# 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.

## 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 | THL130025 | Multidisciplinary Emory Training in Research on Inequities in Cardiovascular Health (METRIC) T32 | V. Vaccarino | 07/01/16 | 06/30/20 | $1,795,815 |
| 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 | 11/30/19 | $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 Dr. Shah’s salary during his research training. Additional support will come from the sponsor’s endowed chair in cardiovascular research. Support for his research project will come XXX

## SPONSOR AND CO-SPONSOR PREVIOUS TRAINEES

State the total number of predoctoral and postdoctoral individuals previously sponsored. Select up to five that are representative, and for those five, provide information on their time spent in the lab, their present employing organizations, and their present position titles or occupations.

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 and 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 | |
| Jun Dai, MD | Predoc (PhD Program) | 2005- 2008 | Mediterranean diet and CVD risk | Assistant Professor, Vanderbilt University |
| 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 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 and Institution** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

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 and 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 |

## TRAINING PLAN, ENVIRONMENT, RESEARCH FACILITIES

### C1. Training Plan

Specific Skills to be Acquired

The main goals of Anish’s mentoring and training plan include gaining 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 section Responsible Conduct of Research.

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 also 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).

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
* Practical experience with big-data that will allow him to study and approach mobile health data challenges
* 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 2-3 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

### C2. 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.

### C3. Research Facilities

Institutional resources

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. Emory Healthcare, which includes Emory’s own or 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 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 Rollins School of Public Health (RSPH) has about 1,000 students pursuing master’s degrees and about 200 PhD students. Many of the over 100 full-time faculty and over 200 adjunct faculty in six academic departments are linked by appointments, shared programs, or research grants within RSPH departments, the School of Medicine as well as the neighboring CDC and other institutions. The school holds more than $70 million in research funding.

Academic cardiology at the Emory University School of Medicine (SOM) has a long-standing and distinguished history. James Warren and Eugene Stead performed the first diagnostic cardiac catheterizations at Emory in the 1940s, and Drs. Stead and Warren did seminal work on the hemodynamics of heart failure and atrial septal defects in the 1940s and 1950s. Dr. Hurst, the Chairman of Medicine at Emory between 1957 and 1986, was an internationally renowned author especially known for The Heart, one of the premier textbooks on Cardiology. Dr. Andreas Grüntzig, the initiator of coronary angioplasty, was on the Emory faculty until his death in 1985. Dr. Leon Goldberg pioneered the use of dopamine as a clinical agent for cardiovascular support at Emory in the 1960s. Emory has a long-standing strong basic research program in vascular biology which was initiated in 1988 by Dr. R. Wayne Alexander, and continued by renowned scientists including Patrice Delafontaine, Kathy Griendling, Bradford Berk, Marschall Runge, David Harrison, and W. Robert Taylor. The cardiology division has continued to grow in faculty, scientific achievements, and funding. It has now over 105 faculty members and a rich pre- and post-doctoral training environment. In additional to over 60 postdoctoral trainees, the division is the research home to graduate students in pharmacology, cell biology, biomedical engineering, mechanical and chemical engineering.

The Georgia Clinical & Translational Science Alliance ([CTSA](http://georgiactsa.org/)), funded by NIH, is an important resource for research and training at Emory. It is led by Emory University, along with partners Morehouse School of Medicine (MSM), Georgia Institute of Technology (GA Tech), and Children's Healthcare of Atlanta. The established partnerships and diverse faculty enables the CTSA to combine the clinical, translational, training and basic discovery programs at Emory with the health disparities, training and community outreach focus of MSM, the engineering and bioinformatics achievements of GA Tech, and the excellence in pediatrics of Children's Healthcare of Atlanta.

Research space and computing environment

Our primary office space is at the RSPH. The RSPH has recently completed an expansion project with the construction of a new state-of-the art 10-story building (CNR), which is adjacent to the pre-existing 10-story building (GCR); the two facilities are connected through a bridge. Both buildings are within the Emory main campus, next to the School of Medicine and close to the Emory University Hospital. The new CNR building houses various departments and laboratories, including the Department of Epidemiology and, within it, our respective offices. RSPH also houses EPICORE, which include the research staff and postdocs. Within the EPICORE facility, databases are stored in a dedicated server. Data are entered into the databases using the TELEFORM application and Web-based systems. Anish will have his own office and computer at the RSPH, in proximity to our offices, with access to printers and to the RSPH and EPICORE database servers. Patient examination for ongoing studies is conducted in the nearby Woodruff Memorial Research building, in a facility entirely dedicated to cardiovascular clinical research, as well as the connected Emory University Hospital.

The computing services at the RSPH allow for advanced computational and biostatistical analyses. The core of our computing services is provided by a Sun SunFire V1280, which has 12 1.2GHz UltraSparc IIIci processors and 24G RAM. Storage is provided through our SAN (storage area network) over a fibre channel network, with 1 terabyte of RAID-protected storage dedicated to the compute server. The server hosts analysis and programming tools including: SAS, SPlus, Fortran 77/90, C, C++, Gauss, Java, R, and IMSL. Database Services. Our main database server is a Dell PowerEdge 2650 with dual Pentium 4 Xeon processors and 8G RAM, running Windows 2003 and MS-SQL Server. The SAN provides access to 265 GB of RAID-protected storage. Web access to this database is provided by Macromedia's ColdFusion application server, which runs on a Dell PowerEdge 2650 (dual P4 Xeon, 4 GB RAM) running RedHat Enterprise Linux. Network Environment. The RSPH network consists of Fast Ethernet hardware running TCP/IP. Gigabit Ethernet provides high speed transmission to each of 10 floors and across three buildings. Ethernet provides high speed (10 Mbps) access to most desktop computers and peripheral devices. The network terminates at over 900 locations. The RSPH network is connected to the Emory Campus backbone via a 100 Mbps Ethernet. RSPH also provides its own high-performance computing cluster, consisting of 256 cores, each with 2 GB RAM, housed in 12 physical nodes. Each node is joined by 1 GB Ethernet. All clusters include access to MATLAB R2019a, Python 2.7 and 3, R 3.6.1, and numerous processing tools and open-source libraries.

## Number of Fellows/Trainees to be Supervised During the Fellowship

Dr. Vaccarino will supervise another postdoctoral fellow and two 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.

## 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.