Chromatin conformation dynamics during T cell development

**Background**

* Metazoan chromatin is highly compact BUT organized.

**Example I: Enhancer-promoter loops**

Chromatin loops bring genes into direct contact with distal regulatory elements, such as enhancers.

**Example II: Topological Associated Domains (TADs)**

The genome is organized into discretely folded megabase-sized regions, denoted as topologically associated domains (TADs), which seem to correlate well with transcriptional activity and histone modifications.

**Method II: Analysis**

**Enhancer-promoter loop developmental dynamics**

Target genes? Timing of loops? Chromatin state?

Known features of enhancers:
- Distant location from TSSs.
- Gene target not necessarily closest on linear chromosome.
- Epigenetic marks such as histone H3 Lys4 mono-methylation (H3K4me1).
- Enrichment for transcription factor binding sites (TFBS).
- Some marks distinguish « active » from « poised » enhancers.

Promoter Cap-C on DP and DN cells. Numbers of sequences are shown for 500 Kb Windows spanning promoters of two differentially-expressed genes, Il17rb (top ; expressed in DN) and Rag1 (bottom ; expressed in DP).

A constitutive interaction with Il17rb is shown by black arrows; a DN-specific interaction with Rag1 is shown by a red arrow.

**References**


**Method I: Cap – Hi-C**

Crosslinking Digestion Ligation DNA shearing Sequence Capture Sequencing

An adaptation of Hi-C to (i) track at high-resolution the conformation of specific TADs surrounding differentially expressed genes; (ii) simultaneously detect all interactions between promoters and distal regulatory elements, across an important developmental transition of T cell; The differentiation from CD4/CD8 double negative (DN) to double positive (DP) cell.