Request for Applications
Investigate Dietary Approaches for Lupus (IDEAL) Initiative
Up to $500,000 over 2 years

CONTENTS

BACKGROUND

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

Lupus is a multifaceted, heterogeneous and complex disease, challenging to diagnose and treat. To date, there are few approved treatment options and disease management is often 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 experience fatigue, pain and comorbidities. Thus, new innovative, holistic and possible unconventional therapeutic approaches are urgently needed. There are many unanswered questions regarding the pathogenesis of lupus, including the relationship of the disease to the microbiome and environmental factors. Over the past years, there have been a number of investigations relating to natural history, interventions, supportive care and lifestyle approaches for individuals living with autoimmune diseases. The impact of diet and microbiome on lupus disease status and lived experience has been an area of high interest for researchers and particularly those living with lupus. While there have been some positive and productive assessments in other therapeutic areas, and many informal reports of potential benefit in lupus, the studies in lupus have been largely nonclinical and limited. To enable the assessment of the impact of diet on the lived experience of lupus, and to address the void of well-

controlled studies in this area, LT/LRA has established the Investigate Dietary Approaches for Lupus (IDEAL) initiative.

PROGRAM DESCRIPTION

The overall objective of the IDEAL initiative is to fund an initial evaluation of the impact of diet on people living with lupus by conducting a pilot clinical study designed and conducted by a collaborative team of investigators/clinicians to provide rapid and actionable outcomes.

The successful proposal will outline a multidisciplinary (potentially multi-institutional) team approach with the aim of developing a study evaluating dietary intervention(s) and the impact on lupus disease status and/or specific clinical measure or patient-reported outcome, elucidation of mechanistic details and/or mediation use. The IDEAL initiative will provide up to $500,000 over two years to fund a scientifically based, well-controlled small clinical pilot study. The desired result will be a clinical outcome or scientific mechanism rather than dietary guidance, although the study may inform the development of dietary guidance. The hope is to conduct a successful proof-of-concept pilot study that could be extrapolated into a larger study and through the process identify a simple, practical and accessible dietary approach that benefits those living with lupus.

The study should be short in duration (e.g., 30-90 days) to provide timely results, but long enough to align with proposed outcomes. Chosen interventions for evaluation (e.g., high fiber or anti-inflammatory diet, fasting) and mode of delivery (e.g., food provision, food source, associated counseling) could encompass varied approaches but should be scientifically driven based upon the current knowledge about lupus and the impact of diet in health and disease especially other autoimmune diseases. If empirical, a thorough rationale for the approach should be provided. Proper controls should be included in the study design. The number of participants should be reflective of a pilot study and the population should be well defined (e.g., the sub-phenotype of lupus). Despite the lower number of participants in a pilot phase, all types of diversity should be part of the inclusion plan for implementation in a larger study. Therefore, a diversity plan should be mentioned in the background for the proposed project.

Outcome measures should include one or more of the following – clinical (flare prevention, disease severity, laboratory values, fatigue measures, mental health assessment, decreased medication), PROs, scientific (immune cell profiling, cytokine/biomarker profiles, microbiome assessments), and defined diet methodologies (e.g., ASA-24, food diaries, apps) or interventions (e.g., controlled diet study, manufactured snack or dietary component, prebiotic, live biotherapeutic products). Investigators with highly innovative ideas are encouraged to apply.

IDEAL supports pioneering, high-risk, high-reward approaches to major challenges in lupus and dietary research. All studies should have a **clear and direct relevance to people with lupus** and should offer the potential to improve standard of care and the daily lived experience for the disease.

ADDITIONAL CLINICAL RESEARCH EMPHASIS

Priority will be given to projects that also align with LRA strategic research priorities of defining human lupus heterogeneity by molecular pathology to stratify patients by active disease mechanisms and integrating the research continuum to bring advances to patients. It is critical for the IDEAL-funded project to keep patients at the center. It is beneficial to include patients as research partners to offer perspective on the proposed stud design and the proposed approach should be one easily adopted by those living with lupus to be considered successful.

Special emphasis is placed on studies that explore fundamental mechanisms and novel pathways, as well as employ interdisciplinary approaches with scientific rationale as the basis for outcome measures. Of particular interest are projects that address, but not limited to, how diet effects on the microbiome impact mechanistic aspects most notably and potentially clinical outcomes or hints of such, the effect of diet on sub-phenotypes of lupus such as cutaneous or neuropsychiatric lupus and molecular signatures of dietary responses. Ancestral, environmental, and socioeconomic drivers of diet and lupus may also be considered but it may not be feasible for a robust evaluation with a small sample size in a pilot study.

Please note that applications involving promotion of a product(s) will <u>not</u> be considered under this RFA. Such submissions will be triaged without review.

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 as the Principal Investigator with co-investigators and collaborators encouraged. All applications must include at least 2 disciplines in the proposed project and a summary of the roles of team contributors. The participation of multiple institutions is encouraged. There are no citizenship requirements for investigators applying to this program.

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.

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.

SPECIAL CONSIDERATIONS

Nutrition, dietary and microbiome research have unique challenges regarding adherence to prescribed diets, tracking food consumption and extrapolation of controlled studies to real world pragmatic application. Proposed projects should address considerations such as dietary assessment methodology, food source/provision, geographic dietary differences and access, biospecimen collection and bioanalytical analysis, heterogeneity of lupus in relation to outcomes, potential differences in age, race, sex, and the impact of current treatments or concomitant medications.

Successful completion of the grant aims detailed in the application should occur within a 2-year period. An external review will be conducted at the end of Year 1 with brief quarterly progress reports and a final report required.

APPLICATION PROCESS AND INSTRUCTIONS

A two-stage application process will be employed. A three-page Letter of Intent (LOI) will be used to judge the innovation, significance, and alignment of the proposed project with the IDEAL 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 with further instructions provided at that time.

Applicants are encouraged to consult with Lupus Therapeutics to discuss the responsiveness of their proposal to this program.

The intent is to fund up to 2 awards at $500,000 each. A budget requirement for the pilot study that exceeds $500,000 may be considered with a detailed rationale or in the case of a joint effort.

KEY DATES

RFA Release:	November 22, 2024
Application Available:	December 6, 2024
Letters of Intent Due:	January 8, 2025
Letter of Intent Decision:	February 14, 2025
Full Applications Due*:	March 28, 2025
Full Application Decision:	June 10, 2025
Expected Start Date:	August 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 that the proposed project will involve the use of human samples and/or data.

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 all other financial support (current as of the date of application submission) 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, and biosketches/CVs as PDFs for all key personnel.

   A. **Letter of Intent (LOI):** The Letter of Intent template provided on ProposalCentral must be used. Margins must not be less than 0.5 inches on each side and 12-point Times New Roman or the equivalent should be used for the text. The LOI and references, **should not exceed three (3) pages**. Figures, tables, and legends are included in the page limit. Biosketches/CVs are not included in the limit. The information listed below must be included in the indicated order.

      i. **Lay Summary:** A brief description of the clinical approach to assess the impact of diet on the lived experience of lupus

      ii. **Brief Background:** Provide a succinct contextual framework for the proposed pilot clinical study/project, methodological approaches, how the project aligns with the IDEAL objectives and how challenges of diet interventions will be addressed.

      iii. **Objective and Specific Aims:** State the overall objective and outline the specific aims/outcomes of the proposed pilot clinical study.

      iv. **Impact Statement**: Provide a succinct statement about the potential of the proposed clinical study to inform dietary/nutrition considerations for those living with lupus.

      v. **Project Plan:** Describe the well-defined, innovation, high level clinical study design, significance, and rationale for the proposed project. Present a realistic, but aggressive timeline and a basic framework for the proposed budget.

      vi. **Resource Assessment:** Summarize the multidisciplinary approach and the resources needed, such as methodologies, partnerships with key collaborators and applicability and access to proposed dietary interventions. 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 dietary intervention for 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.

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 most important LOI review criteria are an innovative multidisciplinary approach, scientifically-based study design with rapid and definitive outcomes and the ability to extrapolate to a larger study leading to pragmatic implementation.

Full Application Review

To facilitate support of high-risk, high-reward projects, full applications will be evaluated using a tripartite scoring system focused on the following components:

- **Innovation & multidisciplinary team** including consideration of the PI's track record, area of expertise, along with the team and environment
- **Clinical design** including outcome measures, timeline, approach and feasibility
- **Potential for pragmatic implementation**

The **Impact Statement** will be used to prioritize funding among the top scoring applications. The rationale for and the novelty of the proposed research rather than the amount of preliminary data may be emphasized if there are limited data in lupus available to date. Obviously strong preliminary data will warrant strong consideration. Continuations of long-term research projects are not appropriate for this grant mechanism. Applications that are not aligned with the goals and the mission of the LRA or the initiative will not be peer-reviewed.

Review Process

All eligible grant applications will be peer-reviewed by a panel of expert reviewers, the results from which will be considered by the LRA Scientific Advisory Board (SAB) and the Lupus Therapeutics Board of Directors (both of which include those living with lupus), and LT/LRA clinical and scientific leadership in the context of the IDEAL initiative goals and the LRA strategic research priorities. Funding recommendations will be presented 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. Scores or application rankings will not be provided to applicants.

AWARD TERMS AND CONDITIONS

The IDEAL initiative provides up to US$500,000 over two years. Indirect costs must not exceed 10% of the total budget and must be included within the overall budget cap.

The grant recipient must attend and present at the LuCIN Community Meeting 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 LuCIN Community meetings.

The LRA is committed to the publication and dissemination of all data/information and materials developed using the LT/LRA resources. All recipients of LRA awards must facilitate availability of data and materials by executing a Data Sharing Plan based on the Final NIH Policy for Data Management and Sharing.

INQUIRIES

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