American Stroke Association-
Bugher Foundation Centers for Stroke Prevention Research

Request for Applications

The Henrietta B. and Frederick H. Bugher Foundation was established during Frederick Bugher’s life and continues to support research in cardiovascular and cerebrovascular diseases. Both of Mr. Bugher's parents suffered from heart ailments. Originally limited to research within the District of Columbia, the foundation now supports research throughout the world. In 1984 the foundation sought the guidance of the American Heart Association in identifying a focus for its research support. The association suggested a program to bring molecular biology training to clinically-trained investigators. This was the beginning of a continuing relationship with the association, initially supporting Centers for Molecular Biology in the Cardiovascular System and more recently the AHA-Bugher Awards for the Investigation of Stroke.

Now the Bugher Foundation has joined with the American Stroke Association (ASA, a division of the American Heart Association) to support a network of three Centers for Stroke Prevention Research for a period of four years. The desired characteristics of these centers, the general requirements of the application and the review criteria are described in this Request for Applications (RFA).

Objectives of Request for Applications

This initiative is designed to produce a network of interacting institutions and scientists for collaborative, multidisciplinary research to improve the prevention of stroke. A major component of the centers will be the interdisciplinary training of a new generation of scientists who, from their earliest experiences in research, will collaborate with other scientists through monthly meetings with established investigators and annual meetings with other investigators participating in the centers. An ultimate product of this program will be the creation of a report on the challenges and results of active collaboration.

The American Stroke Association-Bugher Foundation intends to fund three centers that will encompass the following goals:

- Accelerate generation of important, novel ideas
- Fill large gaps in knowledge and expertise
- Create realistic but dramatic gains (developing new investigators is one such gain)
- Utilize ASA/Bugher Centers as the central work engine
- Link research and training components through the program
- Prioritize multidisciplinary approaches with frequent collaborative communications.
It is anticipated that the results of the funding and formation of the ASA-Bugher Foundation Centers for Stroke Prevention Research and their linking in this structure will:

- Produce a cadre of new investigators who will energize this field and lead to the generation of an expansion of the numbers of such investigators in later years.
- Produce new research results based on the initial ideas of the Centers and on ideas generated by the interaction of the Centers and their investigators.
- Provide insights into and report on the challenges and successful mechanisms for active collaboration.

Figure 1. Overview of implementation process and network structure

**Disciplines and Expertise**

1. Within the scope of stroke prevention, scientific disciplines may range from basic research to clinical research to translational research. A key component for the program includes genetics expertise and related research.

2. Representation on the team should include the breadth of basic, clinical and translational expertise because a key component of the program is a multidisciplinary training program to give fellows basic, clinical and translational research exposure.

3. The Center Director should be recognized nationally for stroke or genetics or disease prevention expertise and for his/her ability to build collaborations. The director is not required to have a successful background in basic laboratory research, but the application must contain a genetic component and stroke prevention component.

4. The centers may be predominantly basic or predominantly clinical provided that significant collaborative research efforts with a view towards translational research are present.

**ASA-Bugher Center Program Structure**
The development of each Center will be the responsibility of the Center Director, who will coordinate the projects and the training program. The Director will provide administrative and scientific leadership and will be responsible for the organization and operation of the Center, and for communication with the AHA and the ASA/Bugher Foundation Stroke Oversight Advisory Group.

Each Center will:
- conduct at least one project that may be basic, clinical and/or translational in nature but that contains a significant genetic component;
- provide a multidisciplinary training program to give fellows basic, clinical and translational research experience;
- train 6 fellows during the period of the award (three two-year fellowships in years one and two, and three two-year fellowships in years three and four);
- be linked to the other Centers by mandatory interactions/meetings to accelerate information exchange and ideas;
- collaborate and participate in producing an end-of-award report about the challenges, mechanisms and successes of the Centers’ collaborations;
- consider itself part of the ASA-Bugher Foundation Stroke Prevention Network.

**Eligible Institutions and Investigators**

Awards are limited to non-profit institutions in Canada, Mexico and the United States, such as universities and colleges, public and voluntary hospitals, laboratories, research institutes, and other non-profit institutions that can demonstrate the ability to conduct projects and organize a center. In the United States, applications will not be accepted for work with funding to be administered through any federal institution or work to be performed by a federal employee with the exception of Veterans Administration employees. In Canada and Mexico, applications will not be accepted from investigators employed at government facilities or by government agencies, even if they also hold a university appointment.

The awards are not transferable to other institutions. The projects described can have no scientific overlap with other funded work. An institution may submit only one ASA-Bugher Center application for this competition. The application may include individuals and/or projects at more than one institution provided there is evidence for a successful close personal and geographical interaction among research and training personnel. It is the responsibility of the submitting institution to ensure that only one proposal is submitted for the institution or to coordinate across several institutions to create a single application. The applicant institution will maintain fiscal responsibility for the Center award. The appropriate Grants/Sponsored Programs Officer and Institutional Officer should sign the proposal.

Directors and Principal Investigators of projects of the Centers must possess an M.D., Ph.D., D.O., D.V.M., or equivalent doctoral degree at time of application. They should be faculty or staff members of the non-profit applicant organization at application. Directors and Principal Investigators of projects of the Centers may hold another AHA award simultaneously. The Center Director may submit a Center project proposal. There is no minimum percent effort requirement for the Director or Principal Investigators (PI) in the Center, though Director or PI salary requested must be proportional to the percent effort devoted to the Center.

The Center Director must demonstrate expertise in the areas of clinical or basic stroke research, with demonstrated ability to build collaborative groups. He/She is not required to have a
successful background in genetics, but the overall application must demonstrate a significant genetics component. The Director must demonstrate a successful history of leadership in training and interdisciplinary collaboration. A clear demonstration of the Director’s commitment to collaboration with other disciplines and other Centers is required.

The responsive application will demonstrate a history of successful clinical and laboratory post-doctoral fellowship training with a plan to continue the program or a strong plan to develop a successful program. Didactic and experiential training in molecular biology and genetics is encouraged. In addition, training in general laboratory research, translational research and clinical research concepts as well as collaborative research should be described in the application. Trainees are not required to be named at the time of the application submission; however, a viable source for identifying and recruiting trainees must be presented. The trainee fellows must possess an M.D., Ph.D. or equivalent doctoral degree at the time of participation in the program. Collaborative interdisciplinary training programs are encouraged. An emphasis on translational research with laboratory training for clinically trained fellows and clinical training for laboratory fellows is also encouraged.

**Citizenship Requirements for U.S. Directors, Principal Investigators and Fellows**

Directors at **U.S. institutions** must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)

Principal Investigators of proposed projects at **U.S. institutions** must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
- H1-B Visa – temporary worker in a specialty occupation
- O-1 Visa – temporary worker with extraordinary abilities in the sciences
- TN Visa – NAFTA professional

Named fellows of the Centers at **U.S. institutions** must have one of the following designations:

- U.S. citizen
- Permanent Resident
- Pending Permanent Resident (must have applied for permanent residency and have filed Form I-485 with the U.S. Citizenship and Immigration Services and have received authorization to legally remain in the U.S., having filed an Application for Employment Form I-765)
- F-1 Visa - student
- H1-B Visa – temporary worker in a specialty occupation
- J-1 Visa – exchange visitor
- O-1 Visa – temporary worker with extraordinary abilities in the sciences
• TN Visa – NAFTA professional

All awardees must meet the citizenship criteria throughout the duration of the award.

Named fellows of the Centers at U.S. institutions must hold a Ph.D., M.D., D.V.M. or equivalent doctoral degree and commit 75 percent effort to research training. Center fellows may commit a minimum of 70 percent effort if justification is accepted by the Oversight Advisory Group. A named fellow may not hold another fellowship award, although the institution may provide supplemental funding. Fellows may not hold a faculty or staff appointment, with the exception of M.D.’s or M.D./Ph.D.’s with clinical responsibilities. These fellows may hold a title of instructor or similar due to their patient care responsibilities, but must devote at least 75 percent of effort to research training. A named fellow may have been the recipient of an AHA fellowship, but may not hold an AHA affiliate fellowship, AHA Fellow-to-Faculty Transition Award and ASA-Bugher Stroke Center fellowship simultaneously.

Additional Eligibility Requirements for Canadian or Mexican Directors, Principal Investigators and Fellows

Directors and Principal Investigators at Canadian or Mexican institutions must be employed (have an academic or institutional appointment) at an eligible institution in a position that permits them to engage in independent research activities for the duration of the award.

Named fellows of the Centers at Canadian or Mexican institutions must hold a Ph.D., M.D., D.V.M. or equivalent doctoral degree and commit 75 percent effort to research training. Center fellows may commit a minimum of 70 percent effort if justification is accepted by the Oversight Advisory Group. A named fellow may not hold another fellowship award, although the institution may provide supplemental funding. Fellows may not hold a faculty or staff appointment, with the exception of M.D.’s or M.D./Ph.D.’s with clinical responsibilities. These fellows may hold a title of instructor or similar due to their patient care responsibilities, but must devote at least 75 percent of effort to research training.

Note: Country of residence is not a selection criterion. The ASA and the Bugher Foundation do not make any assurance that grants will be awarded in all eligible countries in any given award period.

Application Submission Process

Only one Center proposal, including multiple research project proposals, may be submitted from an institution. Institutions that are part of the prospective Center’s application are not eligible to submit a separate Center application. The completed application must include the primary Center application and multiple (at least two) individual research project applications. The components of the application are described below.

Application forms and instructions for the ASA-Bugher Foundation Centers for Stroke Prevention Research will be available on the American Heart Association’s web site (http://www.americanheart.org/presenter.jhtml?identifier=3024775) approximately May 1, 2006. AHA forms and format must be used to apply (electronic submission) via AHA’s web site.

- 5 -
**Components of Application**

**Primary Center Application**

The Director of the proposed Center must submit an umbrella application which consists of the following components:

1) vision for the Center (a clear, unifying central theme to which each research project application relates);
2) information regarding the Director;
3) information regarding any current cerebrovascular research programs and any history of successes in cerebrovascular research;
4) a detailed description of the multidisciplinary training program for the ASA-Bugher Center for Stroke Prevention Fellows' two-year fellowships (basic, clinical and/or translational research exposure), including information regarding the evaluation of prospective fellows and how funded fellows’ ongoing progress will be evaluated; in addition to participating in annual Center meetings, institutions are expected to incorporate collaboration with established investigators at other institutions through regular meetings;
5) information regarding the identification of a faculty/staff member at the Center institution or affiliated institutions (if appropriate) with the leadership skills to bring team-building and professional/organizational development to the collaborative process;
6) information on current training programs and training grants within the Center institution and affiliated institutions (if appropriate);
7) information regarding other faculty/staff members at the Center institution and affiliated institutions (if appropriate) who will be submitting research projects;
8) information on research funding available to the Director and proposed Principal Investigators on Center research projects;
9) information on collaborative research within the Center institution and affiliated institutions (if appropriate) and their ability to integrate and collaborate with other institutions;
10) information on facilities available to support the Center and affiliated institutions’ (if appropriate) research projects;
11) an overview of the estimated four-year budget for the Center.

**Center Research Project Applications**

A Center Research application must include at least two (2) research projects related to stroke prevention. There is a specific requirement for the research projects to have a genetic component and for clear clinical relevance in all programs. While a prospective Center application must contain elements of basic, clinical and/or translational research in the proposed projects, it is possible for the prospective Center to focus primarily on any one of these research areas. The set of projects proposed by a Center will be reviewed as a group. Centers should submit their most competitive projects feasible within the budget described for a Center.

The Principal Investigator of each proposed research project must submit an application which consists of the following components:

1) required application forms
2) investigator’s qualifications
3) specific project aims
4) background and significance
5) previous work on the same or related problems
6) contemplated methods of approach to problem
7) ethical aspects

Peer Review Process

Review of the applications will be conducted by the American Heart Association and will occur in two stages. For the first stage, a peer review committee of volunteer scientists will be assembled to review the Center applications. Appropriate scientific expertise will be sought to review the applications received. Each application will be reviewed in depth by at least two peers, who will present each application to a review panel of twelve or more. At the discretion of the review committee, and based upon the preliminary scores assigned to an application by the assigned reviewers, a streamlined review may be conducted for any application. After discussion of each Center proposal, each panel member will score each application, using the point system described below. The Centers and their projects will be ranked, based upon the average of the panel members’ scores.

A second stage of the review will then be conducted for the highest ranked Center applications, and will include a presentation to the AHA review group by the Center Director and members of the Center team. Reviewers will score the Centers following the presentations, and the average of the reviewers’ scores will provide the final ranked list of applications. The ranked list will be reviewed by the AHA Research Committee, and three Centers with the highest rank will be funded, contingent upon resolution of any policy concerns.

Peer Review Criteria

The following major factors will be considered in the evaluation of each Center. These factors are intended to assist applicants in determining the appropriateness of candidacy. All of the factors will be entered into the deliberations of the peer review committee, and the relative weight given each factor may differ from case to case. These factors are not listed in any specific order of priority.

Review Scoring Algorithm

I. Project – Potential impact of the Center on stroke prevention research; strengths of applicant investigators and collaborations (qualifications, expertise and productivity); scientific content; background; preliminary studies; detailed specific aims; approach detail; analytical plan; sample size; data management; proposed productivity; significance; innovation; individual project scientific merit; and total project coordination (within and among projects). (35 points)

II. Training component – A detailed plan for developing and implementing a training program that includes clinical (M.D.) training in translational research and Ph.D. training in clinical stroke investigation; qualifications and characteristics of current and anticipated trainees; didactic and practicum training opportunities; ability to track trainees; conferences and meeting participation for trainees; documentation of a ready supply of fellows; and history of successful fellowship training for clinicians and academic researchers. (25 points)
III. Collaboration – History, ability and commitment to collaborate with other institutions and within the applicant institution. Defined and detailed process for collaboration with other sites and within and among the different projects; plans to participate in a collaborative network. Evidence of formal training in leadership skills with an emphasis on collaborative leadership will be favorably reviewed. (25 points)

______        points

IV. Investigator team – Qualifications of the Director to provide scientific and administrative leadership for the Center; experience and commitment of the nominated Director; quality of interdisciplinary research team; qualifications of co-investigators; experience with stroke and stroke related studies; training experience. (10 points)

______       points

V. Environment – Institutional commitment, resources and facilities to sustain the Center; institutional resources available to complete the project; analytical resources available to the project. (5 points)

______       points

Total Points ____________ (100 points maximum)

Human Subjects and Ethical Considerations
All applications are expected to adhere to American Heart Association research program policies and standards (http://www.americanheart.org/presenter.jhtml?identifier=12150), including those regarding the ethical treatment of human subjects and animals, as well as the policy addressing inclusiveness of study populations relative to gender, race, age and socioeconomic status. Funding is contingent upon institutional review board approval. Any ethical concerns identified via the review process shall be forwarded to the AHA Research Committee for consideration.

Oversight Advisory Group

Once the Centers are selected, the ASA-Bugher Foundation Oversight Advisory Group will provide external oversight for the centers and serve in an advisory capacity to the centers. Anyone who applies to the Program and is funded will not be considered for membership on the Advisory Group, though Center Directors will report to and meet with the Advisory Group regularly. The Oversight Advisory Group also will offer advice to the AHA Research Committee’s National Research Program Subcommittee on possible changes to the program.

Responsibilities of the Oversight Advisory Group include:
- Monitoring the scientific progress of the Centers and Center Projects
- Overseeing and annually evaluating the program, including an evaluation of the progress of the trainees, making recommendations regarding continuation to the National Research Program Subcommittee
- Monitoring general implementation of collaborative efforts within and among centers. The Advisory Group will exert pressure on the centers to change traditional culture by rewarding collaboration. There will be stated consequences for centers that do not fulfill their obligations, including a statement that annual award renewal is contingent upon appropriate progress
Making recommendations to the AHA Research Committee’s National Research Program Subcommittee regarding management of the program

The Advisory Group will include:
- leading established investigators in stroke who are not funded by the Program
- investigators committed to collaboration and multidisciplinary approaches
- at least one member who is a specialist in organizational development to ensure that the program is structured to facilitate collaboration
- at least one member who is a specialist in statistics
- at least one member of the request for applications (RFA) writing group
- a representative from the AHA Research Committee’s National Research Program Subcommittee.

**Network Membership Responsibilities**

One of the key objectives of this initiative is to encourage collaboration among the stroke prevention centers, both in training and research efforts. An important component of the initiative is a multi-disciplinary approach both within and among centers. The structure of the network will include sufficient components to maximize the collaboration among centers. The Oversight Advisory Group will track collaborative activities, provide incentives for collaboration, and develop and implement a plan for regular dialogue among the Center participants. The entire network should operate as a team.

The initiative will begin with a meeting of all key staff from the Centers and the Oversight Advisory Group. This meeting, among other things, provides a forum for determining the nature and extent of the collaboration. Subsequent meetings, teleconferences, and other interactions among the Centers will occur throughout the duration of the initiative. The institutions in which the Centers are located must provide assurance that no barriers exist to thwart collaboration. A minimum requirement of the Centers is that they agree to change any local data collection system to a common one appropriate to the network. Technological support for this multi-site program with an emphasis on collaboration will be provided to facilitate all the required interactions/meetings in an effective and convenient manner.

**Program Evaluation**

Preliminary measures of the success of the initiative have been identified. Each center will be required to provide an annual and final report of progress. Progress made and plans for the coming year shall be addressed in these annual reports. In addition to the annual and final report of progress from each center, funded centers will be asked to report on the following measures:

- Productivity of centers—track publications and citations; document outcomes of research projects; document other funding resulting from the current initiative
- Transfer of intellectual property to the marketplace
- Impact of the fellowship training experience on career development: track trained fellows over a five-year period for such measures as percent of time in research, publications, other funding, promotion
- Report on the collaborative experience and lessons learned, including measures of level of collaboration, such as heterogeneity of co-authors of papers (number of academic departments represented among co-authors)
**Budget**

The Program will have a total budget of approximately $8 million. The funding will be allocated as follows:

**Projects**
Two or more projects at each of three Centers for four years $5,040,000 ($1.68m/center)

**Fellows**
Three Fellows at each Center during Years One and Two
Three Fellows at each Center during Years Three and Four
(each Fellowship award at $65,000 per year for stipend and other training-related expenses) $2,340,000 ($0.78m/center)

**Program Directors**
One Program Director at each Center for four years
(each Program Director at $50,000 per year) $600,000 ($0.2m/center)

Total $7,980,000 ($2.66m/center)

If awarded, the Director and the institution assume an obligation to expend grant funds for the research purposes set forth in the application and in accordance with all regulations and policies governing the grant programs of the American Heart Association, Inc.

The AHA is currently paying all research payments quarterly on or around the 17th of the month following the end of the calendar quarter. Payments are made to institutions on behalf of the Director or Principal Investigator. If funded July 1, the first payment to the Center would be sent on or around October 17th (and in January, April, July, and October thereafter). All payments would be in U.S. dollars.

**Timeline**

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<tr>
<th>Activity</th>
<th>Date</th>
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<tbody>
<tr>
<td>Promotion of program</td>
<td>February 2006 – September 2006</td>
</tr>
<tr>
<td>Application forms and instructions on AHA web site</td>
<td>May 1, 2006</td>
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<tr>
<td>Letter of intent deadline</td>
<td>September 15, 2006</td>
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<tr>
<td>Peer review committee recruitment</td>
<td>September 2006 – January 2007</td>
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<tr>
<td>Center and Center Projects Deadline</td>
<td>November 15, 2006</td>
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<tr>
<td>Review of proposals</td>
<td>March 2007</td>
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<tr>
<td>Funding decisions made by AHA Research Committee</td>
<td>May 2007</td>
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<tr>
<td>ASA-Bugher Centers for Stroke Prevention Research activated</td>
<td>July 1, 2007</td>
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<tr>
<td>Centers conduct research, train fellows, interact, report results</td>
<td>July 2007 – June 2011</td>
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**Letter of Intent**

Prospective applicants are asked to submit a letter of intent for the ASA-Bugher Center for Stroke Prevention Research on or before September 15, 2006. The letter should include the following information:

- Name, institution, address, telephone, and e-mail of proposed Director
- Names, institutions, addresses and e-mails of proposed Principal Investigators for Center research projects
- Names, institutions, addresses and e-mails of other Key Personnel, such as mentors for the training/fellowship program
- Any additional participating/affiliated institutions not listed above

A letter of intent is not required, is not binding, and does not enter into the review of a subsequent application. It is strongly encouraged, since the information it contains allows AHA staff to estimate the potential peer review workload and to avoid potential conflicts of interest in the peer review process. It also allows AHA to provide potential applicants with updated information about the application process if necessary.

The letter should be sent electronically via e-mail to the American Heart Association at ncrp@heart.org with a subject heading of ASA-Bugher Center.

**Inquiries**

Inquiries regarding this RFA may be sent to:

E-mail    ncrp@heart.org  
Phone    214-706-1458 or 214-706-1457  
Fax    214-706-1341