RUTGERS
School of Graduate Studies

Office of Student Affairs and Admissions
SGS at New Jersey Medical School
Rutgers, The State University of New Jersey
185 South Orange Avenue, MSB C-696
Newark, NJ 07103

http://njms.rutgers.edu/gsbs/
p. 973-972-4511
f. 973-972-7148

YOU ARE INVITED TO ATTEND THE

DEFENSE OF THE DOCTORAL

DISSERTATION

"Unexpected functions of interferons at the gastrointestinal barrier"

by

Connie McElrath
Infection, Immunity and Inflammation Program

B.S. 2005, The Richard Stockton College of New Jersey, Pomona NJ
M.S. 2010, Montclair State University, Montclair NJ

Thesis Advisor, Sergei Kotenko, Ph.D.
Professor
Department of Microbiology, Biochemistry and Molecular Genetics

Thursday, September 6th, 2018
11:00 A.M.
Cancer Center G1196

ABSTRACT

Type I and type III interferons (IFNs) are recognized for their non-redundant importance in limiting viral infection; however their roles as homeostatic and inflammatory mediators are less well characterized. Ulcerative colitis (UC), involves perturbation of the complex interactions between the mucosal immune system and the commensal bacteria of the gut, with cytokines acting as important cross-regulators.

To characterize the contributions of type I and type III IFNs to the formation, progression, and resolution of UC, we used mice deficient in type I IFN, type III IFN, and type I/III IFN signaling and a murine model of acute UC, which followed exposure of mice to dextran sulfate sodium (DSS)-containing water.

Experiments revealed that IFN signaling contributes to the acute inflammatory response and mucosal wound healing. We observed enhanced susceptibility to DSS exposure in mice deficient in type I/III IFN signaling, and decreased proliferative capacity. Analysis of experiments conducted with bone marrow chimera mice revealed that IFN signaling in either the epithelial or hematopoietic compartment supports epithelial regeneration following DSS-induced damage, and is sufficient for protection. We identified a deficiency in amphiregulin when double IFN-deficient mice are exposed to DSS, and determined that both type I and III IFN can up-regulate this EGFR ligand. Furthermore, exogenous administration of amphiregulin rescued double IFN-deficient mice.

Therefore, our data reveals a new role for IFN signaling in supporting epithelial regeneration following DSS-induced damage. Ongoing experiments have revealed that compartmentalized and coordinated action of type I and III IFNs contributes to maintaining intestinal tissue homeostasis and balancing tissue repair and inflammatory responses following acute intestinal injury.