

American Heart Association Strategically Focused Hypertension Research Network Request for Applications

The American Heart Association (AHA) is a non-profit, voluntary health organization funded by private contributions. The mission of the American Heart Association is to build healthier lives, free of cardiovascular disease and stroke. The Guiding Values of the organization include:

- Improving and Extending People's Lives
- Bringing Science to Life
- Speaking with a Trustworthy Voice
- Building Powerful Partnerships
- Inspiring Passionate Commitment
- Meeting People Where They Are
- Making an Extraordinary Impact
- Ensuring Equitable Health for All

A leading priority of the AHA is to fund research that increases an understanding of the causes, prevention and treatments of cardiovascular diseases and stroke. These diseases remain the No. 1 and No. 4 killers of Americans, respectively.

The American Heart Association has a tradition of support for research spanning more than 60 years. Research is the foundation of all other aspects of the AHA's lifesaving work, generating a tremendous impact on people's lives. After the NIH, the AHA is the leading funder of cardiovascular disease (CVD) and stroke research in the U.S. with over \$3.4 billion spent on research since 1949. One of the many striking outcomes of AHA's research program is the funding of 13 scientists who have gone on to be awarded the Nobel Prize.

The Strategically Focused Research Network (SFRN) is a mechanism that provides AHA an opportunity to address key strategic issues as determined by the AHA Board of Directors. This SFRN will focus on "hypertension" with the AHA supporting four (4) Research Centers for a period of four (4) years. These four (4) Centers will constitute the Network and will receive a total of \$15 million award over that period (including costs for Network oversight and administration). The goal is to select and award four (4) Hypertension Centers. The desired characteristics of these Centers, the general requirements of the application and the peer review criteria are described in this Request for Applications (RFA).

Objectives of Request for Applications

The American Heart Association has adopted 2020 goals to improve the cardiovascular health of all Americans by 20% while reducing deaths from cardiovascular disease and stroke by 20%. Scientists and clinicians have played a major role in achieving AHA's 2010 goal to reduce coronary heart disease (CHD), stroke and risk by 25%.

For example, basic scientists have identified the pathophysiologic processes underlying heart disease and stroke, and identified pathways for potential novel therapeutic interventions. Clinical scientists have helped to identify therapeutic agents and approaches that are effective in the prevention and treatment of cardiovascular disease, and traditional and novel risk factors. And population scientists have identified, among others, effective strategies for the prevention of risk factors (primordial prevention), heart disease and stroke targeted to specific populations with varying degrees of susceptibility to these diseases.

However, despite these significant advances, cardiovascular diseases and stroke remain the number 1 and number 4 killers in America, respectively, and among the leading causes of death globally. Additionally, the risk and burden of these diseases is disproportionately greater among underserved minorities. There are many strategies and pathways that researchers can follow to discover new knowledge that support the AHA's goal to promote healthier lives free of cardiovascular diseases and stroke.

For the intention of this particular RFA, AHA's conceptual framework is that the prevalence and control of hypertension are impacted by both heritable and lifestyle factors, as well as the presence of comorbidities, which can bring together multidisciplinary and cross-disciplinary teams. Specifically, this RFA seeks to have basic, clinical and population teams from individual Centers join together and provide proposals which address the topic of hypertension via their individual areas of expertise. A Center may be intra- or inter- institutional. Each Center applies for funding individually and is peer reviewed by the AHA. The most meritorious Center applications and their research projects will be combined by the AHA to form the Strategically Focused Hypertension Research Network (see Illustrations 1 and 1.1).

It should also be noted that the increased availability of consumer-oriented health tools and social media, among others, has created unconventional opportunities for natural experiments and novel interventions that could inform the development of effective health behavior change strategies aligned hypertension awareness and control. Multidisciplinary research that takes advantage of such innovative tools also falls within the scope of this RFA. Furthermore, collaboration is encouraged with social and behavioral scientists, health policy experts, and other experts to identify programs that effectively modify an individual's lifestyle in a fashion that unequivocally reduces the risk and severity of hypertension.

The AHA is committed to an investment of \$15 million to establish this Hypertension Network which provides almost \$4 million per Center. This level of investment will support fully integrated collaboration across science disciplines.

The AHA intends to fund four Centers that will encompass the following goals:

- Accelerate generation of important, novel ideas
- Answer significant questions addressing gaps in knowledge
- Create important gains (developing new investigators is one such gain)
- Link research and training components through the program
- Prioritize multidisciplinary approaches with frequent collaborative interactions
- Demonstrate efficacy through data collection and evaluation
- Demonstrate the effectiveness or the applicability of the findings in clinical, public health or community-based settings such as workplaces, schools, churches or other "real-life" settings.

It is anticipated that the results of the funding and formation of the AHA Strategically Focused Hypertension Research Center Network and their linking in this structure will:

- Produce a cadre of new investigators who will energize the hypertension 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
- Identify programs and policies that result in individual lifestyle modifications that reduce risk and improve control of hypertension.

Although successful applicants are asked to demonstrate effectiveness of the research outcomes by articulating a plan proposing how the results could be implemented in clinical or public health settings, this does not guarantee that funds will be available for the proposed implementation. However, the plan will assist the AHA in exploring opportunities to advance the research findings therefore it is strongly preferred that successful applicants articulate such a plan.

Examples of multidisciplinary research approaches

The intent of this initiative is to support a collaboration of basic, clinical and population researchers from different disciplines whose collective efforts will lead to new approaches, to improve the prevention, treatment, and control of hypertension. Following is an illustrative list of example questions that could be addressed by a Center. The examples below display the spectrum of research that can be performed within a Center, but are not intended to represent the level of integration, from basic to population science. Evidence of synergy among the projects will be expected to comprise the strongest applications.

Example 1: Focus on Hereditary Factors Influencing Hypertension

Basic science questions:

1. What effects do epigenetic changes have on blood pressure control?
2. Are common mitochondrial variants associated with the risk and severity of hypertension?

Clinical science questions:

1. How do *ADRB1* and *AGT* polymorphisms affect response to antihypertensive therapy?
2. How does exposure to specific environmental factors affect blood pressure in cohorts harboring common variants at hypertension-associated loci?

Population science questions:

1. How do age-related changes in the levels of specific sex hormones affect blood pressure?
2. What is the genetic basis for racial disparities in the prevalence of hypertension?

Example 2: Focus on Lifestyle Factors Influencing Hypertension

Basic science questions:

1. Which genetic pathways control salt sensitivity in humans?
2. What molecular mechanisms are involved in abnormal spiral artery remodeling during pregnancy?

Clinical science questions:

1. Can eHealth, exercise or diet effectively lower blood pressure in the intermediate term in ethnic/racial minorities? In older

- adults? In rural settings?
2. Which aspects of physical activity (eg, frequency, duration, intensity) are related to the greatest reductions in blood pressure?

Population science questions:

1. What programs and policies are effective in reducing sodium consumption?
2. Which factors are associated with blood pressure increases related to the use of oral contraceptives?

Example 3: Focus on Comorbidities of Hypertension

Basic science questions:

1. How do *APOL1* variants contribute to the development of renal disease, particularly in African Americans?
2. What is the contribution of specific molecular pathways (eg, inflammation and oxidative stress, dysfunctional baroreflex activation, the renin-angiotensin-aldosterone and sympathetic nervous systems) to obesity-related hypertension versus other subforms of the disease?

Clinical science questions:

1. How should hypertension be managed following acute ischemic stroke? (eg, When should antihypertensive therapy be initiated? What blood pressure targets should be used? Which classes of agents should be used?)
2. How can combination therapy be optimized to reduce or prevent progression of diabetic nephropathy?

Population science questions:

1. What factors determine whether patients will achieve significant blood pressure improvement as a result of treatment for obstructive sleep apnea?
2. Is antihypertensive treatment associated with reduced or altered development of white matter lesions?

Example 4: Focus on Blood Pressure Monitoring & Treatment

Basic science questions:

1. What animal models are most representative of resistant hypertension in humans?
2. Is immunotherapy effective for severe resistant or malignant hypertension in animal models?

Clinical science questions:

1. What assessment of blood pressure (eg, ambulatory blood pressure monitoring [ABPM], blood pressure load, mean arterial pressure) correlates most closely with target organ damage?
2. Does target-based or benefit-based treatment for hypertension lead to superior outcomes?
3. How do nonpharmacological interventions compare in their abilities to reduce blood pressure?

Population science questions:

1. What impact does *Check. Change. Control.* have on blood pressure control at a national level?
2. Which elements of hypertension programs have the greatest impact on control rates?
3. How should the diagnostic schema and reference values for ABPM vary by age, sex, and ethnicity?

Additional investigative areas that would be responsive to this RFA may include, but are not limited to:

- Identification and evaluation of effective strategies for the prevention and control of hypertension
- Understanding the pathophysiology and/or improving disparities in the prevalence of hypertension within specific populations (e.g.: racial, urban vs. rural, men vs. women) across the lifespan
- Research aimed at identifying and characterizing therapeutic targets for the treatment of hypertension
- Research aimed at identifying mechanisms of increased renal sodium reabsorption initiating hypertension.
- Determining the influence of minerals in combination, other than sodium, on blood pressure
- Cross-disciplinary approaches to the prevention and control of hypertension
- Basic, clinical, population and global health strategies to promote blood pressure control
- Research aimed at identifying therapies for hypertensive diastolic heart disease
- Research aimed at identifying new drug targets
- The use of genomics and/or other omics to develop stratified or precision medicine
- Leveraging natural experiments that use novel behavior change strategies in community-based or public settings
- Partnering with social scientists, behavioral psychologists and others to identify best practices for improving treatment compliance

Disciplines and Expertise

Multidisciplinary teams are appropriate and desired and can be broadly defined. Basic disciplines such as cell/molecular biology, biochemistry, bioengineering/biotechnology, immunology/virology, genetics/genomics, physiology, vascular biology, geneticists and bioinformaticians among others are all appropriate. Clinical disciplines, general internal medicine, nutrition and dietetics; cardiology, pediatric cardiology, cardiovascular surgery, exercise physiology, nephrology, anesthesia, nursing, emergency medicine, kinesiology, endocrinology, neurology, psychiatry and behavioral science are all appropriate. In addition, public health disciplines including the fields of health communications, health marketing, informatics, individual and collective behavior are all of interest. Epidemiological, interventional, and behavioral science, biostatistical, and health economic approaches are appropriate to the focus of this program as well as eHealth and related technologies.

Key Requirements of the Center Application

This RFA embraces a Network “Center” concept. Thus, it would be appropriate for three (3) studies to be submitted from each Center applying to be in the Network and to have an integration of these studies within each Center. Each Center will include several components: a designated Center Director, three (3) synergistic projects related to the topic of hypertension, and a research postdoctoral fellowship training component.

In addition to Centers that integrate synergistic projects, as per the four examples above, Centers can also demonstrate a high degree of collaboration by working on one comprehensive research project across all sites. For example, a Center application can be built around a comprehensive but pragmatically designed randomized trial on sodium reduction, using a clinical epidemiology approach to prospectively track the effects of sodium intake on clinical endpoints, while developing ancillary studies of a more basic/biomedical nature.

The development of each Center will be the responsibility of the Center Director, who will coordinate the projects and the training program, to ensure that they are not only complementary, but also effective in producing a greater outcome than if they were executed individually. 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 Strategically Focused Hypertension Research Network Oversight Advisory Committee.

A major component of the Centers selected for funding under this initiative will be their ability to foster a successful program for 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.

Program Structure

Each Center will:

- Conduct three (3) cohesive research projects of scope equivalent to an R01
- Provide a training program for fellows, training three (3) Center-funded postdoctoral fellows during the period of the award
- Be linked to the other Centers by interactions/meetings to accelerate exchange of ideas, encourage sharing of commonly-useful knowledge and methods, and provide networking opportunities for trainees
- Report annually on its efforts towards integration with the other centers, as well as observations on successes/challenges of such integration
- Interact as part of the American Heart Association Strategically Focused Hypertension Research Network

Postdoctoral Fellowship Training Requirements:

- Each Center will provide a multidisciplinary training program to give fellows basic, clinical, population, and translational research experience.
- Each Center will train 3 fellows during the period of the award (one two-year fellowship in years one and two; one two-year fellowship in years two and three and a final two-year fellowship in years three and four).
- Each Center will provide professional, non-medical training in the form of presentation and communication skills.

Collaboration Requirements:

- Centers will be expected to meet and collaborate with each other through interactions and meetings to accelerate information exchange and ideas;
- Centers will be expected to comprise a team that meets on a regular basis and develops one or more collaborative projects;
- Centers will collaborate and participate in producing an end-of-award report about the challenges, mechanisms and successes of the Centers' collaborations;
- Centers will consider themselves part of the AHA Strategically Focused Hypertension Research Network.

Collaboration Expectations

Once awarded, there is an expectation that the four (4) Centers will interact with each other, in particular to provide networking opportunities for trainees, to encourage sharing of commonly-useful knowledge and methods, and to provide a stimulating atmosphere for research collaborations. Strategies for communication and interaction among the Centers should be

addressed in the proposal and could include ways to encourage interaction, augment or expand that Center's study findings, share training opportunities for fellows and junior investigators, etc. Center personnel will be expected to participate in annual meetings and visits to other centers in the network. Annual progress reports describing each Center's efforts towards integration, as well as a report on successes/challenges of such efforts, will be required.

Centers selected for funding will be expected to interact and develop new hypotheses leading to collaborative projects. The collaborating Centers are expected to share everything from "samples to ideas." The Centers will be expected to work with the AHA Oversight Advisory Committee to define the strategies for leadership in training and interdisciplinary collaboration, as well as a clear commitment to collaboration with other disciplines and other centers.

Eligible Institutions and Investigators

Awards are limited to non-profit institutions in 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. 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.

The Centers are not transferable to other institutions. An institution may submit only one AHA Strategically Focused Hypertension Research Network Center application for this competition. Individuals at the applicant institution who are not participating in their institution's center application (and/or its three project applications) may participate in another separate institution's center application. Individuals participating in their institution's center application, other than the Center Director or Center Training Director, may participate in a separate institution's center application. 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 Center Director's institution will maintain fiscal responsibility for the entire award. The appropriate Institutional Officer should sign off on the proposal in AHA's online grants management system, Grants@Heart.

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, and have a faculty or staff appointment. Directors and Principal Investigators of projects at the Centers may hold another AHA award simultaneously. The Center Director may also serve as a Project PI on the Center application. There is a 20% minimum effort requirement for the Director and a 10% minimum effort requirement for Principal Investigators (PI) of Center projects. Director and Project PI salary requested must be proportional to the percent effort devoted to the Center. An individual who holds a Director position within the Center application (Center Director or Center Training Director) may not serve in a director capacity on another institution's application.

The Center Director must demonstrate expertise in the area of hypertension research, with demonstrated ability to build a Center team. The Director should ideally demonstrate a successful history of leadership in a research project team and in career development. A clear demonstration of the Director's commitment to integration with the other Centers is required. Experience in multi-institutional collaboration is encouraged.

The responsive application will demonstrate a history of successful post-doctoral fellowship

training with a plan to continue the program or a strong plan to develop a successful program. In addition, training in clinical outcomes research and translational research concepts as well as collaborative research should be described in the application. Collaborative interdisciplinary training programs are encouraged.

A viable source for identifying and recruiting trainees must be presented in the application and while trainees are not required to be named at the time of the application submission, the first set of fellows must be identified by July 1 of 2015. 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.

Citizenship Requirements for Directors, Principal Investigators and Fellows

Directors 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)
- G-4 Visa – family member of employee of international organizations and NATO

Principal Investigators of proposed projects 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)
- E-3 Visa – specialty occupation worker
- H1-B Visa – temporary worker in a specialty occupation
- O-1 Visa – temporary worker with extraordinary abilities in the sciences
- TN Visa – NAFTA professional
- G-4 Visa - family member of employee of international organizations and NATO

Named fellows of the Centers 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)
- E-3 Visa – specialty occupation worker
- H1-B Visa – temporary worker in a specialty occupation
- O-1 Visa – temporary worker with extraordinary abilities in the sciences
- TN Visa – NAFTA professional
- J-1 Visa – exchange visitor
- F-1 Visa – student
- G-4 Visa - family member of employee of international organizations and NATO

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

Fellowship Qualifications

Named fellows of the Centers at U.S. institutions must hold a Ph.D., M.D., D.O., D.V.M. or equivalent doctoral degree and commit 75% effort to research training. Center fellows may commit a minimum of 70% effort if justification is accepted by the AHA Oversight Advisory Committee. 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% effort to research training. A named fellow may have been a recipient of an AHA fellowship, but may not hold an AHA affiliate fellowship or AHA Fellow-to-Faculty Transition Award at the same time as an AHA Strategically Focused Hypertension Research Network fellowship.

Other Relevant Policies

The Center awards are not transferable to other institutions. The projects described can have no scientific or budgetary overlap with other funded work. Any inventions, intellectual property, and patents resulting from this funding are governed by the AHA Patent, Intellectual Property and Technology Transfer Policy. The applicant/awardee and institution are responsible for compliance with all American Heart Association research award policies and guidelines for the duration of any awards they may receive. Go to Policies Governing All Research Awards to review AHA policies

at http://my.americanheart.org/professional/Research/FundingOpportunities/ForScientists/Policies-Governing-All-Research-Awards_UCM_320256_Article.jsp .

Application Submission Process

Only one Center proposal, including multiple research project proposals, may be submitted from an institution. Each Center application should have only one (1) Center Director. Co-Directors will not be recognized on official documents or publications. The completed application must include the primary Center application, three individual research project applications, and the overall training plan. The components of the application are described below.

Application instructions for the AHA Strategically Focused Hypertension Research Centers will be available on the American Heart Association's [website](#) approximately mid-June 2014. Applications will only be accepted through AHA's online research system – Grants@Heart.

Components of Application

Primary Center Application

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

- 1) Center Science Vision and Synergy (*a clear, unifying central theme to which each research project application relates*); *a center should be viewed as a group of interrelated research projects that are complementary and synergistic.*
- 2) Information regarding the Director
- 3) Information regarding any current hypertension research programs and any history of successes in hypertension research
- 4) A detailed description of the multidisciplinary training program for the AHA Strategically Focused Hypertension Research Center two-year fellowships (basic, clinical and translational research exposure), including information regarding the selection of prospective fellows and how funded fellows' ongoing progress will be guided via an individual development plan (IDP) and evaluated at least annually. In addition to participating in annual SFRN Center meetings, Centers are expected to incorporate collaboration with established investigators at other Hypertension Research Network Center institutions through regular meetings and/or Center-to-Center visits
- 5) Information on current training programs and training grants within the Center institution and affiliated institutions relative to the research being proposed (if appropriate)
- 6) Information regarding other faculty/staff members at the Center institution and affiliated institutions (if appropriate) who will be submitting research projects
- 7) Information on research funding available to the Director and proposed Principal Investigators on Center research projects
- 8) Information on existing collaborative research teams within the Center institution and affiliated institutions (if appropriate) and their ability to share information and methodologies with other institutions. Documented evidence that other collaborations have produced synergistic results.
- 9) Information on facilities available to support the Center and affiliated institutions' (if

- appropriate) research projects
- 10) An overview of the estimated four-year budget for the Center
 - 11) 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

Center Research Project Applications

A Center research application must include three (3) synergistic research projects related to hypertension research. Each project should demonstrate importance and relevance of the research to the field of hypertension. The projects proposed by a Center will be reviewed as a group.

Submitted projects must be feasible within the budget described. American Heart Association research funds will not be awarded to supplement or duplicate any work which is being supported by other funding agencies.

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) Preliminary data on same or related problems
- 6) Contemplated methods of approach to problem
- 7) Evidence of successful collaboration with other Center members
- 8) Ethical and human subject aspects

Peer Review Process

Review of the applications will be conducted by the American Heart Association and will occur in two phases. For the first phase, a peer review committee of volunteer scientists will be assembled to review all the submitted Center applications. Appropriate scientific expertise will be sought to review the applications received. Each application will be reviewed in depth by a minimum of three (3) peers and more than likely four (4) reviewers will be analyzing each aspect of the submission, i.e. Center, Projects, Training Program and Collaboration. These reviews will be presented to a peer review panel of 12 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 current AHA review scoring system. The Centers and their projects will be ranked, based upon the average merit scores and percentile ranking of the panel members' scores.

A second stage of the review will then be conducted with only the highest ranked Center applications, and will include a "reverse site visit" presentation to the AHA review group by the Center Director and select members of the Center team. A minimum number of participants, to be decided by the AHA, will be invited to the reverse site visit. Reviewers will score the Centers as a whole following the presentations, with the average of the reviewers' scores providing the final ranked list of applications. The ranked list will be reviewed by the AHA Research Committee. The four 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 these

factors will be entered into the deliberations of the peer review committee. These factors are not listed in any specific order of priority.

I. Projects – Potential impact of the project on hypertension research; strengths of applicant investigators (qualifications, expertise and productivity); potential for collaboration or synergy of projects; scientific content; background; preliminary studies; detailed specific aims; approach detail; analytical plan; sample size; data management; significance; innovation; individual project scientific merit; and total project coordination (within and among projects). Projects will be rated on the following areas:

- **Approach:** Are the conceptual framework, design, methods and analyses adequately developed, well integrated, well-reasoned and feasible (as determined by preliminary data) and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?
- **Innovation:** Is the project original and innovative? For example: Does the project challenge existing paradigms and address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
- **Investigator:** Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?
- **Significance:** Does this study address an important problem broadly related to cardiovascular disease or stroke? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods and technologies that drive this field?
- **Environment:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?
- **Impact:** How does the project relate to and support the mission of the American Heart Association to **building healthier lives, free of cardiovascular diseases and stroke**?
- **Relationship to other Center projects:** Does the project complement other aspects of the proposed Center, including other Center projects? Is there evidence of synergy among the projects and training component of the Center?

II. Training component – A detailed plan for developing and implementing a postdoctoral training program that includes clinical (M.D.) or Ph.D. training in hypertension research; qualifications and characteristics of current and anticipated trainees; didactic and practicum training opportunities; plan for the selection of prospective fellows and how funded fellows' ongoing progress will be guided via an individual development plan (IDP) and evaluated at least annually. Plan for involving fellows in annual Center meetings and Center-to-Center visits, along with identifying opportunities for fellows to work with established investigators at other network Centers; ability to track trainees; conferences and meeting participation for trainees; documentation of a ready supply of fellows; and history of successful fellowship training for hypertension researchers.

III. Center Team – Qualifications of the Director to provide scientific and administrative leadership for the Center; experience and commitment of the nominated Director; quality of hypertension research team; qualifications of investigators and co-investigators; experience with hypertension related studies; training experience.

IV. Environment – Institutional commitment, resources and facilities to sustain the Center; institutional resources available to complete the project; analytical resources available to the project; letter from Center Director's Department Head assuring the department and institution's support of the Center along with confirmation that the Center Director will devote at least 20% effort towards the Center. Other Center personnel may be appointed to assist the Director in the administration of the Center. However, the Director will be required to devote 20% effort to the Center.

V. Interaction Plan within and among Centers—Plan for and commitment to sharing of commonly-useful knowledge and methods, providing a stimulating atmosphere for research collaborations, and providing networking opportunities for trainees. Cited strategies for communication and interaction among the Centers.

Peer Review Scoring Criteria

I. Projects – Potential impact of the project on hypertension 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).

(30%) of total evaluation

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 hypertension research investigation; opportunities for non-medical training including communication and presentation skills; didactic and practicum training opportunities; ability to track trainees; conferences and meeting participation for trainees; documentation of a ready supply of fellows; qualifications and characteristics of any current or anticipated trainees and history of successful fellowship training for clinicians and academic researchers.

(20%) of total evaluation

III. Collaboration – History, ability and commitment to collaborate with other institutions, investigators and within the applicant institution. Defined and detailed process for collaboration with other sites in addition to within and among the proposed different projects; plans to actively participate in a collaborative network. Evidence of formal training in leadership skills with an emphasis on collaborative leadership will be favorably reviewed.

(25%) of total evaluation

IV. Center Director – Demonstrated ability to lead others, along with experience and commitment to the success of the Center, the projects contained within, and the Network as a whole. Documented evidence of willingness to collaborate with others outside their institution to share ideas, science, etc. to progress the field of hypertension research.

(10%) of total evaluation

V. Investigator team – Qualifications of each PI to provide scientific and administrative leadership for their respective projects; demonstrated commitment of each PI, and experience with hypertension studies; quality of interdisciplinary research team; qualifications of co-investigators; training experience.

(10%) of total evaluation

VI. Environment – Institutional commitment, resources and facilities to sustain the Center; institutional resources available to complete the project; analytical resources available to the project.

(5%) of total evaluation

Reverse Site Visit Expectations

If a Center application is selected to move to the 2nd phase of review, they will have the critiques and committee member comments available electronically at the time of notification. The Center Director and key personnel will have approximately 3-4 weeks to prepare for the reverse site visit. The committee members will listen to the presentation in response to the critiques, plus any additional information that is presented. There will be a question and answer period, so the actual presentation should not be more than 30 minutes, which will allow for responses and follow-up questions from the panel. The entire reverse site visit will last approximately 45 minutes.

Human Subjects and Ethical Considerations

All applications are expected to adhere to American Heart Association research program policies and standards including those regarding the ethical treatment of human subjects, as well as the policy addressing inclusiveness of study populations relative to gender, race, age and socioeconomic status. Institutional review board approval will be handled on a “just in time” basis and will be required by the date of the first quarterly payment made to the institution. Funding is contingent upon institutional review board approval initially and for the duration of the award. Any ethical concerns identified via the review process shall be forwarded to the AHA Research Committee for consideration.

http://my.americanheart.org/professional/Research/FundingOpportunities/ForScientists/Policies-Governing-All-Research-Awards_UCM_320256_Article.jsp

Oversight Advisory Committee

Once the Centers are selected, the AHA Strategically Focused Hypertension Research Oversight Advisory Committee 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 Committee. Center Directors and project PI's will report to and meet with the Advisory Committee regularly. The Oversight Advisory Committee also will offer advice to the AHA Research Committee on the progress of the Centers and any issues that arise in their administration.

Responsibilities of the Oversight Advisory Committee 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 AHA Research Committee
- Monitoring and encouraging interaction efforts within and among Centers. The Advisory Committee will encourage Centers to change traditional culture by rewarding interaction and will request an annual report on the successes and challenges resulting from efforts to interact
- Making recommendations to the AHA Research Committee regarding management of the program

The Advisory Committee will include:

- Leading established investigators in hypertension research who are not funded by the program
- Investigators experienced in multidisciplinary approaches
- at least one (1) member who is a specialist in (bio)statistics
- at least one (1) member who is a specialist in epidemiology
- at least one (1) member who is a specialist in economics and social science

- at least one (1) member of the request for applications (RFA) writing group
- a representative from the AHA Research Committee

Network Membership Responsibilities

One of the key objectives of this initiative is to encourage interaction among the Strategically Focused Hypertension Research Network Centers, both in training and research efforts. An important component of the initiative is a multi-disciplinary approach both within and among Centers that comprise the Network. The structure of the Network will include sufficient components to maximize the interaction and collaboration among the Centers. The AHA Oversight Advisory Committee will track and encourage interactive and collaborative activities, 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 Committee. This meeting, among other things, provides a forum for determining the nature and extent of interactions, collaboration and information sharing. 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 and sharing of ideas. A minimum requirement of the Centers within the Network 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 interim report, as well as a final written scientific 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, and promotions
- Report on the interaction among the Centers 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 \$15 million. The funding will be allocated as follows:

	Network Totals	Center Totals
<u>Projects</u>		
Three projects at each of four Centers for four years <i>Maximum of \$711,000 per year to be divided among the Projects funded at the Center. PI must commit at least</i>	\$11,376,000	\$2.844M/Center

10% effort to project. While there is not a stated maximum on Project PI salary and fringe, these items must be commensurate with percent effort devoted to the project.

Fellows

Three Fellows at each Center for two years each \$ 1,200,000 \$0.3M/Center

Center Director

One Director at each Center for four years \$ 800,000 \$0.2M/Center
*A maximum of \$50,000 per year for each Director.
 Center Director must commit at least 20% effort*

Center Travel Costs

Covers travel for Center personnel to Center network meetings and other integration activities. \$ 112,000 \$28,000/Center
\$7,000 per year must be allocated to Center Travel.

Direct Costs (Total)

Research Dollars \$13,488,000 \$3.372m/Center

Indirect Costs

AHA Policy allows for a maximum of 10% for indirect costs \$ 1,348,800 \$0.3372M/Center

Total **\$14,836,800** **\$3.7092M/Center**

The total amount requested per Center, *including* 10% indirect costs, annually may not exceed approximately \$3.7 million for the 4-year award.

The Center Director will be responsible for overseeing the total budget for his/her Center within the Network. 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. If activated on April 1, the first payment to the Center would be sent on or around July 17th (and in October, January, April and July thereafter).

Timeline

Activity	Date
Promotion of program	March 2014
Request for Applications Published	May 2014
Application instructions on AHA web site	June 2014
Letter of Intent deadline	August 1, 2014
Center and Center Projects Deadline	November 3, 2014
Review of proposals (two phases)	January/February 2015

Funding decisions made by AHA Research Committee / Applicants Notified	March 2015
AHA Strategically Focused Hypertension Research Centers activated	April 1, 2015
Centers conduct research, train fellows, interact, report results	April 2015 – March 2019

Letter of Intent

Prospective applicants are required to submit a Letter of Intent for the AHA Strategically Focused Hypertension Research on or before **August 1, 2014**. The letter should include the following information:

- Name, institution, address, telephone, and e-mail of proposed Center Director
- Name, institution, address, telephone, and email of proposed Center Training Director
- Names, institutions, addresses, telephones, and e-mails of proposed Principal Investigators for Center Research Projects
- Names, institutions, addresses, telephones, and emails of other Key Personnel – collaborators, consultants, etc.
- Information on any additional participating/affiliated institutions not listed above
- Brief overview of the 3 proposed projects – please label project “Basic” “Clinical” or “Population.” Include a maximum 1-2 paragraph project summary on each project along with the proposed project title.

While a Letter of Intent is required it does not enter into the review of said subsequent application. The information provided in a Letter of Intent 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 applicants with updated information about the application process if necessary.

The Letter of Intent should be sent electronically via e-mail to the American Heart Association with a subject heading of AHA Strategically Focused Hypertension Research Network.

Inquiries

Inquiries regarding this RFA may be sent to:
 Phone 214-360-6107

Glossary of Terms

Basic Science	The study of fundamental life processes. This type of research is often purely theoretical with the intent of increasing our understanding of certain phenomena or behaviors but is not directly aimed at solving a specific prevention or treatment issue.
Center	A Center is comprised of a Center Director, Center Training Director and multiple Project PIs. These individuals may be located at the same or separate institutions as long as there is evidence of past and/or current collaboration. Centers will work together to move research forward in the area of study.
Center Director	The Director serves as the leader of his/her Center. This individual is renowned as an expert in the science topic being proposed and provides leadership, training and collaboration experience.
Center Fellow	A Center Fellow has a post-baccalaureate doctoral degree (MD, PhD, DO, DVM, PharmD). These individuals will be highly involved in the work being proposed by the Center and will be encouraged to collaborate with fellows across the network. The Center Fellows will work closely with the Center Training Director and Center Director on their individualized multidisciplinary training plan.
Clinical Science	Addresses important questions of normal function and disease using human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) wherein an investigator or colleague directly interacts with human subjects. It includes research on mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, but does not include in vitro studies using human tissues not linked to a living individual.
Collaboration	Collaboration is defined as a process where two or more individuals or organizations work together to complete a task and achieve shared goals - a deep, collective, determination to reach an identified objective — by sharing knowledge, learning and building consensus.
Letter of Intent	The Letter of Intent is used by the AHA to gather information on prospective applicants – quantity of expected applications, projects being proposed, etc.
Multidisciplinary Research	Multidisciplinary Research brings different disciplines together to explore a topic from different perspectives. Collaboration across the disciplines is key to create new approaches, ideas, knowledge base, etc.
Oversight Advisory Committee	A group of scientific volunteers in the named strategic area tasked with supervising the progress and direction of the Centers in the Network to ensure that the goals of each project, each training program, cross-center collaboration, etc. are met and accomplished during the life of the Network.
Population Science	The science and art of studying the distribution and determinants of health status as influenced by social, economic and physical environments, human biology (including genetics and genomics), health policy and services and of preventing disease, prolonging life and promoting health at the population level. Population health research may include epidemiologic and behavioral

	studies, outcomes research, and health services research.
Project PI	A Project PI is an independent investigator responsible for carrying out the scientific research project proposed in their application. They must provide evidence of successful research accomplishments and their ability and commitment to collaborate and share knowledge with others.
Reverse Site Visit	A reverse site visit occurs during the second phase of peer review for the Strategically Focused Research Network applications. The visit consists of an in-person presentation by the proposed Center Director and Project PIs, to the AHA Peer Review Committee. The reverse site visit is held at a neutral location and will consist of a brief oral presentation followed by a question and answer period.
Strategically Focused Research Network – aka Network	A Network is composed for multiple Centers, each at different institutions, coming together to study a common topic determined by the AHA to encourage collaboration and move the science community forward.
Synergy	Synergy is the ability of a group to produce something greater than the sum of its parts; the ability of the group to outperform even its best individual member.
Training Director	The Training Director is responsible for the direction and execution of the training program of the center postdoctoral fellows. This program should include multidisciplinary approach to training and developing the fellows in the area of research being proposed by the Center.