

March 11, 2019

Georgia Clinical & Translational Science Alliance: TL1 Program

Emory University

Dear Committee Members,

It is with the greatest enthusiasm that I write to offer my support for Anish Shah’s submission for the TL1 Award as a Co-Lead mentor. Anish is a remarkably bright, engaging, and enthusiastic individual who has demonstrated the potential to become an outstanding clinical researcher. He joined Emory for his internal medicine residency training in 2016, and has excelled as a clinician, and has continued to work with the Department of Epidemiology here at Rollins School of Public Health. He has shown a specific passion in cardiovascular epidemiology, with a focus on autonomic dysfunction and associated neuropsychological risk factors. He has repeatedly shown initiative in his own development through project leadership, self-motivated research proposals, and an uncanny capacity for problem-solving through independent study. I can think of no better candidate for this award, and have no reservations in supporting him wholeheartedly.

I completed my MD, PhD, and medical residency in preventive medicine in Spain, with additional training in cardiovascular epidemiology at Harvard School of Public Health. My research mainly focuses on the epidemiology of atrial fibrillation. For the last ten years, I have conducted extensive research in the setting of the Atherosclerosis Risk in Communities (ARIC) Study where I am involved in studies aimed to understand the distribution and determinants of atrial fibrillation in the community. I am also a co-investigator in studies evaluating the impact of cardiovascular risk factors on cognitive decline (e.g. ARIC Neurocognitive Study). I have been continuously funded by grants from the National Heart, Lung, Blood Institute (NHLBI) and the American Heart Association (AHA), and have led numerous studies including the ARIC study and the Multi-Ethnic Study of Atherosclerosis (MESA) on the incidence of AF and its outcomes. I have mentored numerous students and trainees, including PhD graduates, MPH students, and postdoctoral fellows both at the University of Minnesota and now at Emory University. I also have an extensive history of successful collaborations with junior faculty that have led to publications and grant funding, including Amit Shah, MD, MSCR, who will serve alongside me as Anish’s lead mentors.

Anish has had a common thread throughout his education thus far in studying the mind-body connection. As an undergraduate at Emory, he studied linguistics, neuroscience, and behavioral biology. This theme continues as he now has multiple projects that study the relationship of the psychological factors to the heart, including his most recent first-author manuscript entitled “Circadian Changes in Heart Rate Variability Predict Abnormal Myocardial Perfusion”. An important aspect of his research is that Anish independently performed the complex statistics required for twin analysis using linear mixed models, which was verified by our biostatisticians. This work was selected as one of just two top-posters at the AHA Scientific Sessions 2018. One of the interesting sub-group analyses he performed found a strong association of heart rate variability (HRV) with depression, which he has continued to study with Dr. Shah. To highlight his initiative, he independently and successfully wrote a manuscript proposal to examine the relationship of HRV with psychological stress in the ARIC study. As an ARIC investigator, I supported his proposal and have helped him to understand the complexities of large cohort data sets, and will continue to do so as he completes this latest manuscript. He found in this preliminary work that indices of HRV were independently associated with different forms of psychological stress, including exhaustion, anger, and social support, which showcases the importance of studying non-traditional risk factors in understanding cardiovascular risk.

His research proposal follows a similar theme. He intends to measure autonomic dysfunction through a novel HRV index called *Dyx*, and study the relationship with ischemic heart disease and neuropsychological factors including depression and cognitive impairment. He found in his prior work that *Dyx* is a more robust indicator of autonomic dysfunction than traditional HRV indices in a cohort from the Emory Twins Study. Over the last several years I have studied HRV within the ARIC cohort, looking at incidence of stroke, Parkinson’s disease, and AF risk. One inherent limitation of this prior work was the availability of only two to five minutes of ECG recordings for analysis. The current research proposal intends to use several hours of ECG data for analysis, which will give us a much stronger understanding of autonomic dysfunction as it pertains to cardiovascular risk and neuropsychological factors. Autonomic dysfunction has growing evidence of being important in the pathogenesis of mortality from cardiovascular disease, particularly as it relates to susceptibility of arrhythmia. However, little work has been done use measures of autonomic dysfunction to identify at-risk patients, and this will be the first study to look at *Dyx* in the role of multiple important conditions, including obstructive coronary artery disease, depression, life stress, and cognitive impairment. The data generated from this proposal will not only support his prior work, but potentially establish a novel, independent, and non-invasive risk stratification tool for risk-stratification in ischemic heart disease.

As described, the most promising traits that Anish exemplifies are his intellectual curiosity, independent and critical thinking, and combination of clinical and technical expertise (e.g. experience in statistics, programming, and data science), placing him in a unique position to merge his talents to become an outstanding physician and scientist. To his credit, Anish developed the core of this research proposal himself by studying the literature in the multidisciplinary field of neurocardiology independently, and creating a coherent, intentional, and step-wise proposal. More so, he responded to feedback constructively, adapting to problems and providing his own solutions, showcasing his drive and engagement in the research process. Along with his prior manuscript and his current paper on the ARIC cohort, he was invited to join a review article in *Hypertension*, and was requested to write another review on cardiac sympathetic innervation with one of our senior cardiologists, Dr. Marc Thames. Part of his productivity stems from how he actively reaches out for guidance and collaboration within the mentoring team that has grown organically around him, including his other senior advisors Dr. Viola Vaccarino and Dr. Arshed Quyyumi.

In summary, Anish is an exceptional candidate for this award who has the fundamental characteristics to grow into clinical researcher who will contribute substantially to this field. The MSCR will give him the formal training to approach complex research questions with depth and skill. He demonstrates talent and intellectual curiosity fueled by a sincere passion for neurocardiology and innovating the means to help serve his patients. I plan to meet with Anish individually every other week, along with regular interactions through weekly lab meetings, and frequent e-mail and as-needed meetings to help him with study design in cardiovascular epidemiology, interpretation of neurocognitive impairment data, and the assessment of electrophysiology correlates of autonomic dysfunction. I have no doubt about his potential and future success as he continues on to train in preventive cardiology and clinical research, and I wish to endorse Anish with the highest regards. I am fully committed to his academic development, and have no reservations about serving as his Co-Lead mentor along with Dr. Shah. Please contact me with any questions.

Sincerely,



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