:* The signed cover page, which reflects the applicant's agreement to abide by the rules governing grant awards from the LRA, should be uploaded electronically. Instructions are available on the ProposalCENTRAL website.

13. *Supplemental Material:* Applicants can submit supplemental material (limited to 1 page), which: a) was acquired following the submission of the applicant's LOI, and b) substantially bolsters the proposal. Examples of appropriate supplemental information include an accepted relevant manuscript or additional preliminary data. This must be submitted via e-mail to Diomaris Gonzalez (dgonzalez@lupusresearch.org) no later than July 26, 2022.

Review Criteria

LOI

The LOI will be evaluated based on the project plan, its alignment with the LRA's strategic research objectives and the goals of the LMTA.

Full Application

The scientific review group will consider each of the following criteria in assigning the application's overall score, weighting them as appropriate for each application.

1. *Relevance:* Is the proposed project relevant to lupus and aligned with the goals of the LMTA grant mechanism and the mission of the Lupus Research Alliance?

2. *Significance* of the project as indicated by the likelihood that the work will:
    - characterize key steps in the pathogenesis of the disease that will allow for the development of new therapeutic agents or biomarkers.
    - promote basic and clinical research studies to identify and/or better characterize promising lead compounds for lupus treatment.
    - support research that facilitates the clinical evaluation of innovative approaches to the prevention or treatment of lupus and its complications.
3. *Approach*: are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?
4. *Innovation*: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
5. *Feasibility:* Can this project be accomplished within a three-year time frame?
6. *Investigator*: Is the investigator appropriately trained and well-suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?
7. *Environment*: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

Terms of Award

LMTA grants will be supported for up to $200,000/year for up to three years. Indirect costs should not exceed 10% of the total budget and must be included within the $200,000 annual budget cap.

The LRA is committed to the publication and dissemination of all information and materials developed using the LRA's resources. All recipients of LRA awards must agree to this principle and must take steps to facilitate availability of data and materials.

Grant recipients are required to attend the LRA Annual Scientific Conference, Forum for Discovery. Travel funds, provided by the grant award, must be used to attend this meeting.

Resubmission Information

- A resubmission is considered an application that was not selected for funding in the previous application cycle. An applicant may resubmit the revised application only once.
- A brief .5-page resubmission statement (up to 300 words) must be provided at the beginning of LOI for all resubmissions. It should highlight the changes and explain how modifications address the reviewers' concerns. The resubmission statement does not count towards the overall LOI page limit.
- A 1-page resubmission statement (up to 500 words) must be provided at the beginning of the Research Plan if an applicant is invited to submit full application. The resubmission statement should highlight the changes and explain where **(**additions, deletions, revisions) and how the revised application has been modified to address the reviewers' concerns.
- A copy of the summary statement for an application that has not been selected for funding must be included in the appendix of the proposal. If you have not received a summary statement, please contact the LRA research staff.
- If major changes are made to the original application or if the applicant is planning to submit an entirely different/new project, the proposal should not be submitted as a resubmission.
- Applicants should contact the LRA research staff with any questions.

Review Process

All grant applications will be peer-reviewed by a Study Section of the LRA. Results from that peer review will be forwarded to the LRA Scientific Advisory Board (SAB). The SAB will consider the recommendations from the Study Section, in the context of the existing LRA grant portfolio and LRA's strategic research priorities. The SAB will submit their recommendations to the LRA Board of Directors. The Board will consider all the previous recommendations and will also provide a lay perspective. This perspective will include patients' concerns and expectations, as well as deliberations on the business aspect of funding the recommended grants. The LRA Board of Directors will make all final funding decisions.

Review Feedback

For applications receiving a full review, a summary statement containing the reviewers' critiques will be provided. Applications not recommended for full review will receive abridged feedback. The LRA does not provide application scores or rankings to applicants.

Key Dates

RFA Release:	December 7, 2021
Letter of Intent Due:	March 1, 2022
Letter of Intent Decision:	June 15, 2022
Full Applications* Due:	August 1, 2022
Response to Applicants†:	December 2022
Earliest Anticipated Start:	March 2023

*By invitation only with an approved LOI
†Full applications only

Scientific Inquiries:
Jana Barlic-Dicen, PhD
Scientific Program Manager
Lupus Research Alliance
jbarlicdicen@lupusresearch.org
+1-646-884-6086

Administrative Inquiries:
Diomaris Gonzalez
Director of Grant Programs
Lupus Research Alliance
dgonzalez@lupusresearch.org
+1-646-884-6056

proposalCENTRAL:
For help with the electronic grant application process, please contact the help desk of ProposalCENTRAL pcsupport@altum.com; +1-800-875-2562, extension 227.