

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

Title of Project : **How does extracellular ROS induce signaling in acute inflammation and sepsis?**

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Short Description

During innate immune response, macrophages and neutrophils produce large amounts of ROS intracellularly to kill the phagocytosed microbes. However, ROS also causes oxidative stress to the host, which attempts to reduce it using superoxide dismutase, catalase and glutathione peroxidase. ROS acts on cysteine residues of proteins resulting in the conformational modification thereby regulating the activity of protein kinases/phosphatases, eg. ASK, JNK, PI3K, PTPs, which propagates the proinflammatory signals through redox-sensitive transcription factors (e.g. NF- κ B, AP-1). This event induces inflammation-related gene expression during innate immune response. Recently, we have discovered an evolutionarily-conserved ROS-production which occurs extracellularly at the point of infection, killing the microbe effectively. Our hypothesis is that this ROS-antimicrobial strategy occurs in proximity to the invading pathogen and that an infection signal is transduced into the immune-responsive cell to further alarm the host of the invading pathogen. This project aims to examine the co-ordinated role of ROS in innate and adaptive immunity through its immunomodulatory action on the NF- κ B, proinflammatory cytokines (e.g. IL-1 β , TNF α). Some pertinent questions will be addressed: eg: How an extracellular ROS signal is transduced into a host cell? What is the sensor for extracellular ROS? What are the responsive target genes? How are these events immune-regulated?