



## Request for Applications 2023 Lupus Mechanisms and Targets Award \$600,000 over 3 years

### CONTENTS

Background.....	1
Program Description.....	1
Eligibility.....	3
Application Process and Instructions.....	3
Key Dates.....	4
Letter of Intent.....	4
Full Application.....	6
Review Criteria.....	6
Award Terms and Conditions.....	7
Inquiries.....	8

### BACKGROUND

The Lupus Research Alliance (LRA) is the largest private funder of lupus research worldwide. The organization aims to transform lupus treatment while advancing towards a cure by funding cutting-edge, innovative research.

At present, therapy for lupus is mostly empiric and involves largely non-specific anti-inflammatory and immunosuppressive agents. While these treatments are frequently beneficial, many patients do not respond adequately or 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 Lupus Mechanisms and Targets Award (LMTA).

### PROGRAM DESCRIPTION

The LMTA provides up to \$200,000 per year for up to three years. It provides support for 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. Investigators at all stages of their independent research careers are encouraged to apply. To promote a diverse scientific workforce, the program also specifically encourages submissions by underrepresented minority independent research

investigators working in academic or equivalent research institutions across the United States or Canada.

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 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 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 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 or cross-sectional patient samples or data.

**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.**

Applicants are encouraged to consult with LRA scientific staff to discuss the responsiveness of their proposal to this program.

### ***Research Priority Areas***

In keeping with the [LRA's strategic priorities](#), projects that address defining human lupus heterogeneity by molecular pathway or enabling patient stratification based on active disease mechanisms and that also employ emerging technologies to address these areas will be given priority consideration.

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. US federal government research laboratories are not eligible for this award.
- There are no citizenship requirements for investigators applying to this program.
- Applicants with total active LRA funding of US\$600,000 or more (NCEs exempted) are not eligible to receive additional funding from the LRA unless there are exceptional circumstances.
- Applicants who have previously received LRA funding must also be up to date with all progress and financial reports and other Terms and Conditions of the original award(s) at the time of applying.
- Projects with significant overlap with currently active LRA-funded grants will not be considered and may be administratively withdrawn. Applicants are advised to review the [LRA research portfolio](#) to determine if overlap exists and may consult with the LRA's scientific staff if necessary.
- Collaborations between academia and industry can be appropriately supported.

## APPLICATION PROCESS AND INSTRUCTIONS

A two-stage application process will be employed. A two-page Letter of Intent (LOI) will be used to judge the novelty, significance, and alignment of the proposed project with the LMTA funding mechanism. Applicants whose LOIs successfully pass this first review stage will be invited to submit a full application in the second stage of the application process.

### KEY DATES

RFA Release:	December 20, 2022
Letters of Intent Due:	March 1, 2023
Letter of Intent Decision:	June 2023
Full Applications Due*:	August 1, 2023
Full Application Decision:	December 2023
Expected Start Date:	March 2024

\*By invitation only with an approved LOI

### LETTER OF INTENT

LOIs must be submitted electronically, via [ProposalCentral](#), by **11:59pm US ET on the stated deadline**. LOIs will not be accepted via any other means.

The following information is required to submit a complete LOI. Numbers correspond to the application sections found on the left side of the ProposalCentral website.

1. **Title Page:** Enter the title of the proposed project. Indicate whether the LOI is a resubmission and, if so, select the prior application from the dropdown menu.
2. **Download Templates & Instructions:** The Request for Applications and Letter of Intent template can be downloaded from this page.
3. **Enable Other Users to Access this Proposal:** Enter the information for any other users who will need to work on the LOI.
4. **Applicant/PI:** The applicant's information is pre-loaded with the contact information from their ProposalCentral profile. Click the Edit Professional Profile button if any changes need to be made. Upload a standard [NIH Biosketch and Other Support Format Page](#), which should detail other financial support available to the applicant for their research endeavors. Applicants who are not based in the United States may submit a copy of their curriculum vitae, which must be limited to five pages in length.
5. **Institution:** The institution will be pre-loaded with the applicant's institution.
6. **Letter of Intent & Other Attachments:** Upload the Letter of Intent, including Resubmission Statement (if applicable), and biosketches/CVs for all key personnel as PDFs.
  - A. **Letter of Intent (LOI):** The Letter of Intent template provided on ProposalCentral must be used. Margins must not be less than .5 inches on each side and 12-point Times New Roman or the equivalent should be used for the text. The LOI, excluding the resubmission statement (if applicable) and references, **should not exceed two pages**. Figures, tables, and legends are included in the page limit. The information listed below must be included in the indicated order.

- i. **Resubmission Statement (if applicable):** Revised applications are required to include a resubmission statement, not to exceed a half page (300 words). The statement should highlight any major changes and explain how the modifications address the concerns of the original review panel.
    - A resubmission is an application that was not funded in one of the previous two application cycles.
    - An applicant who is unsuccessful may revise their original application only once.
    - If substantial changes are made to the original application, the application should not be submitted as a resubmission.
  - ii. **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.
  - iii. **Objective and Specific Aims:** State the overall objective and outline the specific aims.
  - iv. **Impact Statement:** Provide a succinct statement about the potential of the proposed research to improve the standard of care or quality of life of people with lupus.
  - v. **Project Plan:** Describe the innovation, significance, and approach for the proposed project.
  - vi. **Resource Assessment:** Assess your ability to carry out this project and outline the resources needed, 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 the applicant’s unique knowledge will be applied to address a critical issue in the pathogenesis or treatment of lupus and, importantly, how the applicant will leverage the expertise of their lupus collaborators to maximize the lupus impact of the project.
- B. **Biosketch(es):** Submit a standard NIH-style biosketch for all key personnel working on the project. A curriculum vitae may be submitted for key personnel not based in the United States.
7. **Validate:** Click the “Validate” button to check for any missing required information or attachments.
  8. **Sign:** Click the “Sign” button to electronically sign the LOI. By signing, the applicant certifies that the information contained in the LOI is true, complete, and accurate to the best of their knowledge.

9. **Submit:** After successfully passing the validate check, click the “Submit” button. An e-mail will be sent confirming submission.

### LOI Restrictions

- Only one LOI will be accepted per applicant in a grant cycle.
- Applicants with total active LRA funding of US\$600,000 or more (NCEs exempted) are not eligible for additional funding from the LRA unless there are exceptional circumstances.

### **FULL APPLICATION**

Full applications may be submitted only by applicants whose LOIs have been approved to advance to the next stage of the review process. Applications must be submitted electronically, via [ProposalCentral](#), **by 11:59pm US ET on the stated deadline**. Detailed instructions for the full application will be available on ProposalCentral. The full application site will only be accessible to applicants with approved LOIs.

### **REVIEW CRITERIA**

#### *LOI Review*

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 Review*

The scientific review group will consider each of the following criteria in assigning the application’s overall score, weighing 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 LRA?
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?

The **Impact Statement** will be used by the LRA Scientific Advisory Board to prioritize funding among the top scoring applications.

### Review Process

All eligible grant applications will be peer-reviewed by a panel of external reviewers, the results from which will be considered by the LRA Scientific Advisory Board (SAB) in the context of the LRA grant portfolio and LRA's strategic research priorities. The SAB will make funding recommendations to the LRA Board of Directors, which will, in turn, consider all previous recommendations and provide a lay perspective including patients' concerns and expectations, as well as deliberations on the business aspects of funding the recommended grants. The LRA Board of Directors will make all final funding decisions.

### Review Feedback

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

### AWARD TERMS AND CONDITIONS

The LMTA provides up to US\$200,000 per year for up to three years. Indirect costs must not exceed 10% of the total budget and must be included within the \$200,000 annual budget cap.

Grant recipients must attend and present at Forum for Discovery, the LRA annual scientific conference, each year. Travel funds (up to \$2,000 per year) provided by the grant must be used to pay for travel expenses related to attending Forum for Discovery meetings.

The LRA is committed to the publication and dissemination of all data/information and materials developed using the organization's resources. All recipients of LRA awards must facilitate availability of data and materials by executing a Data Sharing Plan based on the [2023 NIH Data Management and Sharing Policy](#).

## **INQUIRIES**

### **Scientific:**

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### **ProposalCentral:**

For assistance with the electronic grant application process, please contact ProposalCentral at [pcsupport@altum.com](mailto:pcsupport@altum.com) or 800-875-2562, extension 227.