# H. SPONSOR AND CO-SPONSOR STATEMENTS

## H1. RESEARCH SUPPORT AVAILABLE

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Funding Source** | **Grant No.** | **Title** | **Principal Investigator** | **Start** | **End** | **Award Amount** |
| 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 | R01HL10941 | Mental Stress and Myocardial Ischemia after MI: Sex Differences, Mechanisms and Prognosis | V. Vaccarino | 08/15/19 | 07/31/24 | $2,486,076 |
| 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 |

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. Dr. Vaccarino will serve as the primary sponsor and mentor for Anish. Anish is a postdoctoral fellow in epidemiology who has completed training in internal medicine. He will pursue additional research fellowship training prior to applying for career develop awards. The F32 fellowship will support his 2 years of research.

Dr. Vaccarino is well suited to serve as the lead mentor for Anish. She has international recognition for her work on behavioral and psychological determinants of cardiovascular disease and women’s health. An area of growing interest is the role of acute mental stress, negative emotions and mental health on hemodynamic reactivity, and immune, autonomic and vascular responses. She has published over 350 peer-reviewed research publications and has been continuously funded by the NIH as a PI for almost 20 years. She is Professor and former Chair of the Epidemiology Department at the Rollins School of Public Health, where she holds the Wilton Looney endowed chair in cardiovascular research; she is the program director for the NHLBI METRIC T32 for predocs and postdocs, and holds a joint appointment in the Division of Cardiology.

Dr. Vaccarino has worked closely with all the members in Anish’s mentoring and advisory team, including Dr. Arshed Quyyumi, the leader of the Emory Cardiovascular Biobank study, with whom she shares several research grants. Perhaps Dr. Vaccarino’s most important qualification to serve as a mentor to Anish’s F32 application is her commitment towards mentoring. Throughout her career, she has dedicated a large part of her time to mentoring students, postdoctoral fellows and junior faculty members. She has been the primary mentor of 15 PhD students and 24 postdocs in addition to several junior faculty (including Dr. Amit Shah), and was funded for 10 years by a NHLBI K24 to help support her mentoring activities. She has sponsored several funded training/career development awards, including five NIH K awards, five K12/KL2 ACTSI fellowships, six AHA scientist development grants, five NRSA F31/F32 fellowships, and six AHA/ACC predoc/postdoc fellowships. Additionally, several of her trainees have received prestigious national awards for their work, including the Elizabeth-Barrett Connor Award for Young Investigators at the AHA Scientific Sessions, the Jeremiah and Rose Stamler Research Award for New Investigators at the AHA Conference on Epidemiology and Prevention, and the Trudy Bush Award for CVD Research in Women’s Health at the same conference. Many of her trainees have pursued successful academic careers as independent investigators (examples provided in next section).

As the primary sponsor for the proposed F32 award, Dr. Vaccarino will assume primary responsibility for the overall supervision of his research, training and career development. In addition to structured training as described below, and to supervising the applicant’s research progress, Dr. Vaccarino will train him directly in the use of psychological surveys, the study of depressive symptoms in coronary disease, and the conduct of research on psychological stress and physical health outcomes. She will also train him in the practical aspects of implementing the study, including participant recruitment and examination, data collection and data management. For this aspect of the research and training, Anish will also work closely with our staff recruiters, research coordinators and data managers, to learn the day-to-day aspects of recruitment, data collection, and database development. Furthermore, Dr. Amit Shah will work closely with him to train him on ECG analysis and interpretation, and Dr. Alonso will instruct him on epidemiological data analysis.

Dr. Vaccarino currently devotes about 75% of her professional time to research and mentoring. She will meet with Dr. Shah weekly, in addition to other interactions as part of regular research meetings, seminars and conferences, and as need arises. Dr. Shah will meet regularly with his co-mentors as well.

## H2. SPONSOR AND CO-SPONSOR PREVIOUS TRAINEES

Throughout her career, Dr. Vaccarino has mentored 17 PhD students and 24 postdocs as their primary mentor or dissertation chair/co-chair. 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 |

The co-sponsors have extensive mentoring experience as well. Dr. Alonso has mentored 8 predoctoral and 11 postdocs, and Dr. Shah has mentored 4 predoctoral and 11 postdocs.

## H3. TRAINING PLAN, ENVIRONMENT, RESEARCH FACILITIES

### Environment

The central theme of the sponsors’ research programs is focused on the study of the determinants, mechanisms and outcomes of cardiovascular disease (CVD), with particular emphasis on behavioral factors, novel biomarkers, genetic factors, mind-body relationships on cardiometabolic conditions 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, neurobiology 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 established training program within an interactive and interdisciplinary team of accomplished investigators. This is a very stimulating and fruitful environment for the training of Anish.

Dr. Vaccarino is the Director of the Emory Program in Cardiovascular Outcomes Research and Epidemiology (EPICORE), a research group with expert field and data management staff who run Dr. Vaccarino’s research projects and those of collaborators. This center formalizes interdisciplinary collaborations and helps develop common research protocols in cardiovascular diseases and related disciplines. EPICORE, in conjunction with the Department of Epidemiology, the Emory Division of Cardiology, and the METRIC T32, organizes educational activities such as the Epidemiology/METRIC Seminar Series and the Clinical Cardiology Research Conference. All trainees in our training programs (irrespective of whether their funding comes from the T32 or other sources) have access to these and other specialized seminar series in cardiovascular research and individualized research rotations, and participate in the monthly Research in Progress Roundtable where they practice presentation skills, update faculty mentors on their progress, and interact and network with faculty and fellow trainees.

Outside her institution, Dr. Vaccarino has established links in the local Atlanta area, such as the Morehouse School of Medicine and the Centers for Disease Control and Prevention. At the national level, she has extended collaborations with researchers at outside institutions with whom she has developed collaborative projects, including, among others, the University of Washington, the University of Pittsburgh, Boston University, Yale University and Columbia University. In addition, Dr. Alonso, Professor in the Department of Epidemiology, is a co-investigator in the Atherosclerosis Risk in Communities Study (ARIC). He has national and international collaborators that he maintains relationships with. 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. He has multiple institutional relationships, including the Department of Biomedical Informatics and medical technology companies. All these connections will prove useful to Anish.

### 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. Direct training/mentoring will come from regular interactions with his sponsor and co-mentors. Dr. Vaccarino will train him in theanalysis of psychological data, the study of sex differences in cardiovascular epidemiology and pathophysiology, and the practical data collection and execution of cohort studies. Dr. Amit Shah will train him in the methods of ECG analysis and signal processing, and Dr. Alonso will train him in biostatistics and epidemiological data analysis.He 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 activities, 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 is taking several basic statistical and epidemiology methods courses as part of his 2-year Master of Science in Clinical Research (MSCR) coursework through the TL1 program. Since the TL1 program lasts only 1 year, it is anticipated that Anish will complete the MSCR thesis under the F32 award. In addition, the proposed F32 training includes additional classwork on advanced epidemiology and statistical modeling (EPI 538, EPI 545, BIOS 526, BIOS 534, BIOS 731), 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, f) journal club (ECCRI and MSCR)
* 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 come from my direct mentorship and that of his co-mentors. 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 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 provide constructive reviews of his progress. He will be encouraged 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 of 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 provide 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
* Supervise statistical analyses, particularly for 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, his current enrollment in the TL1 and the MSCR program and the fact that he has already conducted a pilot study, I anticipate that he will be able to begin working on his proposed research immediately, with most of the patient enrollment completed prior to the grant start date. Therefore, during the F32 period he will be able to focus on statistical analysis and manuscript preparation. Furthermore, he will be expected to come up with new original research ideas and will be encouraged to pursue them, using existing data or implementing new 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 (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, I 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, I 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 promote his development towards becoming 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
* 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, career development seminars and workshops, and pilot research funds.

### 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 Roundtablewhich 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 three postdoctoral fellows and three PhD students during this fellowship. Dr. Alvaro will supervise two PhD students and Dr. Shah 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 the institutional 1-year TL1 program through the Georgia CTSA. 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 his 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 physician scientist, including preparing him to apply for a career development award at the end of his fellowship.

Anish has a highly unusual background. He has special skills 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 like 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 quantitative 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 proposal. What is most impressive however is that he accomplished all this work while he was a resident during a clinically rigorous training program. During the same time he applied for and received the highly selective TL1 award. Anish remains extremely productive, as not only is he completing the MSCR, but has been actively enrolling and conducting the pilot study for this current proposal.

Anish’s main interest is in the assessment of autonomic dysfunction as a potential novel risk factor and prognostic 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, requiring only minimal guidance from our team, including the execution of 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 junior 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.