# AHA-Allen Distinguished Investigator Awards

Extracellular Matrix Biology in the Cardiovascular System

Application Deadline: Wednesday, May 10, 2017 at 5 p.m. CST

June 19, 2017 - Announcement of two awardees

The application must be submitted by 5 p.m. Central Time in <u>Grants@Heart</u> on the deadline date. The application will be submitted to the designated grant officer, who will submit it to the American Heart Association (AHA).

**Applicant Instructions** 



### Purpose

An AHA-Allen Distinguished Investigator is an active researcher who will lead a compass-driven, leadership-guided research program intended to open an area (scientific "compass" direction) at the frontier of cardiovascular research defined by their own vision, listening tours of The Paul G. Allen Frontiers Group, and ongoing AHA dialogues with science advisors. AHA-Allen Distinguished Investigators are pioneers who will expand the frontiers of bioscience. The purpose of this inaugural funding partnership is to discover and fund highly promising investigators working in research on the cardiovascular extracellular matrix (ECM), who have creative ideas with the potential to move ECM science forward and transform matrix biology.

Awarded investigators are expected to demonstrate a combination of the following attributes:

- Likelihood of transforming and advancing ECM biology and its significance in cardiovascular and stroke science.
- Ability to develop new tools and methods that support creative experimental approaches to questions, utilizing techniques from other disciplines, if appropriate.
- Original research ideas with promise of innovative contributions, if successful.
- Creativity in their scientific ideas.
- Commitment to take risks on forward-looking concepts of major scientific impact.

## Science Focus and Impact Questions

The intent of these AHA-Allen Distinguished Investigator awards is to fund research that will address fundamental knowledge gaps about the role of the ECM in cardiovascular physiology and pathophysiology through approaches such as multi-omic evaluations, data computation, cell biology, bioengineering, multiscale modeling, and/or imaging. ECM plays a defining role in the initiation and progression of major cardiovascular diseases, including ischemic heart disease, hypertensive heart disease, pediatric and adult cardiomyopathies and congenital cardiovascular malformations, atherosclerosis and vascular disease, and cerebrovascular disease. We also seek to explore a new paradigm in ECM biology, which views the ECM as an "information storage medium", that may harbor detailed and long-lasting information of significance to tissue/organ function and remodeling, and outlasts the lifetime of some parenchymal cells. Advances in our understanding of ECM structure and function will yield new approaches to the prevention, detection and treatment of these cardiovascular disease states and also provide potential translation to other organ systems.

The following is an illustrative list of overarching questions that could be addressed. Successful applications might address one or more of the questions below or an alternate innovative approach.

- 1. How does aging change information storage and retrieval in the cardiovascular ECM?
  - o Define ECM function and evolution with aging and pathology.
  - Understand the complex temporal interactions between ECM and cell-signaling growth factors.
- 2. How does inflammation modify structure, function, and information storage in the cardiovascular ECM?
  - o Define what ECM is, beyond collagen, in the healthy and post-MI heart. Expand to other disease states, if appropriate to the new paradigm.
  - Dissect ECM-mediated actions that may increase myocardial stiffness and contribute to heart failure with preserved ejection fraction (HFpEF), in aging and diabetes and with reduced EF (HFrEF), in myocardial infarction and pressure overload.
- 3. How does the cardiovascular ECM direct recruitment, differentiation, and maturation of progenitor cells?
  - Better understand the cell-cell (and cell-ECM interactions) that drive remodeling in pathologic situations.
  - Understand the effects of the ECM on inflammatory, reparative, and progenitor cells to coordinate cardiovascular wound healing and appropriate and inappropriate remodeling post MI.
- 4. How can we edit the ECM to direct cell and tissue function?
  - Develop new therapeutic approaches that focus intentionally on the matrix, based on new understanding of how the cardiovascular ECM communicates with cells.

## Target/Eligibility

- Ph.D. and/or M.D. (or the equivalent).
- Faculty appointment at an eligible nonprofit institution in the U.S. or equivalent faculty position at a foreign University that meets foreign equivalency determinants for a non-profit in the United States
- U.S. Federal government employees are not eligible.

We seek and strongly encourage applications from women and members of minority groups that are under-represented in biomedical sciences.

Awardees will be invited to and expected to attend an annual, two-day research Symposium gathering of all Allen Distinguished Investigators. This event offers time for cross-fertilization of frontier bioscience ideas and new collaborative opportunities.

## **Application Submission**

- 1. The application (5 pages, 12 point Arial font, 1 inch margins on all four edges) Research Proposal Describe:
  - Your creative idea, hypothesis, or solution to an ECM question, and the research plan to produce compelling new knowledge or technology.
  - Likelihood of transforming and advancing the future of one of the ECM science areas outlined in this RFA.
  - o How your plan advances ECM research into new frontiers and/or difficult problems.
  - Your capacity to develop new tools and methods that support creative experimental approaches to guestions, encompassing concepts or techniques from other disciplines.
  - Areas of collaboration with other distinguished scientists, if relevant.
  - The impact of your proposed work, written in clear, concise language that can be understood by a non-scientist reviewer.
- 2. Biosketch (for PI and any co-PIs, up to 5 pages each)

- 3. A list of up to 15 relevant or important publications (1 page)
- 4. Budget

### **Award Amount & Duration**

- Awards are for a three-year period
- \$500,000 annually for 3 years = \$1,500,000 per award
- Budget can cover costs such as PI and any co-PI salary/fringe; salaries/fringe of lab personnel; other expenses such as laboratory supplies; animal costs; equipment, human subject recruitment/reimbursement; travel; publication costs. Up to 10% may be used for institutional indirect costs.

### Peer Review Criteria

#### Impact:

Is the research described by the candidate likely to lead to the development of significant contributions in the ECM science areas outlined in the RFA? Does the research challenge existing paradigms or critical barriers to progress in the field? Does the candidate propose transformative approaches to major research challenges in ECM biology relevant to the areas of CV and stroke?

#### Investigator:

Does the candidate express creative ideas and a commitment to pursue pioneering work at the frontiers? Does his/her record of accomplishment and scientific choices suggest the ability to transform the field?

#### Innovation:

Are there new conceptual innovations in the proposed project? Does the applicant describe the development of new tools and methods that support creative experimental approaches to questions, encompassing concepts or techniques from other disciplines?

### **Review Process**

The first stage of review will evaluate the written proposal against the peer review criteria listed above. A second stage of the review will be conducted with only the highest ranked candidates and will include a video (Skype) interview process. Dates are TBD, but finalists must be available during the period of June 12-13, 2017.

### Timeline

Date	Event
April 10, 2017	Program announcement / funding opportunity published on the Web
May 10, 2017	Application submission deadline
June 12-13, 2017	Review of finalists (via teleconference)
June 19, 2017	Announcement of two awardees