APPLICANT'S BACKGROUND AND GOALS FOR FELLOWSHIP TRAINING

A. Doctoral Dissertation and Research Experience

Doctoral Dissertation

My PhD advisory committee consists of 2 muscle physiologists, an academic cardiologist, and my sponsor (Ken Campbell, PhD, a translational cardiovascular researcher). I presented an early version of this F31 proposal to them as part of my Qualify Exam and they approved my goal to quantify how titin-truncating variants impact cellular turnover pathways, accumulation of cytosolic waste, and cardiac mechanics.

My experiments will use myocardial samples donated by organ donors and patients with non-ischemic cardiomyopathy that I have helped to procure for the Gill Cardiovascular Biorepository led by Dr. Campbell. I will also work with the clinical data associated with each specimen. This will give me a unique background in translational and applied cardiovascular research that will strengthen my applications for postdoc positions in well-respected labs. My long-term goal is to lead my own research program and try to use research to help patients who develop cardiovascular disease due to inherited variants.

Prior Research Experience

Undergraduate Research Experience (2019 – 2022)

Growing up alongside my sister as she battled with an idiopathic neuromuscular disorder fueled my interest in translational research, particularly the interplay between genetics and pathology. My undergraduate institution was a small liberal arts college that lacked extensive research infrastructure, making it difficult to find clinically relevant research labs. I persisted and earned a researcher role in the lab of Rachel Pritchard, PhD, investigating antibiotic production from soil bacteria. 6 months after starting in Dr. Pritchard's lab, I took the lead on a new project and compiled preliminary data to support an application for an institutional award. My project was funded for 2 years during which I identified 13 bacterial isolates that produced broad spectrum antimicrobial compounds. I presented my findings at 6 conferences as 3 posters and 3 podium talks. My podium talks at the 2020 Kentucky-Tennessee American Society for Microbiology and 2021 Kentucky Academy of Science Annual Meetings received 1st-and 2nd-place presenter honors, respectively. Moreover, I served as 1 of 3 invited speakers at the 2022 STEM Bridge Program hosted by my undergraduate institution. These first experiences in research reinforced my interests and led to me applying to the more translational environment at my state's flagship university .

Graduate Research Experience (2023 – Present)

I was admitted into the Integrated Biomedical Sciences PhD Program at the University of Kentucky College of Medicine in August of 2022. The first year of this program involves taking undifferentiated core curriculum prior to joining a lab. Upon completion of these courses, I joined Dr. Campbell's lab, where I began working on the genetic characterization of our large cardiac biobank. The heart contains primarily post-mitotic cells, making it difficult to extract high quality nucleic acids from it. However, I optimized an extraction and purification protocol for tissue in our biobank, which I performed on over 350 human hearts.

Concurrently, I have become proficient and am still improving my skills in coding, particularly for batch data analysis. This has become especially useful for our multi-omics data since it exceeds 10 terabytes. I have used this knowledge to build scripts acceptable for a layperson to parse through the data efficiently (e.g., variants for one gene). This coding skillset has enabled me to identify 24 patients who have both non-ischemic heart failure and a titin-truncating variant. Moreover, I have built an image processing pipeline that executes precise and high-throughput segmentation of fluorescent scans, crucial for Aims 2 and 3 of this proposal. I have also customized this workflow for brightfield scans, making it the standard for analyzing histology in Dr. Campbell's lab.

Since joining Dr. Campbell's lab, I have presented my work at 8 conferences, including the 2024 Madison Myofilament and 2025 Biophysical Society Annual Meetings. In addition, I delivered a departmental podium talk focused on cardiac titin variants.

B. Training Goals and Objectives

My primary training goal during this fellowship is to develop expertise in a range of techniques that will help quantify links between genetics and heart failure pathophysiology. I will strengthen my scientific, collaborative, and communication skills while directly addressing the hypothesis outlined in this proposal. This experience will provide hands-on training in translational research while studying the bases of genetic characterization, RNA/protein turnover, accumulation of cellular waste, and muscle mechanics in human heart failure. I will gain technical expertise in genomic analysis, biochemistry, and biophysics while engaging with scientists across related disciplines. The resulting research outputs will demonstrate meaningful progress and productivity, supporting future applications for postdoctoral positions and extramural awards. Ultimately, this fellowship will serve as a springboard towards achieving my short- and long-term goals (listed below).

Annual Research Product Goals

- Manuscripts/Publications
    - 2 First-Author
    - 2 Co-Author
- Conference Presentations (*1 abstract selected for podium talk)
    - 2 Regional
    - 1 National/International

Short-Term Research and Academic Objectives

Research

1. Develop skills in genomics, biochemical assays, and muscle mechanics to a degree of producing publication-quality data (Aims 1-3).
2. Enhance my writing abilities by producing high quality manuscripts, grant proposals, and conference abstracts, along with participating in the process of peer review.
3. Broaden my network with translational and clinical researchers with attendance and presentation at local and national/international conferences.
4. Supplement my rigor and reproducibility of data collection and analysis by developing and subsequently publishing MATLAB scripts for data management, statistical testing, and figure generation.

Academic

1. Expand my clinical knowledgebase of cardiology and heart failure by auditing the medical school's cardiology course (directed by my sponsor, Dr. Campbell), bi-weekly shadowing of cardiologist Vedant Gupta, MD (advisory committee member), and attending cardiology fellow meetings.
2. Further my understanding of ethical and responsible research by partaking in responsible conduct of research trainings and courses.

Long-Term Research and Academic Objectives

Research

1. Network with NIH-funded labs in search of post-doctoral positions by attending and presenting my work at conferences.
2. Strengthen my public-speaking skills by giving oral presentations at seminars and conferences.

Academic

1. Mentor high school and undergraduate students to develop skills in leadership and scientific communication.
2. Establish myself as a productive and innovative researcher by meeting the benchmarks outlined in *Annual Research Product Goals* and successfully defending my dissertation research.

C. Activities Planned Under This Award

My lab's research focuses on heart failure and spans 4 broad areas: (1) computer modeling of contraction, (2) biochemistry, (3) muscle mechanics, and (4) biobanking. The lab has built a large repository of human myocardium (currently >20,000 samples from 650 patients) and specializes in clinically supported translational research. This expertise and unique access to human samples allow experimental results to extend from sarcomere- to organ-level function. The activities planned under this award include using our experimental techniques and sharpening my scientific repertoire (Table 1).

Table 1. Planned Activities and Percent Effort

Activity	Effort (%)
F31 Research Aims (experimentation, data analysis)	70
Scientific Writing (abstracts, manuscripts)	10
Conferences/Networking	5
Responsible Conduct of Research (trainings)	5
Coursework (department curriculum, communication skills workshops)	4
Leadership (mentor undergraduate/high-school students, collaborative projects)	3
Seminars (seminar series', forums, specialized meetings)	3
Total	**100**

F31 Research Aims

My prime focus will be to complete the 3 Specific Aims described in the Research Strategy and described in Table 2 below.

Table 2. Skills Learned in Specific Aims

Aim		Focus	Resultant Skill(s) Learned
1		RNA turnover pathways	Western blotting to measure protein abundance
2	.1	K48-linked polyubiquitination of titin	Electrophoresis of ultra-large proteins
	.2	Lipofuscin granule accumulation	Cryosectioning, immunostaining, and imaging tissue (slide scanner and confocal microscope); Analyzing fluorescent images
3	.1	Truncated titin in sarcomeres	
	.2	Contractile dysfunction	Tissue permeabilization and multicellular muscle mechanics

Scientific Writing

I will complete "Duke Graduate School Scientific Writing Resource", an online course that will strengthen my conveyance of science into words. Also, I will write and submit at least 2 first-author manuscripts from data collected for this proposal and other research questions explored with the techniques honed during this fellowship.

Conferences/Networking

I will attend at least 2 regional and 1 national/international conference(s) per year to disseminate my work. Examples of such events include the biannual Myofilament Meeting, American Heart Association Basic Cardiovascular Sciences Scientific Sessions, and the European Muscle Conference.

Responsible Conduct for Research

I have and will continue to attend bimonthly, in-person seminars provided by the Bioethics department on a variety of topics related to responsible conduct of research. Also, I will take the “Fundamentals of Bioethics” course offered by the Department of Pharmacology during this award period. This will provide >35 contact hours of RCR training, well above the NIH requirement of 8 hours.

Coursework

I will audit the medical school’s cardiology course (directed by my sponsor, Dr. Campbell) to enhance my understanding of the clinical aspects of our research. Also, I will continue to strengthen my ability to speak about science in communication skills workshops and professionalism courses.

Leadership

I meet, and will continue to meet, one-on-one with Dr. Campbell in-person for 30 minutes every Tuesday . Additionally, we will continue hosting weekly meetings with lab members and collaborators to discuss current projects, grants, and manuscripts in preparation. I will have an advisory committee meeting every 6 months to present updates on my progress toward dissertation defense and receive feedback.

I will mentor at least 1 undergraduate or high-school student each semester throughout this fellowship. I have been mentoring Elizabeth Wilkerson, a junior undergraduate at the University of Kentucky, and Angela Cortazar, a senior at Bryan Station High School, for 1 year. Elizabeth has presented our work as posters at the 2024 Kentucky Chapter of the American Physiological Society Annual Meeting and the 2025 University of Kentucky Center for Clinical and Translational Research Spring Conference. Angela has presented our work as a poster at the 2024 Kentucky Chapter of the American Physiological Society Annual Meeting and a podium talk at the 2024 National Institutes of Health STEP-UP Program Annual Meeting.

This will strengthen my understanding and execution of the experiments within each Aim, along with building mentorship skills.

Seminars

I will continue to attend weekly departmental/cardiovascular seminars and present my work at such gatherings yearly. Also, I will attend weekly cardiology fellow meetings and continue bi-weekly shadowing of cardiologist Vedant Gupta, MD (advisory committee member).

F31 Timeline

Table 3. Activity Timeline During F31 Proposal

Activity	Year 1		Year 2		Year 3	
Courses						
Aim 1: RNA Turnover						
Aim 2: Protein Turnover & Waste Accumulation						
Aim 3: Sarcomere Ultrastructure & Mechanics						
Manuscript Preparation						
Conferences						
Mentoring Students						
Training in RCR						

Proposal Aims

Scientific Dissemination

Professional Development

Research Ethics

Pre-Award Period

During the time of this submission and potential award, I will become proficient at performing muscle mechanics with rat skeletal muscle. Then, I will transition to human cardiac tissue. Concurrently, I will collate summary results from my analysis of our whole exome and transcriptome sequencing results, and continue with allelic phasing, burden analysis, and expression clustering. This will serve as the basis for one of my first-author manuscripts. Also, I will continue to provide around-the-clock support for tissue collections for our myocardial repository.