



Funding Opportunity Title: HIRN New Investigator Pilot Award (2018)

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Key Dates

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| Posted Date: | November 15, 2017 |
| Letter of Intent Due Date: | December 15, 2017 |
| Application Due Date: | January 15, 2018 |
| Scientific Review: | February/March 2018 |
| Start Date: | June 1, 2018 |
| Expiration Date: | January 16, 2018 |

Section I. Funding Opportunity Purpose

The Human Islet Research Network (HIRN) announces a program to support a small number of new investigators of exceptional creativity who propose to apply bold and highly innovative new research approaches to biological problems under current investigation in HIRN. The HIRN New Investigator Pilot Award is designed to provide support for early career investigators who may need funding to explore feasibility of a new concept in support of an eventual R01 application. The research proposed must be relevant to the goals of HIRN consortia.

Section II. Funding Opportunity Description

II-1. Background

Type 1 diabetes is a disease caused by the autoimmune destruction of the insulin-secreting beta cells of the pancreas. Type 1 diabetes requires daily insulin administration, but episodes of hyperglycemia and hypoglycemia are common, and as a result patients with type 1 diabetes often suffer serious diabetes-associated complications. The incidence of type 1 diabetes appears to be increasing worldwide. Although the disease may occur at any age, the onset of type 1 diabetes peaks prior to twenty years of age. In some populations, about one percent of all newborns will develop type 1 diabetes during their lifetime.

Starting in 2014, NIDDK established a new team science program, the Human Islet Research Network (HIRN; www.hirnetwork.org), to support collaborative research related to the loss of functional beta cell mass in type 1 diabetes (T1D). HIRN is jointly supported by NIDDK and the type 1 diabetes special funding program, and its overall mission is to better understand how human beta cells are lost in T1D, and to find innovative strategies to protect or replace functional beta cell mass in diabetic patients. The HIRN program is configured as a modular network of research consortia, each defined by a

specific set of research priorities. The network structure helps to facilitate interactions between small communities of investigators organized around common biological and/or technological challenges, with the overall goal of developing innovative strategies for the treatment, prevention and monitoring of T1D.

All HIRN research consortia are focused on human disease biology, the use of human cells and tissues, and the development of reagents, tools and disease-modeling platforms that can help further our understanding of the human disease process, or that will lead to innovative treatment strategies for patients with severely depleted beta cell mass.

II-2. Objectives and Scope

Research supported by these awards would be expected to address significant barriers in T1D research. Opportunities to be pursued should fit conceptually within the framework of goals of an existing consortium within the Human Islet Research Network.

Current HIRN consortia include:

- The Consortium on Beta Cell Death and Survival ([HIRN-CBDS](#)) is using human tissues to discover highly specific biomarkers of beta cell injury in asymptomatic T1D and developing strategies to stop beta cell destruction early in the disease process.
- The Consortium on Human Islet Biomimetics ([HIRN-CHIB](#)) is combining advances in beta cell and stem cell biology with tissue engineering technologies to develop microdevices that support functional human islets.
- The Consortium on Modeling Autoimmune Interactions ([HIRN-CMAI](#)) is developing innovative approaches to model basic aspects of human T1D immunobiology using novel in vivo and in vitro platforms.
- The Consortium on Targeting and Regeneration ([HIRN-CTAR](#)) is focused on developing methods to increase or maintain functional beta cell mass in T1D through targeted manipulation of islet plasticity, or through engineering protection of islet beta cells from immune-mediated destruction.
- The Human Pancreas Analysis Program ([HIRN-HPAP](#)) is performing deep phenotyping of human endocrine pancreas and its interaction with the immune system to better understand the cellular and molecular events that precede and lead to beta cell loss in type 1 diabetes.

Examples of opportunities that could be pursued to address current roadblocks to progress in T1D research include, but are not limited to:

- Identifying novel biomarkers of type 1 diabetes to monitor disease progression and response to therapy;
- Developing humanized model systems that will allow for exploration of the pathogenesis and potential therapies for human type 1 diabetes;
- Developing new miniaturized assays for metabolism that could be adapted for use in biomimetic systems;
- Developing a biomimetic system that will allow for the exploration of immune-beta cell interactions;
- Identifying components of the beta cell and its environment required for maintenance and function and/or instrumental in its pathogenic destruction; or to restore beta cell function or mass through regeneration;
- Developing methods for the measurement of beta cell mass or function that may be used as endpoints in studies of preventing or ameliorating type 1 diabetes;
- Developing cell based therapies to enhance or restore glycemic control.

Section III. Award Information

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| Funding Instrument: | Subcontract, awarded from the HIRN-Coordinating Center (HIRN-CC) (City of Hope) |
| Application Types Allowed: | New |
| Funds Available & Anticipated Number of Awards: | HIRN intends to commit approximately \$1 million in FY2018 to fund up to 4 awards |
| Award Budget: | Awards are limited to \$150,000 Direct Costs over the lifetime of the award (up to 2 years), plus applicable F&A costs to be determined at the time of award. |
| Project Period: | The maximum project period is 2 years. |

Section IV. Eligibility Information

IV-1. 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 encouraged to apply for 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)

Foreign Institutions

- Non-domestic (non-U.S.) Entities (Foreign Institutions) **are NOT** eligible to apply.
- Non-domestic (non-U.S.) components of U.S. Organizations **are NOT** eligible to apply.
- Foreign components, as [defined in the NIH Grants Policy Statement](#), **are NOT** allowed.

IV-2. Eligible Individuals (Program Director/Principal Investigator)

For the purposes of this FOA:

- **Multiple PD(s)/PI(s) are NOT allowed.**
- **Investigators with New Investigator status who are currently listed as key personnel on a funded HIRN Notice of Award are NOT eligible to apply.**

In addition, applicants must meet the NIH definition of a New Investigator (NI). A New Investigator is defined by NIH as an applicant who has not yet competed successfully for a substantial, competing NIH research grant. For a complete list of NIH grants that do not disqualify a PD/PI from being considered a New Investigator, see information posted [here](#).

Applicants also must hold an independent research position at a domestic (U.S.) institution at the time of submission of the application (January 15, 2018). For the purposes of this FOA, “independent research position” means a position that automatically confers eligibility, by the applicant’s

institutional policy, for an investigator to apply for R01 grants, with an appropriate commitment of facilities to be used for the conduct of the proposed research. Investigators still in training or mentored status (postdoctoral fellows) are not eligible to apply unless they have a written commitment of an independent faculty position as of January 15, 2018 that is certified by the institution.

Applicants may submit or have an R01 grant application pending concurrently with their HIRN New Investigator Pilot Award application. However, if that pending R01 grant is awarded in the fiscal year of the HIRN NI Pilot Award competition with a start date of September 30, 2018 or earlier in that fiscal year, then the applicant is no longer eligible to receive the HIRN Early Stage Investigator Pilot Award.

Section V. Application and Submission Information

V-1. Requesting an Application Package

Applicants may access the application package associated with this funding opportunity at the HIRN-CC website under “Funding”, specifically at: <https://hirnetwork.org/newinvestigator2018>

V-2. Content and Form of Application Submission

Application Forms: It is critical that applicants follow the instructions in the HIRN Application Guide (see Appendix 1). Conformance to the requirements in the Application Guide is required and will be strictly enforced. Applications that are out of compliance with these instructions may be returned without review.

Letter of Intent: By the due date listed above (December 15, 2017), prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity
- Name, address and telephone number of the PD/PI
- Names of other key personnel
- Participating institution
- Name of the one HIRN consortium most closely related to the project aims and goals

The letter of intent should be sent in electronic form to:

The Human Islet Research Network Coordinating Center (HIRN-CC) City of Hope, Duarte, CA
at: hirncc@coh.org

Budget: Budgets are limited to \$150,000 direct costs. Within that budget cap, investigators must set aside \$2,000 to support travel of the PI to the HIRN annual investigator’s retreat for each year of the proposed project period.

V-3. Instructions for Application Submission

Applications should be submitted directly to the HIRN-Coordinating Center, **NOT** to the Division of Receipt and Referral at the NIH.

V-4. HIRN Research Plan

All instructions in the HIRN Application Guide (Appendix 1) must be followed, including provision of a face page, detailed budget, budget justification, Biosketch (up to 5 pages) and research plan. The research plan should conform to the following instructions with careful attention to use of the headers and word limits outlined below:

Relationship to HIRN goals (500 words): Applicants should describe how their objectives and research design are related to, but distinct from, ongoing studies in HIRN.

Statement of research effort commitment: A statement must be included that, if chosen to receive an award, the applicant will commit a minimum of 2 person-months effort to the project supported by the HIRN New Investigator Pilot Award.

Project Description (up to 5 pages): Describe the scientific problem that you propose to address, its importance, and explain how solving this problem would have a major impact on T1D research. Why is the planned research uniquely suited to the HIRN New Investigator Pilot Award program, rather than a traditional grant mechanism? Briefly summarize the project Specific Aims, and describe the overall strategy, methodology, and analyses to be used to accomplish these aims. Describe the experimental design and methods proposed and how they will achieve robust and unbiased results. Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims. If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high-risk aspects of the proposed work. The application should provide a brief overview of future directions and anticipated timeline for securing funding for continuation of the work at the end of the HIRN-NI pilot award.

Innovation (500 words): State clearly and concisely what makes your project unusually innovative. If the approaches entail a high degree of risk, what will you do if these approaches are not successful?

Investigator Qualifications (500 words): Provide evidence to support your claim of innovativeness and creativity in your research at this early stage of your career. For example, which experiences demonstrate your inclination to challenge paradigms and take intellectual risks, develop unique collaborations, integrate diverse sources of information, or develop novel approaches when new challenges or opportunities arise?

Note: Bibliographic citations are not required but if included must fit within the page limit. Figures and illustrations may be included but must also fit within the page limit.

Resource Sharing Plan: Individuals are required to comply with instructions for providing Resource Sharing Plans as provided in [NIH guidance](#). Post-award, grantees will be expected to comply with HIRN consortium-specific resource sharing and confidentiality agreements.

Appendix: Letters from Collaborators should be submitted in the Appendix. Additionally, applicants may include letters of support from up to three individuals currently associated with HIRN to provide validation for the proposal's relationship to current and future aims of the consortium of interest.

V-5. Planned Enrollment Report

DO NOT INCLUDE. Studies meeting the current NIH definitions of Clinical Research or Clinical Trials will **NOT** be eligible for support under this funding opportunity. For current definitions, please see guidance at: <https://grants.nih.gov/grants/glossary.htm#C>

V-6. PHS 398 Cumulative Inclusion Enrollment Report

DO NOT INCLUDE. Studies meeting the current NIH definitions of Clinical Research or Clinical Trials will **NOT** be eligible for support under this funding opportunity. For current definitions, please see guidance at: <https://grants.nih.gov/grants/glossary.htm#C>

Section VI. Application Review Information

VI-1. Criteria

Only the review criteria described below will be considered in the review process. Consistent with the HIRN program mission, all applications submitted will be evaluated for scientific and technical merit using external peer review.

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 there a strong scientific premise for the project? 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? Is the project an appropriate vehicle for a New Investigator? Is the scope of activities proposed appropriate to meet those needs? Will successful completion of the aims bring about unique advantages or capabilities to the NIDDK research community?
- **Investigator(s):** Does the New Investigator have appropriate experience and training to carry out the experiments proposed?
- **Innovation:** Does the application challenge and seek to shift current research 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?
- **Approach:** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Has the investigator 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?
- **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 investigator adequate for the project proposed?

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: DO NOT INCLUDE. Studies meeting the current NIH definitions of Clinical Research or Clinical Trials will **NOT** be eligible for support under this funding opportunity. For current definitions, please see guidance at: <https://grants.nih.gov/grants/glossary.htm#C>

Inclusion of Women, Minorities, and Children: DO NOT INCLUDE. Studies meeting the current NIH definitions of Clinical Research or Clinical Trials will **NOT** be eligible for support under this funding opportunity. For current definitions, please see guidance at: <https://grants.nih.gov/grants/glossary.htm#C>

Vertebrate Animals: When relevant, reviewers 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.

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.

VI-2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by external peer reviewers convened by the HIRN-CC using the stated review criteria.

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.
- Appeals of the HIRN-CC peer review **will NOT** be accepted for applications submitted in response to this funding opportunity.

Applications will compete for available funds with all other recommended applications submitted in response to this funding opportunity. Following initial peer review, recommended applications will receive a second level of review by an *ad hoc* group of HIRN External Science Panel members. NIH staff affiliated with HIRN will make final funding decisions, with consideration of the following:

- 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.

VI-3. Anticipated Announcement and Award Dates

After peer review and secondary review of the applications are complete, the PD/PI will be notified by the HIRN-CC as to funding decisions by May 1, 2018.

Appendix I. Application Guide

The following items will be collected as part of the application:

- [Public Health Service Grant \(PHS\) 398: Face Page \(form page 1\)](#)
- [Public Health Service Grant \(PHS\) 398: Detailed Budget for Initial Budget Period \(form page 4\)](#)
- [Investigator Biographical Sketch \(Biosketch\) \(5 page max length\)](#)
- Research Plan (as detailed in Section V-4)
- [NIH Checklist](#)