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SIgN Immunology Seminar



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The Role of B Cell Metabolism in Immune Homeostasis

Host
Prof Laurent Renia
Singapore Immunology Network, A*Star

Date
Tuesday, 15 November 2016

Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

The immune system protects the host from infection by pathogens. It does this through the action of multiple immune cell types, for example, invariant natural killer T (iNKT) cells that specifically recognize lipid antigens and B cells. iNKT cells provide help to B cells to promote production of antibodies that neutralize the pathogen. When the immune response is directed against molecules expressed by self, iNKT cells also modulate production by B cells of autoantibodies that result in damage to host tissues.

Less well understood is how B cells reciprocally regulate iNKT cell responses, which can occur via presentation of self-lipid antigens by B cells to activate iNKT cells. To address this question, we studied the phenotype of iNKT cells in two autoimmune strains of mice which harbour, separately, B cell-specific loss-of- function mutations in the FAS receptor and SHP-1 phosphatase. As both strains of mutant mice spontaneously developed autoimmunity which worsened with age, they accumulated autoantibodies, produced elevated levels of cytokines and manifested a striking deficiency of iNKT cells. I will discuss how aberrations in lipid metabolism of autoimmune B cells, which can be induced by cytokines, contribute to iNKT depletion in vitro and in vivo.

Our findings collectively unveil a critical link between the B cell lipidome and the maintenance of iNKT cells, and are consistent with the emerging notion that B cells have essential immunomodulatory functions beyond antibody production.

Finally, I will describe how therapeutic strategies used to redress dysregulation of lipid biosynthesis pathways in lipid storage diseases can be re-purposed to target similar pathways in order to correct immune defects in autoimmune diseases.