American Heart Association
Disparities in Cardio-Oncology
Strategically Focused Research Network

Key Dates

- RFA Posted: Fall 2020
- Letter of Intent (Required) Deadline: Feb 9, 2021
- Application Deadline: March 30, 2021
- AHA Peer Review: Spring 2021
- Notification of Awards: mid-June 2021
- Award Start Date: July 1, 2021

Applicant Requirement.

As a reminder, for applicants to AHA SFRN award mechanisms, the Center Director and each project PI must be an AHA Member/Partner. Join or renew when preparing an application in Proposal Central, online, or by phone at 301-223-2307 or 800-787-8984. Membership/Partnership processing takes 3-5 days; do not wait until the application deadline to renew or join.

Award Objectives and Characteristic Announcement

The American Heart Association (AHA) announces a Request for Applications for the Disparities in Cardio-Oncology Strategically Focused Research Network (SFRN).

Purpose

Cardio-oncology represents the intersection of cancer and cardiovascular disease. It has emerged as a new research area as a result of the evolution in cancer therapies which have improved prognosis for many cancer patients. Cardiovascular complications from cancer therapies represent an important challenge for many cancer patients, both at the time of treatment as well as during survivorship. Cancer itself can lead to cardiac disease, ranging from amyloidosis to carcinoid heart disease. While cardiomyopathy associated with traditional cancer therapies (such as anthracyclines and radiation) has been well-studied, novel targeted and immune-based therapies often lead to not only myocardial but also vascular and metabolic toxicities; the mechanisms of these toxicities or the populations at risk are less clear. In addition, emerging data suggest that common genetic and environmental risk factors can lead to both cardiovascular disease (CVD) and cancer. All of these issues have become important in 2020, as there are more than 17,000,000 Americans who are cancer survivors, representing 5% of the U.S. population. Cardiovascular disease represents a major challenge, often competing with cancer as the most common
cause of death in cancer patients. It is in this environment where health disparities often contribute to differential outcomes. Well-known examples of disparities affecting health and healthcare are race/ethnicity, socio-economic status, age, geography (e.g., rural vs urban populations), language, gender, disability status, citizenship status, and sexual identity and orientation.

To address critical deficiencies related to disparities in cardio-oncology, AHA has prioritized funding research that increases the understanding of the etiology, pathophysiology, treatment and prevention of cardiovascular disease among cancer patients and cancer survivors from diverse populations. Cancer patients and/or survivors are often not included in cardiovascular studies. Understanding mechanistic underpinnings of cardiac complications, especially targeted and immune-based therapies, can lead to better diagnostic, preventive and treatment strategies. Furthermore, data describing differences in cardiovascular toxicities associated with cancer therapies are sparse.

This SFRN provides the AHA with a mechanism to advance the understanding of the causes, pathophysiology, risk factors, epidemiology, prevention and treatment of cardiovascular disease in those patients who are currently undergoing or have undergone cancer treatment (or applicable models). Applicants are requested to focus in particular on areas that have not been previously explored in cardio-oncology, and must include diverse and/or underrepresented cohorts in proposed studies.

Topics of Interest
Specific Questions to be Answered by this Grant Opportunity

The intent of this initiative is to support a collaboration of basic, clinical and population (or implementation) researchers whose collective efforts will lead to new approaches to the study of cardio-oncology. Each Center must propose two (2) or three (3) projects representing at least two of the following research disciplines: basic, clinical, and population science. All projects must focus on disparities in cardio-oncology. Population studies are inclusive of projects ranging from cohort studies to translational or implementation research involving community interventions. All projects must address health and health care disparities and/or health equity in the cardio-oncology domain.

Note: Centers are highly encouraged, where applicable, to align with AHA initiatives focusing on cardio-oncology, AHA initiatives addressing the use of digital technology to improve health outcomes, or other AHA programs. These and other AHA programs can be found via www.heart.org.

The following are illustrative descriptions of overarching themes that could be addressed by a Center. Successful applications will provide strong evidence of synergy among the proposed projects and will address at least one of the issues below or an alternate issue of equal importance.

**BASIC/MECHANISTIC**

- What are the basic mechanisms of cardiovascular toxicities associated with cancer therapies, which may include specific chemotherapies, radiation therapy, targeted and immune-based therapies?
- Are there genetic and epigenetic risk factors of cardiovascular disease specific to cancer patient populations?
• What are the patterns and regulators of expression of CVD associated with cancer?

**CO-MORBIDITIES**

• What are the mechanisms of common risk factors associated with both cancer and cardiovascular disease?

• How do cardiovascular co-morbidities affect the cardiovascular toxicities seen with specific cancer therapies?

• What populations are at risk of specific targeted or immune-based therapies, and what risk factors are involved that can be used in risk prediction?

• What new interventions or improvement in current interventions can prevent or reduce development of CVD/Heart Failure (HF) events in patients with cancer?

**DIAGNOSIS AND RISK ASSESSMENT**

• What new biomarkers, tissue markers, cytokine and immune profile, or imaging modalities can identify patients at risk for CVD in the cardio-oncology population?

• What newer biomarkers, tissue markers, cytokines, imaging modalities, non-invasive techniques, etc. can identify *a priori* patients at risk for CVD, CHD, Stroke, CKD (chronic kidney disease), and HF and/or help predict the disease progression or identify patients who are destined to have poor clinical and quality of life outcomes from interventions?

• What are the involvements of the right ventricle and/or left atrium as future risk predictors and/or markers of cardiotoxicity post cancer therapy?

**TREATMENT**

• What are the most effective pharmacologic, device or behavioral treatment strategies for specific disparate cardio-oncology populations?

• Can precision medicine approaches using molecular and clinical phenotyping identify cancer subgroups likely to differentially benefit from specific pharmacotherapies?

• What categories of pharmacologic therapies could possibly prevent or mitigate radiation-associated CVD and vascular and metabolic disease associated with novel targeted cancer therapies?

**LIFESTYLE, BEHAVIOR, AND PRIMARY OR SECONDARY PREVENTIONS**

• What measures, including interventions of lifestyle, behavior, and primary or secondary prevention, can help reduce development of CVD/CKD and HF as well as related complications?

• What is the role of exercise training in prevention of cardiovascular morbidity after chemotherapy and/or stem cell transplantation?

• What is the role of education and any potential connectivity gap (e.g., lack of internet access) on CV outcomes in cancer?
• What measures can be most efficaciously employed in the assessment of care quality within the realm of cardio-oncology?

• Are there existing CV cohorts that could be enhanced by adding relevant oncology information? If so, what information is most critical? Conversely, are there existing cancer cohorts that could be enhanced by adding relevant CV information? If so, what information?

Award Details

Duration: 4 years with opportunity for up to 12-months No-Cost Extension (NCE).

Number of Awards: AHA anticipates awarding four (4) Center grants* to establish the Disparities in Cardio-Oncology SFRN. Awardees will be selected based on scientific merit and how each group aligns with AHA’s mission and goals.

*The AHA reserves the right to determine the final number of awardees.

Award Amount: The maximum budget amount a Center applicant may request is $2,925,000. The AHA reserves the right to determine the final award amount for competitive projects based on need and potential impact.

Collaborative Project: During Year 1 of the Network, the Centers will be required to develop a Network-wide collaborative project in coordination with the Network Oversight Advisory Committee (OAC). The Collaborative project will start in Year 2. AHA has set aside money for this effort, not to exceed $1,500,000 for the Network. More details on the Collaborative project will be made available after the Centers are named.

Appropriate Budget Items:

• Salary and fringe benefits of the Center Director, Training Director, Principal Investigators, three named fellows, collaborating investigator(s), and other participating research staff or faculty.

• Project-related expenses, such as salaries of technical personnel essential to the conduct of the project, supplies, equipment, travel, and publication costs in accordance with institutional and AHA policies.

• Centers may use award dollars to pay for travel to two required face-to-face (as feasible), network-wide meetings (below) and other meetings where SFRN research is presented. One semiannual meeting will be in the Fall. A second semiannual meeting will be held in the Spring; it is anticipated awardee Centers will host both meetings on a rotating basis. The purpose of both meetings is to share results across the network and identify and act on potential collaborative opportunities. Additionally, there will be virtual meetings during the NCE dedicated to the required Network-wide publication. More information will be provided upon award and be more specific once travel becomes possible again.
• Maximum of 10% institutional indirect costs may be claimed on the award.

Sample Budget for a Center:

<table>
<thead>
<tr>
<th>Projects:</th>
<th>Center Totals</th>
</tr>
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<tbody>
<tr>
<td>TWO OR THREE projects for four years.</td>
<td>$2.041M</td>
</tr>
<tr>
<td>Maximum of $2.041M to be divided between the projects. It is not required to spend funds equally across projects or years.</td>
<td></td>
</tr>
<tr>
<td>Fellows</td>
<td>$390K</td>
</tr>
<tr>
<td>Three Fellows for two years each. Minimum fellows’ salary and fringe of $65,000/year. Additional funds to supplement salary and fringe can come from Center Director salary, Center travel budget, Project PI budget, or additional funding sources. (Fellows must maintain 0.75 FTE research effort.)</td>
<td></td>
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<tr>
<td>Center Leadership</td>
<td>$200K</td>
</tr>
<tr>
<td>A maximum of $50,000 per year to cover effort associated with directing the Center (i.e., Center Director, which requires at least 20% effort) and the training program (i.e., Training Director). The Center Director may also serve as the Training Director. If an individual other than the Center Director serves as the Training Director, this $50,000 per year limit remains, and the available funds should be allocated as appropriate to cover the efforts of these individuals.</td>
<td></td>
</tr>
<tr>
<td>Center Travel Costs</td>
<td>$28K</td>
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<tr>
<td>Covers travel for Center personnel to attend network meetings and other integration activities. $7,000 per year must be allocated to Center Travel.</td>
<td></td>
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<tr>
<td>Direct Costs (Total)</td>
<td>$2.659M</td>
</tr>
<tr>
<td>Research Dollars</td>
<td></td>
</tr>
<tr>
<td>Indirect Costs</td>
<td>$266K</td>
</tr>
<tr>
<td>AHA Policy allows for a maximum of 10% for indirect costs</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>$2.925M</td>
</tr>
</tbody>
</table>

The awardee will be responsible for overseeing the total budget for the grant. If awarded, the principal investigator 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.

Relevant Policies and Requirements

NEW TO THIS FUNDING OPPORTUNITY: Required Participation in AHA’s Precision Medicine Platform, powered by Amazon Web Services.

Each Center will receive Amazon Web Services computational credits to cover the cost of cloud computing for a secure and private workspace on the AHA Precision Medicine Platform to enable investigators in each Center to collaborate and analyze data securely.
Data analysis is enabled in secure workspaces by a friendly web user interface that allows researchers to code in various languages, including R and Python and use statistical software including but not limited to SAS and R studio. The most up-to-date machine learning and artificial intelligence software available from Amazon Web Services is also included. For a full list of the analytical tools available, please see precision.heart.org/workspace/about. Researchers are also able to upload their own tools.

The AHA asks that the grantees within the Network also accelerate collaboration with the funded Centers through the sharing of data and code as well as the coordination for interoperability of data to facilitate findability and sustainability. The AHA fully supports the FAIR (Findable, Accessible, Interoperable and Reusable) Guiding Principles of Data Stewardship.

All applications will be reviewed with the expectation that the methods/results section contains:

- a clear description of the tools and types of analysis each Center will perform in the workspace
- how the Precision Medicine Platform will be leveraged to share data and code amongst the staff within the Center and within the entire Network to accelerate collaboration
- a plan for interoperability of data between Centers and with National or International Standards
  - To obtain a 60-day complimentary trial workspace to use during the application period, please Register Here. Once registered, go to the Search page, click Request Workspace, complete the form, and Submit.

**Note:** While the request form mentions billing, there is no charge for use of the PMP during the trial period. View detailed instructions and helpful information (pdf)

To learn more about the Precision Medicine Platform and how it can enable your research, please access the following videos. The first (Learn more about the platform – video 1) provides a high-level overview, while the second (Explore the capabilities of the platform – video 2) provides more detail about accessing data and analytical tools, data storage, and sharing of data.

The Platform is HIPAA (pdf) and FedRAMP (pdf) compliant.

Subjects/Study Cohorts: As this SFRN is specifically focused on disparities in cardio-oncology, all center proposals must include diverse populations in proposed studies.

For clinical and/or population projects enrolling human subjects, it will be important to design studies that incorporate both realistic recruitment goals and sufficient statistical power to ensure valid results.

**NEW TO THIS FUNDING OPPORTUNITY:** Institutional Partnership Policy. In keeping with AHA’s commitment to diversity and inclusion, each Center applicant must partner with at least one institution focused on educating or serving under-represented individuals. Investigators from these partnering institutions must be included in a substantive manner in the scope of the center and projects. AHA staff will review for compliance.

To be considered, an institutional partner must be either of the following:
A. An institution of higher learning focused on the education of Black/Hispanic/American Indian/non-White students, such as a(n):
   - Historically Black College/University (HBCU) or Predominantly Black Institutions
   - Hispanic-Serving Institution
   - Tribal College or University or Native American-Serving, Nontribal Institution
   - Alaskan Native- or Native Hawaiian/Pacific Islander-Serving Institution
   - Other majority-non-white institution of higher learning

B. A non-profit community hospital or other research/care institution:
   - serving a majority non-white population OR
   - located in a non-urban, non-suburban setting (area population <250,000) OR
   - serving an underrepresented population not listed above (e.g., a federally qualified health center (FQHC))

As part of the required Letter of Intent (LOI), each Center Director must upload a letter from a Senior Institutional Official (e.g., Provost, VP/Dean of Academic Affairs, VP for Research, Hospital CEO, Healthcare Center Director, etc.) from the partnering institution indicating they meet the requirement stated above. AHA staff will review for compliance. A non-complying institution will not be permitted to submit a full application.

Interim Assessment: Awardees must report progress on a minimum annual (once per year) basis. Progress may take the form of a required written report in addition to video conferencing, phone calls, and/or face to face visits. Reporting will be focused on achievement of stated milestones as indicated in the project timeline. The OAC reserves the right to request additional updates, site visits, or reporting.

Public Access: The AHA’s public access policy requires that all journal articles resulting from AHA funding be made freely available in PubMed Central (PMC) and attributed to a specific AHA award within 12 months of publication. It is the responsibility of the awardee to ensure journal articles are deposited into PMC.

Open Data: Any factual data that is needed for independent verification of research results must be made freely and publicly available in an AHA-approved repository within 12 months of the end of the funding period (and any no-cost extension).

For more information on the above policies, see AHA’s Open Science Policy webpage.

Other: 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. Visit the Research Programs Awards Policies page for more information on this topic: AHA Policies Governing All Research Awards.
Peer Review

Peer Review is a two-phase process. Projects/Science will be scored during Phase I. Center applications that advance past Phase I will undergo a separate, Phase II review. Criteria for both phases of review follow.

Phase I Review

Each PROJECT within a Center application will be scored individually according to the criteria below.

Projects – Potential impact of the project on research in the field of the designated research topic; 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? Does each applicant develop a plan for data analysis using the tools in a workspace on the Precision Medicine Platform and discuss how the workspace will be leveraged to share data and code amongst the staff within the Center and within the entire Network to accelerate collaboration? Does each applicant develop a plan for interoperability of data between Centers and with National or International Standards?

  *For all applications that include vertebrate animals or human subjects, applicants must explain how relevant biological variables, such as sex, are factored into the research design, analysis and reporting. Furthermore, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.*

- **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(s)**: Is the investigator(s) 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 related to disparities in cardio-oncology? 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 AHA – To be a relentless force for a world of longer, healthier lives?

- **Synergy**: How does this project enhance the Center and the additional science project(s)? i.e., does this project enhance the likelihood that the collective Center outcomes will exceed outcomes of the individual sum of its distinct components? *Only projects that demonstrate synergy will move forward to Phase II.*

- **Summary for Non-Scientists**: How well does this lay summary convey to a non-scientific audience the purpose and importance of the research? Does the summary adequately:
  
  - How well written is the lay summary in explaining to a non-scientist audience the research proposed and its importance?
  - Does the Lay Summary adequately explain the major health problem being addressed by this study?
  - Does it provide specific questions and how the projects will address them?
  - Does it provide information on the overall impact of this work and the potential advances in the field?
  - Does it relay how the proposal supports the mission of the AHA?

**Phase II Review**

**CENTER** application scoring is based on the criteria below.

- **Synergy** – A clear vision of scientific direction is expected. A Strategically Focused Research Center should be viewed as a group of interrelated research projects, each of which is not only individually scientifically meritorious, but also complements the other projects and contributes to an integrating theme. Describe the rationale for the total program. Explain the strategy of achieving the objectives of the overall program and how each individual project relates to the strategy. Describe the synergies and interactions among projects and their investigators. Is there evidence of synergy among the projects and training component of the Center?

- **Collaboration** – History of collaboration, as well as the ability and commitment to collaborate with other institutions, investigators and within the applicant institution as well as within the awarded
Network. Defined and detailed process for collaboration with other sites in addition to within and among the proposed 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. What collaborations do you envision between investigators working on individual projects?

- **Interaction Plan within and among this Network and other AHA Networks** (if appropriate) – Plan for and commitment to sharing 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. Centers proposing clinical projects must document that they have sufficient volume of patients from all study populations to ensure robust results are achievable.

- **Training component** – A detailed plan for developing and implementing a postdoctoral training program that includes clinical (M.D., D.O., PharmD) or Ph.D. training in research in the field outlined by the RFA; 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 researchers in the appropriate research topic.

- **Center Team** – Qualifications of the Director to provide scientific and administrative leadership for the Center; experience and commitment of the nominated Director; quality of research team; qualifications of investigators and co-investigators; diversity of the research team; experience in the field of study outlined by the RFA; training experience. Applicants should comment on the diverse composition of the proposed research teams, in keeping with AHA’s core values of diversity and inclusivity.

- **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. Documented evidence of willingness to collaborate with others outside their institution to share ideas, science, etc. to progress the field of research as outlined in the RFA.

- **Investigator team** – Qualifications of each PI to provide scientific and administrative leadership for their respective projects; demonstrated commitment of each PI, and experience with studies in the field outlined by the RFA; quality of interdisciplinary research team; qualifications of co-investigators; training experience.
• **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.

**Process:**

**Peer Review of Submitted Applications**

The two phases of face-to-face Peer Review for submitted applications will be conducted approximately 4-5 weeks apart.

- Phase I will include a written review of the science (i.e. projects)
- Phase II will include a reverse site visit of a limited set of applicants, with the review focused on the overall vision of the center, synergy and collaborative possibilities, and the training plan and environment

For more information on Peer Review of submitted applications, including information on reverse site visits, see the Peer Review section of the [SFRN General Information](#) page on the [AHA SFRN website](#).

*An applicant is prohibited from contacting AHA peer reviewers. This is a form of scientific misconduct and will result in removal of the application from funding consideration and institutional notification of misconduct.*

**Application Submission**

Applications must be submitted using [ProposalCENTRAL](#), AHA’s online submission portal. For explicit Application Instructions, visit the [AHA SFRN General Application Information](#) page.