

The University of Rochester Intellectual Developmental Disability Research Center (UR IDDRC) Research Project Request for Proposals 2023

The UR IDDRC provides a coordinating hub and scientific infrastructure to support IDD research and works with the research community to respond to emerging IDD research needs through a combination of core services and research projects.

As a precursor to recompeting for the next funding period for the UR IDDRC, applications are being solicited for the new principal research project.

The selected project should pertain to one or more of the seven focus areas listed below. The current research project focuses on Neuronal Ceroid Lipofuscinoses (NCL) or Batten Disease. The application process is open to all faculty members across both the Medical School and the Undergraduate Campus.

Research Projects

Applications must include at least one specific Research Project that has not been previously funded and addresses one or more of the IDD focus themes identified as an area of research need. These are recognized as potentially exploratory, discovery-based, and/or high-risk projects, with the goal of yielding interpretable results that will either prove or disprove the proposed hypothesis.

Each Research Project must utilize at least two cores of the IDDRC, which may include the Administrative Core. A description of the cores can be found [here](#). The project can address a broad array of intellectual disorders, including new, recently characterized, or under-researched areas such as comorbid mental health conditions in IDD. The focus areas are as follows, in no order of priority:

1. Comprehensive -omics Approaches

Comprehensive -omics approaches (e.g., genomic, transcriptomic, epigenomic, proteomic, metabolomic) that will markedly increase our understanding of IDD conditions to improve diagnosis, management, and potentially, treatment. Examples include, but are not limited to:

- Whole exome or whole genome sequencing of a well-defined cohort of subjects with IDD to identify genetic or genomic variants likely to cause the phenotype;

- Methylation, chromatin immunoprecipitation (ChIP), histone modification, or other epigenetic studies on individuals with a shared or related IDD diagnosis but variable manifestations (such as range of cognitive or behavioral function) to identify potential epigenetic contributors;
- Tandem mass spectrometry on biological samples such as saliva, blood or urine from a group of individuals with metabolic or other disorders associated with intellectual disability that might define distinctive biomarkers or metabolic signatures that would allow monitoring of outcomes or response to treatment;
- Single-cell transcriptomics on samples of differentiated human induced pluripotent stem cells (iPSC), brain organoids, or central nervous system tissue.

2. Development of Biomarkers or Assessment Measures in More than one IDD Condition

Development of a biomarker, assessment measure, or clinical intervention for more than one IDD condition or a group of related IDD conditions that share a common feature or metabolic or molecular pathway. Examples include, but are not limited to:

- Use of a human iPSC or brain organoid model to develop a biomarker or measure for a group of related conditions that demonstrates sensitivity to biologically-relevant perturbations to the system;
- Development of an assessment paradigm for an allelic series in an animal model for an IDD condition that exhibits a range of phenotypes;
- Development of an electrophysiological paradigm for two or more IDD conditions that share a common metabolic or molecular pathway;
- Creation of a clinical trial for a plausible target in two or more IDD conditions that reflects a shared etiology or molecular pathway.

3. Outcome Measures or Biomarkers for Interventions or Treatments

Development of preclinical or clinical outcome measures or biomarkers for the cognitive and/or behavioral phenotypes of IDD that have the potential to demonstrate a change in response to intervention or treatment. Examples include, but are not limited to:

- Development of a measure or biomarker for an animal model (e.g., mouse, rat, nonhuman primate) of an IDD disorder that reliably detects changes in cognitive function or behavioral response to a drug treatment;

- Development of a measure of cognitive or behavioral function (e.g., depression, psychotic ideation) in individuals with an IDD condition that is sensitive to an intervention;
- Development of a measure or biomarker that can be applied to more than one IDD conditions that share a common feature or metabolic or molecular pathway;
- Demonstration of changes in an existing measure or biomarker in individuals with an IDD condition in response to therapy.

4. Multi-modal Treatment Approaches

Development of bi- or multi-modal treatment approaches for a single IDD condition or a group of IDD conditions or spectrum disorders to demonstrate combinatorial effects to ameliorate a cognitive or behavioral symptom(s) of the condition(s). The interventions may or may not be disease-specific, and the potential to broaden to multiple IDD disorders is encouraged. A medication can be repurposed from its original indication, but any clinical trial must adhere to NIH Clinical Trial guidelines (<https://grants.nih.gov/policy/clinical-trials.htm>), with defined milestones and go/no-go decision points. Examples include, but are not limited to:

- Use of a drug and a training paradigm in an animal model of an IDD to demonstrate improvement in a cognitive or behavioral measure;
- Use of a medication and behavioral treatment in combination for individuals with an IDD condition to demonstrate improved or synergistic efficacy;
- Use of one well-established intervention plus 1-2 medications to improve general symptoms of a mood disorder in individuals with different IDD conditions who share that mood disorder.

5. Preventing and Mitigating the Impact of Exposures that Can Cause IDD

Exposures of many types – medications, substances of abuse, infectious agents, environmental exposures, toxins – increase the risk of developing IDD. Therefore, therapeutic agents that can prevent or mitigate the risk of IDD following such exposures have the potential for broad clinical and public health impact. Exposures of interest may occur in the pre-conceptual, prenatal, postnatal or childhood period, and may involve the broader family or community. Examples include, but are not limited to:

- A project that develops a therapy or treatment for an animal model subjected to an exposure associated with an IDD-related cognitive or behavioral phenotype;

- A project that proposes an intervention to reduce the risk of developing an IDD due to preterm birth;
- A project looking at factors that may mitigate the impact of a prenatal exposure, such as alcohol, opioid or other medication, other substance of abuse, cytomegalovirus, Zika virus, etc. on a child's risk of IDD;
- Studies of a therapeutic intervention that may mitigate the impact of an environmental toxin (such as lead) that can lead to IDD.

6. Interventions and Management of Co-morbid Mental Health Conditions

Individuals with IDD experience behavioral symptoms and mental health conditions at considerably higher rates than the general population, including behavioral symptoms such as depression, aggression, or suicidal ideation or mental health conditions such as attention deficit hyperactivity disorder (ADHD), bipolar disorder, or psychotic disorders. These can be extremely challenging to manage in individuals with IDD due to the language, cognitive, and sensory impairments that often impede traditional strategies for evaluation and treatment. Many children and adults with IDD are diagnosed with behavioral or mental health conditions in the absence of assessment tools appropriate to IDD populations, and psychotropic medications are often administered to individuals with IDD, without an adequate understanding of their potential interactions and associated safety risks. Studies are encouraged that include individuals with IDD who are on multiple psychotropic medications in the study design. Priority will be given to novel interventions that go beyond traditional behavioral management of symptoms. Examples include, but are not limited to:

- Development of new tools or adaptation of existing tools that can be used in the management of behavioral symptoms or mental health conditions that identify and account for level of cognitive functioning in individuals with IDD;
- Studies of the safety and efficacy of commonly-used psychotropic medications in treating specific behavioral symptoms or mental health conditions in individuals with IDD;
- Studies to delineate variability in pharmacokinetics and pharmacodynamics of psychotropic medications in individuals with IDD;
- Studies that use pharmacogenomic strategies to select the safest and most efficacious psychotropic medications for use in individuals with IDD, which can then be clinically validated.

7. Innovative Technologies to Improve Assessments, Interventions, and Outcomes for Those with IDD

There has been an explosion of new technologies aimed at assessing and improving health, including wearable devices, communication aids, robotics and e-textiles. There have also been enormous advances in technologies that were not created for health-related purposes, but that have potential applicability to health assessments and interventions, including mobile device applications (“apps”) and social media platforms. Most of these technologies were originally developed for use in adults, particularly those with typical development, so there is a need for valid and reliable technological tools and adaptive devices for those with IDD. Examples include, but are not limited to:

- Development of validated eye tracking technologies to identify and monitor social gaze preferences in children with autism receiving interventions targeting their social interactions;
- Use of actimetry sensors to identify and monitor sleep behaviors or activity levels to measure biological indicators and response to interventions;
- Development of devices that monitor physiologic parameters (such as heart rate monitors, multi-channel EEGs, or instruments that measure metabolite levels) for digital phenotyping or to serve as a proxy measure for other outcomes of interest, such as anxiety;
- Validation of apps, devices, and social media platforms to aid communication in individuals with IDD and language impairments;
- Application of mobile technologies to deliver video- or computer-based interventions to individuals unable to travel to academic centers to participate in research or clinical programs.

Application Process

Applicants may request up to \$75,000 to cover a project development phase of 18 months. Principal investigators must be faculty members (with or without tenure) within the University of Rochester community and will need to be a member of the IDDRC. A short membership application is available on the IDDRC website.

Applications will be submitted online with a short informational online page and a **single pdf application file**.

A) The online component includes:

- Title, submitting PI information, co-PI(s) information
- Technical abstract (300 words): This will be used to assign reviewers, and should include overall goal, specific aims, and techniques used.
- Lay abstract (300 words): this will be used to convey information to the public, and should be easily understandable to the non-scientist. This will be public, and so should not contain proprietary information.

B) The written applications should be modeled after a short NIH research proposal (i.e. R21) and should include:

- **Cover letter** with title, investigators, and description that indicates how the proposal addresses one or more of the IDD focus themes identified as an area of research need and can be leveraged into the IDDC research project [one-page limit].
- **Research description** (limited to *7 pages*) including Specific Aims, Background and Significance, Preliminary Studies, Research Design and Methods.
- **Supporting materials** (Human Subjects, Vertebrate Animals, and Literature Cited) can follow on additional pages.
- **Budget** (detailed, *not* modular) with justification (faculty salary support is specifically excluded)
- **Bio-sketches** of all Co-Investigators and key personnel.
- **Other Support**
- **Resources and Environment**
- **18-month project timeline** Provide a detailed timeline with outcomes and deliverables. Describe the project procedures in sufficient detail to assure reviewers that project completion is feasible within 18 months with currently available environment and personnel. Use of IDDC core resources should also be described.

Review criteria will include but are not limited to:

- Likelihood of being a successful IDDC principal project
- The *significance* and *innovation* of the proposed project.
- The *relevance* of the project to the strategic plan of the IDDC.
- Where relevant, the *interdisciplinary/collaborative* character of the project (across faculty, laboratories and IDDC cores).

Application Submission Deadlines

The application deadline is **5:00 pm** on Thursday January 26th 2023. Applications will be submitted online at <https://redcap.link/iddrcproposal2023>. Open Date (Earliest Submission Date) Monday January 2nd 2023.

Address all questions about applications to: sherry_mentor@urmc.rochester.edu

An internal review committee will work with a panel of independent external reviewers to determine the most competitive projects for support. The Program is administered through the Del Monte Institute for Neuroscience.

Funding is scheduled to begin April 3rd 2023. Funds are available for a maximum of 18 months and there will be no option for no cost extensions.

Other details

Recipients should acknowledge the UR IDDRC grant number *P50 HD103536* as a funding source in any publications resulting in IDDRC supported research.

Recipients of the IDDRC research pilot project awards, acknowledge that regular reporting is a requirement of the award. The PI's of the selected project will be required to present project updates at the quarterly IDD Executive committee, beginning after the first 6 months of funding through this mechanism.