Individual Development Plan

T32/F32 to K08/K23 Transition

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# Education

## Clinical Rotations

Table 1:

|  |  |
| --- | --- |
| Coronary/Cardiac Care Unit | 3 blocks |
| General Cardiology Consults | 4 blocks |
| Electrophysiology Consults | 2 blocks |
| Non-invasive Imaging | 6.25 blocks |
| Catheterization Laboratory | 4 blocks |
| Heart Failure | 0.5 blocks |
| Research | 11 blocks |
| Clinic (Half Days) | 117 clinics |

## Academic Training

Table 2:

|  |  |  |
| --- | --- | --- |
| Emory University | Bachelor of Science | 2011 |
| Texas A&M University | Doctor of Medicine | 2016 |
| Emory University | J. Willis Hurst Internal Medicine Residency | 2019 |
| Emory University | Master of Science | 2020 |
| University of Illinois at Chicago | Cardiology Fellowship | - |

# Research Experience

During this time I also developed a research background through projects that focused on computational neurocardiology. The projects and their descriptions are listed below…

Table 3:

|  |  |  |
| --- | --- | --- |
| MSIMI and CV Mortality | A large prospective cohort study measuring myocardial ischemia in response to mental stress, with extensive follow-up. Analytical skills included the development of recurrent event models (AG, PWP, MSM, marginal, conditional). Recurrent event software in R was developed. Middle-author Publication in JAMA | 2019-2020 |
| HRV and Myocardial Perfusion | Evaluated circadian patterns in autonomic function using 24-hour Holter data, generating HRV with a focus on spectral density analyses. Compared these patterns with CFR on quantitate PET, finding a relationship with CFR and early morning low HRV. First-author Publication in IJC | 2017-2020 |
| GEH and Diabetes | Using the CARRS cohort, evaluated ECG-based patterns of GEH and diabetes, finding a strong relationship with cardiac fibrosis and widening of specific GEH parameters. WIP | 2018-2019 |
| HRV and Psychosocial Factors | Evaluated changes in HRV from baseline to several years later in the ARIC Study. Found that psychosomatic stress (in the form of vital exhaustion) led to a persistent decrease in high frequency HRV, a surrogate of vagal tone. First-author Publication in JAHA | 2016-2020 |
| AFL and Family History | Statistical analysis of relationship between early onset AFL and family history, which notably yields different phenotypes in Whites and Blacks. WIP | 2022 |
| Disturbances of Neurocardiac Axis | TL1 and F32 grant focused on evaluating of myocardial ischemia and changes in autonomic function using HRV. Pilot study with completed recruitment. Publication of Thesis and WIP | 2019-now |
| Harmonic Regression Analysis | Measuring circadian patterns and disturbances using a cosinor regression method. First-author Publication of Software Package (CRAN) | 2019 |

*GEH = global electrical heterogeneity; HRV = heart rate variability; CV = cardiovascular; SCD = sudden cardiac death; AFL = family history; MSIMI = mental stress induced myocardial ischemia; PET = positron emission tomography*

Technical research skills:

* epidemiology and biostatistics
* study design (IRB, informed consent, subjection enrollment)
* digital signal processing (HRV, ECG)
* programming in R, MATLAB
* harmonic regression
* advanced survival models with recurrent events

# Personal Goals

Douglas Zipes asked the question “Why did he die on Tuesday and not on Monday?” In the 50 years since the advent of the coronary care unit,1 we have extensively studied sudden cardiac death but it remains a looming challenge - roughly 1/5 deaths are arrhythmogenic in nature.2,3. The problem can be broken down into two components: 1) a substrate and 2) a trigger. My area of focus on this problem is that of the trigger, combining stress epidemiology and triggered arrhythmias as the two major aims of my work in neurocardiology. My computational approach parallels these topics by combining biostatistics and digital signal processing.

## Short Term

My short-term goals are the following…

1. General Cardiology Fellowship, with General and Echocardiography Board Certifications
2. Clinical Electrophysiology Fellowship, focused on Chicago-land training opportunities.
3. K23/K08/CDA grant application

As I have already had an extensive background in biostatistics and epidemiology, my focus is to reframe my training to include “wet lab” methodologies, including applied physiology and genetics. This is to help support my next grant application, by highlighting research strengths in the two core areas of **stress epidmeiology** and **triggered arrhythmias**. I will need 2-3 first-author publications in these areas over the next 1-2 years.

## Long Term

My long-term goal is to be a federally-funded computational neurocardiologist and a clinical electrophysiologist. This entails working as an attending physician-scientist, with a division of time as seen below…

Table 4:

| **FTE** | **Description** |
| --- | --- |
| 0.4 | Electrophysiology Lab |
| 0.1 | Clinic |
| 0.2 | Epidemiology Research |
| 0.2 | Arrhythmia Research |
| 0.1 | Administrative Time |

# Research Plan

## Committee Members

The committee members have multiple R01-level funding, with differential strengths to complement my training plan.

1. Amit J. Shah, MD, MS (Cardiologist): stress epidemiology, autonomic dysfunction
2. Dawood Darbar, MBCHB, MD (Electrophysiologist): atrial arrhythmias, genetics
3. Mark McCauley, MD, PHD (Electrophysiologist): atrial arrhythmias, basic/translational science
4. Alvaro Alonso, MD, PHD (Epidemiologist): atrial fibrillation epidemiology, ARIC investigator
5. Viola Vaccarino, MD, PHD (Epidemiologist): stress epidemiology
6. Jalees Rehman, MD (Cardiologist): computational biology
7. Rachel Lampert, MD (Electrophysiologist): autonomic dysfunction, sudden cardiac death
8. Andrew Boyd, MD (Clinical Bioinformatics): biomedical informatics

This still needs to be narrowed down for the eventual grant proposal after the core aims are formalized.

## Proposal

My proposal is divided into two aims: 1) vagolysis-triggered arrhythmogenesis, 2) arrhythmia phenotyping. Both will be further developed into the aims and sub-aims for my future K-grant.

1. **Explore the role of vagolysis in triggered arrhythmias.** Hypothesis: arrhythmia thresholds will be reduced by blockade of vagolysis (as opposed to only adrenergic stimulation).

The atria are heavily innervated by autonomic ganglionic plexi, leading to the complex activity that regulates cardiac conductive properties.4,5 The key mechanism that we will explore is the intracardiac cross-talk between adrenergic (sympathetic) and cholinergic (vagal) neurons. Adrenergic neurons release catecholamines that directly affect the myocardium, but indirectly as well through neuropeptide Y (NPY).6 NPY binds to cholinergic neurons through the Y2 receptor, inhibiting firing and leading to vagolytic effects on the myocardium.7,8

In a murine model of arrhythmia, I propose to study the characteristics of myocardial conduction properties (phase slope changes, after depolarizations, ectopy) in a series of experiments that modulate the sympathetic nervous system at the level of the myocardium. These models will be prepared as ex-vivo, vagal-sparing whole heart explants in Langendorf preparations.

1. **Identify phenotypes of triggered arrhythmia.** Hypothesis: clinical phenotypes of atrial fibrillation exist that will classify increased burden of pulmonary vein triggers as measured by electrophysiology study.

Using several “big-data” cohorts apart from UIC, including ARIC, MESA, MVP, the VA Research Database, I will create computational models to classify atrial fibrillation phenotypes (based on clinical, ECG, and echocardiographic parameters). These classification clusters will be used to compare findings from intracardiac monitoring during EPS/PVI, such as LA geometry, atrial scar and voltage burden, dominant AF frequencies, ectopy, etc. This project remains a work-in-progress and will need further credentials, computational power, and signal processing efforts to realize.

# Publications and Funding

Publications after fellowship are listed below:

Shah, A. S., Alonso, A., Whitsel, E. A., Soliman, E. Z., Vaccarino, V., & Shah, A. J. (2021). Association of Psychosocial Factors With Short‐Term Resting Heart Rate Variability: The Atherosclerosis Risk in Communities Study. Journal of the American Heart Association, 10(5), e017172. https://doi.org/10.1161/JAHA.120.017172

Shah, A. S. (2021). Stress Reactivity: Disturbances of the Neurocardiac Axis. https://etd.library.emory.edu/concern/etds/tx31qj818

Vaccarino, V., Almuwaqqat, Z., Kim, J. H., Hammadah, M., Shah, A. J. A., Ko, Y. A., Elon, L., Sullivan, S., Shah, A. J. A., Alkhoder, A., Lima, B. B., Pearce, B., Ward, L., Kutner, M., Hu, Y., Lewis, T. T., Garcia, E. v., Nye, J., Sheps, D. S., … Quyyumi, A. A. (2021). Association of Mental Stress-Induced Myocardial Ischemia with Cardiovascular Events in Patients with Coronary Heart Disease. JAMA - Journal of the American Medical Association, 326(18), 1818–1828. https://doi.org/10.1001/jama.2021.17649

Shah, A. S., Shah, A. J., Lampert, R., Goldberg, J., Bremner, J. D., Li, L., Thames, M. D., Vaccarino, V., & Shah, A. S. A. J. (2020). Alterations in heart rate variability are associated with abnormal myocardial perfusion. International Journal of Cardiology, 305, 99–105. https://doi.org/10.1016/j.ijcard.2020.01.069

Pending publications include:

* Manuscript submitted to Circulation: Mental Stress-Induced Autonomic Dysfunction is Associated with Cardiovascular Mortality
* Abstract submitted to ACC: Mental Stress-Induced Autonomic Dysfunction is Associated with Cardiovascular Mortality
* Abstract submitted to HRS: AFL and Family Histoory
* Abstract submitted to HRS: AF Recurrence by Race/Ethnicity

Funding:

* F32 received
* AHA IPA (withdrawn)
* K23 in planning stages

# References

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3. Lown B, Verrier RL, Rabinowitz SH. Neural and psychologic mechanisms and the problem of sudden cardiac death. The American Journal of Cardiology 1977;39:890–902. doi:[10.1016/S0002-9149(77)80044-1](https://doi.org/10.1016/S0002-9149(77)80044-1).

4. Hoover DB, Isaacs ER, Jacques F, Hoard JL, Pagé P, Armour JA. Localization of multiple neurotransmitters in surgically derived specimens of human atrial ganglia. Neuroscience 2009;164:1170–1179. doi:[10.1016/j.neuroscience.2009.09.001](https://doi.org/10.1016/j.neuroscience.2009.09.001).

5. Armour JA, Murphy DA, Yuan BX, Macdonald S, Hopkins DA. Gross and microscopic anatomy of the human intrinsic cardiac nervous system. Anatomical Record 1997;247:289–298. doi:[10.1002/(SICI)1097-0185(199702)247:2<289::AID-AR15>3.0.CO;2-L](https://doi.org/10.1002/(SICI)1097-0185(199702)247:2%3c289::AID-AR15%3e3.0.CO;2-L).

6. Coote JH. Myths and realities of the cardiac vagus 2013;591:4073–4085. doi:[10.1113/jphysiol.2013.257758](https://doi.org/10.1113/jphysiol.2013.257758).

7. Kalla M, Hao G, Tapoulal N, Tomek J, Liu K, Woodward L, et al. The cardiac sympathetic co-transmitter neuropeptide Y is pro-arrhythmic following ST-elevation myocardial infarction despite beta-blockade. European Heart Journal 2020;41:2168–2179. doi:[10.1093/eurheartj/ehz852](https://doi.org/10.1093/eurheartj/ehz852).

8. Herring N, Lokale MN, Danson EJ, Heaton DA, Paterson DJ. Neuropeptide Y reduces acetylcholine release and vagal bradycardia via a Y2 receptor-mediated, protein kinase C-dependent pathway. Journal of Molecular and Cellular Cardiology 2008;44:477–485. doi:[10.1016/j.yjmcc.2007.10.001](https://doi.org/10.1016/j.yjmcc.2007.10.001).