



EXCELLENCE IN GENETICS & IMMUNOLOGY SEMINAR SERIES



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**Talk: “Contextual Control of TLR-induced Responses
by Divergent Signaling Thresholds ”**

Monday, July 27, 2015

Karp Amphitheatre | Room 501, 12:00 PM

Goodman Cancer Research Centre

“The innate immune system generates context-specific responses to microbial products, distinguishing steady-state stimuli from those of invasive pathogens. To date, we lack a detailed mechanistic understanding of the signaling logic that limits inflammatory cytokine production to non-dangerous inputs, thereby avoiding immunopathology. Using single cell quantitative assays and computational modeling, we found multiple thresholds for signaling pathways dictating stimulus-dependent functionality in macrophages exposed to TLR4 ligand. While TNF protein expression was controlled by switch-like MAPK activation, NF- κ B activity occurred at ligand concentrations below the MAPK-mediated threshold for inflammatory cytokine production, and primed cells for a more robust response to subsequent stimulation. Remarkably, macrophages from distinct mouse strains and from multiple human donors showed quantitatively very similar behavior. Our study thus reveals a tightly regulated ‘low-noise robust response’ system, which modeling suggests can be disturbed by small expression variations in regulatory phosphatases, including those showing linkage to human inflammatory diseases”.

This seminar is mandatory for Graduate students

LOCATION: Goodman Cancer Research Centre, Room 501, 12:00 PM

HOSTED BY: DRS SILVIA VIDAL & JUDITH MANDL