American Heart Association Cardiovascular
Genome Phenome Study (CVGPS)
Applications for Grants

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. These diseases remain the No.1 and No.4 killers of Americans, respectively. 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.

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 Cardiovascular Genome Phenome Study (CVGPS)

The Cardiovascular Genome Phenome Study (CVGPS) is a collaborative effort, spearheaded by the American Heart Association (AHA), to accelerate the future of cardiovascular medicine. CVGPS combines the power of long-term population studies with the precision of molecular analysis to unravel key distinctions between and within subgroups of patients. The discoveries it generates will point the way toward better-targeted, safer, and more effective treatments, based on a deeper understanding of patients’ characteristics, including e.g. risk profiles and therapeutic needs.

The CVGPS is a collaboration among AHA, Boston University (BU) and the University of Mississippi Medical Center (UMMC), the academic coordinating center homes, respectively, of the Framingham Heart Study (FHS) and the Jackson Heart Study (JHS). The Jackson Heart Study also involves Jackson State University (JSU) and Tougaloo College (TC) as partner institutions. These institutions are making available these large databases as the initial dataset for new research projects; other diverse population studies will be added to CVGPS via this collaboration. The multi-generational FHS is the nation’s best-known and longest-running heart research program. The JHS is the largest research effort focused on African-Americans, who face increased risks for heart disease and stroke. Population studies such as Framingham and Jackson have helped lay the groundwork for today’s cardiovascular treatments and preventive strategies.

The intent of the CVGPS is to converge these vast repositories of clinical and genomic data and add on other diverse population studies, established and proposed, to create a database unique in scale, diversity, and potential for gleaning new insights. The CVGPS will consolidate disease state and patient-specific data with a bio bank of molecular information from tissue samples meticulously stored, in some cases for decades, from participating population studies. These phenotypic and genotypic resources will be made available to researchers within an integrated network, with strict...
controls on database security and integrity. The ongoing growth of this network of cardiovascular studies will add to the initiative’s value and opportunities for innovation.

Through the rich diversity of its constituent participant/patient populations, CVGPS research will bring inter-individual and patient-to-patient differences into ever sharper focus for common diseases such as atherosclerosis and hypertension. Investigators will be able to correlate genomic variations with disease course and severity, treatment responses, demographics, and both routine and novel diagnostic measures, for a 360-degree look at cardiovascular health and disease. This comprehensive understanding will enable faster and more efficient development of targeted new drugs and implementation of earlier prevention programs.

To accomplish the promise of the CVGPS, AHA is offering 2 grant mechanisms to investigators. They are the:

**CVGPS Pathway Grants and CVGPS Grand Challenge Awards**

The CVGPS Pathway Grants (Pathway) will be funded at $250K/year for 2 years for a total of $500K and the CVGPS Grand Challenge Awards (Challenge) will be funded at $500K/year for 4 years for a total of $2MM. The desired characteristics of these grants, general requirements of the application, letter of application and the peer review criteria are described in this Request for Applications (RFA).

Applications can include: a) use of data from either the FHS and/or the JHS cohort, b) new enhanced data from the FHS and/or JHS cohorts, c) new data from new clinical/population samples or d) new enhanced data from other established cohorts.

**Objectives of Request for Applications**

The broad objectives of the new collaboration are to:

- conduct novel ‘dense’ phenotyping that will substantially add to extant genotypic, OMICs, and phenotypic data collected from an expanded sample set that extends beyond the existing FHS and JHS funded cohorts. The integrative data-exchange across the datasets using varying depths of phenotyping should provide important insights into the pathways to CVD.

- build a state-of-the-art phenotypic and genotypic repository that will integrate previously collected data from FHS/JHS in their current repositories with new phenotypes collected on these cohorts and other new samples (in the new CVGPS biorepository) This repository will be open to qualified investigators.

- build a national network biorepository resource by building upon the foundational population science resources of the AHA-FHS-JHS partnership. Leverage the collective talent and experience of AHA, FHS, and JHS in population science to establish best practice data-sharing standards and harmonize the dense phenotyping across datasets so that the knowledge harnessed will have wider generalizability and facilitate detailed analyses of the determinants of CVD risk and ethnic and socioeconomic differences therein;

- develop (where necessary) and implement analytical methods and tools for trans-ethnic
comparisons and meta-analyses, integration of genetic/OMIC and phenotypic data (standard and novel) with state-of-the-art approaches such as network and systems modeling, and dissemination and distribution of individual level data and meta-data to researchers world-wide (with appropriate protection of participant confidentiality) to promote CVD research; and

- introduce ‘e-health’ methods for digital data collection which would reshape and expand our biorepository, and introduce ‘dynamic testing’ (perturbation) to meet current scientific needs of cardiovascular research.

This RFA seeks to have investigators at all levels and across all disciplines provide proposals that adhere to the above broad objectives while specifically addressing the areas of: phenotypic extremes, longevity and health disparities.

**Phenotypic Extremes**
- Phenotypic extremes refers to sampling of individuals at the extremes of the distributions of select traits with a view to understanding disease biology. These could include participants affected at a very young age, or those affected particularly severely, or those who are protected from disease.

**Longevity**
- Inquiries into longevity could range from identifying mechanisms of longevity and frailty, to determining actual age versus biologic age, to ascertaining gender and racial differences in longevity.

**Health Disparities**
- Explore genetic and lifestyle/environmental determinants of differences in disease incidence, prevalence, lifetime risk, prognosis, and impact of treatments within and across ethnicities.

**Approaches** to conduct these inquiries could include but are not limited to the following:

- Leverage pre-existing data in FHS and JHS cohorts to define mechanisms of cardiovascular disease.
- Use novel approaches to create new individual and/or population samples/ datasets with deeper, richer phenotyping.
- Use novel approaches for deeper, richer phenotyping within the FHS/JHS cohorts, including innovative targeted new phenotyping of subsets of FHS/JHS participants (with no more than minimal participant burden and risk as defined by these studies and consistent with established procedures and policies of these studies).
- Add existing cohorts to expand the efforts of these individual and/or population cohorts and the FHS/JHS cohorts to enhance the understanding of cardiovascular disease.

These above cohorts could support the following example activities:

- The FHS/JHS cohorts have large collections of phenotypes which could identify unique exposures and/or genotypes and/or their combination that influence CVD risk, longevity, and health disparities.
- Large-scale phenomic analysis could identify a subset of individuals that are “outliers” with regards to their risk for or protection from CVD burden.
- Combining genomics, epigenomics, and/or metabolomics, investigation of such subgroups may provide clues about the genetic and environmental factors that contribute to CVD risk, longevity and health disparities (such as HDL.
composition, levels, carotid IMT, concentric LV remodeling, salt-sensitive blood pressure, etc.).

- Comparative genomic analyses across cohorts could further identify underlying differences.
- Use of novel approaches could add new deeper phenotyping to these FHS/JHS cohorts.
- Validation using these new cohorts or using phenotypic extremes from FHS/JHS of novel hypotheses (genes, pathways, targets).
- Building novel analytical infrastructure or novel analytical methods which could include machine learning tools for mining and integrating multi-dimensional data using both longitudinal JHS and FHS data (OMICs and social network datasets) and experimental datasets (non-FHS/JHS) including combining human and experimental datasets, or network medicine approaches to ascertaining disease network structure and response to perturbation (disease mutations or drugs). Example: layering of eQTL or animal model data on human data relevant to specific CVD traits, and building analytical pipelines that can accommodate/integrate these, test these in experimental model systems, and suitably display results.

**Collaboration:** The AHA Guiding Principles for research strongly supports enhancing the collaboration of investigators across disciplines (basic, clinical, translation, and population). If appropriate to the research questions being investigated in this application, AHA encourages the formation of multidisciplinary teams.

**Training/Career development:** Training and development of early career investigators is one of AHA’s major goals. To that end, applications for these CVGPS funds should indicate how early career investigators will be included. An Individual Development Plan (IDP) for the early career investigator is required with submission. Also required is an indication of departmental support to protect the investigator’s time, goals for abstract presentations/manuscripts, and how trainees will utilize data from the project as preliminary data for future applications.

**Study Data and Infrastructure:** It is anticipated that the results of the CVGPS funding and formation of the CVGPS itself will establish an infrastructure and template for national cohort studies that utilize state-of-the-art phenotyping, -omic assessments, and analytical approaches to ensure that these ‘big datasets’ collected en masse over time will provide optimal diagnostic, prognostic, and therapeutic insights in the struggle against cardiovascular diseases. Data, specimens, etc. collected by investigators receiving CVGPS funding will be required to be deposited into a biorepository identified by the AHA.

**Process for Investigators seeking to Access FHS/JHS data.**

**Overview of data/biosample Access Process at FHS/JHS.**
The four potential sources for the data from the FHS and the JHS cohorts are:

1. **Biolincc** (the NHLBI data biorepository; [https://biolincc.nhlbi.nih.gov/home/](https://biolincc.nhlbi.nih.gov/home/)) for non-genetic data;
2. **dbGAP** for genetic/genomic/other OMICs data and for phenotypic data to be used for genome-phenome associations/analyses;
3. Data may also be requested from the parent cohorts (i.e., FHS and JHS) if they are not available in either of the two sources noted above.
4. **Novel approaches** (with minimal participant burden) to new phenotyping of subsets of participants involving targeted examination.
Access to data from Biolincc and dbGAP will follow the established protocols established by the NHLBI and NCBI, respectively, with appropriate data request applications made to these two repository systems. Approvals for such applications will follow the existing review process at these data repositories. Applications that require only data from dbGaP or BioLINCC do not need an application to the parent study itself.

Once LOAs are approved by the initial AHA and FHS/JHS screening and finalized applications are being considered for the final stage of funding, access to FHS and JHS data from the parent cohorts, requests for FHS/JHS biosamples and new phenotyping of participants (requiring targeted examination of subsets of participants) will require additional applications to these studies. They will also require approval by the respective study committees: research, examination, and/or Executive committee in the case of FHS; and publications and presentation subcommittee, or the ancillary studies subcommittee and the Steering committee in the case of JHS.

CVGPS related Processes at FHS/JHS for Approval of data/bio sample access.
Please note that review by the parent studies (FHS and JHS) will occur during the CVGPS application process at two levels as outlined below.

First Level Screening by FHS/ JHS:
An initial screening of the letter of application (LOA; see below) will be conducted at FHS/JHS after the review of the LOA by the AHA (see timeline in Table below). Data abstracted from the LOA will be sent to the FHS/JHS (with de-identification of PI details to maintain anonymity) for this screening. This initial screening at FHS/JHS will determine feasibility (availability of data sought to be used, availability of biosamples at specific examination cycles requested, assay performance characteristics, and participant burden) and also assess scientific overlap with ongoing approved research at the parent studies.

The parent cohort studies may seek the opinion of their laboratory and/or DNA committees at this juncture as deemed appropriate if the application requests bio samples. A lack of feasibility of the proposed research or substantial overlap with ongoing research at the parent study may result in the LOA not being approved by the AHA (which has the final authority to decide based on information on feasibility and scientific overlap received from the parent cohorts after the initial review at FHS/JHS). The PIs of all approved LOA that request data directly from FHS/JHS will receive a packet of information related to each study to guide the applicant through the subsequent processes, including steps required for completion of the application process. This packet will include information on data and biological sample availability, procedures for examining participants consistent with ancillary studies policies of the studies, informed consent considerations, study-specific review processes and timelines, existing publications and other information relevant to the application process.

Second Level Screening by FHS/JHS:
As part of the review of the full applications received by the AHA, a second round of reviews of applications that are deemed meritorious by the AHA peer review panel may be done at FHS/JHS if the applicant requests data and/or bio samples directly from FHS/JHS. This second review will involve the research, laboratory and/or the DNA committees of the parent cohorts, consistent with the policies related to approval of all ancillary study proposals at these studies. The decision of the research, laboratory examination and or DNA committees will be forwarded to the AHA review panel to consider as part of the final decision making process.

This second review will require the completion of an online application form (common to FHS and JHS) that will be available at the website of each of these studies if the applicant request data sets directly from the parent cohorts (see alternatives above) or if there is a request for study biological samples. Please note that this common application is not the same as the full AHA grant application
but focuses on the requirements of each cohort study.

**Actual Steps for data/Bio sample Access. After the AHA peer review process** identifies potential awardees, additional steps must be undertaken to access FHS and JHS data and/or bio samples. Access to data from Biolincc and dbGAP must follow the established protocols established by the NHLBI and NCBI, respectively, with appropriate data request applications and existing review mechanisms at these data repositories as noted above. For requests of data/bio samples from the parent cohorts, a signed Data and Materials Distribution Agreement (DMDA) will be required before the requested data/bio samples are distributed. It is very important that the Distribution Agreement match exactly what was requested in the application and was approved by the Research Committee and other committees (e.g., the approval by the laboratory committee to release a specific volume of a specific bio sample at a specific exam). An IRB approval of the research from the applicant’s institution must be obtained before data and/or bio samples can be released. Redistribution of data obtained from any of the three sources noted above is not permissible. When new measurements are made on bio samples obtained from FHS/JHS, the new data accrued from the CVGPS grant must also be returned to the parent cohorts, consistent with established policies at these studies.

The exact timeline for these procedures as relevant to CVGPS is outlined in the Timeline Table below.

**Program Structure**

**Target Group, Eligibility**

Faculty/staff members conducting independent research at time of application. At application, principal investigator must hold an M.D., Ph.D., D.O. or equivalent doctoral degree and must meet institutional requirements for grant submission.

Other than the requirement that the Principal Investigator be independent, eligibility for the CVGPS Pathway Grants are in no way restricted upon experience level or seniority. While no minimum percent effort is specified, the PI must demonstrate that adequate time will be devoted to ensure successful completion of the proposed project.

Association research awards are limited to non-profit or public institutions, such as: medical, osteopathic and dental schools, veterinary schools, schools of public health, pharmacy schools, nursing schools, universities and colleges, public and voluntary hospitals and other non-profit institutions that can demonstrate the ability to conduct the proposed research. For CVGPS only, applications will be accepted from federal employees and Veterans Administration employees.

At the time of application, the PI must have one of the following designations:

- U.S. citizen
- Permanent resident
- Pending permanent resident. Applicants 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 United States (having filed an Application for Employment Form I-765).
- E-3 Visa - specialty occupation worker
- 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
• G-4 Visa - family member of employee of international organizations and NATO

Fellows 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

Fellows included in CVGPS Grants must hold a Ph.D., M.D., and D.O., D.V.M. or equivalent doctoral degree and commit 75% effort to research training. A 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.

Awardee must meet American Heart Association citizenship criteria throughout the duration of the award.

Applicants are not required to reside in the U.S. for any period of time before applying for American Heart Association funding.

Other Relevant Policies

Awards are not intended to supplement or duplicate currently funded work. Rather, it is expected that submitted applications will describe projects that are clearly distinct from ongoing research activities in the applicant’s laboratory. Minor variations from existing research projects are not sufficient to constitute independent and distinct projects.

Awards are transferable to other institutions. The grantees 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.

Other Relevant Policies

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-
Application Submission Process

Only one application may be submitted per investigator for each grant mechanism. Multiple applications may be submitted from one institution.

Application instructions for the CVGPS Grants are at the American Heart Association’s website http://my.americanheart.org/professional/Research/CardiovascularGenomePhenomeStudyCVGPS/CV-GPS_UCM_461668_SubHomePage.jsp

Peer Review Process

Review of the applications will be conducted by the American Heart Association. Since we began providing research funding in 1948, we’ve required that funds be awarded in strict accordance with peer review committee appraisals of scientific merit. Peer review is mandatory for all national research applications.

The American Heart Association ensures that its peer review process provides a fair evaluation of each and every application submitted. Its review panels consist of scientific expert reviewers familiar with the science of the application and may also include lay reviewers. Lay reviewers are individuals without the formal training of a scientist but who have a strong interest in the prevention and/or management of heart disease and stroke. In the AHA peer review process, lay reviewers will specifically help to evaluate the potential impact of research applications to the mission of the AHA through their scoring (evaluation) of the lay summary portion of an application. The score and assessment of scientific reviewers take into account all of the review criteria for the type of program being reviewed. The panel must maintain a quorum throughout discussion of each proposal's scientific merits.

AHA peer review is impartial. Each committee member assigns each application a priority score. The conflict-of-interest policy prevents a reviewer with a professional or personal interest in an application from reviewing, discussing or scoring it. (AHA’s peer review practices and procedures can be found at the following link: http://my.americanheart.org/professional/Research/AboutOurResearch/OurResearch/Research-Standards_UCM_320231_Article.jsp

Peer Review Criteria

The following major factors will be considered in the evaluation of each CVGPS Grant. 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.

Potential impact of the project on cardiovascular disease genome-phenome 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 including sample size; data management; significance; innovation and overall scientific merit; 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 this project relate to and support the mission of the American Heart Association to building healthier lives, free of cardiovascular diseases and stroke?

**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

**Science Oversight**

There are two science groups providing oversight to the CVGPS science activities: The CVGPS Steering Committee and the Science Advisory Group.

The collaboration will be governed by a **CVGPS Steering Committee** which is responsible for:
- Creating the programmatic vision and high level design parameters;
- Issues related to funding distribution among the entities and programmatic components (infrastructure, Pathways Grants, Grand Challenge);
- Relationship of CVGPS with AHA-Industry collaborations;
- Rules regarding data ownership and usage;
- Agreements about branding and partnership representations externally;
- Accountability back to respective institutions; and
- Receipt and approval of scientific progress reports.

A **Science Advisory Group** will be appointed by the Steering Committee. This group will consist of scientific appointees from the leadership at BU and UMMC/JSU/TC, the Chair of the AHA Research Committee and others as determined by the Steering Committee. This group will be accountable for:

- Designing the specific research programs;
• Announcing the programs to the community and developing criteria for selection of award recipients when grants will be offered;
• Overseeing the application, peer review and awards process;
• Forging additional relationships as needed to broaden the scientific impact;
• Reporting on outcomes back to the Steering Committee
• Providing lay summaries of scientific reports which can be released to the public or potential donors;
  ▪ Monitoring the scientific progress of the investigators to assure completion of these projects
  ▪ Providing support to staff and investigators related to submission of data into the repository
  ▪ Overseeing and annually evaluating the program, including an evaluation of the progress of the awardees, making recommendations regarding continuation or changes of projects to the Steering Committee.
  ▪ Monitoring and encouraging interaction among awardees.

Program Evaluation

Preliminary measures of the success of the initiative have been identified. Each awardee 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. Funded investigators will be asked to report on the following measures:

• Productivity of awardee - track publications and citations; document outcomes of research projects; document other funding resulting from the current initiative
  ▪ Transfer of intellectual property to the marketplace
  ▪ Other metrics as defined by the AHA

Budget

CVGPS Pathway Grants

The Program will have a total budget of $500,000.

$250,000 per year, including up to 10% institutional indirect costs ($227,273 direct costs and up to $22,727 institutional indirect costs).

Principal Investigator salary, fringe benefits, and project support are unrestricted in accordance with institutional and AHA policies.

Total award: $500,000 (based upon this award’s duration of two years).

Appropriate Budget Items: Salary and fringe benefits of the Principal Investigator, collaborating investigator(s), and other participants with faculty appointments. Project-related expenses, such as salaries of technical personnel essential to the conduct of the project, supplies, equipment, travel, volunteer subject costs, and publication costs. 10% institutional indirect costs.

Duration: Two years. Eligible for competitive renewal.
The Awardee will be responsible for overseeing the total budget for his/her grant. If awarded, the PI 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.

**CVGPS Grand Challenge Awards**

The Program will have a total budget of $2,000,000.

$500,000 per year, including up to 10% institutional indirect costs ($454,546 direct costs and up to $45,454 institutional indirect costs).

Principal Investigator salary, fringe benefits, and project support are unrestricted in accordance with institutional and AHA policies.

Total award: $2,000,000 (based upon this award’s duration of four years).

**Appropriate Budget Items:** Salary and fringe benefits of the Principal Investigator, collaborating investigator(s), and other participants with faculty appointments. Project-related expenses, such as salaries of technical personnel essential to the conduct of the project, supplies, equipment, travel, volunteer subject costs, and publication costs. 10% institutional indirect costs.

Duration: Four years. Non-renewable

The Awardee will be responsible for overseeing the total budget for his/her grant. If awarded, the PI 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.
### CVGPS Application and Award Timeline

**Pathway**

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<tr>
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<tr>
<td>April 15, 2014</td>
<td>Final Information on Data Sources available to applicants</td>
</tr>
<tr>
<td>June 3, 2014</td>
<td>LOA Due</td>
</tr>
<tr>
<td>June 3 – 17, 2014</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; Level Peer Review Screen by AHA of LOAs. Accepted LOAs sent to FHS/JHS</td>
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<td>1&lt;sup&gt;st&lt;/sup&gt; Level Screening by FHS, JHS, NHLBI of LOAs for feasibility &amp; overlap with existing projects</td>
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<tr>
<td>July 28 - 30, 2014</td>
<td>Invitations sent for Full Applications</td>
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<tr>
<td>July 30 – Aug 1, 2014</td>
<td>PIs will receive a info packet on FHS/JHS samples, data, informed consent, etc. to assist with their application</td>
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<tr>
<td>October 1, 2014</td>
<td>Applications Due</td>
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<tr>
<td>October 15 – November 6, 2014</td>
<td>Final Peer Review by AHA. If a 2&lt;sup&gt;nd&lt;/sup&gt; NHLBI/FHS/JHS review is required it will be done during this time</td>
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<tr>
<td>November 6 – December 2, 2014</td>
<td>AHA considers any issues raised during second NHLBI/FHS/JHS review</td>
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<tr>
<td>November 14 – 17, 2014</td>
<td>Awardees Announced at Scientific Sessions</td>
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<td>Nov 24 – 28th Thanksgiving Week</td>
<td>Thanksgiving Week</td>
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<tr>
<td>December 2, 2014</td>
<td>Full Applications Due</td>
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<tr>
<td>December 19 – Jan 5, 2015 2014</td>
<td>Holidays</td>
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<tr>
<td>January 19, 2015</td>
<td>Data will be provided to Investigators*</td>
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<td>February 2015</td>
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**Grand Challenge**

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<td>Invitations sent for Full Applications</td>
</tr>
<tr>
<td>July 30 – Aug 1, 2014</td>
<td>PIs will receive a info packet on FHS/JHS samples, data, informed consent, etc. to assist with their application</td>
</tr>
<tr>
<td>October 1, 2014</td>
<td>Applications Due</td>
</tr>
<tr>
<td>October 15 – November 6, 2014</td>
<td>Final Peer Review by AHA. If a 2&lt;sup&gt;nd&lt;/sup&gt; NHLBI/FHS/JHS review is required it will be done during this time</td>
</tr>
<tr>
<td>November 6 – December 2, 2014</td>
<td>AHA considers any issues raised during second NHLBI/FHS/JHS review</td>
</tr>
<tr>
<td>November 14 – 17, 2014</td>
<td>Awardees Announced at Scientific Sessions</td>
</tr>
<tr>
<td>Nov 24 – 28th Thanksgiving Week</td>
<td>Thanksgiving Week</td>
</tr>
<tr>
<td>December 2, 2014</td>
<td>Full Applications Due</td>
</tr>
<tr>
<td>December 19 – Jan 5, 2015 2014</td>
<td>Holidays</td>
</tr>
<tr>
<td>January 19, 2015</td>
<td>Data will be provided to Investigators*</td>
</tr>
<tr>
<td>February 2015</td>
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<tr>
<td>February 15-April 15, 2015</td>
<td></td>
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<tr>
<td>April 15 – May 15, 2015</td>
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<tr>
<td>June 1, 2015</td>
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<tr>
<td>July 1, 2015</td>
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<tr>
<td>AHA Peer Review Review by FHS, JHS, NHLBI for feasibility &amp; overlap with existing projects</td>
<td></td>
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<tr>
<td>AHA reviews all feedback</td>
<td></td>
</tr>
<tr>
<td>Awardees Announced</td>
<td></td>
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<tr>
<td>Data will be provided to Investigators</td>
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</tbody>
</table>

*For this first round of awards, there will be a 6-8 week turn around on providing data to investigators due to the intervening holiday season.
Letter of Application/Letter of Intent

Prospective applicants are requested to submit a Letter of Application (LOA) for the Pathway Grants on or before the date indicated in the table above.

A Letter of Application is required to ensure responsiveness to the unique nature of this program. The Letter of Application should include sufficient information to assist in determining if a formal application will be requested. Our intent is to conduct a rather robust screening at this stage so that the most meritorious proposals are the ones that move on to the full application stage.

Upon receipt of the LOA, a first level science screening will be conducted specifically to assure feasibility, alignment of the specific aims with the goals of CVGPS and the AHA Mission, assure quality data management and appropriate Informed Consent procedures, if required. Once screened at that level, the proposal will be forwarded to the FHS/JHS teams to receive approval as an ancillary study. Applicants will be notified by AHA following these 2 stages as to whether they will be invited to submit a full application. Only invited applicant proposals will be accepted.

Letter of Application: Required documents

I. Title of proposed project:

II. Description of the Project: (limit to 500 words)

III. Specific Aims: (limit to one page single space)

IV. Relevance and Importance to this CVGPS Program: (limit to one page single space)

V. Briefly describe methods: (limit to one page single space)

VI. Identify Data Cohort you will seek to use:
   Framingham Cohort: □ Data* □ Bio samples* □ New Phenotyping on subsets of participants*  
   Number of Participants ________________  
   Number of Specimens ________________
   
   FHS cohort type: □ Original (Gen 1) □ Offspring (Gen 2) □ Third Generation (Gen 3)

   Jackson Cohort: □ Data □ Bio samples* □ New Phenotyping on subsets of participants*  
   Number of Participants ________________  
   Number of Specimens ________________

   Other ____________________________  
   Number of Participants ________________  
   Number of Specimens ________________  
   None ____________________________

   Providing New Cohort  □ Yes* Describe:
* For any requests for data, please indicate the key phenotype and/or genotype variables of interest you will require and from which cycle(s)/exam(s).

• For any requests for bio samples, please indicate the type of bio sample (e.g., serum, plasma, buffy coat, urine, DNA), sample volume requested, and at which examination cycle(s) of which cohort (in the case of FHS), as well as assay performance characteristics.

• For any new phenotyping involving targeted examination of or interviews with a subset of FHS/JHS participants, please indicate participant burden (including number of hours of contact per participant, nature of test/interview) and risks involved.

VII. Describe your Informed Consent procedures if proposing a new cohort or new individual testing of current cohort (only applicants receiving an invitation for a Full Application later in the process will need to provide evidence of IRB consent).

VIII. Describe briefly your quality management protocol for data and bio samples: (limit to 500 words) - may also attach protocol, but must summarize in this section in addition).

IX. Describe your computer security levels and protocols

X. Describe if you have IRB approval for the proposed project at your institution

XI. Describe your statistical methods including your power calculation. (limit to 250 words)

XII. Budget

XIII. Bio sketch for Principal Investigator and other team members: (attach)

XIV. Training Plan for Fellow: (An IDP is preferred).

The Letter of Application and supporting documents must be submitted via the AHA Grants@Heart system before the posted deadline. Visit: https://research.americanheart.org/

**Letter of Intent**

Prospective applicants are requested to submit a Letter of Intent (LOI) for the AHA CVGPS Grand Challenge Award on or before **October 1, 2014**. The letter should include the following information and ideally will not exceed one page in length:

- Name, institution, address, telephone, and email of proposed Principal Investigator
- Names, institutions and emails of other Key Personnel
- Project title
- Brief overview of proposed project – 1 paragraph
- Identification of Data Cohort(s) you will seek to use:

  **Framingham Cohort:**
  - Data
  - Bio samples
  - New Phenotyping on subsets of participants

  **Jackson Cohort:**
- Data
- Bio samples
- New Phenotyping on subsets of participants

Other Cohort: (Name)_______________________________

Providing New Cohort: If yes, please describe (1 sentence)

None:

While a Letter of Intent is not required in order to submit a subsequent full application and does not enter into the review of said subsequent application, the information provided in a Letter of Intent allows AHA staff to estimate the 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 email to the American Heart Association at deb.korns@heart.org with a subject heading of AHA Grand Challenge Award LOI.

Inquiries

Inquiries regarding this RFA may be sent to: E-mail apply@heart.org
Phone 214-360-6107 (select option 1)