Name: Amanda Mauro

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Major Professor: Derek Boeldt

Degree Objective: PhD, Endocrinology and Reproductive Physiology

Background: BS Biology, Bridgewater State University

Current Research Project:

Preeclampsia (PE) is a condition characterized by hypertension during pregnancy. This hypertension is thought to be largely a result of underlying endothelial dysfunction. Endothelial dysfunction reduces sustained phase Ca^{2+} bursting in human umbilical vein endothelial cells (HUVEC) from preeclamptic pregnancies compared to normal pregnancies. This reduction in Ca^{2+} bursting potential reflects a decrease in the activation of endothelial nitric oxide synthase ((eNOS) the enzyme with catalyzes the production of the potent vasodilator nitric oxide), which hinders vascular endothelial cell function especially in the pregnant state. Changes in circulating levels of VEGF, TNFα, and IL-6, can contribute to endothelial cell dysfunction via Src kinase activation. However, the literature surrounding circulating and local, vascular bed-specific VEGF levels remains unclear. In order to mimic PE in various states of endothelial VEGF exposure, we administered three PE cocktails (Low (L), Medium (M), and High (H)) to normal HUVECs, which contained 3ng/ml IL-6 and 0.5 ng/ml TNFα, and either 0.1ng/ml (L), 1ng/ml (M), or 10 ng/ml (H) VEGF. A control cocktail corresponding to normal pregnancy contained 0.1ng/ml IL-6, 0.03 ng/ml TNFa, and 0.5 ng/ml VEGF. To evaluate the efficacy of Src kinase inhibition as a therapy for PE we pretreated the cells using two Src inhibitors conjugated linoleic acid (CLA) and PP2. We found that there was partial burst rescue with the use of the Src inhibitors only in the (H) PE cocktail and no improvement of bursting in the (M) and (L) PE cocktails. The lack of improvement observed in the (M) and (L) PE cocktails led us to believe that there is involvement of another pathway other than Src. To elucidate the signaling pathways at play I am currently using cocktails without IL-6 and treating with Src inhibitors and ERK inhibitors to determine the burst rescue capability of such treatments when only VEGF and TNFα are present. Additionally, experiments with the original PE cocktails will be conducted to investigate the role of other signaling pathways involved in the sustained phase Ca^{2+} response.

Honors:

Grants Received:

Publications:

National Presentations:

Other Presentations:

Poster Presentation: **Amanda Mauro**, Danielle Berdahl, Nauman Khurshid, Dinesh Shah, Ian Bird, Derek Boeldt. Endocrine Cocktails Designed to Mimic Preeclamptic Conditions Promote Endothelial Dysfunction in Part via Src Kinase. ObGyn Research Day 2017 and ERP Symposium 2017

Teaching and Mentorship:

ERP Service: