SIgN Immunology Seminar

Prof Ichiro Taniuchi

RIKEN Center for Integrative Medical Sciences (IMS), Laboratory for Transcriptiopnal Regulation

Roles of Runx Transcription Factor Family During T Lymphocyte Development

Host
Dr Florent Ginhoux
Singapore Immunology Network, A*Star

Date
Thursday
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Time
2pm – 3pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Runx complexes are evolutionally conserved heterodimeric complexes, which consist of Runx protein and non-DNA binding partner Cbfβ protein, and acts as essential regulator in the control of development of multiple types of cells. For instance, we have shown that Runx complexes play an essential role in a CD4 helper versus CD8 cytotoxic lineage choice via repressing expression of helper-signature genes such as *Cd4* and *Zbtb7b*. However, role of Runx complexes in early specification process to T-lineage remain obscure. Recently, we have found that a loss of Cbfβ2 variant, one of two major RNA splicing variants of Cbfβ in mammal, resulted in a small size of thymus due to an impaired generation of paired immunoglobulin-like receptor (PIR) expressing fetal liver subset, which was shown to be a pre-thymic progenitor possessing a thymus colonizing activity. Having these results, we are now attempting to find Runx target molecules, which would be important for differentiation of PIR^+ fetal liver cells

Upon encountering antigen, naïve CD4 T cells differentiate into effector subset that expresses a distinct set of cytokines. During such a process, Runx complexes are necessary to silence *Il4* gees in Th1 cells via direct activation of the silencer in the *Il4* locus. We searched for novel Runx target genes whose expression is also repressed by Runx, and found that Runx complexes repress expression of a CC chemokine gene cluster in $CD4^+$ T cells. An evolutional conserved VWRPY motif present at the C-terminal end of Runx proteins is necessary to repress CC chemokine gene as well as *Il4*. Importantly, impaired Runx complexes function in T cells cause an spontaneous development of airway inflammation in mice. To further understand a mode of Runx-mediated repression of cytokine/chemokine genes, we are now characterizing a long non-coding RNA that can interact with Runx complexes in a VWRPY motif-dependent manner and is involved in *Il4* gene repression.

These two topics will be discussed from the view of transcriptional control of differentiation and function of T lymphocytes.