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

"The Life and Death of Natural Killers: The Inhibitor of Apoptosis Protein, Birc5, critically regulates the NK cell niche."

by
Marc Brillantes

Infection, Immunity and Inflammation Program

B.S. 2011, The College of New Jersey, NJ

Thesis Advisor, Aimee M. Beaulieu, Ph.D.
Assistant Professor and Chancellor Scholar
Center for Immunity and Inflammation
Department of Microbiology, Biochemistry and Molecular Genetics

Friday, February 18th, 2022
10:00 A.M.

Join Zoom presentation
https://rutgers.zoom.us/j/2177278890?pwd=YTdYc2lRU2w5cHBpSVExamw2MnorZz09
Meeting ID: 217 727 8890
Password: 860222

ABSTRACT

Natural killer (NK) cells are cytotoxic lymphocytes that serve as sentinels to defend the body against virally-infected and cancerous cells. Understanding the cellular pathways that regulate NK cell development and function will inform the development of immunotherapies that harness NK cells in the treatment or prevention of cancer and infectious disease. Here, we demonstrate that the Inhibitor of Apoptosis Protein (IAP), Birc5 (also known as Survivin), is essential for NK cell development and maturation. We report that Birc5 is highly but transiently expressed in developing NK cells undergoing expansion to fill the NK cell niche. We report that NK cell-specific deletion of Birc5 results in a near-complete loss of NK cells in the bone marrow and peripheral organs of mice. This NK cell deficit was reflective of maturation defects, increased apoptosis, and arrested cell cycling in developing NK cells. Furthermore, loss of NK cells due to Birc5-deficiency led to increased outgrowth of murine cytomegalovirus (MCMV), consistent with the importance of NK cells in antiviral defense. We show that the cytokine IL-15, which is indispensable for NK cell development and homeostasis, regulates Birc5 expression, acting in part through mechanisms dependent on signaling through phosphatidylinositol 3-kinase, the metabolic regulator mTOR, and the transcription factor STAT5. Finally, we show that Birc5 is essential not only for NK cell development, but also for the development of other innate lymphoid cell subsets (ILCs), including Type 1 and Type 3 ILCs. Collectively, our data support a novel role for Birc5 as a critical regulator of NK cell development and maturation.