Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH (http://www.nih.gov))

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Components of Participating Organizations

National Institute of Mental Health (NIMH (https://www.nimh.nih.gov/index.shtml))

National Eye Institute (NEI (https://www.nei.nih.gov/))

National Institute on Aging (NIA (https://www.nia.nih.gov/))

National Institute on Alcohol Abuse and Alcoholism (NIAAA (https://www.niaaa.nih.gov/))

National Institute of Biomedical Imaging and Bioengineering (NIBIB (https://www.nibib.nih.gov/))

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD (https://www.nichd.nih.gov/))

National Institute on Deafness and Other Communication Disorders (NIDCD (https://www.nidcd.nih.gov/))

National Institute on Drug Abuse (NIDA (https://www.drugabuse.gov/))

National Institute of Neurological Disorders and Stroke (NINDS (https://www.ninds.nih.gov/))

National Center for Complementary and Integrative Health (NCCIH (https://nccih.nih.gov/))

Funding Opportunity Title

BRAIN Initiative: Pilot resources for brain cell type-specific access and manipulation across vertebrate species (U01 Clinical Trial Not Allowed)

Activity Code

U01 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=u01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project – Cooperative Agreements

Announcement Type

New

Related Notices

None

Funding Opportunity Announcement (FOA) Number

RFA-MH-20-556

Companion Funding Opportunity

None

Number of Applications

See Section III. 3. Additional Information on Eligibility.

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

93.242, 93.213, 93.867, 93.866, 93.273, 93.286, 93.865, 93.279, 93.173, 93.853

Funding Opportunity Purpose

This Funding Opportunity Announcement (FOA) from the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is intended to support the development of technologies, production efforts, and dissemination resources for a cell type-specific armamentarium to study brain function across species. The goal is to promote evaluation of molecular or genetic technologies and creation of pilot production and distribution resources for cell type-specific access and manipulation reagents for several vertebrate species, including in human *ex vivo* tissues or cells. Demonstration projects are sought that would develop reagents that: (1) enable access to molecularly defined neural cell types in a complex brain region or significant brain network of a vertebrate; (2) are easily produced, disseminated, utilized, and stored; and (3) are catalogued for users in a brain atlas. In addition to the above required features, reagents are also sought that exhibit the following qualities: (4) are applicable to both genetically tractable and less tractable vertebrate organisms; (5) exhibit high specificity and efficiency of targeting; (6) show low toxic or perturbative effects; (7) provide flexibility to deliver various reporter, sensor, and effector payloads and are compatible with other methods of access to brain cell types; and (8) are potentially usable in human *ex vivo* brain tissue or cells. The pilot projects should be scalable in the future. The long-term goal of a potentially scaled-up effort is to achieve near comprehensive, molecular access for monitoring and manipulation reagents in each defined cell type of vertebrate brains relevant to neuroscience research.

Key Dates

Posted Date

September 17, 2020

Open Date (Earliest Submission Date)

January 11, 2021

Letter of Intent Due Date(s)

30 days prior to the application due date

Application Due Date(s)

February 11, 2021; October 19, 2021, by 5:00 PM local time of applicant organization.

All applications are due by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on the listed date(s).
Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

AIDS Application Due Date(s)

Not Applicable

Scientific Merit Review

June 2021, March 2022

Advisory Council Review

August 2021, May 2022

Earliest Start Date

September 2021, June 2022

Expiration Date

October 20, 2021

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000),except where instructed to do otherwise (in this FOA or in a Notice from NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/)).

Conformance to all requirements (both in the Application Guide and the FOA) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the NIH ASSIST system to prepare, submit and track your application online.

   Apply Online Using ASSIST

2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and eRA Commons (http://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.

3. Use Grants.gov (https://www.grants.gov/web/grants/applicants/download-application-package.html#search=true&oppNum=RFA-MH-20-556) Workspace to prepare and submit your application and eRA Commons (http://public.era.nih.gov/commons/) to track your application.

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Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Background

The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative® (https://braininitiative.nih.gov/) is aimed at revolutionizing our understanding of the human brain. By accelerating the development and application of innovative technologies, researchers will be able to produce a new dynamic picture of the brain that, for the first time, will show how individual cells and complex neural circuits interact in both time and space. It is expected that the application of these new tools and technologies will ultimately lead to new ways to treat and prevent brain disorders.

NIH is one of several federal agencies involved in the BRAIN Initiative. Planning for the NIH component of the BRAIN initiative is guided by the long-term scientific plans, "BRAIN 2025: A Scientific Vision (http://braininitiative.nih.gov/pdf/BRAIN2025_508C.pdf)," which details seven high-priority research areas and calls for a sustained federal commitment of $4.5 billion over 12 years, and "The BRAIN Initiative 2.0: From Cells to Circuits, Toward Cures (https://braininitiative.nih.gov/sites/default/files/images/brain_2.0_6-6-19-final_revised10302019_508c.pdf)." This Funding Opportunity Announcement (FOA) and other FOAs issued in Fiscal Year 2020 are based on careful consideration by the NIH of the recommendations of the BRAIN 2025 and BRAIN 2.0 reports, and input from the NIH BRAIN Multi-Council Working Group. Videocasts of the NIH BRAIN Multi-Council Working Group meetings are available at http://www.braininitiative.nih.gov/about/mcwg.htm (http://www.braininitiative.nih.gov/about/mcwg.htm).

To enable rapid progress in development of new technologies as well as in theory and data analysis, the BRAIN Initiative encourages collaborations between neurobiologists and scientists from statistics, physics, mathematics, engineering, and computer and information sciences; and NIH welcomes applications from investigators in these disciplines.

NIH encourages BRAIN Initiative applications from investigators that are underrepresented in the biomedical, behavioral, or clinical research workforce (see data (http://www.nsf.gov/statistics/showpub.cfm?TopID=2&SubID=27) and the most recent report on Women, Minorities, and Persons with Disabilities in Science and Engineering (http://www.nsf.gov/statistics/women/)). Such individuals include those from underrepresented racial and ethnic groups, those with disabilities, and those from disadvantaged backgrounds.

NIH also encourages businesses to participate in the BRAIN Initiative. It is possible for companies to submit applications directly to BRAIN Initiative program announcements or to collaborate with academic researchers in joint submissions. Small businesses should consider applying to one of the BRAIN Initiative small business FOAs. (http://braininitiative.nih.gov/funding/index.htm)

In addition to the National BRAIN Initiative, the NIH continues to have a substantial annual investment in neuroscience research. The Institutes and Centers contributing to the NIH BRAIN Initiative (http://braininitiative.nih.gov/) support those research efforts through investigator-initiated applications as well as through specific FOAs. Potential applicants to this FOA are strongly encouraged to contact Scientific/Program staff if they have any questions about the best FOA for their research.

The BRAIN Initiative will require a high level of coordination and sharing between investigators.

The data sharing expectations for BRAIN Initiative awards can be found at NOT-MH-19-010. (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-19-010.html)

This FOA is related to the transformative project, "A Cell Type-Specific Armamentarium for Understanding Brain Function and Dysfunction," described in the "The BRAIN Initiative 2.0: From Cells to Circuits, Toward Cures (https://braininitiative.nih.gov/sites/default/files/images/brain_2.0_6-6-19-final_revised10302019_508c.pdf)" report of the Advisory Committee to the NIH Director BRAIN Initiative Working Group 2.0.

An Opportunity to Manipulate Brain Function Based on Cell Types

Different types of cells are found in the brain and shape circuit function. Neurons with long-range versus local projections regulate the spatial extent of brain information flow. In addition, excitatory and inhibitory neurons are configured in circuits with feedback, feedforward, lateral, convergent, divergent, and other architectures. Moreover, various glial cell types regulate neurotransmitter recycling and neuronal ion flux in circuits. Thus, defining the diversity of cell types is critical for understanding circuits. Significant progress has been made in this area through a census of mammalian brain cell types, supported by the BRAIN Initiative Cell Census program. The BRAIN Initiative Cell Census effort was initiated in 2014 to define a brain parts list with unprecedented detail through molecular and anatomical profiling of the mouse, non-human primate, and human brain. By 2020, the program together with other efforts succeeded, for example, in defining at least

55 cell types in regions of mouse primary motor cortex with comprehensive transcriptomic, epigenomic, and anatomical profiles. These neuronal cell types can be related in hierarchical classes defined by neurotransmitter identity, cortical layer position, or projection pattern. Many more cell types have been and will continue to be delineated across the cortex and in subcortical regions.

With cell types defined based on molecular profiles, neuroscientists are well positioned to learn more about circuit function. This is because functional probes can be expressed in or addressed to these circuit components using molecular techniques. Gene regulatory elements and viral vector tropic factors can be used for targeting. Recent work is uncovering transcriptional regulatory sequences for cell type expression. Furthermore, genetically encoded reagents have also been developed to monitor and manipulate cells. Fluorescent protein-based probes for calcium, membrane voltage, and released neurotransmitters are useful at reporting activity across neuronal populations with cellular resolution in the intact animal brain. Optogenetic and chemogenetic effector proteins are capable of controlling neuronal activity. Gene editing technologies can be used to precisely alter the molecular composition of neural cells. Expression of these and other molecular tools in specific cell types enables the functional dissection of circuits with greater precision and scale than prior methods. But expanded genetic access to molecularly defined cell types is needed to apply structure defining, activity monitoring, and perturbing methods more comprehensively. Ultimately, gaining molecular access to the diversity of cell types is critical to understand brain function in model organisms and to explore disease-relevant circuits for brain disorders in humans in the future. Cell type-specific access will also augment brain connectomic information by relating cell type identity to circuit connectivity.

In a prior effort, molecular access to neurons defined by marker gene expression was successfully implemented using genetically engineered mice. The Gene Expression Nervous System Atlas (GENSAT) collection of bacterial artificial chromosome (BAC) transgenic mice encompasses more than 1100 BAC-GFP and 250 BAC-Cre recombinase driver lines. This effort was supported in part by the NIH Blueprint for Neuroscience Research (https://neuroscienceblueprint.nih.gov/). Moreover, responder mouse lines are widely used that express structural markers, activity sensors, and effectors in combination with recombinase or transcription factor drivers. By contrast, reagents not requiring germline modification have also been developed for use both in mice and less genetically tractable organisms like non-human primates. Viral vectors, including adeno-associated virus (AAV) and lentivirus (LV), have been engineered with cell type-specific gene regulatory elements for specific expression and capsids for selective tropism. These can be used to deliver payloads to targeted neural cells. But to further dissect brain circuits based on recently defined cell types, especially in less genetically tractable species, a more comprehensive set of reagents for molecular access is needed. The dissection of brain circuits could lead to identification and functional characterization of human disease-relevant neural cells and circuits.

Research Objectives

What are the desired features of a reagent resource for brain cell type access and manipulation? First, a near comprehensive set of validated reagents would match the scale of brain neural cell diversity. The scope of cell type diversity to be accessed is practically limited by reagent production and validation efforts. But the scale of the ideal resource would be conceptually aimed at enabling unique access to each molecularly defined brain neural cell type that could exhibit a distinct cellular, circuit, or behavioral function. Reagents would be easily produced, disseminated, utilized, and stored. The collection of reagents would be catalogued for users in a brain atlas that is registered to cell types based on molecular, anatomical, or other properties that can be referenced. Technologies would be applicable to both genetically tractable and less tractable vertebrate organisms in common use by neuroscientists. The specificity and efficiency of targeting cell types would be quantitatively high and reproducible. The toxic or perturbative effects to cells, tissues, and organisms would be quantitatively low. The access technologies would provide flexibility to deliver various reporter, sensor, and effector payloads and would be compatible with other methods of access. Finally, in some cases, technologies to access cell types would be potentially usable in humans to target gene editors or other effectors to disease-relevant circuits for future therapies. The envisioned reagents to access and probe cell types encompassing all of these attributes will be challenging to achieve. But different types of reagent production efforts for various areas of neuroscience will likely be needed that prioritize some features over others. It is hoped that a near comprehensive resource will emerge from iterative attempts to achieve these characteristics. This FOA is intended for the pilot projects.

Research Scope

The purpose of this FOA is to evaluate molecular or genetic technologies and create pilot production and distribution resources for cell type-specific access and manipulation reagents for several vertebrate species. Applicants to this FOA should propose demonstration projects for reagent resource production, validation, and dissemination. The proposed projects should be scalable. The proposed projects should demonstrate the potential to achieve as many of the following goals as possible. Applicants are required to address goals 1, 2, and 3:

1. Reagents enable unique access to many molecularly defined neural cell types that are found in a complex brain region

or significant brain network of a vertebrate and that could exhibit distinct cellular, circuit, or behavioral functions.

2. Reagents are easily produced, disseminated, utilized, and stored.

3. Collection of reagents are catalogued for users in a brain atlas and registered to cell types based on molecular, anatomical, or other properties that can be referenced.

4. Reagents are applicable to both genetically tractable and less tractable organisms in common use by neuroscientists.

5. Specificity and efficiency of targeting brain cell types are validated to be quantitatively high and reproducible.

6. Toxic or perturbative effects to cells, tissues, and organisms are quantitatively low.

7. Access technologies provide flexibility to deliver various reporter, sensor, and effector payloads and are compatible with other methods of access.

8. Technologies to access cell types are potentially usable in human *ex vivo* brain tissue or cells to target gene editors or other effectors to disease-relevant circuits for future therapies.

Applicants are strongly encouraged to form multidisciplinary teams for the demonstration projects to work toward the above goals for reagent production, validation, and dissemination. Successful applicants will become part of a research consortium (see further below) encompassing other awardees. The NIH expects the consortium to operate as a cooperative network to promote collaboration and coordination and to achieve the program's overall goals. This will include regular meetings and other coordinated activities within the consortium as well as in the BRAIN Initiative more broadly.

During the funding period, applicants must propose to demonstrate the scalability of reagent production, validation, and dissemination to potentially gain near comprehensive access to each cell type that could exhibit a distinct cellular, circuit, or behavioral function and is molecularly defined in the brain of a vertebrate. The demonstration could encompass achieving access to the cell types of a complex brain region or significant brain network of a vertebrate. Based on promising demonstration results, the scale up of reagent resources will potentially be supported by FOAs subsequent to this announcement. In the demonstration projects, the initially proposed cell types to access should be justified based on their high significance to neuroscience researchers.

Applicants are strongly encouraged to make use of publicly available data that molecularly define brain cell types from the BRAIN Initiative Cell Census program (https://biccn.org/data) or other similar efforts. Applications that include further molecular characterization of cell types (e.g., nucleic sequencing of bulk or single brain cells or nuclei) as part of producing neural cell access reagents will be considered, but such characterization efforts should be thoroughly justified.

Applications may propose to incorporate technology development and optimization, but these efforts should be integrated into a larger reagent production, validation, and dissemination project. For example, technology development and optimization could be incorporated to augment or improve existing methods for molecular access based on feedback from reagent validation studies.

Applicants should propose robust reagent resource sharing plans (including quality control, quality assurance, dissemination plans, etc.) that enable greater cell type access to many neuroscientists as a result of the demonstration projects. Applicants should propose plans for reagent sharing beyond the applicants and named collaborators. Applicants should propose to share all validated reagents from demonstration projects with the neuroscience community to promote their use and refinement. The participation of reagent repositories and industry in multidisciplinary applicant teams is encouraged. It is recognized that future, scaled-up projects subsequent to this FOA likely will require additional support for widescale reagent production and dissemination. Applicants should also propose data sharing plans that are consistent with the Data Sharing Policy for the BRAIN Initiative (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-19-010.html). Applicants should propose to catalogue all validated reagents from demonstration projects for use by the neuroscience community.

Applications must include proposed milestones and a proposed timeline, both of which will be evaluated as part of the review process, but final versions of each will be agreed upon at the time of award. If justified, future year milestones may be revised based on data and information obtained in the current year. The milestones and timeline should include the timing and quantity of dissemination of the validated reagents from the demonstration projects to the neuroscience community.

Examples of responsive research activities include, but are not limited to:

- Production of adeno-associated viral (AAV) or lentiviral (LV) vectors containing transcriptional regulatory elements that enable selective or specific expression of neural activity monitoring or manipulation payloads in molecularly defined brain cell types that could have functional relevance.

- Creation of cell type access and manipulation reagents for brains of vertebrate animals and/or human *ex vivo* brain tissue or cells to identify, characterize, and/or alter potentially disease-relevant neural cells or circuits.
- Bioinformatic analysis of gene promoter, enhancer, splicing sequences, and transcriptomic and epigenomic profiling data within or across species to identify candidate regulatory elements to confer brain cell type selectivity or specificity to constructs.
- Scalable use of somatic cell, CRISPR gene editing to knock in monitoring or manipulation constructs to a collection of gene loci that contain *cis* regulatory elements that drive expression in specific brain cell types.
- Screening and validation of AAV capsid variants to selectively transduce brain neural cell types.
- Screening and validation of lipid nanoparticles containing surface proteins that mediate selective transduction of brain neural cell types with genetic constructs.
- Engineering of LV vectors pseudotyped with antibody or nanobody proteins to mediate selective transduction of brain neural cell types targeting cell surface antigens.
- Screening for viral or non-viral access reagents for defined cell types using nucleic acid barcoding of variants and barcode sequencing of brain cell types.
- Production of transgenic mouse, rat, zebrafish, or other vertebrate responder lines containing widely used reporter, monitoring, or manipulation constructs that can be combined with molecular access driver reagents to be expressed in specific brain neural cell types.
- Scalable transgenic and genome engineering projects to knock in reporter, monitoring, or manipulation constructs through the germline to gene loci for brain cell type-specific expression that very substantially reduce the time, cost, and breeding required for current methods in experimental vertebrate organisms.
- Projects to produce combinations of molecular access reagents that intersectionally refine expression or delivery of monitoring and manipulation constructs to brain cell types with greater specificity.
- Production of high-resolution atlases to validate and catalog produced access reagents for users, showing vector tropism, transcriptional regulatory element activity, or transgene expression in the mouse, primate, or other vertebrate brain using whole brain volume fluorescence microscopy and counterstaining with known reference markers.
- Establishment of atlases where access reagents are validated and assigned to brain cell types based on transcriptomic profiling.
- Creation of a collection of systemically administered viral or non-viral reagents that efficiently cross the blood brain barrier and direct construct expression to molecularly defined brain cell types and that detarget peripheral organs.
- Toxicity and cytomorbidity studies that define parameters and protocols for brain cell type-selective reagent use administered systemically or intracranially to minimize undesirable, perturbative effects of vectors or payloads.
- Establishment of brain cell type-selective reagent manufacturing and dissemination platforms that ensure quality control, quality assurance, and adequate supply for neuroscience community users.
- Production of collections of viral or non-viral vectors that enable neuronal projection mapping of or transsynaptic tracing initiated from defined brain cell types.
- Construction of a library of RNA-based reagents to target brain cell types based on nucleic acid complementarity, protein-RNA interaction, or nanoparticle delivery.

The following research areas are considered outside the research scope of this FOA, and such applications will be considered non-responsive and will not be reviewed:

- Studies that fail to propose to achieve the 3 required goals where: (1) reagents enable unique access to many molecularly defined neural cell types that are found in a complex brain region or significant brain network of a vertebrate and that could exhibit distinct cellular, circuit, or behavioral functions; (2) reagents are easily produced, disseminated, utilized, and stored; (3) collection of reagents are catalogued for users in a brain atlas and registered to cell types based on molecular, anatomical, or other properties that can be referenced.
- Studies primarily focused on the pursuit of a biological mechanism or a hypothesis through basic research that does not result in the generation of a pilot, scalable reagent resource for brain cell types;
- Studies primarily focused on technology development that do not propose a pilot, scalable reagent resource. Note: Applications for technology development may be submitted to a separate BRAIN Initiative FOA (RFA-MH-19-135 (https://grants.nih.gov/grants/guide/rfa-files/rfa-mh-19-135.html), RFA-MH-19-136 (https://grants.nih.gov/grants/guide/rfa-files/rfa-mh-19-136.html), RFA-MH-19-148 (https://grants.nih.gov/grants/guide/rfa-files/rfa-mh-19-148.html), RFA-MH-20-135 (https://grants.nih.gov/grants/guide/rfa-files/rfa-mh-20-135.html)).

Applicants are strongly encouraged to consult the Scientific/Research Contact listed below to discuss the alignment of their proposed work with the FOA goals. A Technical Assistance teleconference will be held for potential applicants on Tuesday, November 17, 2020, from 1:00-2:00 ET. NIH staff will be available to answer questions related to this FOA. To obtain call-in information, please contact by email the Scientific/Research Contact listed below at least 24 hours prior to the call and specify the RFA number in the subject line or in the body of the email.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this FOA.

Application Types Allowed

Revision
New
Resubmission
The OER Glossary (//grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the SF424 (R&R) Application Guide provide details on these application types. Only those application types listed here are allowed for this FOA.

Clinical Trial?

Not Allowed: Only accepting applications that do not propose clinical trials
Need help determining whether you are doing a clinical trial? (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

Issuing IC and partner components intend to commit an estimated total of $10,000,000 per year to fund 4 to 6 awards.

Award Budget

Application budgets are not limited but need to reflect the actual needs of the proposed project.

Award Project Period

The maximum project period is 3 years.

NIH grants policies as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this FOA.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Local Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)

Federal Governments

- Eligible Agencies of the Federal Government - Including the NIH Intramural Program
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Institutions)

Foreign Institutions

Non-domestic (non-U.S.) Entities (Foreign Institutions) **are** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

Foreign components, as defined in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

Required Registrations

Applicant organizations

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications (//grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html) states that failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) (http://fedgov.dnb.com/webform) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) (https://www.sam.gov/portal/public/SAM/) – Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code (//grants.nih.gov/grants/guide/url_redirect.htm?id=11176) – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.
- eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Applicants must have an active DUNS number to register in eRA Commons. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration, but all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one

Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- Grants.gov – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

2. Cost Sharing

This FOA does not require cost sharing as defined in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11126)

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101 (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html)).

Section IV. Application and Submission Information

1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this FOA. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000) except where instructed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Letter of Intent

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

By the date listed in Part 1. Overview Information, prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity

- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

The letter of intent should be sent to:

Email: nimhpeerreview@mail.nih.gov (mailto:nimhpeerreview@mail.nih.gov)

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits (//grants.nih.gov/grants/guide/url_redirect.htm?id=11133) must be followed.

Instructions for Application Submission

The following section supplements the instructions found in the SF424 (R&R) Application Guide and should be used for preparing an application to this FOA.

SF424(R&R) Cover

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Other Project Information

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R or Modular Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R Subaward Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Cover Page Supplement

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Research Plan

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Research Strategy: Applicants must include as part of the research strategy plans to achieve goals number 1, 2, and 3 listed below for a cell type-specific reagent resource. Applicants are also encouraged to plan to achieve as many of goals number 4 to 8 as possible.

1. Reagents enable unique access to many molecularly defined neural cell types that are found in a complex brain region or significant brain network of a vertebrate and that could exhibit distinct cellular, circuit, or behavioral functions.

2. Reagents are easily produced, disseminated, utilized, and stored.

3. Collection of reagents are catalogued for users in a brain atlas and registered to cell types based on molecular, anatomical, or other properties that can be referenced.

4. Reagents are applicable to both genetically tractable and less tractable organisms in common use by neuroscientists.

5. Specificity and efficiency of targeting brain cell types are validated to be quantitatively high and reproducible.

6. Toxic or perturbative effects to cells, tissues, and organisms are quantitatively low.

7. Access technologies provide flexibility to deliver various reporter, sensor, and effector payloads and are compatible with other methods of access.

8. Technologies to access cell types are potentially usable in human *ex vivo* brain tissue or cells to target gene editors or other effectors to disease-relevant circuits for future therapies.

Current State-of-the-Art Statement: Investigators should summarize the current state of knowledge regarding cell type-

selective access for molecular monitoring and manipulation technologies in the vertebrate brain region(s) or network(s) described in the application and how advances will be measured. Applicants are expected to explain how further cell type-selective access in the brain region(s), network(s), and species chosen will be significant to neuroscience researchers.

Proposed Milestones: Proposed milestones should include critical junctures and annual indicators of progress. These should be tailored to the unique scope of each project and written concretely enough to evaluate what exactly will be achieved (e.g., reagent resource validation steps, numbers of cell types accessed for specific circuits, testing methods across brain regions, reagent dissemination metrics, measures of progress for brain atlas cataloguing, etc.) during the course of the project. Given that some projects or aspects of projects are likely to be in early stages, the milestones should indicate the specific proof-of-concept test(s) along with any alternative strategies should that effort fail to perform as expected.

Timeline: In addition to and along-side the proposed milestones, applications should include a proposed Timeline that will describe when key milestones are likely to be met as well as when scalability will be evaluated.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide.

The following modifications also apply:

A central goal of this FOA is to generate transformative reagents that will be widely used throughout the research community. Applications must include a detailed plan for sharing these resources and include the following key elements:

- Project management of resource sharing;
- Description of what specific resources will be shared;
- Schedule/timeline for availability of resources to other users;
- Persons who will have access to the resources (written as broadly as possible to the extent consistent with applicable laws, regulations, rules, and policies);
- Plan for post award disposition of resources.
- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan consistent with data sharing expectations for BRAIN Initiative awards found at NOT-MH-19-010 (https://grants.nih.gov/grants/guide/notice-files/NOT-MH-19-010.html).

Appendix:

Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered “Yes” to the question “Are Human Subjects Involved?” on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed.

Delayed Onset Study

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

PHS Assignment Request Form

All instructions in the SF424 (R&R) Application Guide must be followed.

Foreign Institutions

Foreign (non-U.S.) institutions must follow policies described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign institutions described throughout the SF424 (R&R) Application Guide.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for

completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov.

4. Submission Dates and Times

Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday (https://grants.nih.gov/grants/guide/url_redirect.html?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to Grants.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the NIH Policy on Late Application Submission.

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11142)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11143).

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit How to Apply – Application Guide (https://grants.nih.gov/grants/how-to-apply-application-guide.html). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues (https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this FOA for information on registration requirements.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the SF424 (R&R) Application Guide.

See more tips (//grants.nih.gov/grants/guide/url_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and responsiveness by components of participating organizations (https://grants.nih.gov/grants

/guide/rfa-files/rfa-mh-20-556.html#_Components_of_Participating), NIH. Applications that are incomplete, non-compliant and/or non-responsive will not be reviewed.

In order to expedite review, applicants are requested to notify the NIMH Referral Office by email at nimhreferral@mail.nih.gov (mailto:nimhreferral@mail.nih.gov) when the application has been submitted. Please include the FOA number and title, PD/PI name, and title of the application.

Applications Involving the NIH Intramural Research Program

The requests by NIH intramural scientists will be limited to the incremental costs required for participation. As such, these requests will not include any salary and related fringe benefits for career, career conditional or other Federal employees (civilian or uniformed service) with permanent appointments under existing position ceilings or any costs related to administrative or facilities support (equivalent to Facilities and Administrative or F&A costs). These costs may include salary for staff to be specifically hired under a temporary appointment for the project, consultant costs, equipment, supplies, travel, and other items typically listed under Other Expenses. Applicants should indicate the number of person-months devoted to the project, even if no funds are requested for salary and fringe benefits.

If selected, appropriate funding will be provided by the NIH Intramural Program. NIH intramural scientists will participate in this program as PDs/PIs in accord with the Terms and Conditions provided in this FOA. Intellectual property will be managed in accord with established policy of the NIH in compliance with Executive Order 10096, as amended, 45 CFR Part 7; patent rights for inventions developed in NIH facilities are NIH property unless NIH waives its rights.

Should an extramural application include the collaboration with an intramural scientist, no funds for the support of the intramural scientist may be requested in the application. The intramural scientist may submit a separate request for intramural funding as described above.

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy (//grants.nih.gov/grants/guide/url_redirect.htm?id=82299). Any instructions provided here are in addition to the instructions in the policy.

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the NIH mission (//grants.nih.gov/grants/guide/url_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

For this particular announcement, note the following:

Because this FOA specifically seeks applications to systematically generate brain cell type-specific reagent resources and possibly related tools, the NIH expects that some applications may propose mature and well-established approaches that may not be innovative per se to produce robust high-quality reagents for broad use by the research community. In their evaluation of Innovation, reviewers will be asked to weigh the potential of the applications to develop novel approaches and/or to integrate existing approaches in novel ways.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project proposed).

Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

How well has the current state of the art been described? How likely is the reagent resource to be significant for accessing brain cell types in circuits that are of interest to neuroscience researchers? To what extent will the project likely provide access to brain cell types in species with previously limited access?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

How have the investigators, collaborators, or other researchers demonstrated experience in scalable production and dissemination of reagent resources?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

How well does the application integrate existing approaches in novel ways? To what extent does the application develop technologies for specific access to brain cell types that are thus far inaccessible? To what extent does the application propose targeting methods for brain cell types in species that lack many targeting reagents?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

How well does the application propose to achieve at least the required goals described in questions number 1, 2, and 3 below?

(1) To what extent does the application propose to enable unique access to many molecularly defined neural cell types that are found in a complex brain region or significant brain network of a vertebrate and that could exhibit distinct cellular, circuit, or behavioral functions?

(2) How easily will the reagents be produced, disseminated, utilized, and stored?

(3) To what extent does the application plan to catalogue the collection of reagents for users in a brain atlas and that is registered to cell types based on molecular, anatomical, or other properties that can be referenced?

How well does the application also propose to achieve the optional goals described in questions number 4, 5, 6, 7, and 8 below?

(4) To what extent will the proposed reagents be applicable to both genetically tractable and less tractable vertebrate organisms in common use by neuroscientists?

(5) How well does the application propose development of reagents where specificity and efficiency of targeting brain cell types are validated to be quantitatively high and reproducible?

(6) To what extent will the reagents be developed such that toxic or perturbative effects to cells, tissues, and organisms are quantitatively low?

(7) In what ways does the application propose access technologies that provide flexibility to deliver various reporter, sensor, and effector payloads and are compatible with other methods of access?

(8) To what extent will the technologies to access cell types be potentially usable in human *ex vivo* brain tissue or cells to target gene editors or other effectors to disease-relevant circuits for future therapies?

Beyond the above questions, how effective will the methods proposed be in demonstrating scalability? How appropriate

are the metrics that will help determine the success of scale up (to produce, validate, and disseminate access reagents)? If the application proposes to incorporate technology development and optimization, how well are these efforts integrated into a larger reagent production, validation, and dissemination plan? If proposed, to what extent are technology development and optimization plans incorporated to augment or improve existing methods for molecular access based on feedback from reagent validation studies?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Will the environment likely enable scalable production and dissemination of reagent resources?

Additional Review Criteria

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Milestones and Timeline

Are the Proposed Milestones and Timeline described in sufficient detail and are they appropriate for the project? Is the timeline reasonable? Are the milestones feasible, well developed, and quantifiable with regard to the specific aims? Do the milestones and timeline describe well and reasonably the timing and quantity of dissemination of the validated reagents from the demonstration projects to the neuroscience community?

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects (//grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research (//grants.nih.gov/grants/guide/url_redirect.htm?id=11174).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (//grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmissions

For Resubmissions, the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewals

Not Applicable

Revisions

For Revisions, the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

Additional Review Considerations

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Applications from Foreign Organizations

Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: (1) Data Sharing Plan (//grants.nih.gov/grants/guide/url_redirect.htm?id=11151); (2) Sharing Model Organisms (//grants.nih.gov/grants/guide/url_redirect.htm?id=11152); and (3) Genomic Data Sharing Plan (GDS) (//grants.nih.gov/grants/guide/url_redirect.htm?id=11153).

A major goal of this FOA is to generate reagents that will be widely used throughout the neuroscience community for brain cell type-selective access. In light of this goal, how well does the application include an adequate and detailed plan for sharing these resources as appropriate and consistent with achieving the goals of the program? To what extent does the plan provide a strong rationale for each of the following key elements as appropriate and consistent with achieving the goals of the program?

- Project management of resource sharing;
- Description of what specific resources will be shared;
- Schedule/timeline for availability of resources to other users;
- Persons who will have access to the resources (written as broadly as possible to the extent consistent with applicable laws, regulations, rules, and policies);
- Plan for post award disposition of resources.

Authentication of Key Biological and/or Chemical Resources:

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in

relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by NIMH, in accordance with NIH peer review policy and procedures (//grants.nih.gov/grants/guide/url_redirect.htm?id=11154), using the stated review criteria (file:///C:/Users/mckenziene/AppData/Local/Microsoft/Windows/INetCache/Content.Outlook/13V4QPZR/Research%20Draft.doc#_1._Criteria). Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications will receive a written critique.

Applications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.

Appeals (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-064.html) of initial peer review will not be accepted for applications submitted in response to this FOA.
Applications will be assigned on the basis of established PHS referral guidelines to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications submitted in response to this FOA. Following initial peer review, recommended applications will receive a second level of review by the appropriate national Advisory Council or Board. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.
Information regarding the disposition of applications is available in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11156).

Section VI. Award Administration Information

1. Award Notices

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the grants management officer is the authorizing document and will be sent via email to the grantee's business official.

Awardees must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

Any application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158) website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) as part of the NoA. For these terms of award, see the *NIH Grants Policy Statement* Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157) and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities (//grants.nih.gov/grants/guide/url_redirect.htm?id=11159). More information is provided at Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158).

Recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age and, in some circumstances, religion, conscience, and sex. This includes ensuring programs are accessible to persons with limited

English proficiency. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html (https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html) and http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html (http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html).

HHS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's scientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or exclude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the health or safety of the subjects, the scientific study design, or the purpose of the research. For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. HHS provides guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html (https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html) and https://www.lep.gov (https://www.lep.gov). For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53 (https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53).
- Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html (http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html).
- HHS funded health and education programs must be administered in an environment free of sexual harassment. Please see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html (https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html); https://www2.ed.gov/about/offices/list/ocr/docs/shguide.html; and https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf (https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf). For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm (https://grants.nih.gov/grants/policy/harassment.htm).
- Recipients of FFA must also administer their programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws. Collectively, these laws prohibit exclusion, adverse treatment, coercion, or other discrimination against persons or entities on the basis of their consciences, religious beliefs, or moral convictions. Please see https://www.hhs.gov/conscience/conscience-protections/index.html (https://www.hhs.gov/conscience/conscience-protections/index.html) and https://www.hhs.gov/conscience/religious-freedom/index.html (https://www.hhs.gov/conscience/religious-freedom/index.html).

Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at https://www.hhs.gov/ocr/about-us/contact-us/index.html (https://www.hhs.gov/ocr/about-us/contact-us/index.html) or call 1-800-368-1019 or TDD 1-800-537-7697.

In accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 (Public Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. FAPIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance system (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and performance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is currently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in making a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in 45 CFR Part 75.205 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS)

grant administration regulations at 45 CFR Parts 75, and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the primary responsibilities as described below:

- Determine and coordinate the research approaches and procedures, conduct experiments, and analyze and interpret research data generated under this award.
- Endeavor to meet or exceed the timeline stated in their application.
- Agree to participate as a voting member in a Consortium Steering Group composed of other awardees from this FOA, NIH staff, and an external expert group.
- Share technologies, reagents, and data with consortium members.
- Ensure that results are published in a timely manner.
- Coordinate with other consortium members the publication of research results, dissemination of reagent resources, and dissemination of data.
- Submit reagents and data for quality assessment and/or validation in any manner specified by the Steering Group or the NIH Project Scientist.
- Submit periodic progress reports.
- Accept and implement any other common guidelines and procedures approved by the Steering Group.
- Attend Steering Group meetings. It is likely that there will be one in-person meeting per year and that other meetings will be held by telephone or using internet assisted meeting software.
- Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NIH staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- A Program Officer will be assigned to this award. The Program Officer will be responsible for normal scientific and programmatic stewardship and guidance.
- Prior to award, the Program Officer will negotiate final milestones with the PD/PIs that will be incorporated in the Notice of Award.
- A group of NIH program staff from the ICs that make up the NIH BRAIN Initiative will form a Project Team for this award.
- The Project Team will include the Program Officer for these BRAIN Initiative awards.
- The Project Team will review annual progress reports and other documents from the awardees and will advise the Program Officer about their view of the progress being made by the awardee as well as about progress being made by others in the field.
- One or more extramural NIH program staff member will be assigned as Project Scientist for this award. The same person may serve as a Project Scientist for multiple BRAIN Initiative awards.
- The Project Scientist(s) will interact scientifically with the PDs/PIs of the cooperative agreement and other named key personnel as a partner in the research.
- The Program Officer and the Project Scientist(s) will be members of the Steering Group.

Areas of Joint Responsibility include:

- The purpose of the Steering Group is to transfer information among the awardees and between the awardees and the BRAIN Initiative more broadly in order to achieve the goals outlined in the BRAIN 2025 and BRAIN 2.0 reports.
- The Steering Group will be comprised of the PDs/PIs of the awards, the Project Scientist(s), the Program Officer, and a group of external experts.
- The PDs/PIs and Program Officer will invite a group of external experts to attend Steering Group meetings. The external expert group will be composed of three to five scientists who are not awardees of this FOA, represent the broad research community, and have relevant expertise. The group may be enlarged permanently or on an ad hoc basis as needed.
- A chair of the Steering Group, who is an awardee of this FOA, will be designated by the Steering Group on a rotating basis as needed.
- It is expected that most of the decisions on the activities of the Steering Group will be reached by consensus. If a

vote is needed, each awardee will have one vote and the Project Scientist(s) collectively will have one vote. When a vote is required, at least 60% of the votes will be required for approval.

- The Project Scientist may assist in research planning, may present experimental findings from an award from published sources or from relevant award projects, may participate in the design of experiments agreed to by the group, may participate in the analysis of results, may help ensure that duplication is avoided, and will interact scientifically with the Steering Group.
- The Program Officer and the external expert group members will attend Steering Group meetings as non-voting participants.
- In all cases, the role of NIH staff will be to assist and facilitate, but not to direct activities.

Dispute Resolution:

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel composed of three members will be convened. These three members include: a designee of the Steering Group chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 1.

3. Reporting

When multiple years are involved, awardees will be required to submit the Research Performance Progress Report (RPPR) (//grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161)
A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161).

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for awardees of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All awardees of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11170) on all subawards over $25,000. See the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11171) for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues)

Finding Help Online: http://grants.nih.gov/support/ (//grants.nih.gov/support/) (preferred method of contact)
Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

General Grants Information (Questions regarding application instructions, application processes, and NIH grant

resources)
Email: GrantsInfo@nih.gov (mailto:GrantsInfo@nih.gov) (preferred method of contact)
Telephone: 301-945-7573

Grants.gov Customer Support (Questions regarding Grants.gov registration and Workspace)
Contact Center Telephone: 800-518-4726
Email: support@grants.gov (mailto:support@grants.gov)

Scientific/Research Contact(s)

Douglas S. Kim, Ph.D.
National Institute of Mental Health (NIMH (http://www.nimh.nih.gov/))
Telephone: 301-827-6463
Email:douglas.kim@nih.gov (mailto:douglas.kim@nih.gov)

Peer Review Contact(s)

Nick Gaiano, Ph. D.
National Institute of Mental Health (NIMH (http://www.nimh.nih.gov/index.shtml))
Telephone: 301-827-3420
Email: nick.gaiano@nih.gov (mailto:nick.gaiano@nih.gov)

Financial/Grants Management Contact(s)

Tamara Kees
National Institute of Mental Health (NIMH (http://www.nimh.nih.gov/))
Telephone: 301-443-8811
Email: tkees@mail.nih.gov (mailto:tkees@mail.nih.gov)

Section VIII. Other Information

Recently issued trans-NIH policy notices (//grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Part 75.

Weekly TOC for this Announcement (/grants/guide/WeeklyIndex.cfm?09-18-20)
NIH Funding Opportunities and Notices (/grants/guide/index.html)

Note: For help accessing PDF, RTF, MS Word, Excel, PowerPoint, Audio or Video files, see Help Downloading Files (/grants/edocs.htm).