BIOGRAPHICAL SKETCH

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NAME: Melissa A. Luse

eRA COMMONS USER NAME (credential, e.g., agency login): MALUSE

POSITION TITLE: Ph.D. Candidate, Molecular Physiology and Biological Physics Department, Cardiovascular Research Center, *University of Virginia*

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Maryland, College Park MD	B.S.	05/2019	Physiology and Neurobiology
University of Virginia, Charlottesville VA	M.S	06/21/22	Biomedical Science
University of Virginia, Charlottesville VA	Ph.D.	05/2024	Molecular Physiology and Biological Physics

A. Personal Statement

My research interests lie at the intersection of metabolism and vascular dynamics. Specifically, I am interested in how adipose microvascular endothelial cells communicate with surrounding adipocytes in the pathology of type 2 diabetes (T2D). There is vast heterogeneity among endothelial cells, a concept I came to appreciate during my undergraduate research at the University of Maryland in Dr. Carleton's lab. The Carleton lab gave me the opportunity to study the genetic heterogeneity of opsins within the retina of cichlid fish. I was fascinated with the concept of cell type differences within tissues and how these differences suited physiological function. During my first year at UVA, I had the opportunity to engage in three intellectually stimulating research rotations. However, my exciting hands-on experience in cardiovascular (CV) physiology piqued my interest due to its pertinence to clinical etiologies, as well as the prevalence of CV disease in the United States. This led me to join Dr. Brant Isakson's Laboratory, a part of the Robert M. Berne Cardiovascular Research Center. Broadly, the Isakson lab focuses on understanding heterocellular communication within the vasculature, between endothelial cells (ECs) and smooth muscle cells. Studying the communication between two different cell types is a fascinating topic for me. I also gained an interest in adipose tissue and metabolism during my rotation with Dr. Thurl Harris. Furnished with the metabolic- and adipose-related technical skills I learned in Dr. Harris's lab, I was able to couple my interest in metabolism with the expertise of the Isakson lab. This unique experience facilitated the beginning of a new research project involving endothelial cell and adipocyte communication. The aims I have outlined in this application are to assess the role of EC and adipocyte communication during T2D, for which my research experiences make me well-suited. At the beginning of my time in the Isakson lab, I was the first author on a review examining the endothelial cell specific effect of common T2D medications. This positioned me exceptionally well to create a firm knowledge base of the metabolic role of the endothelium and how it is dysregulated in metabolic diseases, including T2D. Since beginning my research project, I have independently developed a research protocol for a tissue clearing technique, CLARITY. This technique is imperative for my project which requires two weeks to prepare whole adipose tissue for immunohistochemistry imaging to localize genes of interest in whole tissue. I am progressing, with the help of Dr. Brant Isakson as a main pioneer in the field, toward creating an in vitro co-culture system between human endothelial cells and human adipocytes. I am excited to further my research project outlined in this application and look forward to

potentially elucidating a novel role for endothelial cell-adipocyte heterocellular communication in T2D. I will use my graduate degree training and experiences to further my understanding of cellular and molecular physiology and to gain technical expertise necessary to become a competitive researcher. Specifically, I want to pursue a career as a clinical research scientist where I hope to use my knowledge of cardiovascular physiology to develop powerful and impactful therapeutics that could significantly affect large patient populations.

B. Positions and Honors

2016 Undergraduate Research Assistant, *University of Maryland, College Park, MD*
2018 Toxicology Intern, *Boehringer Ingelheim, Ridgefield, CT*
2019 Public Health Research Intern, *Gryphon Scientific, Takoma Park, MD*
2020 Peach Fellowship, Biomedical Sciences Graduate Program, *University of Virginia*
2020 Awardee, University of Virginia Cardiovascular Training Grant (NIHT32HL007284)
2021 Re-appointed Awardee, University of Virginia Cardiovascular Training Grant (NIHT32HL007284)
2022 American Heart Association Predoctoral Fellowship (AHA#915176)
2023 American Physiological Society cardiovascular section "outstanding graduate student" award

Leadership Roles

2016 President, Project Sunshine, *University of Maryland College Park, MD*
2016 Judicial Board Leader, *Alpha Chi Omega, University of Maryland College Park, MD*
2017 Vice President New Member Education, *Alpha Chi Omega, University of Maryland, College Park, MD*
2020 Committee Member, *Career Development Team, Cardiovascular Research Center University of Virginia, VA*
2021-2023 Committee Leader, *Career Development Team, Cardiovascular Research Center University of Virginia, VA*
2021-2023 Academic Chair, *Graduate Biosciences Society, University of Virginia, VA*

Memberships

2020- Present North American Vascular Biology Organization
2020- Present American Heart Association
2021-Present Microcirculation Society
2021-Present American Physiological Society

C. Contributions to Science

1. Undergraduate Research, *Carleton Laboratory, University of Maryland*, 2017

The Honors Biology Department at the University of Maryland gave me the opportunity to create a two- and half-year undergraduate thesis project in an evolutionary biology lab run by Dr. Karen Carleton. My undergraduate research project revolved around identifying a transcription factor for long wave length sensitive (*LWS)* opsin gene expression in Cichlid fishes. It was previously found that a transcription factor Tbx2a was responsible for Rhodopsin-like (*RH2)* opsin expression in certain species of Cichlids. I investigated the mechanism controlling *LWS* expression, one of the seven opsins Cichlids possess. Through the use of genetic tools, QTL mapping and qPCR, I aimed to understand the mechanism by which Cichlid fish undergo visual tuning to allow for maximal fitness in their environment. My goal was to identify a possible transcription factor that was crucial for visual network formation. I proposed a zinc finger protein, *ATMIN*, a transcription factor for *LWS* opsin, possibly explaining the differences in visual tuning between *Aulonocara baenschi* and *Tramitichromis intermedius* cichlid species. Cichlids diverse opsin expression profiles across species is a perfect model for understanding adaptive radiation and the role evolution plays in the regulation of visual systems. These experimental findings inform our knowledge of how species can adapt to their environments, specifically understanding how opsin expression is regulated, could serve as a potential therapeutic for people who are color vision deficient.

2. Rotation Research, Kashatus Laboratory, *University of Virginia* 2019

During an intensive 6-week rotation in the lab of Dr. Dave Kashatus, I performed key experiments that lead to novel findings related to the role of RalA, a small GTPase, in various stressful cellular conditions. Lipid droplets (LDs) are dynamic organelles which oscillate in size and cellular location depending on nutrient status and cellular state. I examined the role RalA plays in LD formation during lipid stimulation, ER stress, and oxidative damage. I performed cellular siRNA knock down of RalA followed by pharmacological treatments and cell imaging via confocal microscopy. In all conditions tested, I observed no changes in lipid droplet formation between RalA knockdown cells when compared with controls. This led the investigators to rule out conditions other than nutrient deprivation for circumstances in which produce increased lipid droplet formation that is RalA dependent. Overall, my contributions during the time I spent in the Kashatus lab aided in the finding that RalA and its binding partner PLD1 increase lipid droplet formation and growth during cellular starvation.

- Hussain, Syed and Tran, Tuyet-Minh and Ware, Timothy B. and **Luse, Melissa A.** and Prevost, Christopher T. and Ferguson, Ashley N. and Kashatus, Jennifer A. and Hsu, Ku-Lung and Kashatus, David, RalA and PLD1 Promote Lipid Droplet Growth in Response to Nutrient Withdrawal.

3. Graduate Dissertation Research, *Isakson Laboratory, University of Virginia 2020*

The vascular endothelium is a heterogenous cell network that adapts locally to the vascular bed in which it innervates. Endothelial dysfunction and insulin resistance are hallmarks of Type 2 Diabetes (T2D) and often precede the metabolic response to insulin, thereby placing endothelial cell (EC) function at the center of glycemic control. In T2D blood lipid levels become severely dysregulated worsening insulin sensitivity and glucose regulation. Adipose tissue is the main site for free fatty acid uptake and re-esterification, exposing capillary adipose endothelial cells (caECs) to high concentrations of free fatty acids. The capillary adipose endothelium has a unique role in up taking and transporting lipids to adipocytes due to the caECs close proximity to adipocytes in the dense capillary network of adipose tissue. To understand how the caEC changes with T2D, I performed single cell RNA sequencing (scRNAseq) on live adipose endothelial cells to identify gene expression changes in this unique population of ECs. The data indicates that in T2D conditions (eg. High fat diet) caEC upregulated fatty acid handling and transport genes that have been commonly associated with adipocytes (FABP4, FABP5, CD36, Gpihbp1). The aims provided in this proposal will illuminate the degree of physical contact and mechanism of heterocellular communication between caECs and adipocytes as well as elucidate the physiological role of these fatty acid genes in the adipose capillary endothelium. These findings are critical for understanding the etiology and progression of T2D in the vasculature and could aid in the discovery of new pharmacological targets for T2D treatment.

- **Melissa A. Luse,** Emily M. Heiston, Steven K. Malin, and Brant E. Isakson. "Cellular and Functional Effects of Insulin Based Therapies and Exercise on Endothelium." *Current Pharmaceutical Design,* 26.30 (2020): 3760-3767.
- **Melissa A. Luse,** Nenja Krüger, Miranda E. Good, Lauren A. Biwer, Vlad Serbulea, Anita Salamon, Rebecca A. Deaton, Norbert Leitinger, Axel Gödecke, and Brant E. Isakson. "Smooth muscle cell FTO regulates contractile function" *American Journal of Physiology-Heart and Circulatory Physiology,* 323.6 (2022): H1212-H1220.
- Granade, Mitchell E., Stefan R. Hargett, Daniel S. Lank, Michael C. Lemke, **Melissa A. Luse**, Brant E. Isakson, Irina M. Bochkis, Joel Linden, and Thurl E. Harris "Feeding desensitizes A1 adenosine receptors in adipose through FOXO1-mediated transcriptional regulation" *Molecular metabolism*, 63 (2022) 101543.
- Tristan J. Ragland, Emily M. Heiston, Anna Ballantyne, Nathan R. Stewart, Sabrina La Salvia, Luca Musante, **Melissa A. Luse**, Brant E Isakson, Uta Erdbrügger, Steven K. Malin "Extracellular Vesicles and Insulin-Mediated Vascular Function in Metabolic Syndrome" *Physiological Reports* In press
- Claire Ruddiman, Richard Peckham, **Melissa A. Luse**, Yen-Lin Chen, Maniselvan Kuppusamy, Bruce Corliss, Jordan Hall, Chien-Jung Lin, Shayn Peirce, Swapnil Sonkusare, Robert Mecham, Jessica

Wagenseil, Brant E. Isakson. “Polarized localization of phosphatidylserine in endothelium regulates Kir2.1” *Journal of Clinical Investigaton-Insight.* 2023;8(9):e165715

- Abigail G. Wolpe, **Melissa A. Luse**, Christopher Baryiames, Jacob B. Wolpe, Scott R. Johnstone, Henry Paige Askew, Yen-Lin Chen, Vikram Sabapathy, Brent Wakefield, Eugenia Cifuentes-Pagano, Mykhaylo V. Artamonov, Kevin Barr, Avril V. Somlyo, Adam Straub, Rahul Sharma, Frank Beier, Iain Greenwood, Patrick Pagano, Swapnil Sonkusare, Stefanie Redemann, Linda Columbus, Silvia Penuela, Brant E. Isakson. “Noncanonical role for pannexin stabilizing the transcription factor BCL6 to regulate oxidative stress” *Science Signaling,* In Review
- **Melissa A. Luse**, Luke Dunaway, Caitlin Pavelec, Rachel Tessema, Alicia Carvalho, Shruthi Nyshadham, Nick Chavkin, Karen Hirschi, Brant E. Isakson. “Endothelial PPARγ and membrane environment independently regulate Caveolin-1 and Cd36 lipid uptake”. In Prep
- Luke Dunaway*, **Melissa A. Luse*,** Shruthi Nyshadham, Nick Chavkin, Karen Hirschi, Brant E. Isakson. “Obesity reduces transcriptomic differences between mesenteric and adipose arterial endothelium” In prep

D. Additional Information: Research Support and/or Scholastic Performance

Research Support

5T32HL007284NIH United States Owens, Gary (PI) 07/01/2020-06/30/2022

Basic Cardiovascular Research Training Grant. The training program is designed to train individuals to become outstanding biomedical scientists who will pioneer major advances in the understanding of cardiovascular biology and disease and novel therapeutic interventions through research. The program facilitates guest seminars, research in progress presentations, grant brewing sessions, and translational/clinical experiences.
Role: Predoctoral Trainee

AHA Predoctoral Fellowship 07/1/2022-06/30/2024

American Heart Association two-year predoctoral fellowship with the purpose of enhancing the integration of research and clinical training for promising students. This fellowship aims to support pre-doctoral students who aspire to obtain careers as scientists with the goal of improving global cardiovascular health.
Role: Predoctoral Trainee

Scholastic Performance

Coursework at The University of Virginia (Graduate)

YEAR	COURSE TITLE	GRADE	YEAR	COURSE TITLE	GRADE
Coursework at the University of Virginia (Graduate)					
2019	Integrative Biosciences	A	2020	Vascular Biology A	A
2020	Research Ethics	S	2020	Vascular Biology B	A
2020	Intro Biomedical Data Science	A	2020	Principles of Pharmacology I	A
2020	Physiology A	A	2020	Principles of Pharmacology II	A
2020	Physiology B	A	2021	Extreme Physiology	A
Coursework at The University of Maryland (Undergraduate)					
YEAR	COURSE TITLE	GRADE	YEAR	COURSE TITLE	GRADE
2015	Anthropology of Global Health	A	2017	General Bioanalytical Chemistry Lab	B

YEAR	COURSE TITLE	GRADE	YEAR	COURSE TITLE	GRADE
2015	Chemistry Fundamentals I	B	2017	Discovering New Ventures	A+
2015	Chemistry I Laboratory	B-	2017	Women, Art and Culture	A+
2015	Academic Writing	A-	2017	Biochemistry I	B+
2015	Precalculus	A	2017	Biology Lab Research	A
2015	Contemporary Moral Issues	B	2017	Molecular Genetics	B
2015	Student in University	A+	2017	Entrepreneurship Opportunity Analysis	A
2016	Principles Biology III	C	2017	Fundamental Physics I	B
2016	Organic Chemistry I	B-	2018	Fundamental Physics II	B
2016	Organic Chemistry II	B	2018	Biology Dept. Honors Seminar	A+
2016	Oral Communications	A-	2018	Biology Dept. Honors Research	A
2016	Calculus I	C	2018	Mammalian Physiology	A
2016	Principles of Genetics	B+	2018	Science Writing	A-
2016	Organic Chemistry II	C+	2018	Cellular Mechanisms of Disease	A
2016	Organic Chemistry Laboratory II	B-	2018	Biology Dept. Honors Seminar	A+
2016	Calculus II	B	2018	Biology Dept. Honors Research	A
2016	Introduction to Psychology	B	2018	Principles of Neuroscience	A
2017	Cell Biology and Physiology	A	2018	Biological Statistics	A
2019	Biology Dept. Honors Seminar	A+			
2019	Biology Dept. Honors Research	A			
2019	Endocrinology	A			

Coursework at The University of Maryland
Cumulative GPA: 3.43, *Honors in Biology*
Lowest passing grade is C-

Coursework at The University of Virginia
Cumulative GPA: 4.0
Lowest passing grade is B- and ungraded courses marked as satisfactory (S) or unsatisfactory (U.)