

# Chan Zuckerberg Initiative

## REQUEST FOR PROPOSALS

### Scaling Up Synthetic Biology

The Chan Zuckerberg Initiative invites applications for two-year research projects addressing key barriers in scaling, throughput, and cost of synthetic biology methods.

## OPPORTUNITY

### Overview

The Chan Zuckerberg Initiative (CZI) is dedicated to accelerating progress in human health and disease through supporting transformative research and technology. We recognize the potential of synthetic biology to improve our current understanding of the cell and the fundamental principles of life. Overcoming current limitations in this area will enable unprecedented insights into complex biological processes, evolutionary dynamics, and genotype-phenotype relationships, ultimately leading to the development of groundbreaking gene therapies, engineered cell lines and tissues for basic research and translational applications.

This Request for Proposals (RFP) focuses on advancing the field of synthetic biology within eukaryotic cells, particularly mammalian cells. Viral, bacterial, archeal, or plant systems are out of scope, unless being used as tools for assembly or delivery into other higher eukaryotic cells. We invite proposals for two-year research projects that address key challenges in scaling, throughput, and cost reduction for synthetic biology methods. Projects should be appropriately scoped for completion within this timeframe, and budgets should align with the project's scope and timeline.

### Scope and Project Specifications

We encourage bold, high-risk, and high-reward approaches that have the potential to transform the field. We are particularly interested in projects that:

- **Develop novel methods and technologies:** We welcome proposals for innovative DNA synthesis, assembly, delivery, integration, and manipulation techniques that overcome the limitations of current approaches.
- **Enhance the design-build-test-learn cycle:** We seek solutions that accelerate the iterative cycle of synthetic biology research, enabling faster prototyping, testing, and optimization of DNA constructs; screening, analysis, and validation of models in vitro/vivo.

- **Improve scalability, throughput, and cost-effectiveness:** We encourage proposals that aim to make synthetic biology more accessible, affordable, and efficient for a broader range of researchers and applications.

### **Areas of Interest**

Projects that intersect and/or address multiple parts of the design-build-test-learn cycle are of particular interest. While not exhaustive, examples of potential project areas within the scope of this RFP include:

- **DNA Synthesis and Assembly:**
  - Novel methods for high-fidelity, low cost, scalable DNA synthesis
  - Advanced strategies for efficient DNA assembly and error correction
  - Methods for shuttling synthetic DNA between cell types
  - Scalable production of long-read nucleotide pools for assembly
- **Genome Engineering and Manipulation:**
  - Novel methods for synthesizing, manipulating, and inserting DNA fragments into eukaryotic genomes
  - Scalable methods for creation and manipulation of larger artificial chromosomes
  - Advances towards whole genome synthesis, assembly, and insertion
  - Efficient methods for whole chromosome transplantation
  - Large-scale epigenome manipulation tools
- **Delivery Systems and In Vitro Platforms:**
  - Targeted delivery systems for DNA molecules
  - In vitro platforms for manipulating DNA molecules

### **Additional Considerations**

- **Big DNA Challenges:** We are particularly interested in projects that address the challenges associated with large DNA molecules (>100kb), such as scalable construction and insertion of large synthetic DNA constructs into the genome, reducing cytotoxicity, improving stability, and developing reliable and efficient transfer methods.
- **Artificial Chromosome Challenges:** We encourage proposals that explore the construction rules for synthetic chromosomes, scale up their construction, and develop efficient transplantation methods.
- **General Synthetic Biology Challenges:** We welcome projects that address fundamental challenges in synthetic biology, such as modularization, immunogenicity, predictability, design cycles, and transgene silencing.

### **Team Composition**

The opportunity aims to support existing or new collaborative teams focused on bridging multiple disciplines to accelerate synthetic biology research and the development of new tools to measure and manipulate cells. Teams may include up to a total of three principal investigators (PIs), composed of the Lead/Coordinating PI and up to two co-PIs. All teams are expected to contribute to the larger community via regular engagement and sharing of learnings, data, samples, and other resources. We strongly encourage interdisciplinary and trans-institutional teams that bring together teams of

researchers with complementary expertise and resources to address high-risk, high-reward problems that address the scope outlined above and are unlikely to be addressable by a single lab.

Proposals should highlight the unique strengths and contributions of each team member and how the combined expertise will synergistically address the challenges of the proposed project. We value diversity in all its forms and encourage the inclusion of individuals from a variety of career stages, institutions, and backgrounds.

### **Open Science and Collaboration**

To accelerate research and synthetic biology methods and technology development in health and disease, CZI seeks investigators who will contribute to a collaborative interdisciplinary network and the advancement of the field.

- Investigators and members of their labs will participate in annual meetings joined by all other funded groups, in smaller meetings focused on specific biological or technical issues, and in monthly webinars.
- Investigators will commit to the rapid dissemination of all resulting data, protocols, code, reagents, and results prior to publication through resources such as the preprints, protocols.io, GitHub, Addgene, and Chan Zuckerberg CELLxGENE data platform.

## **APPLICATION REQUIREMENTS**

**Application form and submission:** All applications must be prepared using the application form provided (attached to the email invitation) and must be **submitted via email directly to Norbert Tavares** ([ntavares@chanzuckerberg.com](mailto:ntavares@chanzuckerberg.com)), the program manager for this RFP, by 5 PM PT on Thursday, August 8, 2024. Deadline extensions will not be granted. Questions should be emailed to [sciencegrants@chanzuckerberg.com](mailto:sciencegrants@chanzuckerberg.com).

### **Key Dates:**

August 8, 2024	Applications due by 5 p.m. Pacific Time (PT)
August 26 - Sept 4, 2024	30-minute virtual interviews with applicant semifinalists
Mid-October 2024	Earliest notification of decisions (subject to change)
December 1, 2024	Expected start date (subject to change)

Semi-finalists who are invited for a virtual interview will be notified by late August, but as the interview dates are firm, we request that all applicants hold August 26-September 4 for the interview period.

**Award period and start date:** Awards are for two years (24 months) in duration with an expected start date of December 1, 2024.

**Budget:** To allow maximum flexibility, and encourage and enable a wide range of projects of varying scope, we are providing minimal budget guidance. However, budgets should reflect the scope of the

project, and the project should be scoped appropriately to be completed within the two year grant period with the available resources and expertise of the team. Indirect costs cannot exceed 15 percent of direct costs. Indirect costs may not be assessed on capital equipment or subcontracts, but subcontractors may include up to 15 percent of indirect costs of their direct costs. International grantees must use all grant funds exclusively for activities conducted outside the United States of America.

CZI suggests that you consult your home institution to determine eligibility to apply for this grant and your institutional policy on indirect costs. For questions about eligibility for this award or the application process, please contact us in advance of the proposal deadline at [sciencegrants@chanzuckerberg.com](mailto:sciencegrants@chanzuckerberg.com). Deadline extensions will not be granted.

### **CONFIDENTIALITY**

All submitted applications will be kept confidential, except (1) as necessary for our evaluation or to comply with any applicable laws; and (2) to the extent that the application is made public or available to others without a duty of confidentiality through no fault of CZI. Notwithstanding, successfully funded proposals may be made publicly available and/or shared with other grantees or collaborators. Unfunded proposals will remain confidential as provided herein; however, information, including brief summaries of the proposed projects, project metrics, and the types of organizations that have applied for funding, may be made publicly available in aggregate form. Application materials will not be returned to applicants.

### **QUESTIONS**

Please contact [sciencegrants@chanzuckerberg.com](mailto:sciencegrants@chanzuckerberg.com).