

To: Faculty of the Children's Hospital of Philadelphia/University of Pennsylvania
(Please distribute to eligible faculty)

From: Michael B. Robinson, Ph.D. & Robert Schultz Ph.D. (Directors); Marc Yudkoff M.D,
(Co-Director), Intellectual and Developmental Disabilities Research Center

Date: January 28, 2019

Re: Internal CHOP/Penn Request for Applications for Support for Research Project
Related to Intellectual and Developmental Disabilities
Applications Due – March 11, 2019

Summary

The Intellectual and Developmental Disabilities Research Center (IDDRC) at CHOP/Penn invites applications for an independent research project that has not previously been funded that will advance the diagnosis, prevention and/or treatment of one or more intellectual and developmental disabilities (IDD). This project will be an essential component for the competitive renewal of the IDDRC in late 2019. We are offering a total award of \$100,000 for the project (\$25,000 in FY19 and \$75,000 in FY20) with a start date of April 1, 2019. Upon renewal of the IDDRC (2020), we anticipate that funding for the project will increase to ~\$200,000 - \$250,000/year. Funding is being offered now so that a competitive project can be formulated in advance for inclusion in the renewal of the IDDRC. This project can address a broad array of IDD, including new, recently characterized, or under-research areas such as comorbid mental health conditions in IDD. The focus areas are as follows, in no order of priority:

- *Comprehensive –omics Approaches*
- *Development of Biomarkers or Assessment Measures in More than one IDD Condition*
- *Outcome Measures or Biomarkers for Interventions or Treatments*
- *Multi-modal Treatment Approaches*
- *Preventing and Mitigating the Impact of Exposures that Can Cause IDD*
- *Interventions and Management of Co-morbid Mental Health Conditions*
- *Innovative Technologies to Improve Assessments, Interventions, and Outcomes for Those with IDD*

Background

The IDDRC at CHOP/Penn is one of 14 Centers in the U.S. (for more information about the network see <http://www.aucd.org/template/page.cfm?id=530>). The IDDRC is intended to facilitate multidisciplinary research and translational research on IDD. We have received continuous funding since 1990 to support both core research facilities and new investigators. Our funded cores include: Administrative, Clinical Translational, Biostatistics and Bioinformatics, Analytical Neurochemistry, Neuroimaging and Neurocircuitry, and Preclinical Models. For more information, please visit the IDDRC website at <https://iddrc.research.chop.edu/index.php>.

The precise configuration of cores for the 2020 renewal application is not yet finalized, but we anticipate supporting similar services to those currently supported. The application must include at least 3 core resources (and no more than 6), including an Administrative Core and a Clinical Translational Core. We anticipate providing members of the IDDRC with research support in a variety of fields, including genetics, behavioral phenotyping, neuroimaging, electrophysiology, biostatistics, bioinformatics, biomarkers, bioenergetics, stem cells and preclinical animal models. The research project selected for this RFA should utilize one or more of these services.

Application for Support from Internal Sources

Applications are due by **Monday, March 11, 2019**. A single PDF should be sent to the Center Administrator, Kristen Pidgeon (pidgeonk@email.chop.edu). The IDDRC Leadership will review

all applications. Applicant(s) selected for support will be notified by the end March with an anticipated start date of April 1, 2019.

The project must address one or more of the following seven focus areas (*in no order of priority*): Please note some areas have full description because they were included in the NICHD Funding Opportunity Announcement in 2014 (<http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-14-012.html>). Other areas (see asterisk) were announced in a more abbreviated announcement from NICHD in December 2018 (<https://grants.nih.gov/grants/guide/notice-files/NOT-HD-18-030.html>).

1. **Comprehensive –omic Approaches** (genomic, epigenomic, metabolomic) that will markedly increase our understanding of IDD conditions with no known etiology or IDD conditions with complex etiologies to improve diagnosis, 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 or other studies on individuals with a shared IDD diagnosis but variable manifestations (such as range of cognitive function) to identify potential epigenetic contributors;
 - tandem mass spectrometry on biological samples (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 or outcomes or response to treatment.
2. **Development of Biomarkers or Assessment Measures in More than one IDD condition***
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 for an animal model (e.g., mouse, rat, nonhuman primate) of an IDD disorder that reliably detects changes in behavior response to a drug treatment;
 - development of a measure of cognitive function in individuals with an IDD condition that is sensitive to an intervention;
 - demonstration of changes in an existing behavioral measure 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. 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 behavioral measure;
 - use of a medication and behavioral treatment in combination for individuals with an IDD condition to demonstrate improved 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***
6. **Interventions and Management of Co-morbid Mental Health Conditions***

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

- B. The project must utilize at least two cores of the IDDRC (including the Administrative Core and/or Clinical Translational Core).

Application Information (in the following order):

1. **Title page:** title of the project, name and academic title of the principal investigator(s)/key personnel, and contact information. **Please confirm that the proposed research project has not been previously funded or submitted for funding.**
2. **Project Summary** and **Project Narrative** per NIH guidelines.
3. **NIH Biosketch** for each PI and any other key personnel.
4. **Budget** for one year for up to \$100,000 (April 1, 2019 through June 30, 2020).
5. **Research Plan**, including **specific aims**, **significance/innovation**, **experimental approach** and **bibliography and references cited** (Maximum of 6 pages including specific aims and excluding bibliography and references cited).

Review Criteria

Applications must be directly relevant to one of the NICHD-designated focus areas indicated above with preference given to applications of manifest translational import. The project must utilize the core services provided by the Center (please see the IDDRC website for information about core services: <https://iddrc.research.chop.edu/cores.php>). The PI should have demonstrable credentials with regard to scientific accomplishment and organizational ability. **The research project must not have been previously funded, and awardees must agree not to seek support for the project independent of the IDDRC while the Center is competing for renewal.** The Leadership will score applications based upon significance, relevance to the intellectual disabilities, translational import, innovation, research plan and qualifications of the PI.

Funding

We will provide \$100,000 from The Children's Hospital Research Institute. \$25,000 will be available in FY19 (as early as April 1st), and \$75,000 will be available in FY20 (starting July 1st). We anticipate that this award will increase to \$200,000 - \$250,000 (direct costs) upon renewal of the IDDRC in 2020.

Expectations

The goal of this solicitation is to enable the acquisition of preliminary data that will form the basis of an independent research project that will be included in the 2020 competitive renewal application of the IDDRC at CHOP/Penn. Thus, the awardee must agree not to seek support for the proposal independent of the IDDRC. The PI should be prepared to expand the proposal into a full-length proposal which accommodates all requirements specified in the FOA that will be issued this year (hopefully summer 2019). The Steering Committee of the IDDRC will meet with the PI in order to obtain regular updates with regard to research progress. The PI should prepare a draft of the final application by the end of September 2019, or 2-3 months before the due date of the IDDRC application. We will solicit external reviews of all of the elements of the IDDRC so that we can craft the best application possible.

Please feel free to contact us with questions: Michael B. Robinson (robinson@pennterapeutics.com); Robert Schultz (schultzrt@email.chop.edu); Marc Yudkoff (YUDKOFF@email.chop.edu); or Kristen Pidgeon (pidgeonk@email.chop.edu).