March 15, 2019

Georgia Clinical & Translational Science Alliance: TL1 Program

Emory University

Dear Committee Members,

I am pleased to write you to support Anish Shah, MD for his application for the TL1 award. I am enthusiastic about serving as an advisor for him as a part of his mentoring team. I met Anish in 2018 as he began his first manuscript on autonomic dysfunction, and am most impressed by his potential to become an outstanding clinical researcher in the field of neurocardiology and epidemiology. He has a distinct passion for studying the autonomic nervous system, understanding mechanisms, and has grown tremendously in the short time that I have known him. I believe that his completion of the TL1 and Master of Science in Clinical Research will be fundamental on his accelerated path towards becoming a clinical researcher.

[Thames training overview from NIH biosketch]

I have worked on several projects with Anish, including his most recent paper under review on heart rate variability (HRV) and myocardial perfusion imaging (MPI) abnormalities. He demonstrated that a marker of autonomic function, heart rate variability, was able to predict those at risk for abnormal myocardial perfusion imaging, and that the finding is most prominent in the early morning hours. The complex math behind generating the *Dyx* variable is conceptually intriguing, as it seems to capture additional information about sympathovagal balance that was less measurable with traditional HRV. Noteworthy is that Anish has a familiarity with the mathematical concepts at play due to his background in computer science, which places him in the rare position of being able to find clinical meaning in the mathetmatical abstractions he is studying. His paper is hypothesis-generating, as now we are faced with the question of whether the abnormal coronary blood flow occurred from epicardial vessels or microvascular resistance vessels, as there is a certain false positive rate with MPI and it is unknown how coronary angiography compares. I have talked with Anish about this specifically on multiple occasions, and helped him refine a pointed research question that is a central part of his upcoming research proposal.

His current research proposal is to look at a unique and relatively new HRV measure named *Dyx* and how it relates to the neurocardiac axis. He will look at cardiac catherization data in an ongoing study at Emory and see if *Dyx* will be predictive of the amount of stenosis. Although epicardial disease is the expected result, a negative finding would be mechanistically very interesting and thus a high-yield hypothesis to explore. I have extensively published in the field of neurocardiology, with an expertise in autonomic innervation of the heart through study of canine models, as a basic scientist and cardiologist. Thus, I am well-suited to serve as his advisor and can guide him in his understanding and interpretation of his findings at a mechanisms level. As part of his mentoring team, I provide a unique perspective that has already shown to be quite helpful in his current work, his academic development, and I suspect that it will continue.

Anish recently gave his senior lecture on sudden cardiac death and the autonomic nervous system, for which I served as a mentor. It was quite well-received. He shows such promise and growing knowledge in the field that I asked him to write a clinical review article on the sympathetic efferent innervation of the heart, which he is currently working on. Not only is the topic clinically relevant and timely, I think it will improve Anish’s overall understanding of the field at an anatomic and physiologic level. Co-authors on this paper are other clinicians with an interest in the neurocardiac axis, including Amit Shah, MD, MSCR, who is the co-lead mentor for Anish on this grant application. Our continual collaboration on his prior work on *Dyx*, this review article, and the upcoming research project are examples of how the mentoring team I think have and will serve for his academic growth.

His current grant proposal also looks at the neurocardiac axis from another direction, the relationship of the autonomic nervous system and psychological factors. This topic is of interest as it begins to answer a well-posed question by a the researcher Douglas Zipes — “Why did he die on a Tuesday and not on a Monday?” Understanding how neuropsychiatric disorders change autonomic tone, change ventricular fibrillatory threshold, and lead to sudden death are burning topics. By measuring *Dyx*, we will add a non-invasive measure of autonomic tone that can help quantify these relationships.

In summary, I support Dr. Anish Shah in his application for the TL1 award. He will benefit tremendously not only from the protected research time, but also developing his background in computer programming and statistics through formal training with the MSCR. As his advisor for this grant, we will plan to meet in-person monthly to review his work and progress, with a particular focusing on mechanisms and interpretation. We will also interact through e-mail and phone as questions arise. I will also provide routine critical feedback in the manuscript drafting process. I have no reservations about Anish’s success this upcoming year. He has my highest recommendations as a young and promising clinical researcher.

Sincerely,

Marc D. Thames, MD

Assistant Professor

Division of Cardiology

Emory University

[marc.thames@emory.edu](mailto:marc.thames@emory.edu)