URLs

Ifng
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=Graphics&list_uids=15978
Il-4
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=Graphics&list_uids=16189
Il-5
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=Graphics&list_uids=16191
Il-13
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=Graphics&list_uids=16163

GENE REGULATION

Cytokine loci co-localized and poised

How are cytokine loci arranged in the nucleus to ensure coordinated and reciprocal expression of cytokine genes by T helper 1 (T_H1) versus T_H2 cells if they are present on different chromosomes? In a recent study in *Nature*, Richard Flavell and colleagues address this conundrum and provide the first direct evidence that cytokine loci on different chromosomes that are alternatively expressed by T_H-cell subsets are brought together in the nucleus, locating them in nuclear sites that are conducive to rapid expression in response to immune stimuli.

Expression of the T_H1-cytokine gene interferon-γ (*Ifng*) is regulated by elements near it on chromosome 10, whereas expression of the T_H2-cytokine genes interleukin-4 (*Il-4*), *Il-5* and *Il-13* on chromosome 11 are regulated by a locus control region (LCR) on the same chromosome, which controls expression of the entire T_H2-gene complex. But, using a recently developed chromosome-conformation capture technique, the authors could detect interchromosomal interactions between the promoter region of *Ifng* and the T_H2 LCR in naive T_H cells, which seems to add a further dimension to the regulation of these genes. After stimulation of naive cells to induce differentiation into T_H1 or T_H2 cells, the chromosomes seemed to move apart. Concomitant with loss of the interchromosomal interactions, in T_H1 cells intrachromosomal interactions between *Ifng* and its downstream regulatory element were favoured, indicating that the interactions are dynamic and cell-subset specific. These results were confirmed using fluorescence *in situ* hybridization (FISH).

The authors proposed that the purpose of such dynamic chromosome interactions was to position genetic loci in subnuclear compartments that poise and prepare these loci for rapid expression after stimulation. Consistent with this, deletion of an LCR regulatory element (RHS7), which disrupted interchromosomal associations, delayed the rapid induction of *Ifng* expression after stimulation under T_H1-cell-promoting conditions. Similarly, under T_H2-cell-promoting conditions, cells that lacked RHS7 expressed less IL-5 at early time points.

So, the T_H2 LCR seems to regulate not only the transcription of the T_H2 cytokines but also the expression of the *Ifng* gene through mediating interchromosomal associations. Whether this phenomenon will be a common feature of other coordinately regulated genes awaits future research.

Lucy Bird

References and links

ORIGINAL RESEARCH PAPER Spilianakis, C. G., Lalioti, M. D., Town, T., Lee, G. R. & Flavell, R. A. Interchromosomal associations between alternatively expressed loci. *Nature* **435**, 637–645 (2005)

FURTHER READING Kioussis, D. Kissing chromosomes. *Nature* **435**, 579–580 (2005)