



## **Request for Applications 2024 Targeted Research Program on Engineered Cell Therapies for Lupus \$300,000 or \$600,000 over 2 years**

### **CONTENTS**

Background .....	1
Program Description .....	2
Eligibility .....	3
Application Process and Instructions.....	4
Key Dates.....	4
Letter of Intent .....	4
Full Application .....	5
Review Criteria.....	6
Award Terms and Conditions .....	6
Inquiries .....	7

### **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, treatment 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 and/or suffer significant side effects. Importantly, even patients with low disease activity accrue organ damage over time. Thus, new conceptual treatments and potential curative approaches with robust and longer-lasting effects are urgently needed. In recent years, the notion of therapeutically resetting or reprogramming the immune system by specifically targeting the autoreactive immune response has become a viable therapeutic strategy attempting to achieve this goal.

Engineered cell therapies have emerged as a powerful potential therapeutic approach to treat and possibly cure lupus. A small, academically led clinical trial using CD19-directed Chimeric Antigen Receptor T-cell (CAR-T) therapy demonstrated complete remission for over three years, with continued effect, in patients with severe lupus nephritis who were previously resistant to standard-of-care medications. Thus far, although very involved, this treatment approach has shown relatively low toxicity or side effects. Since the release of preliminary results of this landmark study, an upsurge of research activities applying CAR-T and other engineered cell therapy approaches to treating lupus is underway, both in academic and commercial settings, with many different clinical trials listed on

clinicaltrials.gov, many other IND approved and early phase evaluations initiated, and numerous biotech companies launched on this premise. Different engineered cell platforms, receptor targets, antigen-binding domain designs and engineering methods are being pre-clinically and clinically evaluated.

Despite these encouraging developments, the current iterations of engineered cell therapies being clinically tested are costly, entail complex cell production and manufacturing processes, and require elaborate and potentially risky pre-conditioning regimens, which could result in limited patient access and a high threshold for treating only the most severe lupus cases. To enable accessibility across all patient demographics and socioeconomic status, as well as heterogeneous lupus pathologies, improved and alternative engineered cell therapy approaches should also be explored. Cost-effective mRNA-based or universal CAR methods, in addition to more efficient cellular platforms that require lower cell infusion or more lenient pre-conditioning regimens, are some examples.

To promote a variety of strategies and seed a robust pipeline, the LRA has established the **Targeted Research Program on Engineered Cell Therapies for Lupus (TRP-ECT)** as a dedicated funding mechanism to support the development and mechanistic understanding of safe and accessible next-generation engineered cell therapies for lupus patients.

### **PROGRAM DESCRIPTION**

The TRP-ECT provides funding for projects that advance the development of potential engineered cell therapies with a **clear and direct relevance to people with lupus**. Two main types of studies will be considered:

1. **Preclinical studies**, including discovery and translational projects, will be supported with **up to \$300,000 over two years**. Projects can investigate a range of cellular platforms, targets, engineering approaches, and experimental models. Late-stage preclinical studies, devising of new processes, procedures, and regimens, as well as IND-enabling activities, will also be supported.

Preclinical studies can encompass the following research areas, including, but not limited to, the examples listed:

- Pre-clinical evaluation of new engineered cell therapies for lupus, including novel platforms such as iPSCs-based therapies or allogeneic CAR immunotherapy
- Investigations of in vivo or transient engineering approaches, such as injectable mRNA and other novel engineering techniques for use in lupus cell therapies
- Evaluation of different antigen-binding domains or lupus specific autoantibody-expressing cellular targets
- New and improved construct design and gene editing approaches for use in lupus cell therapies
- Design and development of new lupus cell therapy experimental model systems, including humanized systems
- Late-stage preclinical studies, such as in vitro or in vivo toxicity and efficacy testing

- Preclinical evaluation of novel production methods or improved pre-conditioning regimens
2. **Ancillary studies** to ongoing or completed lupus engineered cell therapy clinical trials, funded by a third party, will be supported with **up to \$600,000 over two years**. Ancillary study projects can utilize samples and study data from current or completed engineered cell therapy trials, as well as devise new trial-adjacent processes, procedures, and regimens. Clinical trials will not be supported.

Ancillary studies to engineered cell therapy trials in lupus can encompass the following research areas, including, but not limited to, the examples listed:

- Companion biomarker discovery and development, such as for patient stratification or therapeutic response
- Non-standard analysis of patient samples that have undergone CAR-T or another engineered cell therapy to further understand the mechanism of action and/or therapeutic response
- Design of improved lymphodepletion or pre-conditioning regimens as part of an initiated or ongoing trial
- Exploration of novel manufacturing and production methods and processes as part of an initiated or ongoing trial

All proposals should be centered around a well-defined translational plan to advance the project to the next development stage. For project proposals outside of the described scope, please contact LRA research staff to discuss the responsiveness of your application to the program.

## **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.

### ***Special Considerations regarding For-profit Collaborators***

The LRA recognizes the need for for-profit partnerships and collaborations to enable certain ancillary studies. Partnerships and cost sharing agreements between the applicant and for-profit organizations are allowed and encouraged. Should the LOI proceed to full application, for-profit involvement will be evaluated on a case-by-case basis.

Under certain circumstances, with a strong demonstration of financial need, the scientific or medical officer representing a for-profit organization can apply as the primary investigator. Please contact LRA scientific staff to consult on this issue.

Applicants who have previously received LRA funding must also be current and in good standing with all required reports and previously agreed to Terms and Conditions of the LRA-funded project(s) at the time of application submission.

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.

**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.

### APPLICATION PROCESS AND INSTRUCTIONS

A two-stage application process will be employed. A Letter of Intent (LOI) will be used to judge the innovation of the approach, significance, and alignment of the proposed project with the TRP-ECT funding mechanism. For ancillary projects related to clinical trials, emphasis will also be given to feasibility of gaining timely access to samples and/or data from the related clinical trial. Applicants whose LOIs successfully pass this first review stage will be invited to submit a full application. Applicants are encouraged to consult with LRA scientific staff to discuss the responsiveness of their proposal to this program.

#### KEY DATES

RFA Release:	April 15, 2024
Letters of Intent Due:	May 29, 2024
Letter of Intent Decision:	July 2024
Full Applications Due*:	September 9, 2024
Full Application Decision:	December 2024
Expected Start Date:	March 2025

\*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 applicant is currently funded by the LRA. Indicate whether the proposed project involves the use of human samples and/or data.
2. **Download Templates & Instructions:** The Request for Applications and Letter of Intent template and instructions 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 all other financial support (current as of the date of application submission) available to the applicant for all 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 and biosketches/CVs for all key personnel as PDFs.
  - A. **Letter of Intent (LOI):** Adhere to the specific instructions and guidelines and use the Letter of Intent template provided on ProposalCentral. Note that pre-clinical or ancillary study proposals have distinct instructions.
  - 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. **PI Data Sheet:** Please verify the applicant's gender, race, and ethnicity. This information will not be used during the selection process.
8. **Validate:** Click the "Validate" button to check for any missing required information or attachments.
9. **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.
10. **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 per grant mechanism in a grant cycle (LOIs on distinct projects can be submitted to other grant mechanisms).

#### **FULL APPLICATION**

Full applications may be submitted only by applicants whose LOIs have been approved to advance to the second 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**

The most important review criterion is project innovation, significance, and approach. For ancillary projects to clinical trials, emphasis will also be given to feasibility of gaining timely access to samples and/or data from the related clinical trial. Other criteria will also be considered, including patient impact. Applications that are not aligned with the outlined objectives of this funding mechanism, as well as the goals and the mission of the LRA, will not be peer-reviewed.

## **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 within three months of the funding decision notification date. The LRA does not provide scores or application rankings to applicants.

## **AWARD TERMS AND CONDITIONS**

The TRP-ECT provides up to US\$150,000 per year over two years for discovery, translational and preclinical projects, and up to \$300,000 per year over two years for clinical trial ancillary projects. Once an execution payment is made, distribution of periodic scheduled payments will be contingent upon timely and satisfactory completion of progress reports and execution of project milestones, as determined by the Scientific Program Officer with input from external experts where necessary. Indirect costs must not exceed 10% of the total budget and must be included within the \$300,000 or \$600,000 annual budget cap.

Grant recipients must attend and present each year at the Forum for Discovery, LRA's annual scientific conference. 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 data/information and materials developed using the organization's resources. LRA staff will work with the awardees of this funding mechanism to enable this key LRA principle while ensuring intellectual property and commercialization potential.

## **INQUIRIES**

### **Scientific:**

Maya Bader, PhD  
Associate Director of Research  
Lupus Research Alliance  
[mbader@lupusresearch.org](mailto:mbader@lupusresearch.org)  
+1-646-884-6086

### **Administrative:**

Diomaris Gonzalez  
Director of Grant Programs  
Lupus Research Alliance  
[dgonzalez@lupusresearch.org](mailto:dgonzalez@lupusresearch.org)  
+1-646-884-6056

### **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.