Department of Molecular and Cellular Biology Graduate Seminar MCB*7500

Friday, June 2, 2023 @12:00 p.m.

presented by:



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"Impacts of genomic diversity on the capacity of *Lachnospiraceae* to engage in beneficial immunomodulatory crosstalk in the gut"

The loss of beneficial bacterial members of the gut microbiota has been associated with the chronic inflammation underlying inflammatory bowel diseases. This highlights the key role of host-microbe interactions in promoting balanced immune responses in the homeostatic gut environment. The direct crosstalk between the mucosal immune system and the microbiota can be facilitated by intracellular NOD1/2 innate immune receptors, which recognize conserved motifs in bacterial peptidoglycan taken up by gut epithelial cells to activate the Nf-kB inflammatory response pathway. However, homeostatic levels of NOD1/2 receptor stimulation are largely uncharacterized in prominent, commensal members such as the highly abundant and diverse family of gram-positive anaerobes, Lachnospiraceae. This project aims to investigate how different members in Lachnospiraceae engage in a NOD-dependent immune crosstalk and its beneficial impact on regulating the inflammatory response. First, the NOD1/2 receptor activation patterns of different Lachnospiraceae isolates will be screened using stimulation assays. The genetic and structural basis of these stimulation differences will be assessed using bioinformatics and experimental approaches to select target isolates for further testing. Next, the direct immunological outcomes of target NOD-stimulatory Lachnospiraceae isolates will be evaluated in gut epithelial cell line and organoid cultures by measuring the expression and profile of released cytokines, transepithelial resistance and epithelial cell differentiation. Finally, the ability of target NOD-stimulatory Lachnospiraceae isolates to ameliorate induced inflammation will be tested in vivo using an inflammatory mouse model.