UC RIVERSIDE
School of Medicine
DIVISION OF BIOMEDICAL SCIENCES

PH.D. DISSERTATION DEFENSE OF

MARK WILEY

Biomedical Sciences PhD Candidate
DiPatrizio Lab
Dr. Nicholas V. DiPatrizio, Chairperson

Endocannabinoid System Control of Mucosal Function in Health and Disease

The endocannabinoid (eCB) system is the endogenous cannabis signaling system and includes the lipid ligands which signal along the cannabinoid receptors [cannabinoid receptor subtype-1 (CB1R), -2 (CB2R) and others]. My initial work aimed to identify if host CB1R signaling is protective in host-helminth interactions using *Nippostrongylus brasiliensis* (*Nb*) as a model for hookworm infection in rodents. This study identified that peripheral blockade of CB1R, but not CB2R, leads to significant increases in lung tissue damage, lung hemorrhaging, and lung eosinophilia in response to *Nb* infection with no changes in parasite burden. *Nb* can produce eCBs at quantifiable levels, therefore I developed novel enzyme assays to quantitate enzyme activity for the biosynthetic and degradative eCB enzymatic machinery, including a novel assay to determine the rate of AEA metabolism which does not require the use of radioactive materials. Furthermore, when these methods were applied to a mouse model of diet induced obesity (DIO) in the large intestine, I found that the eCB system of the colon is severely dysregulated in response to DIO and that mice lacking intestinal epithelial CB1R signaling have exacerbated metrics of diet-induced gut-barrier dysfunction in the large intestine. RNA analysis identified an upregulation in inflammatory markers with a downregulation in gut-barrier markers in DIO intestinal epithelial CB1R KO mice. These studies suggest a potential role for the eCB system in several disease models in mucosal tissues providing novel methods for quantitation of eCB metabolism and evidence that CB1R signaling has a strong role in inflammatory processes.

Tuesday, August 17, 2021
12:00 pm (PST)
https://ucr-edu-hipaa.zoom.us/j/92269856866?pwd=TjlQS1F6WHQwMGxqK2U5Nks1cGY3dz09