HUNTINGTON’S DISEASE
Human Biology Project

Request for Proposal

2015
HUNTINGTON’S DISEASE SOCIETY OF AMERICA’S
HD HUMAN BIOLOGY PROJECT
REQUEST FOR PROPOSAL

Dates and Deadlines

Online system opens: March 20, 2015
Letter of Intent due: May 29, 2015
Complete applications due: July 31, 2015
Scientific Advisory Board review: September 2015
Notification of award: by October 1, 2015
Fellowship start date: no later than January 1, 2016

Program Goal

Support for investigator-initiated research directed to better understand the biology of Huntington’s disease (HD) as it occurs in humans. The research projects and observations resulting from them should have the potential to directly impact the lives of patients or help guide future drug development for HD.

Statement of Need

The Huntington’s Disease Society of America (HDSA) is interested in sponsoring innovative lines of inquiry of human HD patient data that will shed light on the most proximal biological events caused by the mutant huntingtin gene. All research proposals must incorporate a patient-centric focus to understanding HD. Some examples of the types of projects the HDSA Scientific Advisory Board would like to see addressed by the international research community are listed below:

1. Biomarker discovery/development: Reliable and robust readouts to assess efficacy of huntingtin lowering strategies in the clinic are of the utmost importance to the HD community.
2. Systems Biology studies using analysis of high-throughput transcriptomic, proteomic, lipidomic, metabolomic, etc…data generated from human HD biological samples to uncover proximal biological pathways affected in human HD.
3. Use of human-derived stem cells or HD patient samples to elucidate HD biology and mechanisms.
4. Human-focused drug target identification and validation
5. Research using innovative technologies to improve of quality of life and care of HD patients.

Background and Rationale

Research into neurodegenerative diseases like HD has largely relied on rodent models of disease. However, since HD does not naturally occur in other species and the central nervous system is especially different between rodents and humans, there is a real need to ensure we understand HD in the context in which it occurs: hence the need to conduct clinical research studies in humans whenever possible to test working hypotheses about the disease. The generation of supporting (or refuting) data for these hypotheses will be crucial to ensuring the most promising therapeutic approaches advance to clinical trials as quickly as possible.
The research to be supported by HDSA must meet certain criteria.

- First, the proposals must involve the use of HD patient data, samples or human HD model systems (e.g., human iPSCs) to maximize the impact on the execution of future clinical trials and/or drug discovery programs for HD. For example, this could be achieved by proposing to identify a new biomarker in the blood of patients that could be monitored to assess efficacy of a novel therapeutic.
- **NEW FOR 2015:** The research proposals should involve a collaboration with investigators/clinicians at a reputable HD clinic anywhere around the world. HDSA no longer requires that funded research proposals have a formal collaboration with one of HDSA’s 29 Centers of Excellence. Applicants may propose to work with any HD clinic they desire. However, if possible, we encourage applicants to consider the HDSA Centers of Excellence as a potential collaborator for their research. For a complete listing of the 29 HDSA Centers of Excellence and the contact information for the Center Director, please see Appendix A.

**Eligibility**

**Fellows:** The HD Human Biology Project Fellowships are provided as “seed monies” (up to $75,000) for new clinical or translational research projects that are directly related to understanding Huntington’s disease in the hope that the results can be used to attract funding from other sources. It is NOT required that applicants have an MD and/or a PhD degree from an accredited medical school, university or research institute at the time of application. Applications are welcomed and encouraged from individuals from other areas of research and health care (e.g., biostatisticians, physical therapists, etc…). Applications are welcome from all researchers regardless of their position/title. However, preference will be given to young investigators who are not yet independent investigators. Applications from U.S. and non-U.S. non-profit and for-profit institutions are also welcomed. These institutions include, but are not limited to, universities, hospitals, government and biotech/pharmaceutical companies. Projects submitted from a for-profit organization must be accompanied by a signed letter from an authorized representative stating that publication of the fellow’s work will not be delayed due to proprietary issues.

**Mentors:** If the applicant is a post-doctoral or clinical research fellow, a mentor must be identified before applying for the HD Human Biology Project. All mentors must have a PhD and/or MD/DO degree and be scientific investigators with primary appointments at academic, public or private research institutions. Collaborations between multiple HD clinics are strongly encouraged.

**Awards**

The HDSA Grant provides funds up to $75,000 a year for up to two years, subject to available organizational funds and demonstration of progress on the proposed research to support personnel (other than the mentor(s)) and supplies. Each award includes a competitive stipend up to $50,000 to cover salary and fringe benefits for the recipient, and a maximum $25,000 annual allowance to cover research costs, supplies and professional conference travel. Annual travel costs cannot exceed $2,000. Indirect costs are not allowed.

The number of fellowships HDSA will award will be determined by its available financial resources and the alignment of the proposed research within the HDSA portfolio. Fellows are permitted to obtain additional awards or grants to cover additional salary and research expenses as needed. However, it is required that the awardee dedicate at least 50% effort to the proposal.
Terms

Proposals can be submitted as one or two-year projects. The funds cannot be used to purchase laboratory equipment, nor does the award cover indirect costs. Awards are paid in installments, contingent upon approval of satisfactory progress as documented in progress and financial reports submitted to HDSA. To continue receiving financial support from HDSA in year two of a two year research project, the awardee must demonstrate significant scientific progress towards the agreed upon 6 and 12 month milestones in the form of a detailed progress report (including all raw data). The first progress report will be due no later than 9 months after the start date of the award. Neither one, nor two year awards, are renewable. All publications resulting from research funded by HDSA must acknowledge the Huntington’s Disease Society of America, and should be provided to HDSA when in-press.

All IRB approved projects selected for funding that involve the recruitment of study participants must complete the HD TrialFinder Listing Request Form available on www.HDSA.org. This information will be used to list the clinical study in HDSA’s HD TrialFinder (www.HDTrialFinder.org) that aims to match interested trial participants with HD research studies around North America.

Sharing Research Results: Twenty four months after the award end date, HDSA may share the results (including raw data) of the funded research with third parties without restrictions. Before that time, HDSA can share the results (including raw data) of the funded research with third parties under a confidentiality agreement which will require such third parties to not publish any results they generate using the results of the funded research until twenty-four months after the award end date. Finally, by accepting funds from HDSA, awardees also agree to make (and agree HDSA may make) the raw data of the funded research freely available for inclusion in data repositories in a timely fashion.

Institutional Approvals: Human Participants and Vertebrate Animal Certifications must be documented with a copy of an official letter of approval (or equivalent for non-US applicants), which identifies the Principal Investigator, project title and date of approval, and is signed by the Review Committee Chair or equivalent responsible institutional/government official. Prior certification for another project cannot be substituted, but can be officially amended to include the proposed project (identified by project title). IMPORTANT: IRB, IACUC or equivalent ethical certification are NOT required to submit an application; however, such ethical certification must be submitted as soon as possible following official notification of an award. HDSA will not issue a grant until the appropriate certifications are received.

Projects using postmortem tissue must provide documentation that the necessary tissue is or will be available at the research site at the time of the award. Applications without proper documentation will be returned without review.

Public Access/Dissemination

Funded researchers are also required to submit or have submitted for them to the National Institutes of Health’s PubMed Central database an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. This requirement applies to all grants awarded after January 1, 2013, whether HDSA funds the research in whole or in part.

HDSA reserves the right to make information about funded awards publicly available.
Notification and Announcements

Proposals will be reviewed by the HDSA Scientific Advisory Board. Proposals will be scored in a manner similar to the NIH scoring system. The scoring system utilizes a 9-point rating scale (1 = exceptional; 9 = poor). This scale will be used by all eligible (without conflict of interest) SAB members to provide an overall impact score and for assigned reviewers to score four individual criteria (Significance, Investigator(s), Approach, and Collaboration). Proposals with inter-laboratory or inter-institutional collaborations will be weighed more heavily than non-collaborative efforts.

Applicants will be notified by e-mail after the funding decision process is complete. All fellowship awards shall be posted on the HDSA Research website. Upon completion of the fellowship, the outcomes of each project may be highlighted in various HDSA communication vehicles, such as newsletters, webinars, or the HDSA website. HDSA fellows may also be asked to present their findings in the form of a poster or scientific presentation at the Annual HDSA Convention. If selected to present, HDSA will cover all costs for the research fellow to attend the HDSA Convention.

Payment of Awards

The recipient of any fellowship from HDSA must use the awarded funds for the specific purpose they were originally intended. Any funds not used in the above specified manner must be returned to HDSA within 60 days of the receipt of the final scientific report by HDSA. Payment of the awards is contingent on receiving any institutional approvals (IRB or IACUC) that are required for the proposed research.

A second year continuation of support for the project will be contingent upon HDSA receiving interim progress and financial reports from the investigator 9 months after the award begins. Final reports are due no more than 30 days after the grant end date. The fellow and mentor may request a one-time only, no-cost extension of up to six months if there is a hiatus in the training. Requests for no-cost extensions must be approved by HDSA prior to the extension period and require submission of a progress report and financial report.

Awards will be paid in two installments. The first payment totaling 75% of the first year budget will be made to the researcher’s institution upon acceptance of the HDSA award terms and conditions, including receipt of all required certifications by a post-award official authorized to act for the institution receiving the award. A fellowship award cannot be transferred to another investigator, laboratory or sponsoring institution without prior written approval from HDSA. The second payment equaling 25% of the annual budget will be sent upon receipt and acceptance of a progress report detailing the progress through the first 9 months of the project.

Letter of Intent and Application

Completed letters of intent (LOI) must be received by HDSA no later than Friday, May 29, 2015, at 5:00 pm (EDT). The LOI must be completed online at www.hdsa.org/reschloi. All LOIs will be reviewed by the HDSA Scientific Advisory Board and those most closely aligning with the statement of need will be invited to submit a full proposal.

1. An electronic version of the Human Biology Project application form will be distributed to each applicant if their Letter of Intent is accepted.

2. Each application must be submitted electronically as a single file in MS Word or PDF file format. Paper copies will not be accepted.
3. Submit the completed application and supporting documents to HDSA by July 31, 2015.

Recipients will be selected in September 2015. Awards will be recommended by the HDSA Medical and Scientific Advisory Committee prior to formal approval by the HDSA Board of Trustees. Awardees will be notified by October 1, 2015 via email, with the anticipated start date to be between November 1, 2015 and January 1, 2016.

Supporting Documents

Applications must be accompanied by a letter from project supervisor/mentor of the department in which the work will be done, evaluating the significance of the research to be conducted and potential of the researcher. Proposals involving human research participants must indicate any potential risks (physical or psychological).

Copies of the certified consent form and approval from the sponsoring Institutional Review Board (IRB) for the protection of research participants must accompany the application. If the proposals also include a portion of research involving use of animals, you must include a statement certifying compliance with all applicable federal, state and local laws, and conformity with and adherence to the Animal Welfare Act, the National Research Council Guide for the Care & Use of Laboratory Animals, and any appropriate US Department of Agriculture or National Institutes of Health (NIH) regulations and standards.

A completed application includes, in order, the following:

I. General Application
   a. Administrative Information
   b. Abstract and Lay Summary
   c. Impact on HD Patients and Families
   d. Budget
   e. Biographical Sketches of applicant and mentor (NIH style acceptable)
   f. Other Research Support

II. Research and Training Plan
   a. Summary of Specific Aims*
   b. Background and/or Preliminary Data*
   c. Preliminary Studies with Figures (if applicable)*
   d. Experimental Plan (methods, statistical analysis, etc…)*
   e. Power Calculations (all studies involving human subjects MUST complete a power analysis to determine appropriate sample size)*
   f. 6, 12, 18 and 24 month milestones*
   g. HD Clinic Collaboration Details*
   h. Literature Cited*
   i. Career Plan or Personal Statement of Applicant
   j. Letter(s) of Support
   k. IRB Certifications and Laboratory Animal Welfare Approvals (if applicable)

* Items a-h must not exceed 7 pages of 12 point type.
Return completed application to:

grants@hdsa.org

Huntington’s Disease Society of America
505 Eighth Avenue, Suite 902
New York, NY 10018
Phone: (212) 242-1968
Fax: (212) 239-3430
Appendix A

HDSA Centers of Excellence Directors

HDSA Center of Excellence at
University of Alabama
Birmingham, AL
Director: Victor Sung, MD
Email: Vsung@uabmc.edu

HDSA Center of Excellence at
Boston University Medical Center
Boston MA
Director: Sam Frank, MD
Email: Samuel.frank@bmc.org

HDSA Center of Excellence at
Cleveland Clinic Comprehensive Care Clinic
Cleveland, OH
Director: Mayur Pandya, DO
Email: pandyam@ccf.org

HDSA Center of Excellence at
Columbia Health Sciences/NYS Psychiatric Institute
New York, NY
Director: Karen Marder, MD, MPH
Email: ksm1@cumc.columbia.edu

HDSA Center of Excellence at
Colorado Neurological Institute
Englewood, CO
Director: Rajeev Kumar, MD
Email: Rajeev.kumar@msn.com

HDSA Center of Excellence at
University of California
Davis Medical Center
Sacramento, CA
Director: Vicki Wheelock, MD
Email: Vicki.wheelock@ucdmc.ucdavis.edu
Co-Director: Teresa Tempkin, RN, MSN, ANP
Email: Teresa.tempkin@ucdmc.ucdavis.edu
HDSA Center of Excellence at University of California
Los Angeles, CA
Director: Susan Perlman, MD
Email: sperlman@mednet.ucla.edu

HDSA Center of Excellence at University of California
San Diego, CA
Director: Jody Corey-Bloom, MD, PhD
Email: jcoreybloom@ucsd.edu

HDSA Center of Excellence at University of California San Francisco
Memory and Aging Center
San Francisco, CA
Director: Michael Geschwind, MD, PhD
Email: Michael.geschwind@ucsf.edu

HDSA Center of Excellence at Duke University HD Clinic
Durham, NC
Director: Burton Scott, MD, PhD
Email: burton.scott@dm.duke.edu

HDSA Center of Excellence at University of Florida Center for Movement Disorders and Neurorestoration
Gainesville, FL
Director: Ramon Rodriguez Cruz, MD
Email: ramon.rodriguez@neurology.ufl.edu

HDSA Center of Excellence at Hennepin County Medical Center
Minneapolis, MN
Director: Martha Nance, MD
Email: Martha.namce@parknicollet.com

HDSA Center of Excellence at Johns Hopkins University/Hospital
Baltimore, MD
Director: Christopher Ross, MD, PhD
Email: CAross@jhu.edu
HDSA Center of Excellence at Indiana University
Movement Disorders Program
Indianapolis, IN
Director: Kim Quaid, PhD
Email: kquaid@iu.edu
Co-Director: Joanne Wojcieszek, MD
Email: jwojcies@iu.edu

HDSA Center of Excellence at University of Iowa
Iowa City, IA
Director: Jane Paulsen, PhD
Email: jane-paulsen@uiowa.edu

New England HDSA Center of Excellence
Boston, MA
Director: Steven Hersch, MD, PhD
Email: hersch@helix.mgh.harvard.edu

HDSA Center of Excellence at Nebraska Medicine
Omaha, NE
Director: Amy Hellman, MD
Email: ahellman@unmc.edu

HDSA Center of Excellence at The Ohio State University
Columbus, OH
Director: Sandra Kostyk, MD, PhD
Email: Sandra.kostyk@osumc.edu

HDSA Center of Excellence at University of Pittsburgh Medical Center
Pittsburgh, PA
Director: Valerie Suski, DO
Email: suskivr@upmc.edu

HDSA Center of Excellence at Rush University Medical Center
Chicago, IL
Director: Kathleen Shannon, MD
Email: Kathleen_shannon@rush.edu
HDSA Center of Excellence at
University of Rochester
Rochester, NY
Director: Kevin Biglan, MD, MPH
Email: kevin_biglan@URMC.rochester.edu

HDSA Center of Excellence at
Stanford University HD Clinic
Stanford, CA
Director: Veronica Santini, MD
Email: santiniv@stanford.edu

HDSA Center of Excellence at
University of South Florida
Morsani Health Center
Tampa, FL
Director: Juan Sanchez-Ramos, MD, PhD
Email: jsramos@health.usf.edu

HDSA Center of Excellence at
Vanderbilt University
Huntington’s and Chorea Multidisciplinary Clinic
Nashville, TN
Director: Daniel Claassen, MD
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HDSA Center of Excellence at
Virginia Commonwealth University
Parkinson’s and Movement Disorders Clinic
Richmond, VA
Director: Claudia Testa, MD, PhD
Email: ctesta@vcu.edu

HDSA Center of Excellence at
University of Virginia
Charlottesville, VA
Director: Madeline Harrison, MD
Email: MBH3Y@hscmail.mcc.virginia.edu
HDSA Center of Excellence at
University of Vermont Medical Center
Frederick Binter Center for Parkinson’s Disease and Movement Disorders
Burlington, VT
Director: James Boyd, MD
Email: james.boyd@uvmhealth.org

HDSA Center of Excellence at
University of Washington
Seattle, WA
Director: Suman Jayadev, MD
Email: sumie@uw.edu

HDSA Center of Excellence at
Washington University Medical School
St. Louis, MO
Director: Joel Perlmutter, MD
Email: joel@npg.wustl.edu