2022 Rheumatoid Arthritis Research Request for Proposals (RFP)

I. RFP Overview

Participating Organization	The Arthritis Foundation, Science Department
Expert Advisors	Medical and Scientific Advisory Committee RA Working Group
Funding Opportunity Title	Characterizing Determinants of Response and Non-response to Current Rheumatoid Arthritis (RA) Therapeutic Agents: Request for Proposals on Refractory RA Research
Announcement Type	New
Funding Opportunity Announcement Number	RFP-RA-2022
Funding Opportunity Purpose	This Request for Proposals (RFP) invites applications for characterization of the distinct mechanisms, biomarkers, and therapeutic targets that distinguish RA responders and non-responders to therapy. Research projects that propose the examination of the socio-economic determinants of therapeutic non-response are also of interest. The long-term goal of this AF research program is to improve the lives of RA patients for whom currently available therapies are ineffective. The funding for this initiative will be provided by the Arthritis Foundation's Science Budget. For more information on our work, please visit: www.arthritis.org/science
Posted Date	04.4.2022
Open Date (Earliest Submission Date)	06.1.2022
Letter of Intent Due Date	05.16.2022
Application Due Date	07.18.2022 **All applications are due by 5:00 PM, Eastern Time Zone.**
Award Announcement	11.14.2022

Earliest Project Start Date	01.01.2023
Expiration Date	This RFP will expire after 'Application Due Date' above.

II. RFP Information

1. RFP Purpose and Objectives

This RFP invites research proposals of two types:

A. **One-year pilot research projects** to investigate a novel hypothesis with no preliminary data requirements and a cap on the budget of up to $75,000 total, or

B. **Three-year large research grant proposals** with a budget of up to $150,000 per year for 3 years (up to $450,000 total).

Proposed budget can include up to 8% indirect expenses, if needed.

Research proposals should focus on investigating determinants of treatment response and non-response in patients with Rheumatoid Arthritis (RA). Applicants should ensure that the definition of non-response to be used in the study is clearly articulated. Research studies using clinical samples and/or clinical data are strongly encouraged. Animal studies are not allowed. Proposed research may include, but is not limited to:

- Identifying underlying biological mechanisms, including but not limited to immunologic, genetic, epigenetic, and/or biochemical;
- Revealing novel therapeutic targets;
- Addressing patients with well-controlled disease according to standard assessment tools, but still experiencing RA symptoms, including pain, that are reducing their quality of life; and/or
- Uncovering social determinants of health and their association with lack of response to treatment.

Proposals may also aim to elucidate how patients experiencing treatment non-response differ from those for whom therapy is effective. For proposals including clinical studies, the incorporation into the design of assessment of patient-reported outcomes is highly encouraged. Awardees will become a part of a cohort of investigators that will regularly communicate with other investigators funded by AF as part of the RA Portfolio of research our Foundation supports.

For all proposals, the Arthritis Foundation strongly encourages the inclusion of patient advocate(s) on the research team who are meaningfully engaged in the research project. We define meaningful engagement as active and collaborative interaction between patient(s) and researchers across all stages of the research process from conception to results distribution, where research decision making is guided by patients' contributions as partners, recognizing their specific experiences, values, and expertise.

The long-term goal of this funding mechanism is to support research that would improve the lives of patients with RA for whom currently available therapies are ineffective.

2. Background

The Arthritis Foundation (AF) has previously supported ground-breaking research that led to the development of early biologics used in the treatment of RA. In 2021, the AF Medical and Scientific Advisory Committee formed an Expert Working Group of academic and government RA experts to prioritize the unmet medical needs and potential research areas of interest for funding in RA research. Based on their recommendations, AF is releasing this RFP, which is open to investigators affiliated with US academic institutions and hospitals who are committed to improving the outcomes of the RA patient community through biomedical (translational, clinical) and/or health outcomes research.

3. Why Focus on Treatment Response and Non-response in RA?

A substantial portion of all RA patients are not responsive to the currently available therapies. The reasons for such variation in outcomes are not well understood but are most likely the result of a combination of factors. Recent advances in development of experimental tools and approaches applicable to the study of blood and tissue of RA patients, along with availability of clinical and demographic data linked to biologic data, provide an opportunity to gain novel insights. These insights have the potential to reveal the underlying causes of therapeutic response and non-response in RA.

4. Research Proposal Evaluation Factors

4.1. Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the review criteria below.

4.2. Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of the scientific merit and strategic importance of each proposal. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not original may be essential to advance the RA field. The list of evaluation factors is presented below.

A. Significance

Does the proposal address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments,

services, or interventions for RA patients with refractory disease? Is there an explanation of how this proposal is needed to improve outcomes for RA patients experiencing treatment non-response?

B. *Principal Investigator(s) and Scientific Team*

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If an Early-Career Investigator is proposed as PI, do they have appropriate experience and training, as well as connections/collaborators to make sufficient progress? If the PI(s) are established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; is their leadership approach, governance, and organizational structure appropriate for the project? Do the key personnel possess appropriate and adequate knowledge and experience in the RA field?

C. *Originality*

Does the proposed research project challenge and seek to shift current paradigms by utilizing novel theoretical and practical concepts, approaches, or methodologies? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed? Does the design/research plan include original elements, as appropriate, that enhance its potential to advance scientific knowledge or clinical practice? Does the design/research plan consider the unique challenges of research on RA patients experiencing treatment non-response?

D. *Approach*

Are the overall proposed strategy and methodology well-reasoned and appropriate to accomplish the specific aims of the project? If appropriate, have the investigators included plans to address lessons learned from other similar initiatives? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Is a robust statistical analysis plan included? Are potential problems, alternative strategies, and benchmarks for success presented? At the early stages of development, will the strategy establish feasibility and will particularly risky aspects during formative stage be adequately managed? Have the investigators presented an outline of the anticipated challenges and how they propose to address them? Are potential ethical issues adequately addressed?

E. *Environment*

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements? If proposed, are the administrative, coordinating, enrollment and laboratory/testing centers, appropriate for feasibility and future trials proposed?

F. *Study Timeline*

For clinical trials, does the study timeline consider start-up activities, the anticipated rate of enrollment, and planned follow-up assessment? Is the projected timeline feasible and well justified? Does the project incorporate efficiencies and utilize existing resources (e.g., CTSAs, practice-based research networks, electronic medical records, administrative database, or patient registries) to increase the efficiency of participant enrollment and data collection, as appropriate? Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?

G. *Protections for Human Subjects*

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

H. *Inclusion of Women, Minorities, and Individuals Across the Lifespan*

When the proposed project involves human subjects and/or clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals based on sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed.

I. *Budget and Period of Support*

Reviewers will consider whether the budget, staffing plan and the requested period of support are fully justified and reasonable in relation to the proposed statement of work. Indirect costs (F & A) must be 8% or less as per Arthritis Foundation policy.

III. Award Information & Eligibility Criteria

The Arthritis Foundation encourages applications from a diverse pool of investigators with respect to race, gender, sexual orientation, ethnicity, national origin, and disability. The Arthritis Foundation recognizes that a diverse and inclusive workforce is critical for ensuring that the most creative minds have the opportunity to contribute to realizing our research goals and to ensuring more equitable health outcomes for all.

Multiple awards are expected to be made, with a project period of 1 to 3 years, depending on the mechanism. Proposals using animal studies are not eligible for this funding mechanism.

Eligible organizations include:

- Higher Education Institutions, including:
- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education
- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Non-domestic (non-U.S.) Entities (Foreign Institutions) and Non-domestic (non-U.S.) components of U.S. Organizations are not eligible to apply.

Arthritis Foundation funds are primarily obtained from donations. The amount available for scientific awards each year is determined by the success of the fundraising efforts. Funds for awards are also derived from partnerships established by the Arthritis Foundation, with other groups that share common interests. Funds for subsequent years of a project, after the first, even if initially approved, are contingent upon adequate scientific progress and available funds, and are therefore subject to change.

Applicant organizations are encouraged to work collaboratively and submit a single application.

IV. General Proposal Application and Submission Information

1. Submission

All LOIs and applications should be submitted using the Arthritis Foundation online portal for this program, available at https://proposalcentral.com/. All applications should be submitted by 5:00 PM Eastern time on the deadline date. Please expect that any application submitted after deadline, incomplete, or failing to otherwise adhere to instructions will be administratively declined.

2. Letter of Intent (LOI)

Submit LOIs through Proposal Central at https://proposalcentral.com/ by 5:00pm EST on May 16, 2022. The LOI, 2 pages maximum in length, should describe the fit of your idea to the overarching goals of this program, include a hypothesis and specific aims, and outline at a high level the impact you expect from the work.

LOIs will be evaluated to confirm each applicant's eligibility for subsequent application submission. Additionally, the information provided will allow AF Staff to estimate the potential review workload and plan the review.

3. Formatting and Page Limits

For both the LOI and the proposal submission, please follow the format requirements. Margins should be greater than or equal to 1/2" on all sides. Font size should be no less than 11 points. Applications must be written in English and formatted such that, if printed, would print to 8.5" x 11" paper. PDF file formats are preferred. Editing permissions must not be restricted and files must not be password protected. Proposals need to adhere to a strict limit of:

- 6 pages single space for the pilot proposals
- 12 pages single space for the large grant proposals

The page limits do not include the additional biosketches, references, letters of support, and table of contents that will also be a part of all proposals.

4. Instructions for Full Application

4.1 **Title page**: Enter project title. Select award type (Pilot or Large Grant).

4.2 **Download Templates & Instructions**: Download RFP

4.3 **Enable Other Users to Access this Proposal**: Allow others (e.g., institutional administrators or collaborators) to view, edit, or submit your proposal. Electronic signatures are required to submit the application for submission. The Signing Official from the applicant's institution must be provided at least 'Edit' access on this screen to be able to sign. Please review the Signature Page to confirm the signature roles required and add as appropriate on this page.
PLEASE MAKE SURE TO GRANT ACCESS AHEAD OF TIME TO YOUR INSTITUTION'S SIGNING OFFICIAL TO AVOID ANY LAST-MINUTE ISSUES WITH SIGNING AND SUBMITTING YOUR APPLICATION.

4.4 **Applicant/PI**: Key information about the applicant PI.

4.5 **Institution & Contacts**: Key information about the PI's institution, including name and email address of the financial officer and the signing official who, in addition to the PI, will be contacted if the award is selected for funding. If your institution has a ROR (Research Organization Registry ID), please include.

4.6 **Other Key Personnel**: List and provide contact information for key persons. Include everyone except the applicant who will contribute to the scientific development or execution of the project in a substantive, measurable way whether they receive salaries or compensation under the grant.

4.7 **Abstracts**: Provide a general audience abstract (non-technical) and a technical abstract (2,000 characters, including spaces, maximum each). Please note: the general audience abstract will become public if the award is selected for funding, therefore, it should not contain any proprietary information.

4.8 **Budget Period Detail**: Enter budget detail for each 12-month award period requested. Up to 8% of the total budget may be dedicated to indirect costs (F&A). Fringe benefits for personnel salaries are allowable. Include any costs associated with sharing of resource outputs. The total cost of salary and fringe support must not exceed 50% of total project costs. Requests for salary and fringe support beyond 50% may be considered but require a letter of justification for why this is necessary for the goals of the project to be achieved.

4.9 **Budget Summary & Justification**: A summary of the budget detail will be shown in this step. In addition, provide a detailed explanation for each budget category for the evaluation of the major portions of the budget that are being requested. If more space is required than is provided in the

Proposal Central forms (2,000 characters), applicants may upload the budget justification in document form in step #13.

4.10 **Other Support:** Please list all current and pending support for the Applicant and Co-Investigators. Any overlap of current or pending support with the Arthritis Foundation proposal must be described and explained.

Current and pending support can be added to your (and other Key Personnel's) Professional Profile on Proposal Central by clicking on the 'Professional Profile' tab and going to Step #10: Other Support. To add your entries, please click on the "+" link and all entries previously saved in your Professional Profile will show. Please select the applicable support and save. For other Key Personnel, if they have granted you at least 'View' access to their profile, you can select Other Support from their profile as well. If they have not provided you 'View' access, upload a list of their current and pending support and any overlap in a separate document in step #14 of the application.

4.11 **Data & Resource Sharing Plan:** While not strictly required, data and resource sharing are an expected outcome from grants funded by the Arthritis Foundation. Provide requested information as to how the data and other resources generated as part of the research project will be shared.

4.12 **Organization Assurances:** IRB approvals, if applicable.

4.13 **PI Demographics:** Please enter your ORCID ID and other requested demographic information. If you do not have an ORCID ID, you can register for one here: https://orcid.org/register. Please note that requested demographic information will NOT be shared with reviewers or used by the Arthritis Foundation in any way during the selection process. The Arthritis Foundation collects such data to better understand the demographic make-up of its applicant and awardee pools and detect and address any inequities identified.

4.14 **Proposal & Supporting Documents**: Upload the following:

1. Research Proposal: Applicants are encouraged to use the suggested layout below
    - *Project Summary*: A paragraph that emphasizes the key attributes of the proposed program at the start of the proposal.
    - *Scientific Background and Research Plan*: This section summarizes the overall importance of the proposed work, including the problem statement, hypothesis and when available, the preliminary results, plus a list of the Specific Aims, Proposed Approach and Specific Methodology, including a Statistical Plan, a detailed study timeline, Alternative Hypotheses & Pitfalls, and Rationale and Fit with RFP Purpose & Objectives.
    - *Description of Key Personnel*: Proposed PI, and proposed team governance structure, how patient advocate(s) will be incorporated into research team.

- *Additional Information*: Any additional information relevant to the Review Criteria listed above.

2. NIH Biosketches: For Applicant/PI and relevant Key Personnel (Co-Investigator and Collaborator roles only).
3. Current and Pending Support: For the Applicant and any Co-Investigators. Upload here ONLY when this information cannot be entered in the Other Support section of the application.
4. Budget Justification: 5 pages maximum. Only provide if more space is needed than what is provided in the Budget Summary & Justification section of the application.
5. Letter from Applicant's Division Chief: Documents that % effort is available and confirming Applicant's salary.
6. Letters of Support (optional).

4.15 **Validate:** Check for any missing information.

4.16 **E-Signature: *Before submitting the application***, an electronic signature is required from both the Applicant/PI and a Signing Official from the applicant's institution. Type your name in the text box and click the green 'Sign' button. A date and time stamp will appear next to the button indicating that the electronic signature was successful. To give the Signing official access to sign this application, enter their information in Step #3: "Enable other users to access this proposal" and grant them at least "Edit" access.

4.17 **Submit:** No proposals will be able to be submitted past their deadline. Technical support for the on-line application system is not available after 5:00 p.m. Eastern Time or on weekends.

V. Selection Process and Award Management

1. Review and Selection Process

Applications will be evaluated for scientific merit by a Scientific Review Group, convened by the Arthritis Foundation, and using the above stated review criteria. As part of the scientific peer review, all applications will receive a written critique in Proposal Central. Only those applications deemed to have the highest scientific and technical merit will be discussed and assigned an overall impact score. A final discussion of the review committee may be required to recommend a list of the final applicants to be considered for award. The following factors will be considered in making final AF funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Relevance of the proposed project to program priorities and strategic importance for the Arthritis Foundation and patients with RA.
- Availability of funds.

A formal email notification will be provided to the applicant's organization for successful applications. An award notification is not an authorization to begin

performance. Any costs incurred before receipt of the notice of award are at the recipient's risk.

2. Award Management and Reporting

AF Science Staff will have substantial programmatic involvement, beyond the normal stewardship role in this award. When multiple years are involved, awardees will be required to submit Annual Progress Reports and Annual Accounting Reports via Proposal Central in addition to a final report once the project is complete. Individual awards are based on the application submitted to, and as approved by, the AF and are subject to the specific terms and conditions identified in the notice of award. Additional regulations that need to be observed include the registration of clinical trials within 21 days of protocol approval on ClinicalTrials.gov.

All awardees must acknowledge the support from this funding mechanism in all presentations and publications related to this project by including the following language: "The authors wish to acknowledge the Arthritis Foundation financial support for this work." Any publications supported in full or in part by this funding must also cite the grant Digital Object Identifier (DOI) that will be assigned at the time of award activation.

3. Questions and Additional Information

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

For general grants information and with questions regarding application instructions, application, and processes, please email:
AFscience@arthritis.org (preferred method of contact)

Scientific/Research Contact(s)
Kristen Mueller, PhD, VP of Autoimmune Arthritis Research Programs
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