

SlgN Immunology Seminar



Prof Gabriel Nuñez

Department of Pathology and Comprehensive
Cancer Center

The University of Michigan Med School, USA

**Control of Pathogen Eradication: Role of
NLRs and the Gut Microbiota**

Host

Dr Alessandra
Mortellaro
Singapore
Immunology
Network, A*Star

Date

**Monday,
26 November 2012**

Time

11am – 12pm

Venue

SlgN Seminar Room,
Immunos Building
Level 4
Biopolis

Nod-like receptors (NLRs) are members of a family of intracellular proteins with structural homology to the apoptosis activator Apaf-1 and plant disease resistance (R) gene products. Unlike Toll-like receptors (TLRs) that mediate recognition of microbes at the plasma membrane or within endosomes, NLRs sense conserved microbial structures in the cytosol through their LRRs and upon activation induce host defense signaling pathways. NOD1 and NOD2 sense related, but distinct structural motifs, present in bacterial peptidoglycan and upon activation, they induce NF- κ B and MAPK signaling to induce the production of pro-inflammatory and anti-microbial molecules. In contrast, NLRP3 and NLRC4 are critical for the activation of inflammasomes, molecular platforms that mediate the activation of caspase-1 and processing of pro-IL-1 β and IL-18. NLRC4 recognizes flagellin in a TLR5-independent manner while NLRP3 senses extracellular ATP, bacterial toxins and intracellular membrane-damage. Notably, mutations in NOD2 are associated with Crohn's disease while NLRP3 mutations are linked to several autoinflammatory syndromes that are characterized by inappropriate secretion of IL-1 β in the absence of microbial infection. Recently, we found that NLRC4 plays a critical role in the discrimination between pathogens and commensals in the intestine. Furthermore, we identified an important role for the indigenous microbiota in the eradication of *Citrobacter rodentium*, a natural enteric pathogen of mice that models human infections with attaching-and-effacing bacteria.