Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

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

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 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/))

Funding Opportunity Title

Engineering Next-Generation Human Nervous System Microphysiological Systems (R01 Clinical Trials Not Allowed)

Activity Code

R01 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r01&Search.x=0&Search.y=0&Search_Type=Activity) Research Project Grant

Announcement Type

Reissue of PAR-16-398 (https://grants.nih.gov/grants/guide/pa-files/PAR-16-398.html)

Related Notices

March 10, 2020 - Reminder: FORMS-F Grant Application Forms & Instructions Must be Used for Due Dates On or After May 25, 2020- New Grant Application Instructions Now Available. See Notice NOT-OD-20-077 (/grants/guide/notice-files/NOT-OD-20-077.html).

July 26, 2019- Changes to NIH Requirements Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-128 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-128.html)

August 23, 2019- Clarifying Competing Application Instructions and Notice of Publication of Frequently Asked Questions (FAQs) Regarding Proposed Human Fetal Tissue Research. See Notice NOT-OD-19-137 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-137.html)

Funding Opportunity Announcement (FOA) Number

PAR-20-055

Companion Funding Opportunity

PAR-20-082 (https://grants.nih.gov/grants/guide/pa-files/PAR-20-082.html), R21 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=r21&Search.x=0&Search.y=0&Search_Type=Activity) Exploratory/Developmental Grant

Number of Applications

See Section III. 3. Additional Information on Eligibility.

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

93.242, 93.853, 93.173, 93.867, 93.279, 93.866

Funding Opportunity Purpose

This Funding Opportunity Announcement (FOA) encourages research grant applications directed toward developing next-generation human cell-derived microphysiological systems (MPS) and related assays that replicate complex nervous system architectures and physiology with improved fidelity over current capabilities. Supported projects will be expected to enable future studies of complex nervous system development, function and aging in healthy and disease states.

This FOA is intended to provide support for the further development of projects where preliminary data supports the feasibility of the line of investigation. Applicants without preliminary data may wish to apply to the companion R21 FOA(PAR-20-082 (https://grants.nih.gov/grants/guide/pa-files/PAR-20-082.html)).

Key Dates

Posted Date

January 03, 2020

Open Date (Earliest Submission Date)

January 05, 2020

Letter of Intent Due Date(s)

Not Applicable

Application Due Date(s)

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11111) apply.

The first standard due date for this FOA is February 5, 2020.

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)

Standard AIDS dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11112) apply.

The first AIDS application due date for this FOA is May 7, 2020

All applications are due by 5:00 PM local time of applicant organization. All types of AIDS and AIDS-related 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.

Scientific Merit Review

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Advisory Council Review

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Earliest Start Date

Standard dates (//grants.nih.gov/grants/guide/url_redirect.htm?id=11113) apply

Expiration Date

January 08, 2023

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 (/grants/guide/ApplyButtonSplash.cfm?dest=https://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.

3. Use Grants.gov (/grants/guide/ApplyButtonSplash.cfm?dest=GrantsGov&oppNum=PAR-20-055) Workspace to prepare and submit your application and eRA Commons (/grants/guide/ApplyButtonSplash.cfm?dest=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

Human cell-based assays (e.g., using induced pluripotent stem cells) hold promise for identifying molecular, cellular and circuit defects, identifying novel targets and developing new therapeutics for patients with complex brain and other nervous system disorders. However, the methods to generate and analyze relevant cells and circuits must be made robust, replicable and predictive for normal nervous system function as well as pathophysiology. Cells grown in monolayer culture remain a mainstay for many assays, including high-throughput screening, but a drawback of these reductionist assays is that they cannot resolve many developmental and aging trajectories, anatomical features and circuit activity representative of *in vivo* nervous system function.

As an alternative, there are increased efforts to generate assays with more physiologically-relevant organization. For example, microphysiological systems are structured three-dimensional (3D) culture assays. One version is organoid or spheroid culture, which is a non-adherent suspension culture that relies on the self-organizing properties of stem cells in the absence of a substrate. Another type of microphysiological system is the tissue chip, which is a multicellular structure that represents minimal units of organ function and is embedded in a non-living microfluidic platform; this allows both efficient exposure to test compounds and efficient physiological readout. A third way to evaluate integrative cell function is by introducing human cells into another live species (known as chimeras). While these assays currently reproduce some important features of *in vivo* prenatal development, a major unresolved technical hurdle is the application of human cell-based assays to evaluation of circuit maturation, connectivity and aging, including its relationship to specific circuits involved in disease states. Addressing this complex technical challenge requires the collaboration of experts from diverse fields, including developmental and stem cell biology, circuit and systems level neuroscience, materials science, engineering and bioethics.

Research Objectives

The purpose of this FOA is to stimulate basic technology-focused research to develop next-generation human cell-derived microphysiological systems (MPS) and related assays with improved fidelity to complex human brain, spinal cord, and/or sensory end organ circuit physiology, which will ultimately facilitate analysis of higher order functional deficits relevant to complex nervous system diseases. This FOA is distinct from others that focus on optimization and scalability of assays for compound screening, although projects could, in principle, have utility for late stage evaluation of drug efficacy and toxicity. These models will have a multi-lineage, complex architecture representing the normal characteristics and functions of the relevant nervous system structure (e.g., sensory input systems, brain or spinal integrative systems, motor output systems) and will substantially exceed the state of the art in cellular maturation and integration, allowing reproducible measurement of human-relevant circuit-level activity under physiological conditions over a long period.

This FOA encourages innovative approaches that are first-in-class, those that propose to substantially exceed the state of the art in tissue organization and function. These can be high risk, high impact designs. Additionally, this FOA encourages approaches that aim to improve robustness and reproducibility of physiologically relevant circuit or supportive systems-level measures.

All applications should define the current state of technology as a benchmark against which the new assay system(s) will be developed and measured. Example approaches include, but are not limited to:

- Utilization of novel materials, substrates or synthesis technologies (e.g., 3D printing, bioreactors, microfluidic platforms) to promote anatomically and physiologically relevant tissue organization and/or maturation.
- Integration of defined cell types consistent with relevant nervous system anatomy (e.g., excitatory, inhibitory and modulatory neurons, astrocytes, oligodendrocytes, microglia, pericytes, endothelial cells) into functional units (assembloids) that may include multipartite synapses, vascularization-perfusion, blood-brain barrier, glymphatic system and/or cerebrospinal fluid flow.
- Novel strategies to faithfully reproduce relevant regional cellular organization (e.g., dorsoventral, rostrocaudal, laminar, columnar or nuclei structure), with both short- and long-range anatomical connectivity (e.g., local inhibitory-excitatory and/or modulatory connections, projections to distant lamina or nuclei).
- Novel strategies to promote maturation of metabolism, signaling, synaptic activity, and connectivity in the cell-based assay.
- Development of human cell-based assays with complex functional features potentially relevant to complex nervous system disorders and diseases (e.g., intrinsic and/or dynamical network properties of cell assemblies

such as neural oscillatory activity, activity-dependent plasticity).
- Inclusion of conditional or intersectional strategies that allow temporally and/or spatially cell-selective monitoring or manipulation of gene expression/function or of live cell activity and function.
- Inclusion of innovative approaches to distinguish or deconvolute heterogeneous cell phenotypes in these assays (e.g., multi-parameter single cell analysis), including those that are minimally perturbing.
- Evaluation of how data obtained from the proposed assay compares with human anatomical, histological or systems-level data, or data from other physiologically relevant paradigms, to facilitate assay validation. Investigators are encouraged to explore data and tools being developed under the NIH BRAIN Initiative (https://www.braininitiative.nih.gov/), BrainSpan (http://www.brainspan.org/), PsychENCODE (https://www.synapse.org/#!Synapse:syn4921369/wiki/235539) and the PsychENCODE Human Brain Development Atlas (http://development.psychencode.org/), Human Connectome Project (http://www.humanconnectomeproject.org/about/), AMP-AD (https://www.nia.nih.gov/research/amp-ad), or related efforts which if utilized could further the authentication of human brain cell-derived assays.

Examples of applications that do not fit the research objectives for this announcement include:

- A central focus on scaling assays or adapting for use in compound screening.
- Strategies directed toward cell therapy or regenerative medicine.
- Developing organoid or other microphysiological system assays from exclusively non-human tissues.
- Assays that aim to recapitulate 3-germ-layer gastrula-like structures (e.g., gastruloids).
- Assays based on pre-gastrulation human-nonhuman chimeric manipulation, or those potentially involving human contributions to the germline.
- Utilization of existing technologies that do not significantly advance the state of the art to address disease-relevant questions.

Interests of Specific Institutes/Centers

The scientific interests of participating Institutes and Centers (I/Cs) are summarized below. Applicants are encouraged to contact the Scientific/Research contact of the intended I/C to ensure that the aims of the proposed project are consistent with the I/C mission.

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

NEI is interested in research proposing to develop Next Generation MPS that more closely recapitulates the cornea, lens, retina, RPE, and/or elements of the central visual pathway. Projects suitable for this announcement include, but are not limited to 1) the development of natural and/or synthetic substrates/scaffolds that promote the growth and differentiation of physiologically relevant tissue; 2) the development of microfluidic devices (eye-on-chip) derived from stem cells that model physiological functions of the visual system; 3) the development of 3D tissue platforms that model microenvironments or niches of the visual system; 4) the development of MPS with complex functional features such as circuit structure, function, and connectivity as it relates to the visual system. Demonstration of how MPS systems are improvements over animal models or other 2D in vitro systems is also desired. While it is necessary to evaluate the basic biology of the 3D tissue, the primary focus should be on the improvement of the MPS technology and to more faithfully recapitulate development and not on basic disease mechanisms, transplantation procedures, personalized gene therapy approaches, and/or therapeutic and toxicity screens.

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

NIAAA supports the generation of microphysiological systems that recapitulate nervous system tissues and brain structures throughout the lifespan. NIAAA is seeking applications for new technologies that can assess the effects of alcohol on 1) cellular physiology, 2) neural circuit formation, maintenance and plasticity, and 3) interactions of multiple cell types (neurons, glia, vasculature, and immune cells) during critical developmental stages. The institute is interested in platforms to test underlying genetic and epigenetic consequences of short and long-term alcohol exposure and the actions of drugs and potential therapeutic compounds for prevention of alcohol use disorder or other consequences of alcohol exposure. The microphysiological systems may provide a platform for the generation and testing of predictive models of molecular, cellular and/or neural circuit responses to acute and chronic alcohol exposure (use) and reveal candidates for risk of and resiliency for fetal alcohol spectrum and alcohol use disorders.

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

The National Institute on Deafness and Other Communication Disorders (NIDCD) has a continued interest and effort to support new opportunities that could provide faster, more efficient biological platforms to assess physiological function, disease models, and transplantation potential in the NIDCD mission areas of hearing, balance, taste, smell, voice, speech and language. The institute is interested in a broad variety of approaches and technology/methodology development. Some examples, but not limited to, would be technical development of microarchitecture reagents including appropriate buffers, media, polymers and synthetics to generate improved 3D platforms and

microenvironments to facilitate cellular attachment, proliferation, in areas of differentiation or regeneration of taste buds, hearing/balance sensory epithelium, or vocal folds; experimental improvements of drug assessment studies, high throughput replication and comparative analyses of laryngeal, chemosensory and auditory/vestibular function (e.g., ototoxicity, noise or drug trauma, and age-related sensory loss); experimental improvements to implantable chip or scaffold-derived tissues and cells, such as for vocal fold replacement or inner ear transplantation studies; use of improved stem cell technology for the derivation of multi-cellular chip organoids replicating normal and/or disordered tissue physiology; use of gene and protein manipulation technologies to enhance the imaging and/or assessment of the created chip microsystem (e.g., cellular identities, function, and interactions, neuronal innervation, or molecule activity).

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

NIMH is interested in all example approaches from the Research Objectives that facilitate Next-Generation MPS representing the cellular and circuit substrates of cognitive, social and affective domains of brain function. Examples from the Research Objectives can include, but are not limited to, generating correctly-specified and anatomically organized brain regions that subserve these domains of function, integration of vascularization-perfusion, blood-brain barrier or other systems-level support features into these structures; optimizing local excitatory-inhibitory-modulatory feedback circuits representing cortex or subcortical regions, longer distance cortico-cortical, cortico-striatal, thalamo-cortical and cortico-limbic connections, the emergent systems-level features (e.g., oscillations) that arise from such circuit activity and the effect of changing input on circuit behavior (e.g., transfer functions). Applications should be primarily focused on MPS technology development and basic biology, although the domains of function should be relevant to those potentially dysregulated in mental illnesses, including autism spectrum disorders, mood and anxiety disorders (e.g., bipolar disorder), attention deficit and obsessive-compulsive disorders, and/or schizophrenia. While applications can include independent variables for validating the utility of the MPS for studying a relevant cellular/synaptic/circuit activity or domain of function (e.g., comparison of isogenic lines with and without engineered gene variants), the central focus should be on developing or improving MPS technology and not studying disease biology per se. Applications focusing on developing or utilizing cell-based assays to study mechanisms of mental illnesses can respond to PAR-17-309 (https://grants.nih.gov/grants/guide/pa-files/PAR-17-309.html) and PAR-17-310 (https://grants.nih.gov/grants/guide/pa-files/PAR-17-310.html). Applications focusing on scaling assays or adapting for use in therapeutics development can respond to PAR-18-505 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-505.html).

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

NINDS is interested in microphysiological system development that will facilitate Next Generation MPS representing cellular and circuit substrates relevant to complex central nervous system function where the MPS optimizes cellular architecture and performance readouts from excitatory-inhibitory feedback circuits that control human movement, cognition, and behavior and incorporate vascularization and/or blood brain barrier function into their design. Applications should be primarily focused on MPS technology development and basic biology, although the circuits and brain regions of interest should be relevant to developmental or adult onset neurological disorders, such as, but not limited to stroke, epilepsy, neuromuscular disease, movement disorders, behavioral and cognitive disorders associated with neurodegeneration, CNS related developmental disorders and lysosomal storage disorders. For advances in organoid development and its relevant basic biology, NINDS is interested in the cellular architecture and circuits relevant to CNS development. While applications can include independent variables for validating the utility of the next generation MPS for modeling a complex cellular and synaptic circuit entity, the emphasis should be on developing or improving MPS technology. Applications focused on developing or using cell-based assays for translational research should respond to PAR-18-762 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-762.html).

National Institute on Aging (NIA)

The National Institute on Aging (NIA) is interested in the development of next-generation microphysiological systems that more closely recapitulate the aging brain and diseases of brain aging. While applications should be primarily focused on microphysiological system technology development, the circuits and brain regions of interest should be relevant to either those declining during brain aging or those resilient to the effects of brain aging. NIA is interested in all examples of approaches listed under the Research Objectives that would promote understanding of the aging brain and diseases of brain aging, particularly Alzheimer's disease. Examples of projects that would be appropriate for this announcement include, but are not limited to: 1) using new technologies to develop three-dimensional human cell-based assays that better recapitulate brain aging, including the integration of defined brain cell types into functional units and mechanisms to study cell-cell interactions during aging and Alzheimer's disease; 2) promoting maturation of metabolism, signaling, synaptic activity, and connectivity in the human cell-based assay to recapitulate the aging brain; and 3) developing human cell-based assays with complex functional features relevant to nervous system disorders of aging, including cell-selective manipulation of gene expression or cell function to model normal and disordered brain aging, such as occurs in Alzheimer's disease. Although applications can include disease-relevant perturbations for

model validation and testing assay utility, the focus should be on developing or improving microphysiological system technology. Applications proposing to use existing cell-based assays to study aging-related and Alzheimer's disease mechanisms should respond to PAR-18-516 (https://grants.nih.gov/grants/guide/pa-files/PAR-18-516.html) or PAR-19-070 (https://grants.nih.gov/grants/guide/pa-files/par-19-070.html).

National Institute of Drug Abuse (NIDA)

NIDA supports research to understand, prevent, and treat substance use disorders and mitigate their impact to human health. For the purposes of this FOA, NIDA encourages applications that explore MPS as a new and powerful technology to further our understanding of the mechanisms of substances of abuse. The abused substances of interest include opioids, cannabinoids, methamphetamine, nicotine, amphetamine, cocaine, barbiturates, and hallucinogens. NIDA is especially interested in applications that can reproducibly elucidate and validate cell and neural circuit mechanisms involved in mediating the addictive properties of abused substances; to develop assays to identify small molecule probes that impact drug abuse pathways, and to evaluate and validate effects and toxicities of potential future therapeutic agents. The ultimate goals of these research are to understand the brain mechanisms underlie the tolerance, sensitization, and dependence of these substances and to inform future diagnose, prevention and treatment of substance use disorders.

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

Section II. Award Information

Funding Instrument

Grant: A support mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity.

Application Types Allowed

New
Renewal
Resubmission
Revision
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

The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

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

Award Project Period

The scope of the proposed project should determine the project period. The maximum project period is 5 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)

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)

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.

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.
Note that the application should include expert collaborators appropriate for the particular needs of the assay being optimized, e.g., developmental or aging neurobiology, stem cell biology, circuit and systems level neuroscience, materials science, engineering and/or bioethics.

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: The primary focus of applications responding to this announcement is developing technologies involving human cell-based engineering of microphysiological systems or related assays, directed as described in the Research Objectives toward faithfully representing salient features of *in vivo* brain, spinal, and/or sensory end organ circuit physiology, that may include systems-level features that support circuit function (e.g., myelination, vascularization-perfusion, blood-brain barrier, glymphatic system, cerebrospinal fluid flow). As a result, applications should focus on technical improvements to and capabilities of these cell-based assays relative to current state of the art. While genetic or environmental perturbations relevant to disease states can be incorporated into the research design as a means of validating the specific utility of the assay, these are neither required nor expected.

The research strategy should:

- Exploit novel tools or technologies, including those from other disciplines, to improve the sophistication, robustness or reproducibility of nervous system assay. Alternatively, it should bring a unique conceptualization of analytic approaches being applied to the assay.
- Address an intransigent barrier to (or propose to substantially exceed the state of the art in) cellular maturation and integration within the assay. Alternatively, the plan should aim to improve robustness and reproducibility of physiologically relevant circuit or supportive systems-level measures.
- Address the goal of improving assay's fidelity to salient features of *in vivo* neural circuit structure and function and/or systems-level features that support circuit function.
- Define the current state of the human cell-based assay technology as a benchmark against which the new assay(s) will be developed and measured.

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:

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. Additionally, applicants should describe how protocols for generating and validating the assay, with sufficient detail to facilitate replication, will be disseminated to the research community. Applicants are expected to register resources supported by this FOA in the Neuroscience Information Framework (https://scicrunch.org/ (https://scicrunch.org/)) and use Research Resource Identifiers (RRID) assigned by (http://scicrunch.com/resources (http://scicrunch.com/resources)) in any publication supported by this FOA.

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-definedclinical 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, NIH. Applications that are incomplete or non-compliant will not be reviewed.

Requests of $500,000 or more for direct costs in any year

Applicants requesting $500,000 or more in direct costs in any year (excluding consortium F&A) must contact a Scientific/ Research Contact at least 6 weeks before submitting the application and follow the Policy on the Acceptance for Review of Unsolicited Applications that Request $500,000 or More in Direct Costs as described in the SF424 (R&R) Application Guide.

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:

As this FOA strongly encourages innovative approaches to major methodological challenges, the level of risk is generally expected to be higher than for conventional R01 applications. The primary focus of applications responding to this announcement is developing technologies involving human cell-based engineering of microphysiological systems or related assays, directed as described in the Research Objectives toward faithfully representing salient features of *in vivo* brain, spinal, and/or sensory end organ circuit physiology, that may include systems-level features that support circuit function (e.g., myelination, vascularization-perfusion, blood-brain barrier, glymphatic system, cerebrospinal fluid flow). As a result, reviewers should primarily assess merit based on the technical improvements to and capabilities of these cell-based assays relative to current state of the art. While genetic or environmental perturbations relevant to disease states can be incorporated into the research design as a means of validating the specific utility of assays, these are neither required nor expected.

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?

Does the research strategy define the current state of technology as a benchmark against which the new assay(s) will be developed and measured?

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 well does the project engage expert collaborators appropriate for the particular needs of the assay being optimized, e.g., developmental neurobiology, stem cell biology, circuit and systems level neuroscience, materials science, engineering and/or ethics?

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?

Does the project exploit novel tools or technologies, including those from other disciplines, to improve the sophistication, robustness or reproducibility of the central nervous system assay? Alternatively, does it bring a unique conceptualization of analytic approaches being applied to the assay?

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 project address the goal of improving assay fidelity to salient features of *in vivo* brain, spinal, peripheral nervous system and/or sensory end organ circuit physiology and/or systems-level features that support circuit function? Does the project address an intransigent barrier to, or propose to substantially exceed the state of the art in, cellular maturation and integration within the assay? Alternatively, does it aim to improve robustness and reproducibility of physiologically-relevant circuit or supportive systems-level measures?

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?

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.

Protections for Human Subjects

For research that involves human subjects but does not involve one of thecategories 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

For Renewals, the committee will consider the progress made in the last funding period.

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).

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 the Center for Scientific Review, 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:

- 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.
- Will receive a written critique.

Applications will be assigned on the basis of the Interests of Specific Institutes/Centers stated in this FOA as well as established PHS referral guidelines to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications . 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.

Institutional Review Board or Independent Ethics Committee Approval: Grantee institutions must ensure that protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the awardee must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

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 law. This means that recipients of HHS funds must ensure equal access to their programs without regard to a person's race, color, national origin, disability, age and, in some circumstances, sex and religion. This includes ensuring your programs are accessible to persons with limited English proficiency. 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.

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.

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. HHS provides general 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/index.html (https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/index.html). The HHS Office for Civil Rights also provides guidance on complying with civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-individuals/section-1557/index.html (https://www.hhs.gov/civil-rights/for-individuals/section-1557/index.html)https://www.hhs.gov/civil-rights/for-providers/laws-regulations-guidance/index.html (https://www.hhs.gov/civil-rights/for-providers/laws-regulations-guidance/index.html). Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see https://www.hhs.gov/civil-rights/for-individuals/disability/index.html (https://www.hhs.gov/civil-rights/for-individuals/disability/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. Also note it is an HHS Departmental goal to ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations. 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 http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53 (http://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53).

Cooperative Agreement Terms and Conditions of Award

Not Applicable

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 agreementsare 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 threatensubmission 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)

David M. Panchision, Ph.D.
National Institute of Mental Health (NIMH (https://www.nimh.nih.gov/))
Telephone: 301-443-5288
Email: panchisiond@mail.nih.gov (mailto:panchisiond@mail.nih.gov)

Lisa Neuhold, Ph.D.
National Eye Institute (NEI (https://nei.nih.gov/))
Telephone:301-451-2020
Email: lneuhold@mail.nih.gov

Nancy L. Freeman, Ph.D.
National Institute on Deafness and Other Communication Disorders (NIDCD (https://www.nidcd.nih.gov/))
Telephone: 301-402-3458
Email: FreemanN@mail.NIH.gov

Da-Yu Wu, Ph.D.
National Institute on Drug Abuse (NIDA (https://www.nida.nih.gov/))
Telephone: 301-435-4649
Email: wudy@nida.nih.gov

Tim Lavaute, Ph.D.
National Institute of Neurological Disorders and Stroke (NINDS (https://www.ninds.nih.gov/))
Telephone: 301-496-1447
Email: lavautetm@ninds.nih.gov (mailto:lavautetm@ninds.nih.gov)

Amanda DiBattista, Ph.D.
National Institute on Aging (NIA (https://www.nia.nih.gov/))
Telephone: 301-496-9350
Email: amanda.dibattista@nih.gov (mailto:amanda.dibattista@nih.gov)

Peer Review Contact(s)

Examine your eRA Commons account for review assignment and contact information (information appears two weeks after the submission due date).

Financial/Grants Management Contact(s)

Terri Jarosik
National Institute of Mental Health (NIMH (https://www.nimh.nih.gov/))
Telephone: 301-443-3858
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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.

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