SIgN Immunology Seminar

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Host: Prof Ren Ee Chee
Singapore Immunology Network, A*STAR
Date: Monday, 21st November 2011
Time: 11am – 12pm
Venue: SIgN Seminar Room, Immunos Building Level 4, Biopolis

LUPUS THROUGH THE OMICS LENS

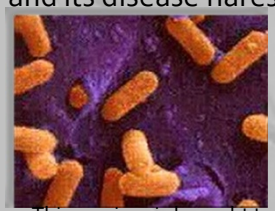
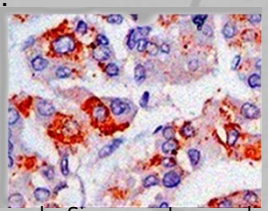
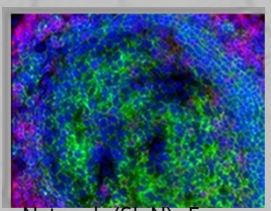
Various "OMICs" platforms are revolutionizing how we study biology and disease. Over the past five years, our understanding of the autoimmune disease lupus (or SLE) has evolved rapidly thanks to insights from various OMICs platforms, including Genomics, Transcriptomics, Proteomics and Metabolomics. Our work has focused on two aspects of the disease, tapping some of these platforms.

I. GENETIC DISSECTION OF LUPUS: Systemic lupus erythematosus is a polygenic disease. The past 2-3 year have witnessed the unraveling of several novel genes for human lupus, largely elucidated through GWAS studies. The challenge ahead is to confirm these associations, and to dissect out the molecular pathways that lead to disease. In this respect, the laboratory mouse has been very useful. Murine lupus is phenotypically similar to human SLE. Genome scans have been reported in almost all commonly studied murine models of lupus. Collectively, these studies highlight the presence of strong disease loci on murine chromosomes 1, 4, 7 and 17. Studies in mice have allowed researchers to engineer mouse models harboring individual genetic loci, also called congenic strains, to understand how each locus operates. Our work has focused on defining the steps leading to lupus, using C57BL/6-based B6.Sle1, B6.Sle2, and B6.Sle3 congenic strains. Collectively, these studies have uncovered at least 3 key mechanisms or checkpoints in lupus pathogenesis:

(a) breach in B and T cell tolerance
(b) peripheral amplification of the autoimmune response by dendritic cells
(c) local processes in the end-organ that facilitate nephritis

Collectively, the above studies indicate that violating tolerance checkpoints in the adaptive immune system and also the innate immune system, coupled with enhanced inflammatory processes in the end organs constitute key events in lupus pathogenesis. More recently, we have begun to define the signaling networks that become activated within lymphocytes as disease evolves. These new leads are uncovering novel therapeutic targets in this disease.

II. DISCOVERY OF NOVEL BIOMARKERS FOR SLE: Over the past few years, we have used proteomic and metabolomic approaches to uncover novel biomarkers in lupus. Several of these molecules have been validated using orthogonal platforms. Longitudinal patient studies are in progress to establish which of these novel proteins or metabolites might be useful in predicting SLE and its disease flares.

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