

The Graduate Program in Biomedical Sciences is proud to announce the



Ph.D. Dissertation Defense of REBECCA HERNANDEZ

Biomedical Sciences Ph.D. Candidate in the Zhou Lab

Dr. Changcheng Zhou, Chairperson

"Novel insights into the mechanisms of Atherosclerosis."

Atherosclerosis is a chronic inflammatory disease characterized by an accumulation of lipids, immune cells, necrotic cells, and other fibrous material in the sub-intimal space of large arteries. The lack of medical intervention or lifestyle changes can lead to advanced plague development and plague rupture, causing complete obstruction of blood flow, and ultimately death. My dissertation work identifies novel contributors of atherosclerosis development that had been previously overlooked. By using the PANDORA-seq method to capture highly modified sncRNAs, I revealed dysregulated tsRNAs and rsRNAs associated with atherosclerosis development in the intima and sperm of high cholesterol-fed male mice. Interestingly, female offspring of those mice developed larger atherosclerotic plagues as compared to female mice from low cholesterol fed sires. As epigenetic regulators, we believe sperm tsRNAs and rsRNAs may become imprinted with an atherogenic "code" that is transmitted to offspring. Lastly, the involvement of the adventitia on plaque development has been largely ignored, but IKKB is a known pro-inflammatory molecule that promotes plaque development. Interestingly, I found fibroblast IKKB-deficiency led to feature of unstable plaques. Single cell-sequencing analysis revealed a decrease in the smooth muscle cell population in fibroblast IKKB deficient aortas, possibly due to reduced fibroblast to smooth muscle cell differentiation. Together, these studies highlight new contributors of atherosclerosis development, including the role of tsRNAs and rsRNAs, paternal diet, and fibroblast IKKB on atherosclerosis development and plague stability.

> Monday, August 5th, 2024 1:00 PM (PST)

School of Medicine Education I Building, Room G650 Join via Zoom:

https://ucr.zoom.us/j/95963041167?pwd=9bf8Xe9O87EbTI6JBEyUo4zlSYRid2.1