Chan Zuckerberg Initiative

REQUEST FOR APPLICATIONS
Measuring Metabolism Across Scales

The Chan Zuckerberg Initiative invites applications for two-year collaborative research projects addressing key outstanding questions in the field of metabolism and metabolic physiology in health and disease.

OPPORTUNITY

Overview

To measure human biology, we need to understand the mysteries of the cell and how cells interact within and as systems. Metabolism is a complex and highly interconnected process, with many different pathways that feed into one another. It encompasses various biochemical processes, chemical reactions, and conversions that transform one form of energy into another, regulating the rate of nutrient uptake from the immediate environment to essentially maintain the living state of a cell or an organism. Metabolic physiology goes beyond studying metabolic pathways and requires consideration of dynamic processes that cross time and space scales. To clarify metabolism and its connection to diseases requires investigating how metabolism is integrated within molecules, organelles, cells, tissues, and organisms, further suggesting that multiple experimental and technological approaches are needed to measure metabolism in action. Mapping, measuring, and integrating metabolism across scales and systems is a path to understanding various facets of human physiology and addressing many common and rare diseases.

Scope and Project Specifications

The Chan Zuckerberg Initiative (CZI) seeks to support two-year collaborative research projects focused on measuring metabolism across organelles and cells. The ability to characterize temporally and spatially the broad molecular profiles, heterogeneity, and phenotypic diversity of organelles and cells and how they interact within and as systems are key to measuring human biology, understanding disease mechanisms, and finding treatments and cures. This Request for Applications (RFA) aims to accelerate innovative discoveries in metabolism and metabolic physiology in health and disease. Applications for two types of grants are welcome: Expanded Projects and Focused Projects. The maximum budgets for proposed projects are $500,000 total costs for *Expanded Projects* and $250,000 total costs for *Focused Projects*. All project awards will be for a 24-month duration.

The long-term goal of this opportunity is to investigate the metabolic processes that maintain physiological homeostasis at the sub-cellular and cellular levels, and understand how and when these normal processes go awry. This two-year funding opportunity is explicitly aimed at addressing the mechanisms of metabolism, including its dynamics and resolution, molecular drivers, and the effects of genetic and environmental risk factors on relevant sub-cellular and cellular properties and interactions, and precisely mapping metabolic changes and states across various scales using a broad range of technologies. The projects should aim to use diverse experimental systems beyond immortalized cell lines to ensure the broadest possible insights into cellular and organelle biology. These grants are not intended to support translational research, clinical trials, or drug development.

Examples of potential areas within the scope of this RFA include, but are not limited to:

- Profiling organelles and cells to understand their heterogeneity and metabolic regulation in maintaining homeostasis and how they dynamically evolve to adapt to all types of diverse stressors and metabolic conditions;
- Using metabolic rewiring to study the state and fate of specialized cells (e.g., immune cells, adipocytes, neurons, hepatocytes, etc.) programmed by metabolic processes;
- Using mechanistic studies to understand the function and dysfunction of metabolism at the systems physiology level and provide a framework for understanding the molecular and cellular basis of metabolic diseases;
- Identifying, measuring, and studying molecular level metabolite-protein interactions at scale with high sensitivity and selectivity;
- Developing techniques for metabolic tracing to help identify the origin and fate of metabolites and their contribution to cellular processes and interactions; and
- Establishing metabolomics and/or proteomics methodologies (Mass Spectrometry- and non-Mass Spectrometry-based approaches) to enable high-quality spatial biomolecular analysis of individual organelles and cells.

Team Composition

This opportunity is intended to support active collaborative teams of researchers with access to established resources ready to be extended, scaled, and applied to address key biological questions in the field of metabolism or metabolic physiology in health and disease. The opportunity also aims to support new collaborative teams focused on bridging multiple biology fields to accelerate metabolism research and the development of new tools to measure human biology. Teams may include up to a total of three principal investigators (PIs) with at least one PI with expertise in metabolism, metabolic reprogramming and/or homeostasis, organelle biology, metabolomics tools, or any other related field. All teams within the CZI Single-Cell Biology Network are expected to contribute to the larger community via regular engagement and sharing of learnings, data, samples, and other resources.

Open Science and Collaboration

CZ Science is committed to open and collaborative science to accelerate scientific discovery and support training and development opportunities for next generation researchers (staff scientists, postdoctoral fellows, and graduate students). This is particularly true of early-stage technology development that benefits from rapid and iterative improvements coupled with community feedback to ensure utility. We highly encourage researchers to participate in the development of training materials, courses, etc., and to participate in cross-disciplinary training opportunities across teams.

To accelerate research in the area of metabolism across scales and systems and metabolic physiology 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 and CZI staff will work together to identify resources and technology that will support the metabolism field as a whole.
- Investigators will commit to the rapid dissemination of all resulting data, protocols, code, reagents, and results prior to publication through resources such as the Human Cell Atlas Data Coordination Platform, Chan Zuckerberg CELL by GENE, protocols.io, GitHub, Addgene, and preprints.

ELIGIBILITY

- Applications may be submitted by domestic and foreign nonprofit organizations, including public and private institutions, such as colleges, universities, hospitals, laboratories, units of state and local government, and eligible agencies of the federal government. For-profit organizations are not eligible to receive funding but may be involved in projects as a collaborator. All grants will be awarded to institutions, not individuals.
- An organization may submit more than one application.
- Each application should designate one Principal Investigator (PI) as the Coordinating Principal Investigator (Coordinating PI). The Coordinating PI will act as the administrative contact between CZI and all other PIs on the grant (Co-PIs). The Coordinating PI must submit the application on behalf of all PIs. The Coordinating PI must be affiliated with the institution submitting the application, and grant funds will be awarded to that institution, which will take responsibility for distributing funds to any other institution. Note that institutions outside the U.S. may not subcontract to U.S. institutions, so please be mindful when selecting the Coordinating PI/institution.
- Teams may include a total of three PIs. Each application must have one Coordinating PI, but may designate up to three total PIs (one Coordinating PI and up to two Co-PIs). All additional PIs should be listed as Co-PIs.
- Principal Investigators may only apply to join and serve as Coordinating PI or Co-PI on one application. Funding will be restricted to one project per PI. Participation in multiple projects as an unfunded collaborator is allowed and encouraged.
- At least one Principal Investigator of the team must have expertise in metabolism or another related field.

- PIs/Co-PIs on one application may be employed at the same or different institutions.
- PIs and Co-PIs must each be permitted to receive grant support from the organization they are applying with. This criterion may be defined differently in different types of organizations. Examples of eligible positions are:
    - Tenure track faculty;
    - Non-tenure track faculty or staff scientists who lead a lab or are engaged in academic activities and are permitted to apply for grants by their institution;
    - Researchers with expertise in the relevant areas that are affiliated with or supported by an institution and permitted to apply for grants; and
    - Co-PIs from companies are permitted as long as no funds are requested to support them or their work.
- Early-career investigators are strongly encouraged to apply as Coordinating PIs and Co-PIs.
- We believe that the strongest teams incorporate a wide range of voices. Those underrepresented in science and technology are strongly encouraged to apply.
- Meta employees, including employees of any subsidiary Meta entities, as well as employees of Chan Zuckerberg Initiative, LLC, are not permitted to apply.
- CZI reserves the sole right to decide if an applicant and the applicant organization meet the eligibility requirements.
- CZI reserves the right to request budget changes prior to award.
- We welcome applications from any country, provided the proposed work is compliant with the United States Treasury Department's Office of Foreign Asset Control (OFAC) sanctions program. Prior to award, all grant applications will be reviewed for compliance with the United States Treasury Department's Office of Foreign Asset Control (OFAC) sanctions program, the United States Department of Commerce's export administration regulations, the Foreign Corrupt Practices Act (FCPA), any other applicable U.S. laws and regulations, and any corresponding laws and regulations in the country where the applicant is based. All grant agreements will also require the grantee to comply with these laws and regulations. For additional information, please refer to the U.S. Treasury Department's resources, the International Trade Administration's website on US Export Controls, and the Department of Justice's website on the FCPA.
- While applicants from all countries are welcome to apply, because of required ongoing compliance with U.S. sanctions and export controls, an applicant's funding eligibility may need to be reassessed if the applicable laws and regulations change at any time. As a result, even if an applicant is eligible to receive funding at the time the application is reviewed, the applicant's status may change later in the process or during the course of the grant term.

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. Deadline extensions will not be granted.

APPLICATION REQUIREMENTS

All applications must be completed and submitted through CZI's online grants management portal at https://apply.chanzuckerberg.com. It is recommended that applicants familiarize themselves with this portal well in advance of the application deadline. Detailed application instructions are available on the Chan Zuckerberg Initiative website, as well as in the grants management portal.

Key Dates:

April 13, 2023	Application portal opens
June 1, 2023	Applications due by 5 p.m. Pacific Time (PT)
Mid-October 2023	Earliest notification of decisions (subject to change)
December 1, 2023	Expected start date (subject to change)

Award period and start date: Awards will be for two years (24 months) in duration with an expected start date of December 1, 2023.

Budget: Grants will be awarded at two levels:

- *Focused Projects*: $250,000 USD total costs (inclusive of up to 15 percent indirect costs) over 24 months for exploratory, risky technology development strategies; and
- *Expanded Projects*: $500,000 USD total costs (inclusive of up to 15 percent indirect costs) over 24 months for projects that look into hypothesis-driven biological questions that rely on applying, scaling, and/or improving existing technology to measure metabolism across organelles and cells.

Proposed budgets should reflect the project scope. Indirect costs cannot exceed 15 percent of direct costs.

SELECTION PROCESS

The Chan Zuckerberg Initiative adheres to our core values in both proposal selection and evaluation of progress.

CZI will evaluate all applications for scientific merit and will seek independent expert review. Final decisions will be made by CZI staff in consultation with our scientific advisors. There is no expectation of any specific number of awards, as this will depend on team size and project budgets, and the Chan Zuckerberg Initiative reserves the sole right not to recommend the funding of any applications. CZI does not provide feedback on decisions for unfunded proposals.

Reporting & Progress: Production and availability of intermediate outputs that demonstrate progress is a key mechanism by which CZI evaluates the progress and impact of a project. Annual reports will be required to ensure that the CZI Measuring Metabolism Across Scales projects are progressing toward their defined set of deliverables, which include:

- Project-specific deliverables might include milestones related to depth, throughput, coverage, accessibility, adoptability, etc;
- Depositing data to an appropriate open source repository for deidentified raw and processed data that make it possible for the scientific community to explore;
- Regular engagement with the community and CZI Single-Cell Biology Program to ensure timely data deposition, hosting on platforms such as CZ CELLxGENE that promote use, and curation of interoperable formats;
- Submitting, updating, or modifying protocols on open repositories such as protocols.io;
- Publishing results along with submission to open-access preprint servers (e.g. bioRxiv, medRxiv, aRxiv, etc.);
- Interacting with other teams within the Measuring Metabolism Across Scales network and the broader CZI and HCA communities. All investigators will meet annually. Technology method developers will have dedicated meetings to identify common bottlenecks and work toward solutions that cut across all network teams; and
- Interacting and engaging with the CZI Single-Cell Biology community. Investigators are expected to participate in the CZI Single-Cell Biology Annual Meeting as well as quarterly working group calls focused on facilitating collaboration and allowing opportunities for groups to discuss progress and challenges to accelerate progress.

POLICIES

- Funds from this award are intended to support research activities. Grants are made to organizations to support the work of the named Principal Investigator, and reasonable flexibility on how these funds are utilized is allowed, provided that funds are used to support research activities related to the project. A detailed budget is required at the time of application.
- For awarded projects, financial statements and progress reports will be due at the conclusion of each grant year and occasionally more frequently. Specific deliverable requirements will be outlined in the award notification. Grantees of funded projects will be required to participate in regular meetings, including annual scientist meetings (which may be in person or virtual). Travel support for these meetings will be provided by CZI separately from the requested grant funds.
- Grantees may obtain funds for their research from other funding sources, provided that there is no conflict with meeting the terms of the CZI award.
- Unused research funds may be carried over to the following year, and requests for no-cost extensions will be considered at the end of the overall project period and upon receipt of an annual report.
- 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. Travel expenses to the United States must not be covered by the requested grant funds.
- **Ethical conduct:** CZI advocates the highest standards for the ethical conduct of research. In addition to the requirements of their own countries, grantees must adopt procedures for the

use of animals in research and the ethical treatment of human subjects and tissue donors, including obtaining their or their appropriate proxy's written informed consent. CZI regards the policies of the National Institutes of Health as a strong model for such procedures.

- **Data, publication, and dissemination policies:** To accelerate scientific discovery and collaboration, CZI supports a consent, sharing, and publication policy for open and rapid dissemination of proposal results, including methods, data, and reagents, and a policy for software development that maximizes accessibility, reuse, and shared development. Under rare circumstances, exceptions to the above may be considered where there are specific situations that make meeting these goals impossible or counterproductive to the project.
    - **Software code:** CZI requires sharing of software code developed by its grantees generally to be made publicly available on GitHub (or a similar public service). All new code must be released under a permissive open source license (MIT, BSD 2-Clause, BSD 3-Clause, or Apache v2.0). All pre-existing and derivative codes must be licensed under the most permissive license possible, given the licensing terms of the pre-existing code. All analysis packages must be released through the appropriate language-specific package manager (e.g., PyPi for Python, Bioconductor, and CRAN for R) with documentation, example data, and interactive demos (e.g., Jupyter notebooks), and the use of Docker or similar container technologies to ensure portability and reproducibility. Software code supported by CZI should be archived for long-term digital preservation and citability, when applicable.
    - **Content and data sharing:** CZI is committed to developing and using platforms that disseminate data openly and freely. Any datasets either curated or generated through the proposal must be made as publicly available and easily accessible through an appropriate data repository as legally permissible, when applicable, under an Open Definition conformant license. Ideally data sets would not include personally identifiable information, but if they do, consent to sharing the data must be obtained. Metadata, documentation, and intended use cases, as appropriate, must be made available under an Open Definition conformant license, preferably CC0 or CC BY/CC BY SA for content that requires explicit attribution.
    - **Publications:** To encourage rapid dissemination of results, any publications related to this funded work must be submitted to a preprint server (such as bioRxiv, medRxiv, arXiv, or any appropriate preprint repository), at or before the first submission to a journal. Experimental protocols must be made publicly available through a protocol-sharing service, such as protocols.io. Scientific publications, preprints, and presentations that result from this award should acknowledge support from this funding.
    - **Reagent sharing:** Resources and reagents developed with this funding support must be available for rapid dissemination to the community, where possible, in an accessible community repository, such as Addgene (for plasmids/DNA reagents/viruses) and Jackson Labs (for model systems lines), etc. This requirement applies to cell lines, transgenic organisms, plasmids/clones, antibodies, and other reagents.
    - **Consent:** All human tissues must be adequately and fully consented to permit maximal sharing of the resulting data and any resulting tools, subject to applicable laws,

regulations, or institutional ethical requirements. Any desired exceptions to this policy must be identified at the time of application, and such requests may affect the application's chance of success. We are aware that there may be circumstances where broad consent may be challenging, and in some cases consent may be subject to alteration or revocation; we encourage investigators to discuss these cases with CZI scientific staff. As a reference, the Human Cell Atlas (HCA) community has developed ethics guidelines and a tool kit with template consent forms.

    - **Intellectual property rights:** CZI does not require the assignment of ownership to any data, published results, or any other intellectual property that results from the work funded by these grants but will have the same rights generally granted to others. CZI supports and promotes policies that enable results and technologies to have the broadest reach and impact. To this end, all newly developed software must be made available through permissive open source licenses as described more fully above. Other technology and intellectual property rights (such as patents) must be made freely available for all academic and non-commercial use, and where intellectual property rights are commercialized, they must generally be subject to non-exclusive commercial licenses that enable broad availability and dissemination.
- Applications selected through this process will either be funded by the Chan Zuckerberg Initiative Foundation (CZIF) or recommended for funding through the Chan Zuckerberg Initiative Donor-Advised Fund (CZI DAF) at the Silicon Valley Community Foundation (SVCF).

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.

RFA CONTACT

For administrative and programmatic inquiries, or other questions pertaining to this RFA, please contact sciencegrants@chanzuckerberg.com.

IMPORTANT DOCUMENTS

Application Instructions
Institutional Approval Form

Chan Zuckerberg Initiative

APPLICATION INSTRUCTIONS
Measuring Metabolism Across Scales

Some helpful information as you get started:

- This document contains:
  - General guidance on using the portal
  - How to submit an application
  - Application details specific to this Mapping Metabolism Across Scale RFA

- Please review the Request for Applications.

- The Chan Zuckerberg Initiative uses SurveyMonkey Apply (SMApply) as its grants management portal. All applications must be submitted through this portal (https://apply.chanzuckerberg.com). SMApply is configured to work best using the Google Chrome browser. It is recommended that you familiarize yourself with this portal well in advance of any deadlines. Deadline extensions will not be granted.

- **Key dates:**

April 13, 2023	Application portal opens
June 1, 2023	Applications due by 5 p.m. Pacific Time (PT)
Mid-October 2023	Earliest notification of decisions (subject to change)
December 1, 2023	Expected start date (subject to change)

- **Application specifics:**
  - **Eligibility:** Please refer to the RFA announcement.
  - **Award period and start date:** Awards will be for two years (24 months) in duration with an expected start date of December 1, 2023.
  - **Budget:** Grants will be awarded at two levels. Proposed budgets should reflect the project scope. Indirect costs cannot exceed 15 percent of direct costs:
    - *Focused Projects*: $250,000 USD total costs (inclusive of up to 15 percent indirect costs) over 24 months for exploratory, risky technology development strategies; and
    - *Expanded Projects*: $500,000 USD total costs (inclusive of up to 15 percent indirect costs) over 24 months for projects that look into hypothesis-driven

biological questions that rely on applying, scaling and/or improving existing technology to measure metabolism across organelles and cells.

- **Number of Principal Investigators:** Each application must have one coordinating Principal Investigator (PI), but may designate up to three total PIs (one Coordinating Principal Investigator and up to two Co-PIs) in the application portal.
- **Institutional sign-off** is required at the time of submission.

GETTING STARTED

Account setup: The applicant (Coordinating PI) must first set up an account in the CZI online grants portal at https://apply.chanzuckerberg.com/. Only the Coordinating PI needs to set up an account.

To set up an account:

1. Go to https://apply.chanzuckerberg.com/.
2. Click the green Register button in the upper right corner.
3. Complete the requested fields and then click the green Create Account button.
4. Click the green Continue button to proceed to the site.

Please note you will need to verify your account through the auto-email that you receive after registering. You will not be able to submit an application until your account is verified.

Personal data: Where we ask for personal data of individuals in grant applications, please only submit personal data that you have a right to provide. We will use and store any personal data collected through the application process for grant-related purposes (e.g., administering the grant, analyzing and improving our grant practices). The Chan Zuckerberg Initiative Foundation and Chan Zuckerberg Initiative, LLC (collectively "CZI") will be the "data controllers" for any such personal information, and the data may be stored on servers outside of your home country, including within the United States. If you have any questions or concerns regarding our privacy practices or collection or use of personal data, you can contact us at privacy@chanzuckerberg.com.

Navigating the portal: Once you have set up an account, you can log into the grants portal at https://apply.chanzuckerberg.com/. Using the links in the upper right corner, you can access available programs (which includes RFAs for all CZI areas, not just Science) and any applications you have in preparation or previously submitted. Use the information ("i") link to get help with the portal. To access your account information, click on your name in the upper right. Your application will pre-populate with the name and email listed in your account information so if you need to edit it, click on your name in the upper right corner to make any necessary changes.

Forgotten username or password: Please note that your username is your email address. If you have forgotten your password, please navigate to the grants portal at https://apply.chanzuckerberg.com/ and click on the **Log In** button. Click the Forgot your password link and then enter the email address associated with your SMApply account. You will then receive an email with information to reset your password.

Other questions: If you have other questions about using the portal, please use the information ("i") link in the upper right corner of the window. Here you will find a link to FAQs about using the portal, as well as links to submit specific help requests. If you have specific questions about the RFA, please contact us at sciencegrants@chanzuckerberg.com.

SUBMITTING AN APPLICATION

To submit an application:

1. Go to https://apply.chanzuckerberg.com.
2. Log in.
3. Click the green View Programs button that is displayed or click on the Programs link in the upper right corner. This will bring you to a listing of all programs/RFAs that CZI is hosting in SMApply. To **find the program/RFA** you are looking for, you may need to scroll down.
4. Find the program/RFA you are interested in and click the green More button.
5. Click the green Apply button in the upper right and complete all sections (details below).
    a. You will first be prompted to **enter the title** of your application, after which you will have access to the application tasks to complete. Project title is limited to 60 characters, including spaces. If you need to **edit your project title**, click on the My Applications link in upper right and click the green Continue button on the application you wish to edit. Once the application page opens, click on the three dots to the right of the application title (next to the Preview link) and select Rename from the dropdown menu.
    b. The application is made up of several sections called tasks that are listed in a menu on the left side of the page. To **open a task**, click on the one you would like to work on. You can edit and complete tasks in any order. You may need to scroll down to see the remaining tasks.
    c. Once you **complete a task**, click the green Mark as Complete button within the task. All tasks must be marked as complete before submitting. To **edit a task** after marking it as complete, click the three dots in the upper right of the task and select edit, which will re-open the task.
    d. Your application will autosave every few seconds, but you can also click the Save & Continue Editing on each task as you go along to **save your application**.
    e. In the tasks that require a PDF upload: If you need to **delete and replace a PDF** after you have uploaded it, click on the three dots to the right of the file under the Attach File section within the task and select Remove from the dropdown menu.
    f. To **download your application**, click on the three dots in the upper right corner of the application page and select download. If you are within a task, first click on the Back to application link in the upper left. Please **be aware of any pop-up blockers** in your browser that may prevent downloading your application.
    g. To **access an application that you have previously saved**, click on the My Applications link in upper right and click the green Continue button on the application you wish to edit.

6. Once all tasks are completed, click the green Submit button **to submit your application**.
    a. If the button is grayed out, it means your application is not yet complete; please be sure all required fields and uploads are complete within each task and that you have clicked the Mark as Complete button within each task.
    b. To **download your application**, click on the download link in the upper right corner. Please be mindful of **any pop-up blockers** that may be active in your browser that prevent/hide downloads.
    c. Review your application in the window (or in the PDF that you have downloaded). If you want to make changes, navigate back to your application and reopen/edit any tasks that need editing. **It is strongly recommended that you download your application as a PDF (instructions above in b.) to review your application before clicking submit.**
    d. Once you are **ready to submit**, click the green Submit Your Application button on the left side of the window. You will need to confirm your submission by clicking the green Submit button in the pop-up window. **Once your application has been submitted, it cannot be edited. Please be sure that your application is complete BEFORE submitting**. If you inadvertently submit your application and it is before the deadline, please contact sciencegrants@chanzuckerberg.com.
7. Once your application is submitted, you will **receive an auto-email** confirming submission within a few minutes. If you do not receive a confirmation email within a few minutes, please check your spam folder. If you still did not receive your confirmation email, please email sciencegrants@chanzuckerberg.com.
8. If you would like to view your application after you have submitted it, it can be accessed through the My Applications link in the upper right corner.

The application consists of the following sections (called tasks in the grants portal): Coordinating PI Details, Equal Opportunity & Diversity (optional), Organization Details for Coordinating PI, Project Details, Project Proposal, Budget, Biosketches for Coordinating PI and Co-PIs, and Letters of Commitment (optional).

- **Coordinating PI Details:** Complete all fields in this task; **all fields are required.** The information entered should be for the Coordinating Principal Investigator (Coordinating PI), who will be the person submitting the application on behalf of the team. The Coordinating PI will take responsibility for managing the group collaboration and be the administrative point of contact for CZI and any partners. Note that institutions outside the U.S. may not subcontract to U.S. institutions, so please be mindful when selecting the Coordinating PI/institution. Information about the Co-Principal Investigator(s) on the proposal should be entered where requested in the Project Details part of the application.
    - Name and email (auto-filled): To edit your name or email, please do so in your account information by clicking your name in the upper right corner and clicking My Account in the dropdown menu.
    - Degree(s).
    - Organization, Title/Position, Department or equivalent.

- Career status: Select early-career (0 to 6 years), mid-career (6+ to 10 years), or neither. **Note: Early- or mid-career status is not required to be eligible for this RFA, although we encourage participation and leadership from early-career researchers.**
    - Early-Career Definition: In the context of this RFA, an early-career investigator is someone who has been in an independent position for zero to six years at the time of application, i.e. have started their first independent position between June 1, 2017, and June 1, 2023.
    - Mid-Career Definition: In the context of this RFA, a mid-career investigator is someone who has been in an independent position for more than six to 10 years at the time of application, i.e. have started their first independent position between June 1, 2013, and May 31, 2017.
- Short narrative biography of the Coordinating PI (maximum of 100 words).
- ORCID iD: Enter in format XXXX-XXXX-XXXX-XXXX. ORCID iDs are unique, digital identifiers that distinguish individual scientists and unambiguously connect their contributions to science over time and across changes of name, location, and institutional affiliation. ORCID iDs will be used to streamline reporting in our applications and grant reports to reduce the burden on grantees. For more information, please visit https://orcid.org/register. (Please contact us at sciencegrants@chanzuckerberg.com if you wish to opt-out).

- **Equal Opportunity & Diversity (optional):** CZ Science supports the science and technology that will make it possible to cure, prevent, or manage all diseases by the end of this century. Different communities are affected by or experience disease in different ways. Moreover, due to systemic barriers, the scientific enterprise itself is not a place where all voices and talents thrive. We believe the strongest scientific teams — encompassing ourselves, our grantees, and our partners — incorporate a wide range of backgrounds, lived experiences, and perspectives that guide them to the most important unsolved problems. To enable our work, we incorporate diverse perspectives into our strategy and processes, and we also seek to empower community partners to engage in science.

  We request demographic information associated with applications submitted to CZI in response to our open calls. This information helps us learn from the RFA process, as well as improve our strategies to help ensure members of underrepresented or marginalized groups in science are aware of and able to apply to CZI opportunities. **Please note that answering the questions below is voluntary, and receiving funding is not contingent on providing this information. Demographic information provided may be used in our grant-making process but will not be used as the sole or determinative factor in our grant funding decisions.** We may also publish aggregated data in various public forums, such as a website or blog. All responses will be shared only with limited personnel and service providers, who will use that information only for the purposes described in this paragraph.

  If you have any additional questions about why we ask this, what we do with the data, or to share suggestions for improvement, please reach out to sciencegrants@chanzuckerberg.com.

The information below may be entered for the Coordinating PI, who will be submitting the application on behalf of the team. The categories listed below may not capture all possible identities; in the event that the categories do not accurately reflect your identities, please use the space provided to self-describe.

- What is your race/ethnicity? (optional)
- What is the year of your last academic degree? (optional)
- What is your gender? (optional)
- Are you transgender? (optional)
- Are you a member of the LGBTQ community? (optional)
- Do you have one or more disabilities? (optional)

The Coordinating PI may also provide aggregated information on the demographics of the Co-Prinicipal Investigators (Co-PIs) listed in the Project Details section of the application if those Co-PIs agree to share that information with CZI. The categories listed below may not capture all possible identities; in the event that the categories do not accurately reflect their identities, please use the space provided to describe.

- How many of the Co-PIs self-identify as each of the following genders?
  - Woman, Man, Non-binary/Third gender, Prefer not to state, Prefer to describe (optional)
- How many of the Co-PIs self-identify as each of the following races/ethnicities?
  - Two or More Races, Black and/or African American, Asian, White, Hispanic or Latinx, Middle Eastern or North African, Native Hawaiian or Other Pacific Islander, American Indian or Alaska Native, Prefer not to state, Prefer to describe (optional)

- **Organization Details for Coordinating PI:** Complete all fields in this task; **all fields are required.** The information entered should be for the organization of the Coordinating Principal Investigator (Coordinating PI), who will be the person submitting the application on behalf of the team. The Coordinating PI must be affiliated with the organization listed, and grant funds will be awarded to this organization, which will take responsibility for distributing funds to the institutions of the other team members.
  - Organization name/Street address/City/State/Country/Website.
  - Type of Organization (Academic, Other Non-profit, Government, Other).
  - Tax ID: Enter your organization's Employer Identification Number (EIN), as assigned by the Internal Revenue Service in the 9-digit format (XX-XXXXXXX; 10 characters total). Foreign organizations or others who do not have an EIN should enter 44-4444444.
  - Organizational/Administrative Contact: List the name and contact information for the administrative contact to discuss additional information needed, if selected for award.
    - First name, Last name, Title/Position, Email.
  - Signing Official: List the name and contact information of the person authorized to sign on behalf of your organization.
    - First name, Last name, Title/Position, Email.

- Press Contact / Public Relations Official: List the name and contact information for the person to discuss press releases and media.
  - First name, Last name, Title/Position, Email.
- Institutional Approval Form: Upload as a single PDF. This form should be reviewed and signed by a person authorized to sign on behalf of your institution agreeing to the stated institutional and investigator requirements and commitments on data, resource sharing, and publication policies, as well as endorsing/verifying your application materials and confirming their ability to receive funding for the proposal. In the event of an award, all funds will be awarded to the Coordinating PI institution as the prime institution, and the Coordinating PI institution will be responsible for ensuring compliance of all of the terms, including compliance of all partners/subcontract institutions. **These policies are non-negotiable so this form should only be signed if the organization is able to comply with the terms as stated.** While CZI does not require sign-off by all of your partner institutions, please refer to what your institution requires. **Note: digital signatures are permitted as long as the document is not encrypted or password-protected.**

- **Project Details:** Complete all fields in this task; all fields are required.
  - Project Title: Auto-filled; limited to 60 characters, including spaces. If you need to edit your project title, navigate to your application summary page, click on the three dots to the right of the application title (next to the Preview link), and select Rename from the dropdown menu.
  - Type of project: Designate if the project is a Focused ($250K limit) or Expanded ($500K limit) project.
  - Category:
    - Scale: select one:
      - Organelles (mitochondria, lysosome, endoplasmic reticulum, Golgi apparatus, etc.)
      - Cells (primary cells, immune cells, tissue-resident cells, etc.)
      - Other, please specify
    - Technology: select all that apply:
      - Single-Cell (Transcriptomics, Proteomics, Metabolomics)
      - Spatial (Transcriptomics, Proteomics, Metabolomics)
      - Untargeted approaches (Mass Spectrometry-based or non-Mass Spectrometry-based)
      - Targeted approaches (Mass Spectrometry-based or non-Mass Spectrometry-based)
      - Imaging approaches
      - Biochemical tools (metabolic biosensors, isotope labeling, fluxomics, organelle purification, etc.)
      - Other, please specify
    - Biological applications: select all that apply:
      - Metabolic reprogramming
      - Metabolic flux measurement

        - Immunometabolism
        - Inflammaging/senescence
        - Inflammation
        - Tumor microenvironment
        - Circadian rhythm
        - Exercise
        - Sleep
        - Nutrition and nutrient sensing
        - Other, please specify
- Amount Requested: Enter the amount requested per year, as well as the total budget requested for all years in U.S. dollars, including indirect costs; these numbers should match those described in the Budget section. Enter whole numbers only (no dollar signs, commas, or cents).
- Number of Co-Principal Investigators: Indicate the number of Co-Principal Investigators, not including the Coordinating PI. Provide the following information for each Co-PI (maximum of two). **Do not include the Coordinating PI in this section**. For each Co-PI, please provide:
    - Co-PI name, Title/Position, Degrees, ORCID iD (format: XXXX-XXXX-XXXX-XXXX), Email, Career status
        - In the context of this RFA, an early-career investigator is someone who has been in an independent position for zero to six years at the time of application, i.e. have started their first independent position between June1, 2017, and June 1, 2023, and mid-career as someone who has been in an independent position for more than six to 10 years at the time of application, i.e. have started their first independent position between June 1, 2013, and May 31, 2017.
    - Organization Name, Country, Website
    - Type of organization (drop-down menu: Academic, Other Nonprofit, Government, Company/industry, Other).
    - Tax ID: Enter your organization's Employer Identification Number (EIN), as assigned by the Internal Revenue Service in the 9-digit format (XX-XXXXXXX; total of 10 characters). Foreign organizations or others who do not have an EIN should enter 44-4444444.
- Role Description of Each PI: (maximum of 500 words) Describe the role of each PI on the project.
- Project Purpose: (maximum of 200 characters including spaces) Summarize your research project; limited to one sentence. Please use a third-person voice.
    - Example: *to develop a comprehensive, validated atlas of the healthy human kidney of African and South Asian ancestries at single-cell resolution open to the entire scientific and clinical community*
- Abstract/Project Summary: (maximum of 250 words) Describe your project. Please use a third-person voice (example).
- Milestones: (maximum of 250 words, list format) Summarize the main milestones for your project, including yearly deliverables that demonstrate progress. Please use a

third-person voice.

- Diversity, Equity, and Inclusion (DEI) Statement: (maximum of 250 words) Advancing DEI is a core value for CZI, and we are requesting information on your efforts in this area. Please describe how your proposal or your team seeks to promote diversity, equity, and inclusion in this project.

- **Project Proposal:** Upload your project proposal as a single PDF; the font must be 11 point or larger, and margins must be at least one-half inch (top, bottom, left, and right) for all pages (letter size required). Include the following sections:
  - Proposal Body: (maximum of 2500 words, which includes 250 words for the Abstract)
    - Abstract: Copy your Abstract/Project Summary entered in the Project Details section here.
    - Scientific proposal:
      - Define the scientific question or problem related to measuring metabolism across organelles and cells that the team aims to investigate.
      - Clarify the rationale for how this project addresses a critical gap in the field, how the team is poised to address this gap, and why it requires an interdisciplinary approach.
      - Detail the scientific goals of the project.
      - Tools and Resources: Provide a brief summary of the tools, technology, data modalities and other resources that your team may be bringing to this project and/or aims to develop as a part of the project.
      - Describe clearly the research and development strategy to be employed.
      - List expected outcomes, learnings from data generated, main deliverables, and associated timeline.
  - Figures/Preliminary Data (optional): Limited to two pages, including legends. Figure legends do not count toward the word count.
  - References Cited in Your Proposal: No word/page limit; include complete source references.

- **Budget (one-page maximum per PI):** Upload in PDF format; budgets can be uploaded in a combined single PDF or one PDF for each Co-PI; one-page maximum per PI; font must be 11 point or larger, and margins must be at least one-half inch (top, bottom, left, and right) for all pages (letter size required). Provide a detailed description of the costs to be funded by this grant at a high level and in tabular form, outlining costs for personnel (including names, if known), supplies, equipment, travel, meetings/hackathons/sprints, subcontracts, other costs, and up to 15 percent indirect costs (excluding equipment and subcontracts). If budgets are provided for individual components, the PI should also generate a summary of no more than one page highlighting the distribution of grant funds across the PIs.
  - Grants can be requested at two levels. Proposed budgets should reflect the project scope:
    - *Focused Projects*: $250,000 USD total costs (inclusive of up to 15 percent indirect costs) over 24 months for exploratory, risky technology development strategies; and

        - *Expanded Projects*: $500,000 USD total costs (inclusive of up to 15 percent indirect costs) over 24 months for projects that look into hypothesis-driven biological questions that rely on applying, scaling, and/or improving existing technology to measure metabolism across organelles and cells.
    - Indirect costs are limited to up to 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.
    - Budget should be requested in U.S. dollars.
    - International grantees must use all grant funds exclusively for activities conducted outside the United States of America. Travel expenses to the United States (including round-trip tickets) should not be covered by the requested grant funds. Any attendance at CZI meetings in the U.S. will be covered by CZI outside of requested grant funds.
    - Application budgets must reflect the actual needs of the proposal. The Chan Zuckerberg Initiative will work closely with successful applicants to arrive at a mutually acceptable budget after review.

- **Biosketches for Coordinating PI and Co-PIs:** Upload the biosketches in PDF format for the Coordinating PI and for each of the Co-PIs. Biosketches can be uploaded in a combined single PDF or one PDF for each Co-PI, a maximum of 5 pages per biosketch; NIH format or similar. **Do not include any biosketches for any additional collaborators beyond the Coordinating PI and Co-PIs, as listed.**

- **Letters of Commitment (optional):** Upload a signed letter from each Co-PI briefly describing their role and contribution of the Co-PI to the overall team and project; **do not** include a letter from the Coordinating PI. Letters should be in PDF format (letter size) and can be uploaded in a combined single PDF or one PDF for each Co-PI and/or partner. **Note: digital signatures are permitted as long as the document is not encrypted or password-protected.**

The formatting and component requirements, including word and page limits indicated above, will be enforced by the review team. Any submitted materials that exceed the word and page limits or do not follow the requirements will not be considered during the application review process.

QUESTIONS?

For administrative and programmatic inquiries pertaining to this RFA, please contact sciencegrants@chanzuckerberg.com. For technical assistance with SMApply, please contact support@smapply.io or while logged into SMApply, click on the information ”i” link in the upper right corner and submit a help request ticket.