UNIVERSITY of VIRGINIA
SCHOOL OF MEDICINE

# The Robert M. Berne Cardiovascular Research Center



December 15, 2022

Dear APS CV Awards Committee:

It is my real pleasure to introduce Melissa Luse, a fourth year Physiology PhD student in my lab at UVA.

*Melissa has performed a simply incredible amount of work over her tenure in my lab.* Through one of the biggest competitions ever, Melissa was chosen to be a part of our Cardiovascular T32. From there she was able to transition to her own AHA Pre-doctoral award. In terms of publications, she has two first author publications (her first one in *AJP-Heart*!) and has two first author papers in preparation. She also has 3 co-author papers and 2 co-author papers in review!

Melissa is possibly the hardest working graduate student I have ever had. In my original letter for her AHA award, I noted that she was “an ambitious, thoughtful, intelligent, and careful experimentalist” and those words couldn’t ring truer. She has outlined her thesis project with a range of exciting data. Her thesis project is focusing on the endothelium of adipose tissue, and their handling and transport of lipids, especially in relation to the heterocellular interaction between the capillary endothelium and adipocyte. The idea was generated by data generated by Melissa’s own scRNAseq experiments on isolated endothelium from adipose that she learned to do while stuck at home during COVID. Based on these results Melissa focused on the regulation of caveolin1 specifically in capillaries. To that end, Melissa has produced amazing data with the new endothelial cell (EC) $Cav1^{fl/fl}$ animals, showing they are completely protected against weight gain, insulin resistance, and glucose tolerance in high fat diet conditions. Regardless of diet, these EC Cav1fl/fl mice are hyperlipidemic. These results begin to call into question the role of caveolin1 in adipocytes, and push the concept of lipid uptake by caveola in endothelium as being an imperative first step. This is the exciting story her APS abstract is based on.

Remarkably, Melissa has three other projects she is working on. In collaboration with Karen Hirshi, Melissa created EC and adipocyte $Cx43^{fl/fl}$ mice to determine how the heterocellular communication with adipocytes may regulate lipid transport between the two cell types. Merging this project and the work on Cav1, Melissa is working in collaboration with a post-doc in the lab on scRNAseq of endothelium from adipose and mesenteric in normal chow and high fat diet. They found arterial endothelium uniquely susceptible to obesity compared to veins, lymphatics and capillaries, and the reason may be due to altered fatty acid oxidation. In addition, Melissa, ever dedicated to understanding the role of the vasculature in metabolism, decided to finish a barely started side-project that would normally require another 2-3 years of work. She provided strong experimental data that the fat mass obesity (*Fto*) gene, when selectively deleted from SMC, has a dramatic change in contractility of arterioles in terms of their myogenic tone, with a stable and significant drop in blood pressure. In microarray experiments from knockout animal aortas, serum response factor (*Srf*) is significantly downregulated, indicating possible regulation by *Fto.* Because *Srf* is a key regulator of SMC-specific contractile genes, this matched the inability of SMC to contract in the absence of *Fto*. This was the work she has recently published in *AJP-Heart*.

Academically, Melissa received one of the top scores in the PhD BIMS core class at UVA (A) and received a 100% (A+) in Graduate Physiology (again, top

of her class). Melissa was awarded the Peach Award for first year students, placing her at the very top of all the incoming 2019-2020 BIMS students. She also won top prize at the Physiology Department Retreat for her oral presentation on her project.

Melissa brings an enthusiasm and passion for her science that makes the lab environment fun and exciting. While on the Cardiovascular T32 here, she has lead the Career Development Seminar series, and organized the first AHA-based 5K (Haunted Heart Walk/Run 5K). She leads by example, not only in terms of work ethic, but also in terms of depth of knowledge and critique of her own, and her lab mates science. She is headed to great things and I feel fortunate to have her in my lab.

Sincerely,

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