# H. SPONSOR AND CO-SPONSOR STATEMENTS

Dr. Anish Shah will work closely with the sponsor (Dr. Vaccarino), and co-sponsors (Drs. Alonso and Shah). As the sponsorship team works closely together in a multidisciplinary team in the Department of Epidemiology, the statement below has been written collaboratively.

## H1. RESEARCH SUPPORT AVAILABLE

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Funding Source | Grant No. | Title | Principal Investigator | Start | End | Award Amount |
| Current | | | | | | |
| NIH/NHLBI | R01 HL109413 | Mental Stress and Myocardial Ischemia after MI: Sex Differences and Mechanisms | V. Vaccarino | 05/01/12 | 07/31/20 | $3,803,371 |
| NIH/NHLBI | R01 HL125246 | PTSD and Ischemic Heart Disease Progression: A Longitudinal Twin Study | V. Vaccarino | 07/15/15 | 04/30/20 | $3,396,769 |
| NIH/NHLBI | R01 HL136205 | Sleep Disturbance as a Mechanism for Ischemic Heart Disease in PTSD | V. Vaccarino | 03/17/17 | 02/29/20 | $2,320,825 |
| NIH/NHLBI | T32 HL130025 | Multidisciplinary Emory Training in Research on Inequities in Cardiovascular Health (METRIC) T32 | V. Vaccarino | 07/15/16 | 04/30/21 | $3,396,353 |
| NIH/NHLBI | R01 HL137338 | Effect of an Intensive Lifestyle Intervention on the Atrial Fibrillation Substrate | A. Alonso | 05/15/18 | 04/30/20 | $1,290,526 |
| NIH/NIA | R21 AG058445 | Atrial Fibrillation Treatment in Older Adults | A. Alonso | 12/01/17 | 11/30/20 | $441,436 |
| NIH/NHLBI | K24 HL148521 | Mentoring in Patient-Oriented Atrial Fibrillation and Cardiovascular Research | A. Alonso | 07/15/19 | 05/31/20 | $118,502 |
| NIH/NHLBI | R03 HL146879 | Cardiac Electrical Instability in Posttraumatic Stress Disorder: A Twin Study | A. J. Shah | 04/15/19 | 03/31/20 | $78,000 |
| NIH/NHLBI | R03 HL146879 | Emotional Stress as a Risk Factor for Arrhythmia: Ischemic and Genetic Mechanisms | A. J. Shah | 01/15/16 | 12/31/19 | $748,812 |
| Pending | | | | | | |
|  |  |  |  |  |  |  |

The F32 fellowship will support Anish’s salary during his research training. Additional support for his research will come from the sponsor’s endowed chair in cardiovascular research.

## H2. SPONSOR AND CO-SPONSOR PREVIOUS TRAINEES

Throughout her career, Dr. Vaccarino has mentored 15 PhD students and 24 postdocs. A representative sample of five trainees in the past 10 years is below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mentee** | **Initial Position** | **Training Period** | **Area of Research** | **Present Position/Institution** |
| Shaoyong Su, PhD | Postdoc | 2005-2009 | Shared genes between depression and inflammation; genes for heart rate variability | Assistant Professor, Georgia Regents University |
| Amit Shah, MD, MSCR | Postdoc | 2009-2013 | Autonomic mechanisms of cardiovascular disease | Assistant Professor, Emory Rollins School of Public Health |
| Susmita Parashar, MD, MPH, MSCR | Postdoc | 2004-2009 | Depression and outcome of acute myocardial infarction | Assistant Professor, Emory Univ. School of Medicine |
| Samaah Sullivan, PhD | Postdoc | 2016-2018 | Sex differences in vascular and inflammatory responses to acute stress | Instructor, Dept. of Epidemiology, Emory Rollins SPH |
| Ambar Kulshreshtha, MBBS, MPH | Predoc (PhD Program) | 2008-2013 | Life Simple Seven and Risk of Stroke | Assistant Professor, Emory Univ. School of Medicine |

Throughout his career, Dr. Alonso has mentored 8 predoctoral and 11 postdocs. A representative sample of five trainees in the past 10 years is below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mentee** | **Initial Position** | **Training Period** | **Area of Research** | **Present Position/Institution** |
| Lindsay Bengtson, PhD | Predoc (PhD program) | 2010-13 | Epidemiology and outcomes in atrial fibrillation | Senior Researcher, Health Economics and Outcomes Research, Optum |
| Danni Li, PhD | Assistant Professor | 2012-18 | Biomarkers of cognitive and functional decline | Associate Professor of Laboratory Medicine, University of Minnesota |
| Amber Fyfe-Johnson, ND, PhD | Predoc (PhD Program) | 2013-17 | Cardiovascular health in children and adolescents | Research Assistant Professor, Washington State University |
| Antonio Arenas de Larriva, MD | Postdoc | 2015-16 | Epidemiology of cardiovascular diseases | Adjunct Assistant Professor, U. of Córdoba, Spain |

Throughout his career, Dr. Shah has mentored 4 predoctoral and 11 postdocs. A representative sample of five trainees in the past 10 years is below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mentee** | **Initial Position** | **Training Period** | **Area of Research** | **Present Position/Institution** |
| Arash Harzand, MD | Postdoc | 2016-2019 | Smartphone enabled exercise therapy in CVD | Assistant Professor, Emory University |
| Erik Reinertsen, MD, PhD | Predoc (MD-PhD Program) | 2015-2019 | Classification of mental health disorders | Postdoctoral Fellow, Harvard University |
| Giulia Da Poian, PhD | Postdoc | 2017-2019 | Autonomic function and sleep in PTSD | Postdoctoral Fellow, ETH Zürich, Switzerland |
| Nil Gurel | Predoc (PhD Program) | 2017-present | Noninvasive vagal nerve stimulation in PTSD | PhD Student, Georgia Tech |
| Nino Isakadze, MD | Postdoc | 2016-2019 | Atrial fibrillation and depression | Postdoctoral Fellow, Johns Hopkins University |

## H3. TRAINING PLAN, ENVIRONMENT, RESEARCH FACILITIES

### Training Plan

Specific Skills to be Acquired

The main goals of Anish’s mentoring and training plan include first-hand research experience, applying important principles of clinical research methods and research ethics, acquiring proficiency in data analysis, paper writing and scientific presentations, developing research collaborations through regular interactions with the research team and other collaborators, and, ultimately, developing a successful trajectory of research excellence and independence. Anish will participate in the acquisition of key data for his proposed studies. He will interpret and analyze a large and complex set of electrocardiographic data and contribute to data quality control by checking for artifact error. He will contribute to creating adjudication methods for the novel ECG measurements. In addition to these objectives, Anish will learn basic skills of every-day clinical and epidemiological research, such as subject screening, consenting, examination, interviewing, tracking and follow-up, maintaining and monitoring a research database, and performing statistical analyses. He will obtain research expertise primarily through hands-on experience with his own projects as well as through participation in other ongoing studies. However, it will be important for him to also have more formal and structured training opportunities in specific areas as described below.

Formal Teaching

The applicant has taken several basic statistical and epidemiology methods courses during his Master of Science in Clinical Research (MSCR) coursework. The proposed training includes classwork on advanced epidemiology and statistical modeling (EPI 538, EPI 545, BIOS 526, BIOS 534, BIOS 731) and which will be needed to advance his research and grant writing skills. He will also take coursework on responsible conduct of research as described under **Training in the Responsible Conduct of Research** (section G).

Additional Training Opportunities

In addition to the above, Anish will participate in a number of activities which will enhance his opportunities to *interact with the research team and other investigators.* He will be a member of the EPICORE research team in the Department of Epidemiology, and a member of the Emory Clinical Cardiovascular Research Institute (ECCRI) in Cardiology. EPICORE and ECCRI are closely integrated and include experts in translational sciences, population research, risk stratification, imaging, behavioral and preventive cardiology, data management, among others. EPICORE also houses data management and data entry personnel and works closely with faculty and staff in the Biostatistics Department which is located in the same building one floor below. He will thus have ready access to several specialists, statistical assistance and data sources. Regular investigator meetings are scheduled where all investigators, research staff and trainees participate. During these meetings, research in progress is presented by trainees or investigators. Specific training opportunities are listed below.

* Conferences and meetings, locally: a) weekly research meeting (Dr. Vaccarino’s program), b) bi-weekly Epidemiology Grand Rounds, c) monthly Public Health Grand Rounds, d) weekly clinical cardiology research conference, e) weekly Medicine Grand Rounds
* Conferences, national: a) American Heart Association (AHA) Scientific Sessions; b) AHA Epidemiolgoy
* Presentations: a) research-in-progress at investigator meetings; b) conference abstract presentations at national meetings.

Mentoring Plan

A large part of Anish’s training will be through our direct mentorship. He has an impressive skill set and tremendous potential, and with the correct coaching he will be prepared to develop independence. We will guide him in toward growing his now his knowledge of this content area through readings and literature searches, and discussion of new research topics, research methodology and ethics. At the same time, we will supervise the implementation of his proposed project and be constructive reviewers of his progress. We will also encourage him to take an active role in other ongoing research, and to generate new hypotheses leading to new projects. We will advise him on available funding sources, research ethics, and will provide general career counseling and advice. As a mentoring team, we will contribute to his growth in various ways. We have broken down our contributions below:

Dr. Viola Vaccarino:

* Weekly meetings through one-on-one discussion and research/lab meetings, with more contact as needed
* Supervise the implementation his proposed project and engage in regular conversations with him to address problems and methodological issues
* Discuss preliminary results, particularly as it relates to depression and autonomic function
* Ensure access to expert support (biostatisticians, data managers, etc.) and other resources as needed
* Review his papers, providing not only constructive criticism but guide him through the peer-review process
* Coach him on submitting abstracts to scientific conferences and on preparing effective presentations
* Encourage him to take an active role in other ongoing research, seek new collaborators and generate new research hypotheses that may lead to new projects
* Advise him on research ethics
* Provide general career counseling, such as advice on career directions, interacting with superiors and colleagues, managing time, and networking

Dr. Alvaro Alonso:

* Weekly to biweekly meetings to assess milestones and challenges
* Assist with study design, particularly as it relates to confounding, mediation, and interaction
* Serve as a guide for research and grant opportunities
* Review and constructive criticism of papers from data interpretation to hypothesis generation
* Teach and discuss epidemiological concepts as they arise from formal coursework and from hands-on research experience

Dr. Amit Shah:

* Weekly one-on-one meetings to assess challenges and potential new directions for research
* Serve as a role model for a recently independent clinical investigator, providing guidance in the path towards applying for a K award
* Serve as a guide for ECG analysis, both from technical expertise to global challenges in time-series data
* Provide collaboration and networking with colleagues in the Department of Biomedical Informatics, which developed the HRV toolbox that this proposal utilizes
* Teach and discussion the relationship of HRV analysis with psychological and cardiovascular variables
* Supervision in statistical analyses, particularly with repeat measure data
* Provide clinical expertise in coronary artery disease and cardiac catherization as a practicing cardiologist

In terms of timeline, because of Anish’s research productivity, including the MSCR and implementation of the pilot study, we anticipate that he will be able to begin working on his proposed research immediately, with a majority of the patient enrollment completed prior to the grant start date. He will be expected to come up with new original research ideas and will be encouraged to pursue them, using existing data or implementing pilot projects. It is anticipated that towards the end of his training he will be able to perform his first independent step in the form of an original grant proposal. He will be encouraged to apply for a new research grant (e.g. research grants from AHA or NIH K series).

Milestones and Evaluation

Anish will be evaluated at regular intervals during the fellowship using two strategies: 1) self-evaluation using an individual development plan (IDP); and 2) externally by the mentoring team during scheduled intervals. The IDP provides a framework for trainees to monitor progress towards their goals. On a semi-annual basis, we will have individual meetings with Anish to evaluate his progress towards meeting expectations in the following areas: overall research, progress towards becoming an independent researcher, progress towards scholarly goals, technical skills, collaboration skills, communication, and adherence to ethical standards in the conduct of research. In addition to completion of coursework, we will evaluate the number/quality of research products: 1-2-3 research abstracts and presentations at national conferences per year, 1-2 first author papers per year, 2-3 collaborative papers per year, and a research grant application (K series) by the end of the fellowship.

Relationship of the Proposed Research Training to the Applicant’s Career Goals

The ultimate goal of Anish’s training will be to become an independent clinical investigator. During the award period, his independence will be fostered through the following activities:

* Through formal classwork, he will learn research methods and statistical skills that are fundamental in advancing his research independence and successfully completing his project
* With coaching for research presentations, he will present at local and national meetings and gain skills to be an effective and rigorous presenter
* He will be expected to publish first author, original research publications on this project each year to increase his research portfolio and prepare him for career development awards
* In addition, he will be expected to participate in collaborative papers with other research groups to broaden his portfolio and open doors to new directions
* He will be expected to participate in professional committees or other professional work which will allow him to gradually gain visibility
* He will be encouraged to form new collaborations outside of his mentoring/advisory team, both within and outside Emory to enhance his independence
* He will take advantage of institutional opportunities through the graduate school and other mechanisms to support independence, including grant writing classes, funding mechanism seminars, and career development seminars and workshops

### Environment

We are all core members of the Emory Program in Cardiovascular Outcomes Research and Epidemiology ([EPICORE](https://www.sph.emory.edu/departments/epi/research/centers/epicore/index.html)), a research group that formalizes interdisciplinary collaborations and helps develop common research protocols in cardiovascular diseases and related disciplines. Dr. Vaccarino is the Wilton Looney Chair of Cardiovascular Research, Professor and Chair of the Department of Epidemiology at the Rollins School of Public Health (RSPH) and Professor in the Department of Medicine, School of Medicine, as well as the Director of EPICORE. She has established connections to local institutions, such as the Morehouse School of Medicine and the Centers for Disease Control and Prevention, as well as national levels, including participating on study sections with the NIH. Dr. Alvaro is Associate Professor in the Department of Epidemiology, and is a co-investigator in the Atherosclerosis Risk in Communities Study (ARIC). Dr. Amit Shah is Assistant Professor in the Department of Epidemiology and Assistant Professor in the Department of Medicine in the Division of Cardiology, with an active clinical cardiology practice at the Atlanta Veterans Affairs Medical Center. Our institutional collaborations and national connections will prove useful to Anish.

We have we have worked together extensively and collaborate on several projects through EPICORE. The central theme of our overlapping research focuses is focused on the study of the occurrence and outcomes of cardiovascular disease, with particularly emphasis on behavioral factors, novel biomarkers, genetic factors, mind-body relationships, metabolic disorder, and women’s health. We are particularly interested in the study of emotional determinants of cardiovascular risk and the underlying mechanisms such as autonomic function, genetics, and immunity. We have multiple ongoing projects in these areas. Our program combines the rigorous application of research methods through a strong epidemiology program, with an outstanding clinical cardiology research environment and basic science research in vascular biology. We have an interactive and interdisciplinary team of accomplished investigators and other postdoctoral research fellows. EPICORE, in conjunction with the Department of Epidemiology and the Emory Division of Cardiology, organizes educational activities such as the Epidemiology Grand Rounds and the Clinical Cardiology Research Conference. This is a very stimulating and fruitful environment for the further development of our trainee.

### Research Facilities

Details of the training and research environment and facilities are under “**Description of Institutional Environment and Commitment to Training**” (section J). Emory is one of the top biomedical research institutions in the nation, ranking among the top 20 schools of medicine in NIH research funding. Emory has more than 2,500 faculty members. The Rollins School of Public Health (RSPH) ranks 5th nationally according to the US News and World Report, and 5th in total federal funding among all schools of public health. Emory Healthcare, which includes Emory’s own and affiliated clinics and hospitals, is the largest service provider in Georgia. The clinics and hospitals, with almost 3,000 inpatient beds and more than 2 million annual outpatient and emergency visits, create an exceptional environment for clinical research.

Emory offers a rich interdisciplinary environment to foster research collaborations and the career development of junior investigators. Emory has more than 6,000 undergraduate and more than 5,000 graduate and professional students. One of the highlights of working at Emory is the opportunity to collaborate with other scientists in different departments and institutions, including the School of Medicine, the School of Public Health, the Morehouse School of Medicine, the Centers for Disease Control and Prevention (CDC), the Georgia Institute of Technology (GA Tech) and the Atlanta Veterans Administration Medical Center. These institutions are all located in proximity to each other.

The **T32 Multidisciplinary Research Training to Reduce Inequalities in Cardiovascular Health (METRIC)**, directed by Dr. Vaccarino, and co-directed by Dr. Quyyumi (ECCRI/Cardiology), was funded in 2016, and utilizes a multidisciplinary approach and a mentor-based model to train diverse pre-doctoral and post-doctoral candidates in the study of broadly defined inequalities in cardiovascular health and health care. The program supports 4 predoctoral and 4 postdoctoral trainees per year for 2 years.

In addition to **EPICORE** (see J2), The **Emory Clinical Cardiovascular Research Institute (ECCRI)**, based in the Division of Cardiology,is another resource available to the applicant. This is a clinical and translational research center engaged in cardiovascular research which houses faculty, post-doctoral fellows, research coordinators, and technical personnel involved in multiple patient-oriented cardiovascular research protocols. ECCRI’s training and research activities are integrated with those of EPICORE. This applicant will have the opportunity to interact and work directly with investigators at this center. ECCRI and EPICORE also jointly organize the **Clinical Cardiovascular Research Conference series**, a bi-weekly interdisciplinary seminar series, and the **METRIC Seminar Series and Roundtable** which provide excellent opportunities for fellows, including the applicant, to interact/network with faculty in different departments and other fellows.

## H4. NUMBER OF FELLOWS/TRAINEES TO BE SUPERVISED DURING THE FELLOWSHIP

Dr. Vaccarino will supervise two postdoctoral fellow and three PhD students this this fellowship. Dr. Alvaro will supervise two PhD students during this fellowship. Dr. Shah will supervise two predoctoral students during this fellowship.

## H5. APPLICANT'S QUALIFICATIONS AND POTENTIAL FOR A RESEARCH CAREER

Anish completed his residency training at the Emory University J. Willis Hurst Internal Residency Program in June 2019 and is currently completing his MSCR after being selected for TL1 award. He will continue as a postdoctoral fellow in the Department of Epidemiology, where he will have two years of dedicated research time. We will be his main supervisors during this time. The purpose of his training is to develop the solid research skills needed to become an independently funded physician scientist. We have each had many conversations over the past year on his research interests, career direction, and current research application. Our mentorship team will allow him to benefit from each of our unique strengths. We will assist him in his development as a clinical investigator, including preparing him to apply for an early career development award at the end of his fellowship.

Anish has a highly unusual background. He has a special skill and interest in computer science, and an advanced understanding of mathematical concepts. It is rare to find someone in cardiovascular research with both clinical and engineering skills as Anish. He joined the EPICORE group as an intern, working with Dr. Amit Shah and Dr. Vaccarino to study the relationship of autonomic function and ischemic heart disease. He performed an intensive time-series analysis that showed the relationship between heart rate and coronary flow reserve. This work was presented at the 2018 AHA meeting and was chosen by AHA to be one of two posters that were highlighted for the donor luncheon based on its real-world relevance and impact on science. With his statistical background and Dr. Alonso’s guidance, he was able to perform a rigorous epidemiological study of the ARIC cohort, and found that somatic depressive symptoms were strongly associated with autonomic function. Both of these projects are now manuscripts under review with Anish as the first author and are the basis for this current research project. What is most impressive however is that he accomplished this as a resident during a clinically rigorous training program, as well as applying for and receiving the highly selective TL1 award. Anish remains extremely productive, as not only is he completing his MSCR, but has been actively enrolling and conducting the pilot study for this current proposal.

His interest is in the assessment of autonomic dysfunction as a novel risk factor for major cardiovascular events. He is particularly interested in electrocardiographic markers for the prediction and quantification of autonomic dysfunction, as reflected in this proposal. It is a sign of his tremendous potential that he has written this research proposal himself, with minimal guidance from our team, including the pilot study and its analysis. This is likely due to his in-depth understanding of the field, both from an engineering/computational perspective (extracting and analyzing raw data from an ECG device) and from a clinical perspective (classification of depression and coronary artery disease). He has gone above-and-beyond as a trainee and researcher, and this proposal, his prior work, and the preliminary analysis he has done are the best proof of his promise to not only succeed in this research proposal but as a future independent clinical investigator.

This grant award will be instrumental to support Anish during his research training. Because the proposed studies stem from existing projects, most of the research expenses are already covered. This award will fulfill the goals of providing formal methods/biostatistical training and hands-on research experience, as well as mentoring, a network of contacts and collaborations. We are eager to work with this outstanding trainee and guide him towards an accomplished future career as an investigator in an academic setting. He is exceptionally qualified to be part of our program and conduct the proposed research. We each have no doubt that he will be highly successful and a model for others.