CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

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Transcriptional and Epigenetic Views of CD4/CD8 Lineage Commitment in Thymus

Date: Friday, 17 August 2012
Time: 1pm – 2pm
Venue: #01-02 Active Learning Rm, Centre for Translational Med. (CeTM)
14 Medical Drive, MD 6, Singapore 117599
Chair: A/Prof Motomi OSATO

Abstract:

Both $CD4^+$ helper-lineage and $CD8^+$ cytotoxic-lineage T cells are differentiated from common precursor $CD4^+CD8^+$ DP thymocytes. ThPOK transcription factor has been shown to play a central role in the CD4/CD8 lineage choice by activating as well as repressing helper- and cytotoxic-fate, respectively in dosage- and stage-dependent manner. Developmental programming towards the helper-lineage depends upon ThPOK expression with correct kinetics, whereas it must be repressed to guide MHC class I-restricted TCR to become cytotoxic-lineage. Thus Thpok gene regulation under TCR signals serves as a good model to study how bi-potential precursors choose one developmental path by converting external stimuli. We have identified several cis-regulatory regions including a transcriptional silencer in the Thpok gene and are characterizing their functions in regulating Thpok expression mainly by using mutagenesis on the endogenous Thpok loci including conditional excision of them. Our results are revealing that distinct epigenetic mechanisms are involved in regulating two promoters to initiate and fix Thpok expression. We are also investigating relevance of interactions between multiple cis-regulatory regions by combined mutagenesis and by synthetic reconstitution of regulatory regions.

In my seminar, I would like to discuss above results with a perspective view toward understanding of how regulatory regions on a particular gene sense and convert external stimuli and how they evolutionally acquire such function.

References

Setoguchi R. et al, Science 319:816, 2008.
Muroi S. et al. Nat. Immunol. 9:1113, 2008.
Collins A. et al. Nat. Rev. Immunol. 9:106 2009.
Seo W. et al. Immunol. Cell. Biol. doi:10.1038/icb.2012.6

All are welcome to attend.