



Request for Applications 2026 Mechanistic Clinical Award \$750,000 over 3 years

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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, and translationally relevant research.

Despite significant translational advances in recent years, and a continuously expanding therapeutic pipeline, major clinical needs remain unaddressed in lupus. While existing treatments are frequently beneficial, many patients do not respond adequately or suffer significant side effects—further confounded by the heterogeneity of the disease and the diverse population impacted. Importantly, even patients with low disease activity accrue organ damage over time. Thus, new conceptual and therapeutic approaches to augment currently available treatment options are urgently needed.

In addition to pharmacologic agents, lifestyle interventions hold great promise for improving outcomes in lupus. Defined as evidence-based clinical care that supports behavior change, lifestyle interventions can be applied to improve mental health, social connection, diet, exercise, and sleep, as well as to minimize stress and harmful exposures. In the context of lupus, these interventions have the potential to affect both clinical outcomes and quality of life. Many individuals with lupus may already employ some form of lifestyle modification to manage their disease, be it diet, exercise, or monitoring with personal health devices. A more comprehensive and evidence-based

understanding of lifestyle intervention effects and underlying mechanisms would enable broader adoption and expand our therapeutic armamentarium.

To advance a precision medicine framework for therapeutic development in lupus, the LRA has developed the **Mechanistic Clinical Award (MCA)**. In 2026, the MCA will focus on the exploration of **lifestyle interventions** and leverage LRA capabilities across the research continuum, including its Research Program and the Lupus Nexus, as well as the Lupus Therapeutic's led Lupus Clinical Investigators Network (LuCIN).

- **Lupus Nexus (LNx)** is the LRA's lupus registry, biorepository, and knowledge portal. It offers a rich source of highly curated, longitudinal, clinical and patient-reported data with linked biospecimens, allowing investigators to address emerging questions in lupus research. Biospecimens from 600 patients (a number that is continuously growing) include whole blood and blood derivatives, urine, saliva, and stool. Applicants using pre-existing clinical data or patient biospecimens available are encouraged to use LNx samples as part of their research plan. For more information on LNx, please contact lupusnexus@lupusresearch.org.
- **Lupus Clinical Investigators Network (LuCIN)** is a network of 60+ premier lupus medical research centers across North America comprised of 250+ providers with expertise in lupus care and clinical trials. Founded and sponsored by the LRA, with oversight by its fully owned affiliate, Lupus Therapeutics, LuCIN brings together experts to evaluate the safety and effectiveness of potential new treatments for lupus. As the clinical research affiliate of LRA, Lupus Therapeutics partners with biopharmaceutical companies, clinical investigators, and community organizations to improve and accelerate the clinical research process.

PROGRAM OBJECTIVES AND SCOPE

The award will fund pilot studies with the goal of testing lifestyle interventions in concert with hypothesis-driven mechanistic analysis to illuminate the underlying effects. Areas of focus for interventions may include physical activity and exercise, diet and nutrition, mental health, mindfulness practices, harmful exposure prevention (e.g., sun exposure, smoking, alcohol, etc.), sleep, and social relation-based interventions. While findings in these studies may eventually support efficacy improvements in both clinical and patient-reported measures, **the primary outcome of the MCA studies must be mechanistic**. Please note that all mechanistic analyses must be designed to identify hypothesis-driven molecular, cellular, or physiologic changes. If the sole mechanistic aim *lacks* the pursuit of specific, pre-identified markers or measures, detailed below, the proposal will not be considered.

RESEARCH EMPHASIS AREAS

Research projects should focus on testing lifestyle interventions that have the potential to **improve the well-being of those living with lupus**—with an eye toward supporting future efficacy studies that influence laboratory, clinical, or patient-reported outcomes (e.g., fatigue, social interactions, cognitive impairment). Examples include, but are not limited to:

- Comprehensive serum analysis following guided exercise training, in pursuit of specific inflammatory markers
- Wearable device measures and corresponding molecular analysis in response to a sleep regimen
- Cognitive behavioral therapy followed by neuroimaging
- Dietary supplement regimen coupled with cellular fecal analysis

Mechanistic analyses must include pre-identified molecular markers or measures, such as specific gene expression changes, epigenetic alterations on pre-specified genes of interest, spatial analysis in pursuit of discrete cell population changes, etc. They may also include physiological or morphological changes, such as those detected by MRI, tissue imaging, electrophysiologic analysis, etc.

Please consult with LRA Scientific Staff (kfischer@lupusresearch.org) for any questions regarding the relevance of your proposed project.

PROGRAM CONSIDERATIONS

The MCA will support pilot lifestyle intervention studies with up to \$750,000 for up to three years. The primary outcome of any studies submitted for consideration must be mechanistic in nature; studies with efficacy as a primary outcome will not be considered.

- To ensure a robust analysis that would inform the underlying mechanism of interventions, project teams must include the appropriate expertise, such as:
 - Clinical investigators to ensure safe and appropriate study design and execution
 - Biomedical scientists for the pursuit of molecular analysis or other mechanistic measures
 - Experts in the proposed lifestyle intervention, e.g. behavioral science, nutrition, exercise science, etc.
- Studies exceeding 20 participants must provide justification and demonstrate recruitment feasibility. There should be no more than three clinical study sites.
- Applicants must demonstrate project feasibility, including administrative and regulatory approvals, access to the intervention and letters of support from third-party participants, if applicable.
- Where possible, the LRA prefers that trials be conducted within LuCIN, utilizing LuCIN centers. Investigators who are outside the LuCIN network may wish to establish a collaboration within the network to apply. *For further information on connecting with LuCIN centers, please consult the [LuCIN Center Directory](#) and contact scientific staff at least four weeks prior to the application due date.*
- Regulatory and IRB approval are required, as appropriate, at the first study site; and submission of the full clinical protocol will be required within three months of the date of the grant award letter. Failure to do so may result in termination of the award.
- Demonstration that individuals with lupus and/or their advocates contributed to or were consulted on the study design is strongly encouraged.

For project proposals outside of the described scope (number of participants or sites), please contact LRA scientific staff to discuss the responsiveness of your application to the program.

ELIGIBILITY

Applicants must have a doctoral degree (MD, PhD, DO, or equivalent); hold a faculty or equivalent position; and lead an independent research team—i.e., your institution enables you to apply for a non-training grant independently as the primary PI—at an academic, nonprofit, or government research institution. 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 studies. Partnerships and cost sharing agreements between academic applicants and for-profit organizations are allowed and encouraged. Please contact LRA scientific staff to consult on this issue.

Applicants who previously received LRA funding must be 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.

Applicants who previously submitted a lifestyle intervention proposal to the 2025 Mechanistic Clinical Award are permitted to submit the same topic but should carefully review this RFA to ensure they meet all updated requirements.

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 LRA scientific staff if necessary.

Only one application will be accepted per applicant in a grant cycle (applications on distinct projects can be submitted to other grant mechanisms).

APPLICATION PROCESS

A single-stage application process will be employed. Applicants are encouraged to consult with LRA scientific staff to discuss the responsiveness of their proposal to this program. **LRA will host a webinar on December 15, 2025, at 1:00pm ET** for interested applicants to provide further context to this RFA and to answer any questions. A recording of the presentation will be made available.

KEY DATES

RFA Release:	November 14, 2025
Full Applications Due:	February 12, 2026
Application Decision:	June 2025
Expected Start Date:	August 2025

SUMMARY OF REQUIRED MATERIALS

If the following required information is not available at the time of application, it must be supplied prior to receiving this award:

- IRB (or waiver)
- Regulatory approval or waiver (if applicable)
- Material Transfer Agreement (if applicable)
- Letter of Support from third-party providing intervention (if applicable)

Applications must be submitted electronically, via the [LRA Grants Management System](#) **by 11:59pm US ET on the stated deadline**. Applications will not be accepted via any other means. Detailed application instructions are available within the LRA Grants Management System.

REVIEW

The most important review criteria are approach, feasibility, alignment with the RFA and 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

A summary statement containing the reviewers' critiques will be provided within three months of the funding decision notification date for all applications that proceed to review. The LRA does not provide scores or application rankings to applicants.

AWARD TERMS AND CONDITIONS

The MCA provides up to US\$750,000 for up to three years. Once an execution payment is made, distribution of periodic scheduled payments will be contingent upon successful completion of project milestones, timely and satisfactory completion of progress reports, financial reports and 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 total annual budget.

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 information and materials developed using the organization's resources. All recipients of LRA awards must agree to this principle and must take steps to facilitate availability of data and materials as similarly required by NIH. A data sharing plan describing how data generated from the project will be managed and shared must be part of the application submission. As such, awardees are expected to account for data sharing activities in project budgets, including but not limited to data storage and sharing costs, data analysis and processing costs (including software and online platforms), as well as dedicated expert personnel. LRA funding must be acknowledged in all publications and presentations of the supported research.

INQUIRIES

Scientific:

Kari Fischer, PhD
Scientific Program Officer
Lupus Research Alliance
kfischer@lupusresearch.org
+1-646- 884-6022

Administrative:

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

LRA Grants Management System:

For assistance with the electronic grant application process, please contact Erin McLaughlin, Manager, Grant Programs, at emclaughlin@lupusresearch.org.