SIgN Immunology Seminar

Dr Wen Qi Ho

A*STAR and Stanford University, Multidisciplinary Program in Immunology

Dyrk1a is essential for cell cycle regulation during T cell development

Host
Dr Maria Lafaille
Singapore Immunology Network, A*Star

Date
Friday, 8 February 2013

Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

The dosage sensitivity of the nuclear kinase Dyrk1a is thought to play a role in Down's syndrome (DS). Dyrk1a functions in concert with GSK3 to export NFAT from the nucleus, which plays diverse roles in neural, cardiac, bone and lymphocyte development. The leading cause of morbidity in DS patients is attributed to a compromised immune system, but the role of Dyrk1a in immune function and development remains unknown. We generated Dyrk1a conditional knockout mice to study the role of Dyrk1a in T cells. Our studies on peripheral T cells support the role of Dyrk1a as an NFAT priming kinase. Unexpectedly, we found that conditional deletion of Dyrk1a leads to the inability of double positive (DP) thymocytes to exit the cell cycle, a step required for T cell receptor (TCR) gene recombination. Dryk1a-deficient thymocytes display ineffective TCRα gene recombination and expression, resulting in reduced TCR-mediated signaling. Inappropriate S-phase entry in the absence of Dyrk1a does not effectively expand the number of T cells, but instead leads to checkpoint-induced cell death. Our study demonstrates that Dyrk1a is required for mitotic quiescence in DP thymocytes, and reveals an unexpected but complex role for Dyrk1a in cell cycle regulation during thymocyte development.