



CONGENITAL HYPERINSULINISM INTERNATIONAL HIHA PILOT GRANT PROGRAM

Background:

Hyperinsulinism Hyperammonemia (HIHA) is the second most common form of congenital hyperinsulinism (HI). HIHA is commonly referred to as GDH-HI and is caused by a defective GDH (glutamate dehydrogenase) gene.

GDH is an enzyme which plays an important role in amino acid metabolism. People with HIHA secrete too much insulin which causes hypoglycemia, especially after a protein rich intake. Those with HIHA also have high ammonia levels in their blood, and often have epilepsy and other neurological issues that are thought to stem from the change in the GDH gene. The only currently available treatment for HIHA is diazoxide, which inhibits insulin secretion. It helps in the management of hypoglycemia but leaves the high ammonia levels untreated. In addition, diazoxide has adverse effects including hirsutism which occurs in almost all who take the medication, changes in facial appearance, and less frequent but serious side effects like pulmonary hypertension, edema, neutropenia, thrombocytopenia, and hyperuricemia.

One grant of \$70,000 is available for an innovative, preclinical, or clinical study that has the potential to lead to: (1) a better HIHA treatment; (2) a cure for HIHA; or (3) a quality of life improvement for those affected by HIHA. This grant is made possible by generous donors to Congenital Hyperinsulinism International.

Application Instructions and Review Procedure

I. Eligibility:

All individuals holding a PHD or MD, tenure-track faculty, non-tenure-track faculty or staff, or an equivalent level at a research institution or at a biotechnology/pharmaceutical company.

Application Due Date: April 8, 2019 no later than 24:00 EDT.

Application documents should be emailed to Jacqueline Kraska, jkraska@congenitalhi.org, CHI Research and HI Global Registry Program Director.

II. FORMAT for documents:

Font and Page Margins: Use Arial typeface, a black font color, and a font size of 11 points. A symbol font may be used to insert Greek letters or special characters. Use 0.5 inch margins (top, bottom, left, and right) for all pages, including continuation pages. Print must be clear and legible; all text should be single-spaced.

Header: There should be a header at the top right on all pages of the PDF indicating the full name of the Principal Investigator – PI (e.g., **PI: Smith, John D.**)

File names: ALL emailed files should start with the LAST NAME of the PI followed by the brief name of the document. Examples: SMITH CV, SMITH Cover Page, SMITH Budget. **If files are not labeled properly, you will be asked to resubmit the PDFs before your application can be considered.**

III. CONTENT to be emailed:

National Institute of Health (NIH)-style Bio sketch with Other Support of PI and key personnel (5 pages max). **[PDF]** The PI must include accurate and complete information regarding all other sources of grant support (current and pending), including title, abstract, annual and total amount of grant, inclusive funding period, and percent effort.

Detailed Budget of Expenses

Provide budget with breakdown of expenses and applicable details.

Grant will be awarded for one year.

Allowable direct costs:

- Salary for PI
- Salary/stipend and related benefits for graduate student/postdoctoral fellow/technical support
- Travel (up to \$1500)
- Laboratory supplies and other research expenses
- Indirect Costs of 10% are included in the total award amount

Unallowable costs:

- Consultant costs
- Tuition
- Professional membership dues
- Equipment >\$5,000
- General office supplies
- Institutional administrative charges (e.g., telephone, other electronic communication, IT network, etc.)
- Pre-award charges
- Any other expenses not directly related to the project

□ **Research Proposal** (5 pages max) and **Bibliography** (1-page max). [combined into one PDF] Include the following sections: Specific Aims, Background and Significance, Preliminary Studies/Data, Research Design and Methods. Research plan should also address the following questions: 1) Do you require access to reagents, cell lines, animal models, IRB/ethical board approvals, and/or equipment necessary to complete work? If so, please describe your plan to gain access within the time-frame of this grant period. Text citations should use a numbered format. Include all author names in the reference list.

IV. Grant Review Procedure:

1) Grants will be reviewed for scientific content and relevance to the goals of the Request for Application (RFA).

2) Full applications are reviewed and rated with an assessment of the strengths and weaknesses of each application based on the defined review criteria described below. Final decision of funding will be made by the CHI Research and Development Committee of the CHI Board of Directors.

3) Research Proposal Content and Review Criteria; the following criteria will be utilized in proposal review:

- RFA Goals – Does the proposed work address one or more of the RFA study goals of (1) a better HIHA treatment; (2) a cure for HIHA; or (3) a quality of life improvement for those affected by HIHA?
- Research Project - Is the proposed project of high scientific quality?
- Background - Is the fundamental objective of the study and hypothesis to be addressed clearly defined?
- Scientific Approach - Will the proposed specific aims answer the study hypothesis? Will the scientific approach effectively test and answer each specific aim? Are the study goals supported by existing data?
- Clinical Impact - Will the proposed research lead to substantial advances and/or contribute to large leaps of understanding or knowledge that will contribute to reductions in disease burden within the decade?
- Research Significance - Does the study address an important question that is not likely to be addressed without this funding? Does the proposed study offer a unique opportunity to explore an important issue and/or employ a novel approach to this disease research? Will the study outcomes advance our knowledge of HIHA and/or contribute to changes in the focus of future

research questions or the way we conduct research on this issue?

- Budget – Is the budget fully justified and reasonable in relation to the proposed project?
- Investigator Qualifications – Does the investigator hold a track record of outstanding research accomplishments? Does the investigator have access to the resources and environment necessary to complete the study as outlined?

V. Fund Disbursement:

Details of invoicing schedules and reporting requirements will be made available upon award.

For additional information, please contact Jacqueline Kraska, *Research and HI Global Registry Program Director*, at jkraska@congenitalhi.org or call (973) 842-7559.

Award will be announced on May 20, 2019.