

**Name:** Amanda Mauro

**Email:** amauro2@wisc.edu

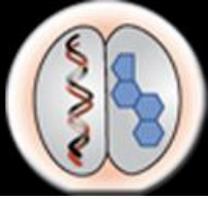
**Major Professor:** Derek Boeldt

**Degree Objective:** PhD, Endocrinology and Reproductive Physiology

**Background:** BS Biology, Bridgewater State University

**Current Research Project:**

Preeclampsia (PE) is a disease of pregnancy diagnosed after 20 weeks and characterized by high blood pressure and proteinuria, but the severity of the disease varies. The exact cause of PE is not fully known, but impaired spiral artery remodeling, inflammation, and reduced vasodilator production due to endothelial dysfunction are hallmarks of the disease. Signal transduction pathways such as JAK/STAT and NF- $\kappa$ B are important factors involved in inflammatory responses. Other signaling pathways, such as Src and MEK/ERK, are known to phosphorylate Cx43 gap junctions at inhibitory residues blocking  $\text{Ca}^{2+}$  signaling that is necessary for the production of the potent vasodilator nitric oxide (NO). Disruption of NO production contributes to endothelial dysfunction and leads to an overall hypertensive state. Currently there is no treatment for the underlying endothelial dysfunction of PE. Dysregulated levels of many growth factors and cytokines, such as VEGF, TNF $\alpha$ , and IL-6, have been associated with PE, but the way in which different levels of each affects the severity of the disease has not been fully investigated. It is crucial to determine the effect that different levels of each growth factor and cytokine has on endothelial dysfunction and the severity of PE. Detailed knowledge of these interactions also allows for a more efficient targeting of the dysfunction with pharmaceutical products. Targeting the shared signaling mechanisms of the growth factors and cytokines is a logical treatment strategy and is likely to be more broadly effective than a treatment strategy targeting just one specific factor. So therapeutic products that act on Src, MEK/ERK, JAK/STAT, or NF- $\kappa$ B (the pathways utilized by some of the growth factors and cytokines of PE) may be valid treatments for PE. Conjugated linoleic acid (CLA) is an example of the kinds of products that could potentially be used to treat PE; its 10t,12c isomer is a known Src inhibitor while its 9c,11t isomer is a known NF- $\kappa$ B inhibitor, and the 10t,12c isomer has been shown acutely to improve  $\text{Ca}^{2+}$  bursting in human umbilical vein endothelial cells (HUVECs). My project aims to untangle the interactions of differing levels of growth factors and cytokines to determine their impact on endothelial cell function, utilizing a kinase inhibitor library to evaluate methods for rescuing  $\text{Ca}^{2+}$  signaling and monolayer integrity from growth factor and cytokine-mediated insult. Additionally I plan on working with a new method for HUVEC isolation resulting in a more physiologically relevant cell model for which future experiments can be conducted on. Preliminary experiments utilizing this new HUVEC "fresh" preparation indicate that the cells' behavior resembles intact umbilical vein vessels, therefore providing a more physiologically relevant model than the pooled HUVEC preparations that is also more technically manageable than working with the intact vessels.



**Honors:** Douglas W. Laube Best Trainee Paper Award, Department of Obstetrics and Gynecology, June 2020

**Grants Received:**

NIH T32 Training Fellowship (5T32HD041921-17), July 2019-July 2020

**Publications:**

Rengarajan A, **Mauro AK**, Boeldt DS. 2020. Maternal Disease and Gasotransmitters. *Nitric Oxide*.

**Mauro AK**, Berdahl DM, Khurshid N, Clemente L, Ampey AC, Shah DM, Bird IM, Boeldt DS. 2020. Conjugated linoleic acid improves endothelial Ca<sup>2+</sup> signaling by blocking growth factor and cytokine-mediated Cx43 phosphorylation. *Mol Cell Endocrinol*.

**Mauro AK**, Khurshid N, Berdahl DM, Ampey AC, Adu D, Shah DM, Boeldt DS. 2020. Cytokine concentrations direct endothelial function in pregnancy and preeclampsia. *J Endocrinology*.

**National Presentations:**

Poster Presentation: **Amanda Mauro**, Ian Bird, Derek Boeldt (2018). CLA Isomers Offer Potential Therapeutic Benefits for Endothelial Dysfunction in Preeclampsia by Improving the Monolayer and Ca<sup>2+</sup> Signaling in HUVECs. 65th Annual Meeting for the Society for Reproductive Investigation. San Diego, CA, March 2018

Poster Presentation: **Amanda Mauro**, Aishwarya Rengarajan, Ian Bird, Derek Boeldt (2019) CLA Rescues VEGF-inhibited Ca<sup>2+</sup> Signaling While Preserving Monolayer Integrity in HUVECs. 66th Annual Meeting for the Society for Reproductive Investigation. Paris, France, March 2019

**Other Presentations:**

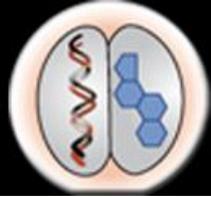
Poster Presentation: **Amanda Mauro**, Danielle Berdahl, Nauman Khurshid, Dinesh Shah, Ian Bird, Derek Boeldt (2017). Endocrine Cocktails Designed to Mimic Preeclamptic Conditions Promote Endothelial Dysfunction in Part via Src Kinase. ObGyn Research Day, May 2017, ERP Symposium, June 2017, and Women's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

Poster Presentation: **Amanda Mauro**, Nauman Khurshid, Ian Bird, Derek Boeldt. (2020). Inhibition of Src but not MEK/ERK Signaling Supports HUVEC Monolayer Integrity. ERP Symposium, June 2020, Women's Health and Health Equity Symposium, October 2020.

**Teaching and Mentorship:**

Teaching Assistant: ObGyn 955: Responsible Conduct of Research for Biomedical Students, Fall 2017

Mentoring of Aishu: HUVEC primary cell culture, Fura-2 Ca<sup>2+</sup> imaging, Fluo-8 Ca<sup>2+</sup> response screening, and data analysis and handling.



Mentoring of Dr. Daniel Adu during his fellowship in the Boeldt Lab: HUVEC primary cell culture, Fluo-8 Ca<sup>2+</sup> response screening, and data analysis and handling.

Mentoring of Rachel Dahn: ECIS (electric cell-substrate impedance sensing) methods, troubleshooting, and data analysis and handling.

Mentoring of Carly Albright: Served as primary mentor as part of her independent project for Introductory Biology 152 "Agonist- Dependent Effects on Sustained Ca<sup>2+</sup> Signaling"

## **ERP Service:**

Member of the Student Committee (2017-present), Social subcommittee (2019-present)

ERP Recruitment Volunteer (2017-present)