BIOGRAPHICAL SKETCH

NAME OF FELLOWSHIP APPLICANT Gunawardena, Naomi D	POSITION TITLE PSTP Trainee
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Carnegie Mellon University	B.S.	2013	Biological Sciences
University of Pittsburgh School of Medicine Physician Scientist Training Program	M.D.	2018 (anticipated)	Medicine

A. Personal Statement

I am currently a trainee of the Physician Scientist Training Program at the University of Pittsburgh School of Medicine. Taking part in this program has given me the opportunity to immerse myself in a basic science research project and the world of academic medicine, greatly enhanced my medical school experience, and provided me with valuable training for my future career with the goal of becoming an independent physician-scientist. My previous research experiences during my undergraduate years at Carnegie Mellon University and at the Children's Hospital of Pittsburgh have prepared me well to take part in this program and taught me valuable skills that have been especially relevant to the process of conducting basic science research. I found great reward in spending the time to develop experiments and achieving results that provided insight into subjects like natural killer cell function, the *Candida albicans* stress response, and the role of mitochondrial aconitase and erythropoietin signaling in iron deficiency anemia. The long-term goals of all of my research experiences have been to understand mechanisms and pathways in order to identify novel therapeutic targets that will enable more effective healthcare, and this has allowed me to develop a true passion for the work. I chose to pursue a career in medicine to help patients by utilizing scientific evidence to make good clinical decisions. I plan to complete a residency in internal medicine and/or pediatrics and a fellowship in hematology/oncology and am planning to conduct basic science research and practice clinical medicine at an academic medical center in the future. The field of hematology includes some of the most prevalent yet complex diseases worldwide and I believe that a career as a physician treating these disorders would be especially stimulating, due to the constant innovations in the field, and rewarding, as physicians are able to help more and more patients with complicated disorders. This will only become more possible in the future as research in this field is continually yielding advances in clinical care. I believe that as a physician scientist, my basic science research activities will enhance my understanding of the diseases that affect my patients, provide me with unique perspectives on current and novel therapeutic options, and ultimately allow me to improve upon the care and advice that I provide to my patients.

My project in the laboratory of Dr. Grant Bullock at the University of Pittsburgh School of Medicine and the Vascular Medicine Institute is entitled "*Mitochondrial aconitase connects iron metabolism to oxidative phosphorylation.*" Previous studies by Bullock et al. have led to the conclusion that there is an iron-regulated checkpoint in erythropoiesis that can dial back red blood cell production in low-iron states and that the aconitase enzymes are key to this pathway. Recent unpublished data suggests that decreased mitochondrial aconitase activity reduces mitochondrial oxidative phosphorylation in iron-deprived erythroid progenitors, suggesting a possible mitochondrial mechanism for the iron restriction response. We propose that mitochondrial aconitase inhibition due to iron deficiency decreases flux through the electron transport chain, which disrupts a reactive oxygen species (ROS) signal that is required for erythroid progenitor cell transition past the iron-responsive differentiation checkpoint. In this model, mitochondrial aconitase activity is essential for erythropoiesis and regulates erythroid mitochondrial function. The specific aims of my project are to determine the role of mitochondrial aconitase in erythroid induction and mitochondrial function in K562 erythroleukemia cells and in the iron restriction checkpoint in primary human CD34+ hematopoietic progenitor cells. Completion of these two aims will allow us to further characterize the role of mitochondrial aconitase in downregulating erythropoiesis in the setting of iron deficiency. The Physician Scientist Training Program has been the perfect training opportunity for me to develop valuable skills in scientific thinking and conducting

research, while also maintaining my focus on its relevance to clinical medicine and this will serve me well during the clinical portion of my medical school career and as a practicing physician in the future.

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	END DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
MD Candidate	8/13	Present	Medicine	University of Pittsburgh School of Medicine	
Medical Student Researcher	5/15	Present (5/16)	Hematology	University of Pittsburgh	Dr. Grant Bullock
Laboratory Teaching Assistant	8/12	5/13	Modern Biology	Carnegie Mellon University	Dr. Linda Visomirski-Robic
Undergraduate Research Student	5/11	5/13	Genetics	Carnegie Mellon University	Dr. Aaron Mitchell
Undergraduate Research Student	6/10	8/10	Immunology	UPMC Children's Hospital of Pittsburgh	Dr. Abbe de Vallejo

Academic Honors/Awards

2015 – 2018 Physician Scientist Training Program at University of Pittsburgh School of Medicine
2014 National Institutes of Health (NIH) T35 Summer Student in Hematology
2013 Carnegie Mellon University: University Honors
2012 – 2013 Carnegie Mellon Mortar Board Senior Honor Society
2009 – 2013 Mellon College of Science Dean's List with High Honors (every semester)
2012 Howard Hughes Medical Institute (HHMI) Undergraduate Summer Scholar
2011 HHMI Undergraduate Summer Researcher

Professional Memberships and Leadership Positions

2015 – Medical Student Member, American Society of Hematology
2014 – 2015 Coordinator, Pediatric and Adolescent Medicine Interest Group
University of Pittsburgh School of Medicine
2012 – 2013 Student Member, University Disciplinary Committee and Academic Review Board
Carnegie Mellon University
2012 – 2013 Membership Co-Chair, Mortar Board Senior Honor Society
Carnegie Mellon University

C. Contributions to Science

Medical Student Researcher (August 2014 – present)
Laboratory of Grant Bullock, MD, PhD. Department of Pathology, Division of Hematopathology and Vascular Medicine Institute. University of Pittsburgh School of Medicine, Pittsburgh, PA.
Funding: University of Pittsburgh School of Medicine Physician Scientist Training Program
Project Title: *Mitochondrial aconitase connects iron metabolism to oxidative phosphorylation*
My role has included transducing lentiviral vectors carrying mitochondrial aconitase-targeting antisense shRNA into K562 erythroleukemia cells, confirming sufficient knockdown of mitochondrial aconitase expression, and investigating the effect of mitochondrial aconitase knockdown on erythroid induction and mitochondrial metabolism in these cells. Preliminary data indicates that aconitase knockdown cell lines have decreased levels of mitochondrial oxidative phosphorylation compared to control cell lines. We are also in the process of transducing primary human hematopoietic progenitor cells with these shRNA constructs in order to knockdown mitochondrial aconitase in these cells and will conduct similar functional analyses on these cells as I have on the K562 cells. Further educational enrichment has included my

participation in lab meetings and journal clubs and attending many of the weekly Vascular Medicine Institute research seminars. I presented my preliminary results at the University of Pittsburgh School of Medicine Dean's Summer Research Program Poster Session and at the Physician Scientist Training Program Annual Symposium in September 2015. I also attended the 2015 American Society of Hematology Annual Meeting in December 2015.

Presented:

Naomi Gunawardena BS, Valerie Schrott MS, Teague Cole BS, Michael Reynolds, Chanté Richardson PhD, Anh Nguyen PhD, Adam Straub PhD, Sruti Shiva PhD, and Grant Bullock MD, PhD. Mitochondrial aconitase connects iron metabolism to oxidative phosphorylation. Physician Scientist Training Program Annual Retreat Poster Session. September 2015.

Bullock GC, Richardson CL, Schrott VM, **Gunawardena N**, Cole T, Corey C, Wang Y, Shiva, S. The Role of Mitochondrial Metabolism and Redox Signaling in Iron Deficiency Anemia. 57th American Society of Hematology Annual Meeting and Exposition Poster Session. Orlando, Florida. December 2015.

Medical Student Researcher (May 2014 – August 2014)

Laboratory of Grant Bullock, MD, PhD. Department of Pathology, Division of Hematopathology and Vascular Medicine Institute. University of Pittsburgh School of Medicine, Pittsburgh, PA.

Funding: NIH T35 Training Grant for Student Research in Hematology/Oncology

Project Title: *Investigating the Connection Between Mitochondrial Aconitase and Erythropoietin Signaling During Iron Deficiency Anemia Using Gene Transfer Techniques*

My role included using retroviral gene transduction to express a series of mutant erythropoietin receptors in primary human hematopoietic progenitor cells and shRNA lentiviral transduction to knock down expression of mitochondrial aconitase in human K562 erythroleukemia cells. I have continued to work on this project since August 2014 and anticipate working on it throughout my medical school career.

Presented: Dean's Summer Research Program Poster Session, University of Pittsburgh School of Medicine. October 2014.

Teaching Assistant (2012 – 2013)

Modern Biology Laboratory Course, Carnegie Mellon University, Pittsburgh, PA.

My role included preparing for the laboratory periods, assisting students and the instructor during class, and helping to grade. I really enjoyed this opportunity to spend time in the laboratory environment and teach other students how to work through biological laboratory techniques, including DNA isolation, DNA transformation, bacteriophage assays, yeast mutagenesis, gram staining, polymerase chain reaction, and dissections.

Undergraduate Researcher (2011 – May 2013)

Laboratory of Aaron Mitchell, PhD. Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA.

Funding: Howard Hughes Medical Institute (HHMI) Summer Researcher (2011) and Scholar (2012) Awards

Project Title: *Screening of Various Candida albicans Mutants for Stress Phenotypes*

Project Title: *Candida albicans Plasma Membrane Proteins that Govern Cell Wall Integrity*

My role included screening a number of insertion and deletion mutant libraries for altered sensitivity to a variety of stresses in order to identify gene targets for antifungal therapies.

Presented: Oral presentation at HHMI Summer Scholars Symposium. Carnegie Mellon University. July 2012.

Undergraduate Summer Research Intern (Summer 2010)

Laboratory of Abbe de Vallejo, PhD

Division of Pediatric Rheumatology, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA.

Funding: Children's Hospital of Pittsburgh Summer Student Research Program

Project Title: *CD56 is a Bona Fide Activating Receptor for Natural Killer Cells*

My role included performing CD56-driven activations of natural killer cells and analyzing effects of CD56 on NK cell activation by flow cytometry.

Presented: Children's Hospital of Pittsburgh Summer Student Research Program Poster Session. July 2010.

E. Abstracts

Vallejo AN*, Griffin P, Montag D, Nussbaum R, **Gunawardena N**, Studenski S. 2013. CD56 is a legitimate immune receptor regulating T and NK cell effector function, and its expression level predicts successful aging. J Immunol 190:119.18.