

REVISED TIMELINE



Request for Applications: GLOBAL TEAM SCIENCE AWARD

\$3 Million Grants

Purpose

The Lupus Research Alliance (LRA) is soliciting Letters of Intent (LOIs) from established investigators across scientific disciplines and geographies to make major advances in understanding the heterogeneity of systemic lupus erythematosus (SLE) using highly collaborative, synergistic, innovative, and ambitious approaches. Incomplete understanding of the tremendous clinical and mechanistic heterogeneity of SLE remains a central challenge to developing safer and more effective treatments and to improving the standard of care for lupus patients. To address this impediment, the Lupus Research Alliance has established the Global Team Science Award (up to \$3M over three years) and invites investigators to apply, through LOIs, for 4-month planning grants (up to \$10,000 each) to assemble competitive Teams to develop, and submit full applications. *It is anticipated that up to six planning grants and then up to three Global Team Science Awards will be awarded.*

Objectives and Principles

The Lupus Research Alliance Global Team Science Awards will support *interdisciplinary*, *collaborative*, and *highly synergistic* projects that push the boundaries of *innovation* and bridge research and clinical efforts in lupus. The successful Teams will focus on unravelling human lupus heterogeneity by applying *cutting-edge technologies* to address critical questions that could bring about *breakthroughs* in lupus care, research or drug development.

Interdisciplinary research, for the purpose of this Request for Applications (RFA), refers to research across disciplinary boundaries that attracts and engages scientific talent from diverse research and clinical fields such as systems biology, computational biology and bioinformatics, biomedical engineering, immunology, microbiology, molecular biology, biochemistry, rheumatology, nephrology, neurology, infectious disease, etc. Achieving the objectives of the proposed Team Project requires combining research tools and resources—such as concepts, technologies, methodologies, use of biologic samples, etc.—as well as unifying investigators who bring different backgrounds and expertise to the Team. Thus, each successful team would be able to bring expertise in cutting edge technologies to bear on understanding the clinical and molecular heterogeneity that is characteristic of SLE.

Collaborative denotes that the relevant research goals can only be achieved if all Co-Principal Investigators (Co-PIs) combine their complementary expertise and resources in a novel and strongly integrated research program. The emphasis on *synergy* indicates the requirement that the Team's research constitutes an effort much greater than the sum of the individual Team member's efforts should they be working alone.

Cutting edge technologies for the purpose of this RFA denote the expectation that patient

samples and clinical data will be studied using state-of-the-art analytic approaches such as but not restricted to scRNA-Seq, REAP-Seq, CITE-Seq, ATAC-Seq, CyTOF, proteomic, metabolomic, machine learning algorithms, etc. There are many other cutting edge approaches that investigators may wish to use. While this RFA requires the application of new technologies, it does not support their development.

Breakthrough research in the context of this RFA is characterized by a high potential for shifting or creating new paradigms. It goes beyond existing doctrines, models, approaches, etc. to open new research areas and/or deliver critical knowledge to transform lupus care and research.

Background

SLE is a severe systemic autoimmune disease characterized by the loss of tolerance to nuclear antigens and the associated presence of autoantibodies against these antigens as well as an increased type I interferon production and dysregulation in numerous other components of the immune system. Lupus is the fifth leading cause of death among young females, and 90% of the affected individuals are women. Yet, the currently available treatments lag far behind those for other autoimmune disease and are largely inadequate to control disease progression and avert long-term complications. Only one lupus-specific therapy has been approved in the past 65 years. Thus, new conceptual and therapeutic advances are urgently needed.

A major challenge in understanding and treating lupus is the extreme disease heterogeneity at both the clinical and molecular levels. Clinically, the disease manifests through a wide array of clinical symptoms and organ involvement affecting patients to varying degrees. Mechanistically, there is a high degree of immunological diversity apparent from numerous serological, cellular, genetic and genomic studies. Distinct pathogenic pathways appear to be at play in different SLE patients as well as within the same patient. Even among individuals whose diseases look similar, different molecular mechanisms likely drive disease in individual patients. Lupus heterogeneity appears to be at the core of the many therapeutic failures in the field. This underscores the need for 1) a molecular definition of disease diversity between patients and within patients; and 2) patient stratification, by active disease mechanism(s), in clinical research and practice.

Recent advances in human immunology as well as rapid technological developments, including advancing computational capabilities, provide an unprecedented opportunity to make major advances in the molecular deconstruction of lupus heterogeneity. Additionally, the large number of data sets from multiple lupus trials/studies and a growing knowledge about disease pathways in SLE offer a fertile ground for applying the emerging technologies to lupus. The Global Team Science Award aims to catalyze these opportunities most effectively by nurturing interdisciplinary and highly interconnected collaborations that bridge lupus clinical research with cutting edge technologies and other relevant research domains.

As a prototypic systemic autoimmune disease, SLE offers a unique platform for both inquiry into the fundamental principles of self-reactivity/inflammation, as well as for applying

learnings from other relevant scientific fields. The Lupus Research Alliance invites investigators across all relevant scientific disciplines to bring their talents to bear on deconstructing lupus heterogeneity through the application of powerful new experimental and collaborative approaches. The ultimate goal is to pave the way for SLE patient stratification and a precision medicine approach to lupus treatment and drug development.

Research Emphasis Areas

The Global Team Science Award mechanism is *strongly aligned with the Lupus Research Alliance's strategic priorities* to 1) Define human lupus heterogeneity by molecular pathology; 2) Enable patient stratification based on active disease mechanisms; and 3) Facilitate global research collaborations.

The Team Award must apply cutting-edge technologies to the study of lupus clinical samples or data sets and do this in a way that interconnects technology and human immunology experts with clinical scientists to realize cross-disciplinary synergies and bring about breakthroughs in the molecular understanding of heterogeneity in human lupus.

Examples of the type of questions that could be explored under the Global Team Science Award include but are not limited to the following in the context of human lupus:

- Understand functional consequences of variants, genes and pathways implicated by human genetic studies
- Understand the role of the microbiome in lupus development and/or progression
- Characterize the immunologic, genetic and molecular factors differentiating responders and non-responders to approved and/or investigational therapies in SLE
- Correlate clinical subsets of SLE with peripheral biomarkers
- Understand how the mechanisms of disease differ for different clinical manifestations of lupus (e.g., in skin, joints, the central nervous system, and kidney)
- Define genetic and/or molecular factors conferring susceptibility to developing lupus nephritis
- Utilize the Accelerating Medicines Partnership (AMP) SLE samples/data or other high-quality samples/data sets to examine racial and ethnic differences in key cellular/molecular pathways.

Activities that will **not** be supported as part of this funding mechanism:

- Generation of new clinical cohorts
- Development of new technologies
- Clinical trials. However, mechanistic studies related to already funded clinical trials will be considered.
- Discovery and/or validation of novel therapeutic targets as the sole focus of the project
- Development of clinical outcome measures
- Exclusively clinical collaborations studying heterogeneity from a purely clinical angle.

Applicants who wish to consult with program staff to discuss the responsiveness of their proposal to this program or to discuss ideas for resources that might benefit this initiative

are invited to do so. Inquiries in this area should be referred to the contacts shown below.

Key Requirements

The following components are required, unless otherwise noted, for the Global Team Science Award:

- The project must fulfill the rules outlined in the “Objectives and Principles” section.
- The core team must consist of at least three but ideally not more than five Co-Principal Investigators. (Co-PIs)
- One of the Co-PIs must serve as the corresponding Co-PI.
- The core team must be multi-disciplinary, and it is encouraged to be inter-institutional and/or multi-national. There are no restrictions on the number of disciplines represented on the Team.
- The proposed research must be strongly aligned with LRA’s strategic priorities described under the “Research Emphasis Areas” section.
- The Team must utilize cutting-edge research technologies and/or computational approaches to tackle the proposed Team project.
- Studies must be done on existing cohorts and/or samples/data. Limited funding for the acquisition of samples/data from already existing resources may be available. Examples of potential sources of samples/data is provided in Appendix I.
- If animal studies are proposed, they must constitute a focused component linked to the results of human studies and aimed towards further understanding of human lupus.

Award Structure

The Global Team Science Award has a unique structure. Unlike other collaborative awards where individual investigators work on their own, distinct projects under the umbrella of the overall collaborative program or center such as a Program Project Grant, the Global Team Science Award requires that all Team Co-PIs work on a common project from distinct angles. Specifically, the Team should address a single overall question/challenge by employing the complementary skills and contributions of the Co-PIs and realizing the synergies within this exclusive collaborative environment. Within this overall structure, the individual Teams can establish the optimal assembly to accomplish their collective research objective. General operational expectations for the Team include sharing of data among Team members in real time, frequent interactions among Co-PIs and their research teams, etc. At a minimum, this should include frequent conference calls and one to two in-person meetings per year one of which should coincide with the annual LRA site visit.

Eligibility

Applicants must hold an MD, PhD, DVM or equivalent academic degree and hold a faculty position or equivalent at a college, university, medical school, or comparable institution.

Applications may be submitted by domestic or foreign non-profit organizations, public or private, such as colleges, universities, hospitals or laboratories.

The Lupus Research Alliance does not impose geographic restrictions on its applicants and researchers working outside of the USA are also encouraged to apply. There are no citizenship requirements.

For-profit entities such as pharmaceutical or biotechnology companies may participate as collaborators but are not eligible to receive any financial support through the grant award.

This funding mechanism requires the participation of parties with complementary expertise coalescing to form a highly synergistic research team. Collaborations between human immunology researchers, technology experts, and lupus clinicians is strongly encouraged. Of course, investigators coming from different areas of specialization can be included.

Application Guidelines

Applications must be submitted electronically, via [proposalCENTRAL](#) by 11:59pm ET on the stated deadline. Paper applications are not accepted.

A two-stage application process—bridged by a planning grant—will be employed. A Letter of Intent (LOI) will be used to judge the significance, innovation and alignment of the proposed project concept with the Global Team Science Award funding mechanism. The specific LOI review criteria are detailed below. Applicants with approved LOIs will be invited to submit a full application and will be provided a 4-month planning grant of up to US\$10,000 to develop the full proposal.

I. Letter of Intent

A Letter of Intent is required and must be submitted electronically, via [proposalCENTRAL](#), by 11:59pm ET on the stated deadline. Applications are not accepted via any other means. The LOI template provided on [proposalCENTRAL](#) must be used. It should contain the information listed below. Items #2-9 should not exceed four pages. Section word limits are offered as suggestions only. Submissions must be completed using one-half inch margins & 12-point Times New Roman font or its equivalent.

1. *Co-PIs*: Provide the name, position, institution and role on the Team for each Co-PI.
2. *Brief background*: Provide a succinct contextual framework for the proposed Global Team Science Award. (100 words)
3. *Objective*: State the overall research question and aim of the Global Team Science Award. (75 words)
4. *Innovation*: What novel questions, approaches or areas does the Team plan to explore? (250 words)
5. *Research plan*: Outline the research approaches anticipated to be pursued by each core team member in addressing the Team's overall question. (500 words for all Co-PIs)
6. *Team attributes*: How will the Team members work together, i.e. what is the general collaboration plan? How will the Team's activities be integrated? What synergies does the Team plan to realize? Explain how the research efforts described in #5 above will be interlaced to create a truly integrated endeavor that is much greater than the sum of

its parts. (300 words)

7. *Significance*: Briefly state the anticipated impact of the outcomes of the Global Team Science Award on improving lupus treatments and clinical care. (75 words)
8. *Resource assessment*: Provide an overview of the Team's ability to carry out this project and outline resources and/or expertise each team member will contribute. (200 words)
9. *Planning grant*: Describe the key activities to be undertaken during the 4-month planning grant stage should the LOI be approved. Describe how the planning grant funds will be used to generate the Global Team Science Award application and provide a corresponding itemized budget for the planning grant. (500 words, excluding budget)
10. *Biosketch*: Provide a standard NIH-style Biosketch for all Co-PIs. This should include a description of other financial support available to the applicant(s) for his/her research endeavors. Applicants who are not based in the United States may submit a copy of their curriculum vitae.
11. *Letters of collaboration*: Each Co-PI, except the corresponding PI, must provide a letter confirming her/his willingness to be an active participant in the proposed Global Team Science Award.

Restriction on Number of Applications Only one LOI will be accepted per corresponding principal investigator in a grant cycle. The corresponding PI may not participate on any other Global Team Science Award. However, other Co-PIs may do so as long as the projects they are involved with are non-overlapping and a compelling justification for the multiple participation has been provided.

II. Full Application

Full applications may be submitted only by applicants whose LOIs have been approved and who have been invited by the Lupus Research Alliance to advance to the next stage of the review process.

Approval of the LOI will trigger the release of a 4-month planning grant from the Lupus Research Alliance to be used for the sole purpose of developing a well-coordinated and synergistic Global Team Science Award application. The planning grant will provide up to US\$10,000 which must be used between **December 1, 2020 and March 31, 2021¹**. During this period, the Team must develop a detailed plan of the proposed research activities for the 3-year grant term. Detailed instructions for completing the full application will be provided after the LOI approval. In brief, the following sections will be included in the research plan: 1) Goals of the project; 2) Interdisciplinary aspects; 3) Relevance and significance; State of the art of the field relevant to the project; 4) Research approach; 5) Description of the collaborative and synergistic aspects of the Team; 6) Project implementation and coordination; 7) Risk management; 8) Milestones and corresponding timeline.

Applications should be submitted via proposalCENTRAL by 11:59pm ET on the stated deadline. Please log on to this site for detailed instructions. The full application site will be accessible only to applicants with approved LOIs.

¹ **Revised timeline**

Review Criteria

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

LOI Review

- Alignment of the concept proposal with the objectives and scope of the Global Team Science Award and the Lupus Research Alliance's strategic research priorities
- Potential of the proposed collaborative team: Do the Co-PIs have demonstrated track record of innovation and of shifting scientific paradigms and breaking open new areas of research? Do the Co-PIs have a history of creating and maintaining meaningful scientific collaborations with investigators in other disciplines and/or within the same discipline. Please note that prior collaborations among the proposed Team members are not required. Do the core team members complement each other's expertise? Does the proposed Team create a unique research environment that can serve as a catalyst for scientific breakthroughs in lupus? Does the Team have compelling preliminary collaboration and integration plans? Please note that the planning grant will enable the full development of these components.
- Novelty of the proposed research: 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?
- Potential impact of the overall effort on lupus treatments and/or care
- Environments: Do the proposed projects take advantage of unique features of the scientific environments at each site? Is there evidence of institutional support?

Full Application Review

- Assessment of the proposed research approach
- Evaluation of the interdisciplinary character of the Team—in relation to the proposed project—and the added value of the collaboration
- Assessment of the proposal's innovation
- Potential for research breakthroughs in lupus
- Assessment of the implementation and coordination aspects of the proposal
- Alignment with LRA's strategic priorities

Terms of Award

Planning grant

The purpose of the planning grant is to facilitate the interactions between the prospective Team members required for the preparation of a highly coordinated and synergistic proposal. This is particularly fitting for the Global Team Science Award mechanism given the prerequisite for effective integration of investigators across diverse disciplines and sites.

Applicants invited to submit a full application will receive a planning grant for up to

US\$10,000 for the period between **December 1, 2020 and March 31, 2021**². The level of support will depend partially on the geographic distribution of the proposed Team members and must be well-justified within the Letter of Intent. Indirect costs on the planning grant are not allowed. Any unused planning grant funds in excess of \$500 must be returned to the LRA by June 1, 2021.

Global Team Science Award

The Global Team Science Award will be supported for up to US \$1,000,000 per year for up to three years. Indirect costs must not exceed 10% of the total budget (excluding equipment) and must be included within the \$1,000,000 annual budget cap. The Co-PIs, including the corresponding Co-PI, must devote a minimum of 15% effort on this award. Equipment purchase is discouraged unless indispensable for the conduct of the project. If so, a compelling justification must be included within the grant application and the equipment purchase, if approved, needs to occur during the first year of the award. The LRA will provide all award funds to the corresponding Co-PI's institution, which will be responsible for distributing the monies to the other Co-PI's institutions according to the LRA approved budget.

The formal start of the 3-year program must follow a *2-month start-up period* intended to complete all administrative and research preparatory tasks required to initiate fully the research activities of the Team. These should include but are not limited to the execution of subcontracts, acquisition of institutional resources at the sites, finalization of common protocols, establishment of a common data sharing platform, finalization of operating processes for the Team, etc. The start-up phase will culminate in an LRA site visit to ensure that the Team is well poised to launch the research effort. The successful completion of these preparatory activities, as determined during the site visit, will trigger the standard award payments. Funds for the start-up phase must be budgeted within the overall \$3 million grant budget.

Continued funding beyond the first year of the grant is contingent on demonstrating research progress and on meeting the pre-established project milestones. Progress reports are required at the end of each year and are reviewed by Lupus Research Alliance staff and external scientific advisors. In addition, site visits will be conducted at the end of year 1 and year 2 of the grant as well as at the end of the start-up phase as noted above.

The Lupus Research Alliance is committed to the publication and dissemination of all information and materials developed using the organization's resources. All recipients of Lupus Research Alliance awards must agree to this principle and must take steps to facilitate availability of data and materials. LRA funding must be acknowledged in all publications and presentations of the supported research.

Forming partnerships with the grant recipients is one of the cornerstones of the Lupus Research Alliance's funding philosophy. Towards this end, awardees are required to attend the Lupus Research Alliance annual scientific conference, Forum for Discovery, and share the

² Revised timeline

concepts and progress of their research. Travel funds, provided by the grant award, should be used to attend this meeting.

Review Process

The Global Team Science Award applications are reviewed by a scientific committee specifically empaneled by the LRA for this grant mechanism. This expert panel makes funding recommendations to the Scientific Advisory Board and the Research Committee of the Board. The Board of Directors of the LRA makes the final funding decisions.

Review Feedback

For applicants invited to submit full proposals, a summary statement, containing the reviewers' critiques, will be provided within three months of the review date. Applications not recommended to advance to the full proposal stage will not receive written critiques. The Lupus Research Alliance does not provide scores nor applications' rankings to applicants.

Key Dates

Please note that the timeline has been updated due to the COVID-19 pandemic.

RFA Release:	February 1, 2020
Letter of Intent Due:	September 15, 2020
Letter of Intent Decision:	November 30, 2020
Planning grant timeline:	December - March 2021
Full Application* Due:	April 1, 2021
Response to Applicants^:	June 30, 2021
Anticipated Start:	September 1, 2021

*By invitation only with an approved LOI

^For full applications only

Inquiries

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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

APPENDIX I

Examples of potential sources of data and samples from lupus studies

Accelerating Medicines Partnership (AMP) RA/SLE data available through the [Immunology Database and Analysis Portal](https://www.immport.org/home) (<https://www.immport.org/home>)

Lupus Family Registry and Repository (LFRR)
<https://ordrcc.omrf.org/about-lupus-family-registry-and-repository/>

Multiple lupus data sets can be accessed through the database of genotypes and phenotypes (dbGAP) (<https://www.ncbi.nlm.nih.gov/gap/>), including:

- Accelerating Medicines Partnership (AMP) RA/SLE
- The International Consortium on the Genetics of Systemic Lupus Erythematosus (SLEGEN)
- OMRF SLEGEN GWAS Data from European-American Women with Lupus
- Whole Genome Association Study of Systemic Lupus Erythematosus
- CLRR-Cincinnati Lupus Registry and Repository

Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry
<https://carragroup.org/>

Vivli – Center for Global Clinical Research Data
<https://vivli.org/>

ClinicalStudyDataRequest.com (CSDR)
<https://www.clinicalstudydatarequest.com/Default.aspx>

GSK Study Register and patient level data
<https://www.gsk.com/en-gb/research-and-development/trials-in-people/gsk-study-register-and-patient-level-data/>

Pfizer Data Access Requests
[https://www.pfizer.com/science/clinical trials/trial data and results/data requests](https://www.pfizer.com/science/clinical%20trials/trial%20data%20and%20results/data%20requests)