

SUMMER 2024 – SC INBRE RET PROJECT DESCRIPTION FORM

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| Mentor's Name | R. Clinton Webb |
| Institution | University of South Carolina |
| Center | Cardiovascular Translational Research Center (CTRC) |
| Mailing Address | 6311 Garners Ferry Road, Bldg 3, Rm 250 |
| Telephone | 706-691-5041 |
| Email | clinton.webb@uscmed.sc.edu |
| Research Subject Area | Mechanisms of vascular injury in hypertension |

A. Briefly describe overall research program at your laboratory:

The overarching goal of our research is to achieve an understanding of how the innate immune response participates in the pathogenesis of hypertension. Innate immunity is beneficial in the vasculature in the short-term, by providing cytoprotective mechanisms, and it facilitates tissue repair. However, sustained activation is maladaptive, leading to increased tissue destruction and end-organ failure.

Hypertension is a chronic disease characterized by systemic high blood pressure and is the most common and important risk factor for the development of cardiovascular diseases. The etiology of hypertension is heterogeneous and remains elusive. In the last decade, oxidative stress and activation of the innate immune response have been shown to be pivotal to the pathophysiology of hypertension. Yet, there is a knowledge gap in how these two critical components are linked to cause blood pressure elevation. In our current work, we propose the **transformative hypothesis** that in hypertension, mitochondrial oxidative stress elevates reactive oxygen species (ROS) and release of mitochondrial DNA (mtDNA) into the cytosol. This cytosolic mtDNA activates the NLRP3 inflammasome leading to endothelial dysfunction and hypertension. This **hypothesis is compelling and barrier-breaking** because it links oxidative stress to activation of the innate immune response to cause hypertensive vascular disease.

B. Briefly describe specific project(s) for your teacher:

Experiments will be performed in isolated vascular segments from hypertensive animals to pharmacologically block components of cell signaling that are critical to activation of the NLRP3 inflammasome. Endothelial function will be characterized using myograph techniques and expression levels of proteins that regulate vascular function will be studied. These experiments require approximately 6-8 hours to perform on any given day.

C. Will any other people (post docs, grad students, undergraduate students, colleagues, etc.) be involved directly with your teacher?

The Webb laboratory is staffed by one associate level research scientist (Dr. Fernanda Priviero), one visiting professor (Dr. Gisele Bomfim), one postdoctoral fellow (Dr. Rinaldo dos Passos), two graduate students (Stephanie Wilczynski and Cintia Santos) and a technician (Anne Bailey). Additionally, within the Cardiovascular Translational Research Center there are two other professors (Drs. Camilla Wenceslau and Cameron McCarthy) who participate in research activities closely related to this ongoing research

D. Will you require any advanced reading/preparation for the teacher?

No advanced preparation is needed. The following provides information about the CTRC:

https://sc.edu/study/colleges_schools/medicine/centers_and_institutes_new/cardiovascular_translational_research_center/index.php