Dark Dimensions of the RNA Regulome (D2R2)

An Ideas Lab Activity

PROGRAM SOLICITATION

NSF 22-510

National Science Foundation

Directorate for Biological Sciences

Preliminary Proposal Due Date(s) ***(required)*** (due by 5 p.m. submitter's local time):

January 31, 2022

Full Proposal Deadline(s) (due by 5 p.m. submitter's local time):

August 31, 2022

IMPORTANT INFORMATION AND REVISION NOTES

Innovating and migrating proposal preparation and submission capabilities from FastLane to Research.gov is part of the ongoing NSF information technology modernization efforts, as described in Important Notice No. 147. In support of these efforts, research proposals submitted in response to this program solicitation must be prepared and submitted via Research.gov or via Grants.gov, and may not be prepared or submitted via FastLane.

Any proposal submitted in response to this solicitation should be submitted in accordance with the revised *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) (NSF 22-1), which is effective for proposals submitted, or due, on or after October 4, 2021.

SUMMARY OF PROGRAM REQUIREMENTS

General Information

Program Title:

Dark Dimensions of the RNA Regulome (D2R2)
An Ideas Lab Activity

Synopsis of Program:

This solicitation invites participation in an Ideas Lab whose focus will be the exploration of novel approaches to elucidate the evolutionary and functional significance of RNA transcripts that do not encode proteins as well as the technological innovations that may arise from the ability to harness the power of non-coding RNA to solve pressing societal problems. Ideas Labs are intensive, facilitated workshops to find innovative solutions to grand challenge problems. The overarching aim of this Ideas Lab is to bring together a diverse set of researchers from multiple disciplines spanning biology, chemistry, physics, mathematics, computer and information sciences, and engineering, to stimulate generation and execution of innovative research that advances our understanding of the origin, diversity, and functions of non-coding RNAs. Outcomes from this Ideas lab should lead to new theories and models for understanding non-coding RNAs, new approaches to manipulate and control non-coding RNA activity, and biotechnological innovations based on the expected research results that spur the bioeconomy and enhance our ability to predict and mitigate the effects of changing environments on organisms and ecosystems.

Although our ability to sequence, analyze, and manipulate genomes has significantly advanced in the last two decades, we still have not solved the grand challenge of understanding how genomes produce phenotypic variation and give rise to taxonomic and functional diversity. Despite substantial investments and widespread implementation, genome-wide association studies have only succeeded in explaining a small fraction of the genetic variation in most organisms, and much of this variation maps onto poorly characterized non-protein-coding regions of genomes. Many of those "dark" regions of the genome are transcribed into RNAs that do not encode proteins but may show signatures of evolutionary conservation, unusual structural features, and/or non-random expression patterns that are suggestive of their functional roles.

There has been a surge of interest in uncovering the cellular, physiological, and developmental roles of non-coding RNAs in recent years, and it is now clear that non-coding RNAs affect a wide range of cellular processes, including regulation of gene expression, developmental processes, metabolism, physiology, and even interactions with other organisms. Understanding the role of non-coding RNA in these cellular processes will be essential to enable the rational design of biological systems for biotechnology applications. Nevertheless, the vast majority of non-coding RNAs remain uncharacterized, and our understanding of their functional roles remains in its infancy. It is likely that the underlying rules governing the evolution and function of non-coding RNAs are different from those of protein-coding ones; hence fresh perspectives and novel approaches are needed to unveil the syntax and semantics of this hidden language. A wealth of new biology awaits discovery, along with hitherto unimagined biotechnology innovations, powered by transformative technologies and approaches to illuminate the dark

dimensions of the RNA regulome, and decipher the role of non-coding RNAs in shaping the form and function of living organisms through evolution.

Cognizant Program Officer(s):

Please note that the following information is current at the time of publishing. See program website for any updates to the points of contact.

- Stephen DiFazio, telephone: (703) 292-4517, email: sdifazio@nsf.gov
- Jean X. Gao, telephone: (703) 292-7253, email: jgao@nsf.gov
- Leslie J. Rissler, telephone: (703) 292-4628, email: lrissler@nsf.gov
- Gerald Schoenknecht, telephone: (703) 292-5076, email: gschoenk@nsf.gov

Applicable Catalog of Federal Domestic Assistance (CFDA) Number(s):

- 47.074 --- Biological Sciences

Award Information

Anticipated Type of Award: Standard Grant or Continuing Grant

Estimated Number of Awards: 4 to 7

Anticipated Funding Amount: $15,000,000

Subject to availability of funds

Eligibility Information

Who May Submit Proposals:

The categories of proposers eligible to submit proposals to the National Science Foundation are identified in the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG), Chapter I.E. Unaffiliated individuals are not eligible to submit proposals in response to this solicitation.

Who May Serve as PI:

There are no restrictions or limits.

Limit on Number of Proposals per Organization:

There are no restrictions or limits.

Limit on Number of Proposals per PI or co-PI: 1

An individual may serve as PI or coPI on only one proposal.

Proposal Preparation and Submission Instructions

A. Proposal Preparation Instructions

- **Letters of Intent:** Not required
- **Preliminary Proposals:** Submission of Preliminary Proposals is required. Please see the full text of this solicitation for further information.
- **Full Proposals:**
    - Full Proposals submitted via Research.gov: *NSF Proposal and Award Policies and Procedures Guide* (PAPPG) guidelines apply. The complete text of the PAPPG is available electronically on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.
    - Full Proposals submitted via Grants.gov: *NSF Grants.gov Application Guide: A Guide for the Preparation and Submission of NSF Applications via Grants.gov* guidelines apply (Note: The *NSF Grants.gov Application Guide* is available on the Grants.gov website and on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=grantsgovguide).

B. Budgetary Information

- **Cost Sharing Requirements:**

  Inclusion of voluntary committed cost sharing is prohibited.

- **Indirect Cost (F&A) Limitations:**

  Not Applicable

- **Other Budgetary Limitations:**

  Not Applicable

C. Due Dates

- **Preliminary Proposal Due Date(s)** ***(required)*** (due by 5 p.m. submitter's local time):

  January 31, 2022

- **Full Proposal Deadline(s)** (due by 5 p.m. submitter's local time):

  August 31, 2022

Proposal Review Information Criteria

Merit Review Criteria:

National Science Board approved criteria. Additional merit review criteria apply. Please see the full text of this solicitation for further information.

Award Administration Information

Award Conditions:

Standard NSF award conditions apply.

Reporting Requirements:

Standard NSF reporting requirements apply.

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I. INTRODUCTION

Understanding how an organism's genome controls its phenotype under varying conditions remains a grand challenge in biology. Significant advances in our ability to sequence, analyze and manipulate genomes over the past two decades have yielded unprecedented insights into the parts of the genome that code for proteins, at least in some model and emerging model systems. However, in eukaryotes, large regions of the genome do not code for proteins, and the functions of those regions for the most part remain unknown – hence the reference to the "dark" genome. Emerging evidence indicates the importance of many of these genomic regions in biological functions; for example, genome-wide studies to associate heritable genetic variation with phenotypic variation indicate they are significant determinants of phenotypic diversity. Thus, identifying how "dark" regions of the genome manifest their functions will illuminate how the genome controls living systems in all their diversity and complexity.

Ongoing research indicates that much of the "dark" genome is transcribed, producing a diverse array of non-coding RNAs, some of which show signatures of evolutionary conservation, unusual structural features, and/or non-random, cell-type dependent expression patterns that are suggestive of regulatory or other critical roles in organismal development and function. Some classes of non-coding RNAs, such as micro-RNAs and small-interfering RNAs, have been extensively characterized in numerous organisms. Although much remains to be learned about these RNAs, the field is advanced enough that many of them can be predicted computationally, and details of the molecular machinery responsible for their production and processing have been determined. In contrast, relatively little is known about the origin, evolution, production, and functions of other classes of short non-coding RNAs, including fragments derived from ribosomal and transfer RNA, as well as most longer noncoding transcripts, including long non-coding RNAs, long intergenic non-coding RNAs, and circular RNAs. These knowledge gaps present substantial challenges for the following reasons:

- A large fraction of eukaryotic genomes is transcribed at some level, but much of this transcription is likely to be spurious and therefore inconsequential for organismal phenotypes. This creates substantial background noise that obscures the functional components of the transcriptome.

- Some non-coding RNAs have low levels of expression in narrow functional contexts (often confined to a single cell type or developmental stage), hence phenotypic consequences of their ablation are difficult to observe and predict in different organisms and environmental contexts.
- The sequences of many functional non-coding RNAs evolve rapidly, which inhibits identification of orthologous sequences and creates challenges for phylogenomic approaches aimed at pinpointing origins, establishing evolutionary relationships, and inferring function.
- Relationships among different classes of non-coding RNAs are poorly understood, and higher order interactions among these RNAs may be key to discovering regulatory networks of these molecules and their emergent functions.
- The non-coding regulatory architecture has not yet been characterized for the genomes of most organisms, posing a substantial obstacle to evolutionary and ecological research that by and large does not rely on model or single-organism approaches.
- The biological functions of non-coding RNAs remain to be determined for most eukaryotic clades, as most of the research in this area has been performed in humans. Biological functions of many non-coding RNAs in bacteria and archaea also remain elusive.
- The role of non-coding RNA in microbe-microbe interactions and host-microbe interactions is beginning to emerge. In the case of pathogens, interaction of a pathogen's non-coding RNA with the host and the host's non-coding RNA with the pathogen may determine the outcome of the infection. Disentangling how microbes and host non-coding RNA modulate these interactions is even more challenging in the context of dynamic host-microbiome interactions.

Many traditional approaches, such as the codon-based models of sequence evolution, are inadequate for understanding the origin and evolution of non-coding RNAs, hence novel conceptual frameworks and fresh perspectives are needed for this purpose. New technologies are required to surmount the challenges of detecting and functionally characterizing non-coding RNAs on a large scale in a wide range of organisms, developmental stages, and environmental contexts. State-of-the-art computational methodologies, including artificial intelligence, are needed for predicting structure and function and inferring regulatory networks from existing public data and the scientific literature. Automated platforms must be developed for submitting, curating, and annotating non-coding RNAs across diverse genomes. Open-source, accessible and user-friendly data analysis cyberinfrastructure is necessary to facilitate integration of non-coding RNA data across sites and scales. Breakthrough tools and approaches that address the challenges noted above are critical to advancing the field.

Insights gained from investigating non-coding RNAs promise considerable practical consequences. Technologies based on non-coding RNAs are likely to create new ways of interrogating and manipulating biological systems, and thus spur the bioeconomy. Indeed, some of the most impactful recent advances in genetic engineering are mediated by non-coding RNAs, including CRISPR-Cas9-based genome editing and RNA interference techniques. Moreover, regulation of gene expression by non-coding RNAs appears key to rapid responses to environmental stress; thus, a more complete understanding of non-coding RNA capabilities will enhance prediction of organismal, community and ecosystem responses to climate change and other perturbations and enable design of mitigation strategies. Finally, the new knowledge will expand the synthetic toolkit for creating organisms with desired characteristics and functionalities, such as robustness and resilience in the face of a changing environment.

The goal of this Ideas Lab is to bring together researchers from diverse backgrounds in a stimulating interactive setting to foster creative solutions to these challenging problems, thereby accelerating the pace of discovery in a way that would not be possible within typical disciplinary confines. The lab should stimulate innovative and transformative research proposals that leverage developments in computational biology, artificial intelligence, information sciences, molecular biology, synthetic biology, chemistry, physics, evolutionary biology, and ecology to find new ways to discover, interrogate, and functionally characterize the non-coding portion of the RNA regulome.

Participation in the Ideas Lab requires an invitation in response to a preliminary proposal. Submission of a full proposal derived from the Ideas Lab requires both participation in the Ideas Lab and an invitation to submit a full proposal.

Full proposals derived from the Ideas Lab must include ideas that could lead to a step-change, rather than to incremental advances in our knowledge. It is expected that these full proposals will be generated by multidisciplinary teams; the teams may include researchers with expertise in biology, physics, biophysics, mathematical modeling, statistics, chemistry, engineering, computer science, or any other discipline suited to shed light on the topic. Additionally, each proposing group should develop an educational plan to train students and technicians who will participate in the project, as well as to provide generalized instruction about non-coding RNAs for graduate and undergraduate students and for the lay public. Given the likely complexity of the proposed research, the participation of specialists in other relevant areas is strongly encouraged.

II. PROGRAM DESCRIPTION

The Ideas Lab

An Ideas Lab is an interactive workshop on a focused problem and typically involves approximately 30 participants. This Ideas Lab aims to stimulate thinking in promising new, or currently under-developed research areas relevant to non-coding RNAs.

Participants will be expected to engage constructively in dialogue with one another, the facilitators, and the Director and Mentors to develop collaborative research proposals. Collaboration is an integral aspect of the activity.

The Ideas Lab is sponsored by NSF. As such, only those eligible to apply for funding from NSF will be eligible to apply to attend the Ideas Lab.

The Ideas Lab will run for five days starting mid-morning on Day One and finishing mid-afternoon on Day Five. At the outset, the participants will work collaboratively to identify and define the scope of the research challenges relating to non-coding RNAs. As the Ideas Lab progresses, participants will dynamically develop and hone novel ideas about how the identified challenges may be addressed. These ideas and approaches will be used in the development of research projects that are genuinely innovative and high risk. The Ideas Lab will include inputs from a variety of sources and will aim to develop collaborative research projects. Following the Ideas Lab, proposals may be submitted by teams selected to submit a full proposal.

How will the Ideas Lab Work?

The Ideas Lab is an intensive, interactive, and free-thinking environment, where a diverse group of participants from a range of disciplines and backgrounds gets together for five days – away from their everyday worlds – to immerse themselves in collaborative thinking and come up with innovative approaches.

The nature of the Ideas Lab requires a high degree of trust among participants to make the required breakthroughs in scientific thinking. This trust extends to allowing the free and frank exchange of scientific ideas, some being in the very early stages of development. The discussion should not be about ideas that are already well-developed but not yet published. Rather, the goal is to bring individuals from different disciplines together to interact and engage in free thinking based on first principles, to learn from one another, and to create an integrated vision for future research projects. It is expected that these ideas would be shared within the Ideas Lab, but their confidentiality would be respected outside the Ideas Lab.

The Ideas Lab will be led by a Director whose role is to assist in defining the topics and help facilitate discussions at the event. The Director will be joined by a small number of Mentors. The Director and Mentors will be selected by NSF based on their intellectual standing, their impartiality and objectivity, and their broad understanding of, and enthusiasm for, the subject area. The Director and Mentors will fully participate in the Ideas Lab but will not be eligible to receive research funding under this collaborative activity. They will therefore act as impartial peer reviewers in the process, providing a function analogous to that of an NSF review panel.

The process can be broken down into several stages:

- Defining the scope of the challenges
- Evolving common languages and terminologies among people from a diverse range of backgrounds and disciplines
- Sharing perspectives and understanding of the scientific challenges, as well as the diverse expertise brought by the participants to the Ideas Lab
- Taking part in break-out sessions focused on the challenges, using creative thinking techniques
- Capturing the outputs in the form of highly innovative research projects
- Using "real-time" peer review to develop projects at the Ideas Lab

The Ideas Lab will be an intensive event. For the well-being of participants, the venue offers opportunities for relaxation, and the timetable will include networking and other activities as a break from the detailed technical discussions.

Who Should Apply to Participate?

Having the right mix of participants influences the success or failure of such an activity. Applications are encouraged from individuals representing diverse research areas across a range of disciplines including, biology, physics, biophysics, mathematical modeling, statistics, chemistry, engineering, computer science, or any other discipline suited to shed light on the topic. However, we are not defining the disciplines that should be represented at this Ideas Lab; rather we are asking potential participants to indicate how their expertise can address the challenges associated with understanding function and evolution of non-coding RNAs.

The ability to develop and pursue a new approach will also be crucial. Expertise is required from a broad range of disciplines, and applicants should not feel limited by conventional perceptions: the Ideas Lab approach is about bringing together people who would not normally interact. We actively encourage applications from people who are experts in their own research areas but have not yet applied it to this challenge.

This is an opportunity to share ideas and develop future collaborations. Participants at any stage of their research career are welcomed; however, they must be eligible to apply for funding from NSF.

Location and Date

This Ideas Lab will take place in person at a location to be determined, in the vicinity of NSF headquarters in Northern Virginia from June 13 - 17, 2022. The environment will encourage free and open-minded thinking, which are vital for the success of such an event. Additional information about the venue and meeting logistics will be provided to the selected participants. All travel to the Ideas Lab, accommodation, refreshments, breakfast, lunch and dinner costs will be covered by NSF. However, all incidental costs incurred while at the event will be borne by the participant.

Applications for this Activity

In brief, any individual interested in participating in the Ideas Lab should respond to this solicitation by submitting a preliminary proposal. Participation in the Ideas Lab is by invitation only from the pool of applicants who submitted a preliminary proposal.

Submission of the preliminary proposal will be considered an indication of availability to attend and participate through the full course of the five-day residential workshop.

Participants will be selected based on their expertise, interests, and other characteristics described in their submitted preliminary proposals. The participants should be willing to engage in frank disclosure and assessment of ideas in a collegial, professional, and responsible fashion. An independent selection committee will recommend a list of potential participants from all applicants. NSF Staff in consultation with the Ideas Lab Director and Mentors will select the final list of participants from the submitted preliminary proposals.

Following the Ideas Lab, participants will be invited to submit to NSF full proposals, based on the outline developed at the Ideas Lab, by the **August 31, 2022** deadline.

III. AWARD INFORMATION

Approximately $15,000,000 will be available in fiscal year 2023. Up to 7 awards will be made pending availability of funds and the type, scale, and variety of project ideas developed at the Ideas Lab.

IV. ELIGIBILITY INFORMATION

Who May Submit Proposals:

The categories of proposers eligible to submit proposals to the National Science Foundation are identified in the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG), Chapter I.E. Unaffiliated individuals are not eligible to submit proposals in response to this solicitation.

Who May Serve as PI:

There are no restrictions or limits.

Limit on Number of Proposals per Organization:

There are no restrictions or limits.

Limit on Number of Proposals per PI or co-PI: 1

An individual may serve as PI or coPI on only one proposal.

V. PROPOSAL PREPARATION AND SUBMISSION INSTRUCTIONS

A. Proposal Preparation Instructions

Preliminary Proposals *(required)*: Preliminary proposals are required and must be submitted via Research.gov, even if full proposals will be submitted via Grants.gov.

Submission of Preliminary Proposals is required for participation in the Ideas Lab. Please note, the preliminary proposal must come from one individual and cannot include co-PIs or collaborators. Participants in the Idea Lab will be selected on the basis of information submitted in the preliminary proposal. The applications are limited to **two pages of "Project Description,"** which should be submitted as a preliminary proposal through Research.gov. Standard NSF formatting guidelines apply. See the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) for guidance. Proposers are reminded to identify the program solicitation number (located on the first page of this document) in the Research.gov preliminary proposal set-up wizard and populated on the NSF Cover Sheet. Compliance with this requirement is critical to determining the relevant proposal processing guidelines. Please note that even though proposals must be submitted to BIO/IOS, once received the proposals will be managed by a BIO-wide team of NSF Program Directors.

The Project Description section of the preliminary proposal applications should conform to the following guidelines:

Page One:

- Please include the sentence, "I am available June 13 - 17, 2022 and can commit to attend all 5 days of the event". If you cannot commit to attend all 5 days of the event, please explain.
- Provide a brief summary of your professional background (no more than half a page). Please note, if you are selected as a participant, information provided in answer to this question will be made available to the other participants to facilitate networking at the Ideas Lab workshop.
- How do you see your expertise and interests contributing to realizing the goal of this workshop? (no more than half a page).

Page Two:

Please spend some time considering your answers to the following questions. Your responses (no more than 150 words each) will help us assess your suitability (unrelated to your research track record) for the innovative and collaborative setting of this intensive, interactive, fast-paced event.

- What is your approach to teamwork? What strengths do you bring to a team effort?
- How would you explain your area of interest to individuals with different expertise to your own? How easy do you find this?
- This workshop is especially suited to individuals who enjoy stepping outside their areas of expertise or interest, are positively driven, enjoy creative activity, and can think innovatively. It is an intensive setting requiring you to develop novel approaches with individuals you may not know. How do you consider yourself suited?
- What do you hope to gain from participating in this workshop, personally and professionally?

Applicants must include a **Biographical Sketch** and a **Current and Pending Support** document (prepared in accordance with standard NSF formatting guidelines).

No appendices or supplementary documents may be submitted.

Full Proposal Preparation Instructions: Proposers may opt to submit proposals in response to this Program Solicitation via Research.gov or Grants.gov.

- Full Proposals submitted via Research.gov: Proposals submitted in response to this program solicitation should be prepared and submitted in accordance with the general guidelines contained in the *NSF Proposal and Award Policies and Procedures Guide* (PAPPG). The complete text of the PAPPG is available electronically on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg. Paper copies of the PAPPG may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-8134 or by e-mail from nsfpubs@nsf.gov. The Prepare New Proposal setup will prompt you for the program solicitation number.
- Full proposals submitted via Grants.gov: Proposals submitted in response to this program solicitation via Grants.gov should be prepared and submitted in accordance with the *NSF Grants.gov Application Guide: A Guide for the Preparation and Submission of NSF Applications via Grants.gov*. The complete text of the *NSF Grants.gov Application Guide* is available on the Grants.gov website and on the NSF website at: (https://www.nsf.gov/publications/pub_summ.jsp?ods_key=grantsgovguide). To obtain copies of the Application Guide and Application Forms Package, click on the Apply tab on the Grants.gov site, then click on the Apply Step 1: Download a Grant Application Package and Application Instructions link and enter the funding opportunity number, (the program solicitation number without the NSF prefix) and press the Download Package button. Paper copies of the Grants.gov Application Guide also may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-8134 or by e-mail from nsfpubs@nsf.gov.

In determining which method to utilize in the electronic preparation and submission of the proposal, please note the following:

Collaborative Proposals. All collaborative proposals submitted as separate submissions from multiple organizations must be submitted via Research.gov. PAPPG Chapter II.D.3 provides additional information on collaborative proposals.

See PAPPG Chapter II.C.2 for guidance on the required sections of a full research proposal submitted to NSF. Please note that the proposal preparation instructions provided in this program solicitation may deviate from the PAPPG instructions.

Special instructions for submitting full proposals to this solicitation.

As stated previously, even though proposals must be submitted to BIO/IOS, once received the proposals will be managed by a BIO-wide team of NSF Program Directors.

Full proposals based on project ideas developed through interactions at the Ideas lab should conform to the project outline developed at the conclusion of the workshop. If substantive changes are contemplated, an NSF Program Director should be contacted for guidance.

B. Budgetary Information

Cost Sharing:

Inclusion of voluntary committed cost sharing is prohibited.

C. Due Dates

- **Preliminary Proposal Due Date(s)** ***(required)*** (due by 5 p.m. submitter's local time):

  January 31, 2022

- **Full Proposal Deadline(s)** (due by 5 p.m. submitter's local time):

  August 31, 2022

D. Research.gov/Grants.gov Requirements

For Proposals Submitted Via Research.gov:

To prepare and submit a proposal via Research.gov, see detailed technical instructions available at: https://www.research.gov/research-portal/appmanager/base/desktop?_nfpb=true&_pageLabel=research_node_display&_nodePath=/researchGov/Service/Desktop/ProposalPreparationandSubmission.html. For Research.gov user support, call the Research.gov Help Desk at 1-800-673-6188 or e-mail rgov@nsf.gov. The Research.gov Help Desk answers general technical questions related to the use of the Research.gov system. Specific questions related to this program solicitation should be referred to the NSF program staff contact(s) listed in Section VIII of this funding opportunity.

For Proposals Submitted Via Grants.gov:

Before using Grants.gov for the first time, each organization must register to create an institutional profile. Once registered, the applicant's organization can then apply for any federal grant on the Grants.gov website. Comprehensive information about using Grants.gov is available on the Grants.gov Applicant Resources webpage: https://www.grants.gov/web/grants/applicants.html. In addition, the NSF Grants.gov Application Guide (see link in Section V.A) provides instructions regarding the technical preparation of proposals via Grants.gov. For Grants.gov user support, contact the Grants.gov Contact Center at 1-800-518-4726 or by email: support@grants.gov. The Grants.gov Contact Center answers general technical questions related to the use of Grants.gov. Specific questions related to this program solicitation should be referred to the NSF program staff contact(s) listed in Section VIII of this solicitation.

Submitting the Proposal: Once all documents have been completed, the Authorized Organizational Representative (AOR) must submit the application to Grants.gov and verify the desired funding opportunity and agency to which the application is submitted. The AOR must then sign and submit the application to Grants.gov. The completed application will be transferred to the NSF FastLane system for further processing.

Proposers that submitted via Research.gov may use Research.gov to verify the status of their submission to NSF. For proposers that submitted via Grants.gov, until an application has been received and validated by NSF, the Authorized Organizational Representative may check the status of an application on Grants.gov. After proposers have received an e-mail notification from NSF, Research.gov should be used to check the status of an application.

VI. NSF PROPOSAL PROCESSING AND REVIEW PROCEDURES

Proposals received by NSF are assigned to the appropriate NSF program for acknowledgement and, if they meet NSF requirements, for review. All proposals are carefully reviewed by a scientist, engineer, or educator serving as an NSF Program Officer, and usually by three to ten other persons outside NSF either as *ad hoc* reviewers, panelists, or both, who are experts in the particular fields represented by the proposal. These reviewers are selected by Program Officers charged with oversight of the review process. Proposers are invited to suggest names of persons they believe are especially well qualified to review the proposal and/or persons they would prefer not review the proposal. These suggestions may serve as one source in the reviewer selection process at the Program Officer's discretion. Submission of such names, however, is optional. Care is taken to ensure that reviewers have no conflicts of interest with the proposal. In addition, Program Officers may obtain comments from site visits before recommending final action on proposals. Senior NSF staff further review recommendations for awards. A flowchart that depicts the entire NSF proposal and award process (and associated timeline) is included in PAPPG Exhibit III-1.

A comprehensive description of the Foundation's merit review process is available on the NSF website at: https://www.nsf.gov/bfa/dias/policy/merit_review/.

Proposers should also be aware of core strategies that are essential to the fulfillment of NSF's mission, as articulated in *Building the Future: Investing in Discovery and Innovation - NSF Strategic Plan for Fiscal Years (FY) 2018 – 2022*. These strategies are integrated in the program planning and implementation process, of which proposal review is one part. NSF's mission is particularly well-implemented through the integration of research and education and broadening participation in NSF programs, projects, and activities.

One of the strategic objectives in support of NSF's mission is to foster integration of research and education through the programs, projects, and activities it supports at academic and research institutions. These institutions must recruit, train, and prepare a diverse STEM workforce to advance the frontiers of science and participate in the U.S. technology-based economy. NSF's contribution to the national innovation ecosystem is to provide cutting-edge research under the guidance of the Nation's most creative scientists and engineers. NSF also supports development of a strong science, technology, engineering, and mathematics (STEM) workforce by investing in building the knowledge that informs improvements in STEM teaching and learning.

NSF's mission calls for the broadening of opportunities and expanding participation of groups, institutions, and geographic regions that are underrepresented in STEM disciplines, which is essential to the health and vitality of science and engineering. NSF is committed to this principle of diversity and deems it central to the programs, projects, and activities it considers and supports.

A. Merit Review Principles and Criteria

The National Science Foundation strives to invest in a robust and diverse portfolio of projects that creates new knowledge and enables breakthroughs in understanding across all areas of science and engineering research and education. To identify which projects to support, NSF relies on a merit review process that incorporates consideration of both the technical aspects of a proposed project and its potential to contribute more broadly to advancing NSF's mission "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense; and for other purposes." NSF makes every effort to conduct a fair, competitive, transparent merit review process for the selection of projects.

1. Merit Review Principles

These principles are to be given due diligence by PIs and organizations when preparing proposals and managing projects, by reviewers when reading and evaluating proposals, and by NSF program staff when determining whether or not to recommend proposals for funding and while overseeing awards. Given that NSF is the primary federal agency charged with nurturing and supporting excellence in basic research and education, the following three principles apply:

- All NSF projects should be of the highest quality and have the potential to advance, if not transform, the frontiers of knowledge.
- NSF projects, in the aggregate, should contribute more broadly to achieving societal goals. These "Broader Impacts" may be accomplished through the research itself, through activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project. The project activities may be based on previously established and/or innovative methods and approaches, but in either case must be well justified.
- Meaningful assessment and evaluation of NSF funded projects should be based on appropriate metrics, keeping in mind the likely correlation between the effect of broader impacts and the resources provided to implement projects. If the size of the activity is limited, evaluation of that activity in isolation is not likely to be meaningful. Thus, assessing the effectiveness of these activities may best be done at a higher, more aggregated, level than the individual project.

With respect to the third principle, even if assessment of Broader Impacts outcomes for particular projects is done at an aggregated level, PIs are expected to be accountable for carrying out the activities described in the funded project. Thus, individual projects should include clearly stated goals, specific descriptions of the activities that the PI intends to do, and a plan in place to document the outputs of those activities.

These three merit review principles provide the basis for the merit review criteria, as well as a context within which the users of the criteria can better understand their intent.

2. Merit Review Criteria

All NSF proposals are evaluated through use of the two National Science Board approved merit review criteria. In some instances, however, NSF will employ additional criteria as required to highlight the specific objectives of certain programs and activities.

The two merit review criteria are listed below. **Both** criteria are to be given **full consideration** during the review and decision-making processes; each criterion is necessary but neither, by itself, is sufficient. Therefore, proposers must fully address both criteria. (PAPPG Chapter II.C.2.d(i). contains additional information for use by proposers in development of the Project Description section of the proposal). Reviewers are strongly encouraged to review the criteria, including PAPPG Chapter II.C.2.d(i), prior to the review of a proposal.

When evaluating NSF proposals, reviewers will be asked to consider what the proposers want to do, why they want to do it, how they plan to do it, how they will know if they succeed, and what benefits could accrue if the project is successful. These issues apply both to the technical aspects of the proposal and the way in which the project may make broader contributions. To that end, reviewers will be asked to evaluate all proposals against two criteria:

- **Intellectual Merit:** The Intellectual Merit criterion encompasses the potential to advance knowledge; and
- **Broader Impacts:** The Broader Impacts criterion encompasses the potential to benefit society and contribute to the achievement of specific, desired societal outcomes.

The following elements should be considered in the review for both criteria:

1. What is the potential for the proposed activity to
    a. Advance knowledge and understanding within its own field or across different fields (Intellectual Merit); and
    b. Benefit society or advance desired societal outcomes (Broader Impacts)?
2. To what extent do the proposed activities suggest and explore creative, original, or potentially transformative concepts?
3. Is the plan for carrying out the proposed activities well-reasoned, well-organized, and based on a sound rationale? Does the plan incorporate a mechanism to assess success?
4. How well qualified is the individual, team, or organization to conduct the proposed activities?
5. Are there adequate resources available to the PI (either at the home organization or through collaborations) to carry out the proposed activities?

Broader impacts may be accomplished through the research itself, through the activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project. NSF values the advancement of scientific knowledge and activities that contribute to achievement of societally relevant outcomes. Such outcomes include, but are not limited to: full participation of women, persons with disabilities, and other underrepresented groups in science, technology, engineering, and mathematics (STEM); improved STEM education and educator development at any level; increased public scientific literacy and public engagement with science and technology; improved well-being of individuals in society; development of a diverse, globally competitive STEM workforce; increased partnerships between academia, industry, and others; improved national security; increased economic competitiveness of the United States; and enhanced infrastructure for research and education.

Proposers are reminded that reviewers will also be asked to review the Data Management Plan and the Postdoctoral Researcher Mentoring Plan, as appropriate.

Additional Solicitation Specific Review Criteria

This activity, particularly the Ideas Lab approach, is designed to foster the development and implementation of creative and innovative project ideas that have the potential to transform research paradigms and/or solve previously intractable problems. We anticipate that awards made through this solicitation will be high-risk/high-impact, as they represent new and unproven ideas, approaches and/or technologies. Projects that involve the application of novel, collaborative, or interdisciplinary approaches will therefore receive priority during the consideration process. In addition, full proposals derived from the Ideas Lab will be evaluated to determine whether the scientific themes/objectives in the proposal are congruent with the ideas presented at the Ideas Lab, and whether any significant changes in project scope or resources from those presented at the Ideas Lab have been justified.

B. Review and Selection Process

Proposals submitted in response to this program solicitation will be reviewed by Ad hoc Review and/or Panel Review, or Ideas Lab.

The competition will be consistent with the guidelines for an Ideas Lab described in the PAPPG Chapter II.E.6.

Stage 1. Selection of Participants:

NSF Program Directors will convene a panel of external reviewers to advise on the selection of participants in the Ideas Lab. This group will comprise individuals who will be barred from receiving any research funding through, or in any other way collaborating on, the Ideas Lab. These individuals will be subject matter experts from diverse disciplines pertinent to the topic of the Ideas Lab. The selection panel will review the preliminary proposals submitted by applicants and will advise NSF Program Directors on participant selection. Final selection decisions regarding participation in the Ideas Lab workshop will be made by NSF.

Overall, the panel will seek to ensure that a balance of expertise and experience is present at the Ideas Lab workshop; their assessment will be based on the specific criteria outlined below:

- The ability to develop new and highly original research ideas;
- The potential to contribute to research between disciplines; and
- The ability to work in interdisciplinary teams.

Submission of the preliminary proposal will be considered an indication of commitment to attend and participate through the full course of the five-day residential Ideas Lab workshop on June 13 - 17, 2022, should the proposer be invited. The decisions of NSF about whom to invite will be final and binding.

Stage 2. Ideas Lab:

Applicants selected by NSF will participate in the Ideas Lab workshop, building collaborations and refining ideas. Organizing NSF Program Directors will select up to 6 qualified persons to serve as Mentors during the workshop. This group will also comprise individuals who will be barred from receiving any research funding through, or in any other way collaborating on, the Ideas Lab. These individuals will be subject matter experts from diverse disciplines pertinent to the topic of the Ideas Lab. One of the Mentors will act as the Director of the workshop and will be responsible for leading the activities of the Mentors.

Anonymous real-time peer review involving the participants and the Mentors will be incorporated into a workshop format, providing iterative constructive feedback during the development of project ideas. The workshop will use a team of facilitators to guide the creation of interdisciplinary teams and the creative development of ideas, and to ensure that the workshop progresses in a productive manner. At the end of the workshop, the Mentors will provide a consensus report summarizing their evaluation of each project idea. The recommendations of the Mentors are advisory to NSF. Informed by their advice, within seven to fourteen days following the workshop, NSF Program Directors will consider which projects to invite for submission as full proposals. At their discretion, NSF Program Directors may invite some, all or none of the Ideas Lab projects for submission to NSF as full proposals. NSF Program Directors will issue written invite/not invite full proposal decisions to the Ideas Lab participants with instructions to submit invited full proposals to NSF by August 31, 2022. These invited full proposals must be prepared according to standard NSF *Proposal & Award Policies & Procedures Guide*.

It is anticipated that these full proposals developed through the Ideas Lab workshop will feature the following:

- Novel, highly multidisciplinary research projects, clearly reflecting the distinctive opportunity for creating such projects that the Ideas Lab mechanism provides;
- Clear evidence that the team has the capability to deliver its project as a high-quality multidisciplinary activity; and
- Clear relevance and potential to make a distinctive and novel contribution to addressing the research challenges of understanding function and evolution on non-coding RNAs.

Inclusion of international partners as Senior Investigators is encouraged; however, no NSF funding can be directed to research in overseas labs. NSF funds can be used for travel and student exchange essential to the project.

Stage 3. Review and recommendation of full proposals:

NSF-invited full proposals arising from the Ideas Lab will be submitted *via* Research.gov or Grants.gov by August 31, 2022. NSF-invited proposals will be reviewed internally by the cognizant NSF Program Officers and other external reviewers, as appropriate.

Reviewers will be asked to evaluate proposals using two National Science Board approved merit review criteria and, if applicable, additional program specific criteria. A summary rating and accompanying narrative will generally be completed and submitted by each reviewer and/or panel. The Program Officer assigned to manage the proposal's review will consider the advice of reviewers and will formulate a recommendation.

After scientific, technical and programmatic review and consideration of appropriate factors, the NSF Program Officer recommends to the cognizant Division Director whether the proposal should be declined or recommended for award. NSF strives to be able to tell applicants whether their proposals have been declined or recommended for funding within six months. Large or particularly complex proposals or proposals from new awardees may require additional review and processing time. The time interval begins on the deadline or target date, or receipt date, whichever is later. The interval ends when the Division Director acts upon the Program Officer's recommendation.

After programmatic approval has been obtained, the proposals recommended for funding will be forwarded to the Division of Grants and Agreements for review

of business, financial, and policy implications. After an administrative review has occurred, Grants and Agreements Officers perform the processing and issuance of a grant or other agreement. Proposers are cautioned that only a Grants and Agreements Officer may make commitments, obligations or awards on behalf of NSF or authorize the expenditure of funds. No commitment on the part of NSF should be inferred from technical or budgetary discussions with a NSF Program Officer. A Principal Investigator or organization that makes financial or personnel commitments in the absence of a grant or cooperative agreement signed by the NSF Grants and Agreements Officer does so at their own risk.

Once an award or declination decision has been made, Principal Investigators are provided feedback about their proposals. In all cases, reviews are treated as confidential documents. Verbatim copies of reviews, excluding the names of the reviewers or any reviewer-identifying information, are sent to the Principal Investigator/Project Director by the Program Officer. In addition, the proposer will receive an explanation of the decision to award or decline funding.

VII. AWARD ADMINISTRATION INFORMATION

A. Notification of the Award

Notification of the award is made to *the submitting organization* by a Grants Officer in the Division of Grants and Agreements. Organizations whose proposals are declined will be advised as promptly as possible by the cognizant NSF Program administering the program. Verbatim copies of reviews, not including the identity of the reviewer, will be provided automatically to the Principal Investigator. (See Section VI.B. for additional information on the review process.)

B. Award Conditions

An NSF award consists of: (1) the award notice, which includes any special provisions applicable to the award and any numbered amendments thereto; (2) the budget, which indicates the amounts, by categories of expense, on which NSF has based its support (or otherwise communicates any specific approvals or disapprovals of proposed expenditures); (3) the proposal referenced in the award notice; (4) the applicable award conditions, such as Grant General Conditions (GC-1)*; or Research Terms and Conditions* and (5) any announcement or other NSF issuance that may be incorporated by reference in the award notice. Cooperative agreements also are administered in accordance with NSF Cooperative Agreement Financial and Administrative Terms and Conditions (CA-FATC) and the applicable Programmatic Terms and Conditions. NSF awards are electronically signed by an NSF Grants and Agreements Officer and transmitted electronically to the organization via e-mail.

*These documents may be accessed electronically on NSF's Website at https://www.nsf.gov/awards/managing/award_conditions.jsp?org=NSF. Paper copies may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-8134 or by e-mail from nsfpubs@nsf.gov.

More comprehensive information on NSF Award Conditions and other important information on the administration of NSF awards is contained in the NSF *Proposal & Award Policies & Procedures Guide* (PAPPG) Chapter VII, available electronically on the NSF Website at https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

C. Reporting Requirements

For all multi-year grants (including both standard and continuing grants), the Principal Investigator must submit an annual project report to the cognizant Program Officer no later than 90 days prior to the end of the current budget period. (Some programs or awards require submission of more frequent project reports). No later than 120 days following expiration of a grant, the PI also is required to submit a final project report, and a project outcomes report for the general public.

Failure to provide the required annual or final project reports, or the project outcomes report, will delay NSF review and processing of any future funding increments as well as any pending proposals for all identified PIs and co-PIs on a given award. PIs should examine the formats of the required reports in advance to assure availability of required data.

PIs are required to use NSF's electronic project-reporting system, available through Research.gov, for preparation and submission of annual and final project reports. Such reports provide information on accomplishments, project participants (individual and organizational), publications, and other specific products and impacts of the project. Submission of the report via Research.gov constitutes certification by the PI that the contents of the report are accurate and complete. The project outcomes report also must be prepared and submitted using Research.gov. This report serves as a brief summary, prepared specifically for the public, of the nature and outcomes of the project. This report will be posted on the NSF website exactly as it is submitted by the PI.

More comprehensive information on NSF Reporting Requirements and other important information on the administration of NSF awards is contained in the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) Chapter VII, available electronically on the NSF Website at https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

VIII. AGENCY CONTACTS

Please note that the program contact information is current at the time of publishing. See program website for any updates to the points of contact.

General inquiries regarding this program should be made to:

- Stephen DiFazio, telephone: (703) 292-4517, email: sdifazio@nsf.gov
- Jean X. Gao, telephone: (703) 292-7253, email: jgao@nsf.gov
- Leslie J. Rissler, telephone: (703) 292-4628, email: lrissler@nsf.gov
- Gerald Schoenknecht, telephone: (703) 292-5076, email: gschoenk@nsf.gov

For questions related to the use of FastLane or Research.gov, contact:

- FastLane and Research.gov Help Desk: 1-800-673-6188
- FastLane Help Desk e-mail: fastlane@nsf.gov
- Research.gov Help Desk e-mail: rgov@nsf.gov

For questions relating to Grants.gov contact:

- Grants.gov Contact Center: If the Authorized Organizational Representatives (AOR) has not received a confirmation message from Grants.gov within 48 hours of submission of application, please contact via telephone: 1-800-518-4726; e-mail support@grants.gov.

IX. OTHER INFORMATION

The NSF website provides the most comprehensive source of information on NSF Directorates (including contact information), programs and funding opportunities. Use of this website by potential proposers is strongly encouraged. In addition, "NSF Update" is an information-delivery system designed to keep potential proposers and other interested parties apprised of new NSF funding opportunities and publications, important changes in proposal and award policies and procedures, and upcoming NSF Grants Conferences. Subscribers are informed through e-mail or the user's Web browser each time new publications are issued that match their identified interests. "NSF Update" also is available on NSF's website.

Grants.gov provides an additional electronic capability to search for Federal government-wide grant opportunities. NSF funding opportunities may be accessed via this mechanism. Further information on Grants.gov may be obtained at https://www.grants.gov.

ABOUT THE NATIONAL SCIENCE FOUNDATION

The National Science Foundation (NSF) is an independent Federal agency created by the National Science Foundation Act of 1950, as amended (42 USC 1861-75). The Act states the purpose of the NSF is "to promote the progress of science; [and] to advance the national health, prosperity, and welfare by supporting research and education in all fields of science and engineering."

NSF funds research and education in most fields of science and engineering. It does this through grants and cooperative agreements to more than 2,000 colleges, universities, K-12 school systems, businesses, informal science organizations and other research organizations throughout the US. The Foundation accounts for about one-fourth of Federal support to academic institutions for basic research.

NSF receives approximately 55,000 proposals each year for research, education and training projects, of which approximately 11,000 are funded. In addition, the Foundation receives several thousand applications for graduate and postdoctoral fellowships. The agency operates no laboratories itself but does support National Research Centers, user facilities, certain oceanographic vessels and Arctic and Antarctic research stations. The Foundation also supports cooperative research between universities and industry, US participation in international scientific and engineering efforts, and educational activities at every academic level.

Facilitation Awards for Scientists and Engineers with Disabilities (FASED) provide funding for special assistance or equipment to enable persons with disabilities to work on NSF-supported projects. See the *NSF Proposal & Award Policies & Procedures Guide* Chapter II.E.6 for instructions regarding preparation of these types of proposals.

The National Science Foundation has Telephonic Device for the Deaf (TDD) and Federal Information Relay Service (FIRS) capabilities that enable individuals with hearing impairments to communicate with the Foundation about NSF programs, employment or general information. TDD may be accessed at (703) 292-5090 and (800) 281-8749, FIRS at (800) 877-8339.

The National Science Foundation Information Center may be reached at (703) 292-5111.

The National Science Foundation promotes and advances scientific progress in the United States by competitively awarding grants and cooperative agreements for research and education in the sciences, mathematics, and engineering.

To get the latest information about program deadlines, to download copies of NSF publications, and to access abstracts of awards, visit the NSF Website at https://www.nsf.gov

- **Location:** 2415 Eisenhower Avenue, Alexandria, VA 22314
- **For General Information** (NSF Information Center)**:** (703) 292-5111
- **TDD (for the hearing-impaired):** (703) 292-5090
- **To Order Publications or Forms:**

  Send an e-mail to: nsfpubs@nsf.gov

  or telephone: (703) 292-8134
- **To Locate NSF Employees:** (703) 292-5111

PRIVACY ACT AND PUBLIC BURDEN STATEMENTS

The information requested on proposal forms and project reports is solicited under the authority of the National Science Foundation Act of 1950, as amended. The information on proposal forms will be used in connection with the selection of qualified proposals; and project reports submitted by awardees will be used for program evaluation and reporting within the Executive Branch and to Congress. The information requested may be disclosed to qualified reviewers and staff assistants as part of the proposal review process; to proposer institutions/grantees to provide or obtain data regarding the proposal review process, award decisions, or the administration of awards; to government contractors, experts, volunteers and researchers and educators as necessary to complete assigned work; to other government agencies or other entities needing information regarding applicants or nominees as part of a joint application review process, or in order to coordinate programs or policy; and to another Federal agency, court, or party in a court or Federal administrative proceeding if the government is a party. Information about Principal Investigators may be added to the Reviewer file and used to select potential candidates to serve as peer reviewers or advisory committee members. See System of Record Notices, NSF-50, "Principal Investigator/Proposal File and Associated Records," andNSF-51, "Reviewer/Proposal File and Associated Records." Submission of the information is voluntary. Failure to provide full and complete information, however, may reduce the possibility of receiving an award.

An agency may not conduct or sponsor, and a person is not required to respond to, an information collection unless it displays a valid Office of Management and Budget (OMB) control number. The OMB control number for this collection is 3145-0058. Public reporting burden for this collection of information is estimated to average 120 hours per response, including the time for reviewing instructions. Send comments regarding the burden estimate and any other aspect of this collection of information, including suggestions for reducing this burden, to:

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