Welcome!

We will begin at 2pm ET

Questions and Answers

Submit your questions via the Q&A box on your screen

- You may elect to submit your question anonymously.

- For specific questions about your project, please contact a Program Director.

Slides and recording will be available at:

MCB blog: https://mcbblog.nsfbio.com/office-hours/2/

and the MFB program website

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Molecular Foundations for Biotechnology

Partnerships to Transform Emerging Industries

RNA Tools/Biotechnology

NSF 23-554

NSF + NHGRI/NIH

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MFB 2023: RNA Tools/Biotechnology – NSF + NHGRI Funding Call

Program Directors:

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Molecular Foundations for Biotechnology (MFB)

- Effort led by the NSF Division of Chemistry to address biotechnology and biomanufacturing priorities of the Executive Branch.
- Multi-year campaign on different themes to catalyze fundamentally new approaches and advance biotechnology through collaborative high risk/high reward projects.
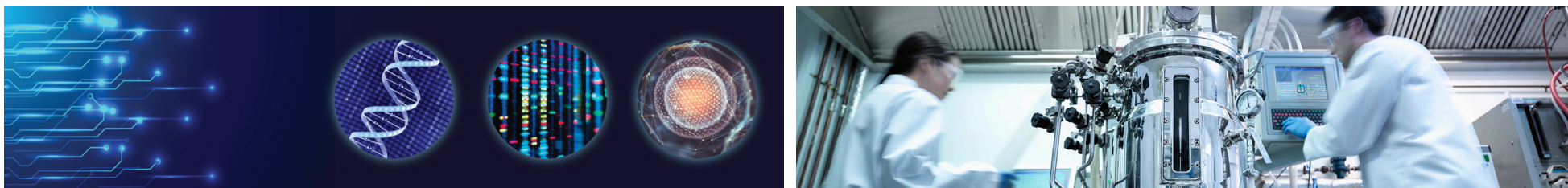
Biotechnology harnesses the power of biology to create new services and products, which provide opportunities to grow the United States economy and workforce and improve the quality of our lives and the environment.

Executive Order 14081

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MFB 2021:
Small Molecule-Protein Interactions Modifying Structure, Function and/or Fate of Proteins

Jointly funded by PHY/MPS, MCB/BIO, CBET/ENG

- **Ultra-Fast Development of Portable Small Molecule Sensor-Actuators**

  Tim Whitehead (U Colorado Boulder)/Sean Cutler, Ian Wheeldon (UC Riverside)/Francis Peterson (Med Coll Wisconsin) - 2128287

- **Bioorthogonal Chemistries Targeting 5-hydroxytryptophan for Biological Discovery and Biologics Development**

  Abhishek Chatterjee, Tim van Opijnen and Eranthie Weerapana (Boston College) - 2128185

- **Developing Next-Generation Approaches to Targeted Protein Degradation**

  Daniel Nomura/Thomas Maimone (UC-Berkeley) - 2127788

- **Deciphering the Logic of PTM Crosstalk via Novel Chemical Technology: Histones and Beyond**

  Philip Cole/Ben Garcia (Harvard/Wash U) - 2127882

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MFB 2022:
Innovative Machine Learning Methods for Research on Biomacromolecular Systems

Jointly funded by MCB/BIO, PHY/MPS, DMS/MPS, CBET/ENG, IIS/CISE

- **Deciphering RNA-based regulatory logic with interpretable machine learning**
  Oded Regev (NYU)/Shu-Bing Qian (Cornell) - 2226731, 2226633

- **Integrating Deep Learning and High-throughput Experimentation to Rapidly Navigate Protein Fitness Landscapes for Non-native Enzyme Catalysis**
  Philip Romero (Wisconsin-Madison)/Jared Lewis (Indiana U.)/Anthony Gitter (Morgridge Institute for Research) - 2226383, 2226475, 2226451

- **Accelerating the Discovery of Novel Liposome Formations with Origins-of-Life Insights, Laboratory Automation, and Machine Learning**
  Joshua Schrier (Fordham U), Sarah Maurer (CCSU) - 2226511

- **Deep-Learning Enabled Structure Prediction and Design of Protein-DNA Assemblies**
  David Baker, Frank DiMaio (U of Washington), Barry Stoddard (Fred Hutchinson Cancer Center) - 2226466

- **Novel Graph Neural Networks to Understand, Predict, and Design Allosteric Transcription Factors**
  Corey Wilson, Yao Xie, Matthew Realff (Georgia Tech) - 2226663

- **Data-Adaptive and Metamorphosis Machine Learning Architectures for Generative Protein Design of Metal Biosensors**
  Joanna Slusky (U of Kansas), Margarita Osadchy, Rachel Kolodny (U of Haifa) - 2226804

- **Targeting the Dark Proteome by Machine-learning-guided Protein Design**
  Sagar Khare, Adam Gormley, Guillaume Lamoureux, Sijian Wang (Rutgers U) - 2226816

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MFB 2023: RNA Tools/Biotechnology

Opportunity:

Fundamental discoveries and technological breakthroughs have revealed a rich landscape of coding and noncoding RNA functions in the cell. The variety of RNA types and cellular roles present exciting opportunities for mechanistic research coupled with technological development centered on this versatile nucleic acid.

Goals:

Catalyze synergies among biological, chemical, computational, mathematical, and physical sciences researchers to:

- pursue creative technological approaches that address questions about RNA function in complex biological systems, and
- harness RNA research to advance biotechnology.

NSF Directorates for MPS, BIO and CISE, and NIH-NHGRI are participants in MFB 2023, emphasizing partnerships across disciplines.

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MFB 2023: Requirements

- Proposals have to develop and provide proof-of-concept testing of tools, methodology and/or theory that address one or both themes below:

  I. Accelerate fundamental discoveries about RNA structure, interactions, and functions at molecular or genome and transcriptome-wide scales.

  and/or

  II. Create innovative RNA-based applications for various sectors of the bioeconomy such as agriculture, energy production, or efforts to mitigate the effects of climate change, improve environmental sustainability, and/or combat global pandemics.

- All proposals must include innovative, interdisciplinary approaches that have the potential to drive fundamentally new directions in biotechnology.

- Proposals must also be motivated by questions or hypotheses about RNA function in biological systems, with an emphasis on molecular and cellular science.

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MFB 2023: For Example

Approaches that:

- Identify, predict, detect, quantify, characterize and/or selectively manipulate RNA, including isoforms, modifications, non-natural RNAs;

- Enable prediction and analysis of the molecular structure, interactions and function of RNA, especially in complex assemblies and compartments;

- Discover or develop new chemical and biochemical tools that target RNA and modulate its properties;

- Develop novel computational methods, algorithms and tools to enable data science-driven approaches to understanding RNA structure, interactions and function;

- Advance design and synthesis of RNAs with novel form and function by leveraging biological diversity and evolution.

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MFB 2023: Required Letter of Intent

1. **Project Title**
   - Proposal titles must have the form "MFB: Title".
     The title should describe the project in concise, informative language that is understandable to a technically literate reader.

2. **List of Senior Project Personnel and Participating Organizations**

3. **Project Synopsis (2500 characters)**
   - Include statements on the intellectual merit and on the broader impacts.
   - Outline the specific goals of the research and testable hypotheses for each goal, and the related technology or methods to be developed.
   - Also highlight innovative aspects of the work and the significance of potential outcomes.

4. **Research Disciplines (255 characters)**
   - Identify the disciplines in which the research is grounded.

Note:

Submission of multiple Letters of Intent as PI, co-PI, or other senior personnel (including on subaward) is not permitted.

No evaluative feedback will be provided by NSF at this stage.

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MFB 2023: Key Elements of Full Proposal

Solicitation-specific information (supplements guidelines and requirements in NSF PAPPG)

- **Project Title:** "MFB: Title"

- **Project Description:**

  Due: May 11, 2023

  - List of PIs, co-PIs, senior personnel and collaborators on first page
  - Challenge driving the research, approach, and tool/method development
  - Anticipated outcomes and significance
  - Innovative, high risk/high reward aspects
  - Cross-disciplinary synergies and roles of collaborators
  - Plans to ensure reproducibility of methods, data

- **Broader Impacts:**
  - Generalizability of outcomes (tools, methods, concepts, findings)
  - Potential impact on future technology
  - Educational and training opportunities

Note:

Submission of multiple full proposals as PI, co-PI, or other senior personnel (including on subaward) is not permitted.

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MFB 2023: Review Process

Review of full proposals will be managed by NSF in consultation with NHGRI

- Proposals will be evaluated in panels and/or by ad hoc reviews using the two NSF merit review criteria and additional solicitation-specific criteria.

- Meritorious proposals may be recommended for funding either by NSF or NHGRI.

- NHGRI will select proposals for funding based on additional considerations.

- Proposals selected for NHGRI funding will be invited to submit reformatted applications to the NIH.

  (note: the budget and scientific content of the reformatted application must be the same)

- Following award/decline decisions, all PIs will be provided verbatim reviews excluding reviewer information and a panel ranking and summary (as appropriate).

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MFB 2023: Review Criteria

- **Intellectual Merit**

- **Broader Impacts**

- **Additional Solicitation-Specific Criteria:**

  - Innovation in tools, methodology and/or theory to advance research on RNA or to develop RNA-based applications;

  - Interdisciplinary approach employed to solve complex challenges;

  - Potential catalytic impact on driving new directions in biotechnology; and

  - Prospect of the outcomes to be generalizable beyond the specific system under study.

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NSF Merit Review Criteria

Intellectual Merit

Potential to advance knowledge within/across fields

- Creative, original, potentially transformative concepts

- Well reasoned and organized ideas and experiments

- Qualified investigators

- Adequate resources

Broader Impacts

Potential to benefit society

- Well reasoned, organized and resourced plans to (for example):

  o Promote training and education

  o Enhance infrastructure, resources

  o Engage in outreach to community

  o Broaden participation of underrepresented groups in STEM

Note: Broader impacts can include research outcomes that benefit society, e.g., inform novel therapeutic strategies in the long term.

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MFB 2023: NHGRI Considerations

NHGRI will consider MFB applications that accelerate genomic research focused on the structure and biology of genomes and can demonstrate utility or relevance to human or disease-relevant model organisms.

NHGRI is interested in approaches that are comprehensive across the genome or are generalizable across variants, tissues, diseases, or function and that address priority areas described in the NHGRI 2020 Strategic Vision.

NIH Review Criteria:

- Overall Impact
- Significance
- Investigators
- Innovation
- Approach
- Environment

https://grants.nih.gov/grants/peer/critiques/rpg.htm

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MFB 2023: What's Not In Scope

NSF (from the PAPPG)

- Biological research on mechanisms of disease in humans, including on the etiology, diagnosis, or treatment of disease or disorder, is normally not supported.
- Biological research to develop animal models of such conditions, or the development or testing of procedures for their treatment, also are not normally eligible for support.
- However, research with etiology, diagnosis- or treatment-related goals that advances knowledge in engineering, mathematical, physical, computer, or information sciences is eligible for support.

NHGRI

- Studies relevant only to a particular disease or organ system are not in scope for NHGRI.
- Similarly, applications whose primary scientific objective is to understand a single biological or behavioral process, the pathophysiology of a disease, the mechanism of action of an intervention, or the direct development of therapeutic research are not in scope.

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MFB 2023: Additional Information

- **Anticipated Funding:**
  - The program will support projects with a budgetary range of ~$250,000 – $400,000 per year in direct costs and a duration of up to 3 years.
  - Up to 7 awards are expected.

- **Collaborations:**
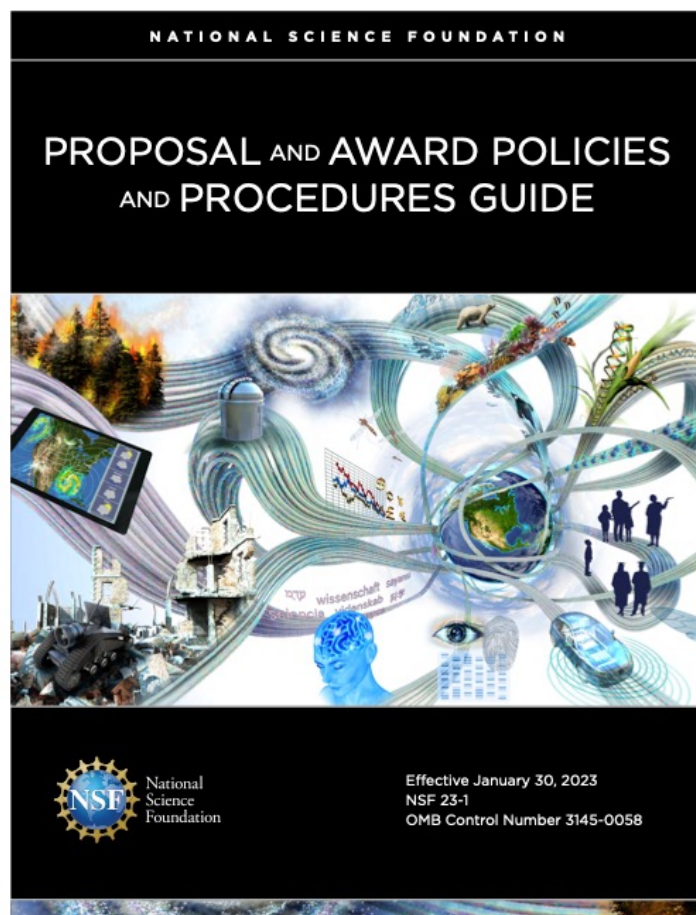 - This solicitation allows only a single proposal submission with subawards administered by the lead organization.

- **Timeline:**
  - **March 16, 2023**   **Required Letter of Intent due**
  - **May 11, 2023**   **Full proposal due**
  - **Mid-summer 2023**   **Panel/ad hoc review**
  - **Fall 2023**   **Funding decisions**

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MFB 2023: New NSF PAPPG 23-1 in Effect

Summary of Changes to the PAPPG (NSF 23-1)
Effective date January 30, 2023

https://beta.nsf.gov/policies/pappg/23-1/summary-changes

Chapter II.E.9, Safe and Inclusive Working Environments for Off-Campus or Off-Site Research, describes the new requirement for the AOR to certify that an organization has a plan in place for safe and inclusive research for any proposal that proposes to conduct off-campus or off-site research. This section also provides considerations for plan development, communication, and dissemination.

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MFB 2023: Resources

- **Email**: mfb@nsf.gov

- **Website**: https://beta.nsf.gov/funding/opportunities/molecular-foundations-biotechnology-mfb-0

- **Slides and recording available:** MCB blog and MFB program website

- **Additional webinar on Friday, February 24 at 1-2 pm ET**
  Registration link via MFB program website

  - **P. Shing Ho** – Division of Chemistry, MPS
  - **Manju M. Hingorani** – Division of Molecular and Cellular Biosciences, BIO
  - **Stephen DiFazio** – Division of Molecular and Cellular Biosciences, BIO
  - **Christine Chow** – Division of Chemistry, MPS
  - **Sorin Draghici** – Division of Information and Intelligent Systems, CISE
  - **Zhilan J. Feng** – Division of Mathematical Sciences, MPS
  - **Angel E. Garcia** – Division of Physics, MPS

  - **Jennifer Strasburger** – National Human Genome Research Institute/NIH

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Monthly Virtual Office Hours

Division of Molecular and Cellular Biosciences (MCB blog)

- **March 8th, 2023, 2-3 pm ET**
  New MCB Solicitation for Core Programs (NSF 23-548)

- **April 12th, 2023, 2-3 pm ET**
  How to Write a Great NSF Proposal

Send topic suggestions to:
Olaf Corning: ocorning@nsf.gov

Division of Chemistry

- **Friday, 1-2 pm ET**
  Topic: Chemistry Virtual Office Hours

Send topic suggestions to:
cheminfo@nsf.gov

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