

**NUS Graduate School for Integrative Sciences and Engineering
Research Project Write-up**

Title of Project : **Host-pathogen interaction - Regulation and fate of immune-responsive signaling molecules**

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Short Description

Toll-like receptors (TLRs) are the key components in cell-signaling of the innate immune system, responsible for detection of invading pathogens. Different TLRs recognize different pathogen-associated molecular patterns (PAMPs), leading to the activation of distinct gene expression patterns. This process is involved in differential usage of adaptor molecules by different TLRs. It was recently shown that the Sterile alpha and HEAT/Armadillo motif containing protein (SARM) is a new member of the adaptor family of the TLR signaling pathways. Studies on *C. elegans* and human SARM revealed that this molecule is essential for pathogen resistance and may mediate signal transduction within a novel TLR signaling pathway. However, the exact role that SARM plays in innate immune response remains unclear. We hypothesize that SARM is responsible for downregulating the hyperactivity of signaling molecules after the initial infection phase. We have shown that SARM is highly conserved in the worm, fly and mammals. Transcription profiling showed an upregulation of SARM in response to acute phase *Pseudomonas* infection. We have preliminary evidence to show that SARM terminates certain infection-induced signaling molecules. The new graduate student will study the interaction partners of human SARM to investigate how SARM & its partners regulate the action and fate of various signaling molecules during infection and immunity.

Questions to Address:

- How does a host downregulate its immune response signals after an infection?
- How is SARM involved? What are the intracellular molecules which collaborate with SARM? Which part of the SARM molecule is responsible for its role?