TEXAS HEART® INSTITUTE

NIH Exploratory/Developmental Research Grant Award (R21)

The R21 grant mechanism supports high-risk, high-reward projects that are still in the early/conceptual stages of development. Preliminary data are not required. R21s cannot be renewed.

Note: NHLBI does not accept investigator-initiated (unsolicited) R21s. NHLBI only accepts R21 applications in response to specific RFAs.

Project period: ≤ 2 years

Budget: Varies depending on the specific FOA. The parent announcement states ≤ $275,000 total direct costs with no more than $200,000 in a single year.

Formatting

- Font: Use only Arial, Helvetica, Palatino Linotype, or Georgia fonts in black color with a size of 11 points or larger.
- Margins: Margins must be at least ½ inch on all sides.

  No information should appear in the margins. For example, don't make headers or footers with the PI's name, or with page numbers.
- Spacing: The text should be single-spaced.
- Figures: Within the figure/chart itself, you may use one of the approved fonts listed above in a smaller type size; however, it must be easily legible and black in color. For the figure legend, use the same font type and size as the main text.
- File format: All documents should be converted to PDF format before being uploaded. Use a descriptive file name of 50 characters or less. Do NOT use any special characters (&, -, *, %, /, #) OR SPACES in file names. To separate words, use an underscore ("My_Attached_File.pdf").

Give As Soon As Possible to the Office of Sponsored Projects (OSP)

- Title of the proposal
- Funding opportunity announcement (FOA) number and title
- DRAFT Budget

  The OSP can assist you with preparing your budget. Contact OSP > 2 weeks in advance of the deadline.
- Contact information for subaward recipients (consortium members)
- A Statement of Work (SOW) for each subaward

  Briefly describe the work to be conducted by the subrecipient, define the deliverables (if applicable), and outline the time frame in which they are to be delivered. Provide enough detail that someone could read it and determine whether the other lab lived up to its commitment. If the PI deems it necessary, the SOW can also define all personnel and their responsibilities. It should be accurate and concise as to what, when, and (if appropriate) how your organization will accomplish the work to be performed. The SOW usually includes a timeline in the form of a chart.
- The subaward institution must provide
  - An institutional letter of intent to establish a consortium
  - A detailed budget
  - A detailed Budget Justification

Application Documents

- **Letter of Intent** (optional)

  Check the specific RFA to see if an LOI is requested. Even if requested, often it is not required and it is not reviewed. It is used to plan the scientific review.

- **Cover Letter** (optional)

  The cover letter should contain any of the following information, as applicable:

  - Application title
  - Title of the FOA (PA or RFA)
  - For late applications, specific information about the timing and nature of the delay
  - For changed/corrected applications submitted after the due date, a cover letter that explains the reason for late submission of the changed/corrected applications. If you already submitted a cover letter with a previous submission and are now submitting a late change/corrected application, you must include all previous cover letter text in the revised cover letter. The system does not retain any previously submitted cover letters; therefore, you must repeat all information previously submitted in the cover letter, as well as any additional information.
  - Explanation for subaward budget components that are not active for all budget periods of the proposed grant
  - If a video is to be submitted as part of the application, information about the intent to submit it
  - If applicable, a statement indicating that the proposed studies will generate large-scale genomic data that will be shared according to the NIH Genomic Data Sharing Policy (see NIH Guide Notices on the Implementation of the NIH Genomic Data Sharing Policy and Reminder about the Implementation of the Genomic Data Sharing Policy).

- **PHS Assignment Request**

  This information is entered directly into the SF424 application. Provide this information to OSP:

  - Funding opportunity number and funding opportunity title
  - For unsolicited R21s, suggest up to 3 NIH institutes/centers (You may also exclude up to 3 NIH Institutes/centers).
  - For unsolicited R21s, suggest up to 3 study sections (You may also exclude up to 3 study sections).
  - (Optional) A list of individuals who should not review your application and the reason why (usually a conflict of interest)
  - Up to 5 scientific areas of expertise needed to review your application (e.g. cardiovascular physiology, stem cell biology)

- **Project Summary**

  An abstract. No more than 30 lines of text.

- **Project Narrative**

  A concise lay summary. 2-3 sentences only. Think big picture/human health.

- **Multiple PD/PI Leadership Plan** (uncommon for R21)

- **Consortium/Contractual Arrangements** (for subawards)

  Describe the arrangement, stating the roles/responsibilities of the people and organizations involved. Explain the plan for adequate communication.

- **Facilities & Other Resources**

  A separate Facilities & Other Resources document is required for each subaward institution.

- **Major Equipment**

  A separate Major Equipment document is required for each subaward institution.

- **Budget Justification:**

  R21s use modular budgets. The budget justification should include

  - **Personnel Justification**

    List *Senior/Key Personnel* (the PI and those essential to the project), *Other Significant Contributors* (individuals who have committed to contribute to the scientific development or execution of the project, but are not committing any specified measurable effort, e.g. unpaid collaborators, unpaid consultants), and *Other Personnel* (e.g. students, postdocs, technicians). State their title, % effort in person months, and role in the project.

    The *Senior/Key Personnel* comprise all individuals who contribute in a substantive, meaningful way to the scientific development or execution of the project (regardless of whether salary is requested). Consultants should be included if they meet this definition. List individuals that meet the definition of senior/key regardless of what organization they work for.

  - **Consortium Justification** (for subawards)

    Include the total costs (direct costs plus F&A costs), rounded to the nearest $1,000, for each consortium/subcontract. List all subcontract personnel, their % effort in person months, and their role in the project. Indicate if a consortium component is foreign.

  - **Additional Narrative Justification** (if applicable)

    Include explanations for variations in the number of modules requested annually. Describe any direct costs that were excluded from the total direct costs (such as equipment, tuition remission) and any work being conducted off-site, especially if it involves a foreign study site or an off-site F&A rate.

- **Biosketches** for all Senior/Key Personnel and Other Significant Contributors listed in the Personnel Justification (≤ 5 pages/biosketch).

  The biosketch should include the following sections: A) Personal Statement, B) Positions and Honors (listed in chronological order), C) Contributions to Science (briefly describe up to 5), and D) Research Support (list both ongoing and completed research projects for the past 3 years). *Do not* state % effort or direct costs. Include PubMed Central ID (PMCID) numbers (if available) on all references. Include a link to your NCBI MyBibliography webpage. An eRA Commons username is only required for the PI.

- **Protection of Human Subjects** (if applicable)

- **Vertebrate Animals** (if applicable)

  Include these 4 sections:

  1. **Description of Procedures**

Concisely describe all procedures involving live vertebrate animals (Don't explain anything done after euthanasia). Identify the species, strains, ages, sex, and total number of animals by species. If dogs or cats are involved, indicate the source of the animals.

2. Justifications

Describe why the species is appropriate for the proposed research. Explain why the research goals cannot be accomplished by using an alternative model (e.g. computational, human, invertebrate, *in vitro* model).

3. Minimization of Pain and Distress

Describe the measures that will be taken to minimize discomfort, distress, pain, and injury. These include analgesia, anesthesia, sedation, palliative care, and humane endpoints.

4. Method of Euthanasia

For most applications, state that the animals will be euthanatized in a manner consistent with the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals. If a method is not consistent with AVMA guidelines, describe the method, provide a scientific justification, and indicate steps that will be taken to minimize pain and distress.

- **Select Agent Research** (if applicable)
- **Resource Sharing Plan** (check the RFA for specific requirements)
  - *Sharing Model Organisms*. If the project involves developing a model organism, include a plan to share and distribute that resource or explain why sharing is restricted or not possible.
  - *Genomic Data Sharing*. Describe your plan for sharing large-scale genomic data or an explanation for why sharing is not possible.
- **Authentication of Key Biological and/or Chemical Resources**

  Briefly describe methods to ensure the identity and validity of key biological and/or chemical resources.

  Key biological and/or chemical resources are those that
  1) may differ from laboratory to laboratory or over time;
  2) may have qualities and/or qualifications that could influence the research data; and
  3) are integral to the proposed research.
  (e.g. cell lines, specialty chemicals, antibodies, and other biologics)

  Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common reagents or chemicals.
- **Letters of Support** (if applicable)

  New/early investigators—letters to demonstrate independence and institutional support
  Letters of commitment from collaborators, consultants, and co-investigators
- **Introduction to Resubmission** (if applicable, 1 page)
- **Research Plan:**
  - **Specific Aims** (1 page)

    Suggested format:

    Paragraph 1. Introduce the problem. What is known and unknown? What is the critical need?

Paragraph 2. Rationale, preliminary data (if any), overall hypothesis, and objective(s). Why is your lab particularly qualified to do this?

Specific Aims. R21s typically have 2 specific aims. Give each aim a title that is the overall objective. Briefly summarize the rationale, objective, and experimental approach for each aim. If relevant, include a sub-hypothesis.

Summary. In 2-3 sentences, state the expected outcome, why the project is innovative, and why the project is significant.

- **Research Strategy** (6 pages)

  The RFA may include guidance for the research strategy. Read the RFA and make sure to address any requests specific to that program.

  Subsections:

  A. Significance

  Rigor and Transparency guidance: Describe the scientific premise for the proposed project, including the strengths and weaknesses of published research, or preliminary data crucial to the support of your application.

  B. Innovation

  C. Approach

  a. Preliminary Studies (not required for R21)

  b. Research Design and Methods

  Rigor and Transparency guidance: Describe the experimental design and methods in sufficient detail to convey how you will obtain robust and unbiased results. Indicate what statistical tests will be used and the number of biological replicates to be performed.

  Sex as a Biological Variable guidance: Explain how relevant biological variables, such as sex, are factored into your research designs and analyses for studies in vertebrate animals and humans. For example, strong justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex.

  c. Timeline (optional)

  d. Summary/Concluding Remarks (optional)

  Important notices: Implementing Rigor and Transparency (NOT-OD-16-011)
  Consideration of Sex as a Biological Variable (NOT-OD-15-102)

- **References Cited**

  No specific format is required. Include the names of all authors (don't use "et al"). Include PMCID numbers (if available) when citing applicable papers that you author or that arise from your NIH-funded research. Here are instructions to add PMCID numbers to all your EndNote references.

Consultants, Collaborators, and Co-investigators

A **consultant** provides advice or services. List consultants as key personnel only if they contribute substantively and measurably to the scientific development or execution of a project. Typically, consultants do not receive a salary from your grant, but in some cases, they may receive a fee.

For paid consultants, don't indicate % effort in the personnel justification; instead, indicate their commitment in hours/week and cost/hour. List fees for paid consultants in the 'Consultant Services' section of the detailed budget. Their letter of support should complement the budget justification by stating their hourly commitment and cost per hour.

A **collaborator** is a scientist whose distinct expertise complements your own. Collaborators always play an active role in the research and are typically listed as key personnel. They may or may not receive salary from the grant.

A **co-investigator** shares your area of expertise and therefore contributes in guiding the scientific direction of the overall project.

Collaborators or co-investigators at other institutions can have their salary paid through a consortium agreement (subaward).

Subawards

Subawards allow another organization to perform some activities for your grant under your supervision. They enable collaborations between you—the grantee—and the subawardee. You must still include the details of the work in your application because the initial peer review committee needs to evaluate it (unlike a purchase contract). A subaward requires a financial agreement between THI and the other organization.

THI (not the subawardee) is accountable to the NIH for the performance of the research project, spending of grant funds by all parties, fulfilling reporting requirements, negotiating assurances for animal and human subjects, and meeting other obligations for the grant.