# IN BRIEF

DEVELOPMENTAL IMMUNOLOGY

## Abnormal bone marrow stroma in mice deficient for nemo-like kinase, Nlk.

Kortenjann, M. *et al*. *Eur. J. Immunol.* **31**, 3580–3587 (2001)

Kortenjann *et al.* investigated the *in vivo* role of Nemo-like kinase (Nlk), a serine/threonine kinase that connects MAP kinase and Wnt signalling pathways, by generating *Nlk*$^{-/-}$ mice. The complex phenotype of these mice depended on their genetic background. 129/Sv *Nlk*$^{-/-}$ mice, among other defects, developed abnormal bone marrow stroma, resulting in increased numbers of adipocytes, large blood sinuses and an absence of bone-lining cells. These mice represent a new model in which the genetic requirements of bone marrow stromal differentiation can be studied.

AUTOIMMUNITY

## Systemic sclerosis (scleroderma): specific autoantigen genes are selectively overexpressed in scleroderma fibroblasts.

Zhou, X. *et al. J. Immunol.* **167**, 7126–7133 (2001)

Autoimmune mechanisms have been implicated in the pathogenesis of systemic sclerosis (SSc), a multisystem disorder of connective tissue. Here, cDNA microarrays were used to analyse the gene-expression profiles of SSc dermal fibroblasts. In comparison to normal control fibroblasts, SSc fibroblasts from either affected or unaffected skin selectively overexpressed specific autoantigen genes.

T-CELL DEVELOPMENT

## Friend of GATA-1 represses GATA-3-dependent activity in CD4$^+$ T cells.

Zhou, M. *et al. J. Exp. Med.* **194**, 1461–1471 (2001)

The friend of GATA (FOG)-1 protein is known to regulate activity of GATA transcription factors at several stages of haematopoietic development, but whether it regulates GATA-3 activity in developing T cells was unknown. Here, Zhou *et al.* show that FOG-1 represses GATA-3-dependent activation of the *IL5* promoter in T cells, and that overexpression of FOG-1 during primary activation of naive T cells inhibits $T_H2$ development in CD4$^+$ T cells.

ANTIGEN PRESENTATION

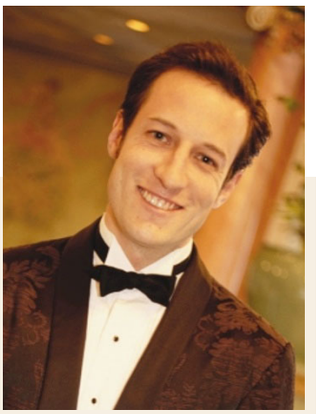
## Multiple defects in antigen presentation and T-cell development by mice expressing cytoplasmic tail-truncated CD1d.

Chiu, Y-H. *et al*. *Nature Immunol.* **3**, 55–60 (2002)

CD1 molecules are non-polymorphic, MHC class I-like molecules that present lipid antigens to T cells. To investigate the trafficking and presentation pathway for CD1d, Chiu *et al.* generated knock-in mice expressing CD1d with a truncated cytoplasmic tail. The results show that the tyrosine motif in the cytoplasmic tail is important for intracellular trafficking of CD1 and the development of subsets of CD1d-restricted T cells.

THYMOCYTE DEVELOPMENT

# Jacket and tie required



**Dress codes are often used by exclusive restaurants to prevent undesirable clientele lowering the tone of their premises. In the same way, chromatin codes, defined by patterns of histone modifications such as acetylation and methylation, dictate whether a gene locus is open (allowing for transcription), or closed (meaning transcription is inhibited). T-cell receptor (TCR) rearrangement, which occurs during thymocyte development and enables a broad range of TCR specificities to be generated, might also be affected by chromatin codes. An open structure might allow access for recombination-activating gene (RAG) products, in a similar way as it does for transcriptional machinery.**

**Interleukin-7 (IL-7) is required for normal lymphoid development and survival, and for rearrangement at the TCRγ locus, but the mechanism of its action in this process is unknown. Two reports, from Muegge's group in *The Journal of Immunology*, and from Ikuta's laboratory in *Immunity*, now show that IL-7 signalling regulates TCRγ gene rearrangement by specifically altering histone acetylation within the TCRγ locus.**

**Both groups performed chromatin-immunoprecipitation (ChIP) analysis to study the acetylation status of histones 3 and 4 within regulatory sites of the TCRγ locus in thymocytes from wild-type and IL-7 receptor-α (*Il7Rα*)$^{-/-}$ mice. Acetylation of histone tails is thought to result in an open chromatin structure. Muegge and colleagues found that, in comparison with other sites within the genome, histone acetylation of the TCRγ locus was enhanced in wild-type thymocytes. Results from both groups showed that this hyperacetylation was not seen in thymocytes from *Il7Rα*$^{-/-}$ mice, indicating that the specific acetylation of the TCRγ locus is dependent on IL-7 signalling.**

**Does IL-7 have a direct effect on accessibility at the TCRγ locus? Muegge and colleagues investigated this by treating thymocytes from *Il7*$^{-/-}$*Rag2*$^{-/-}$ mice with IL-7, and assessing the production of constant-region transcripts. Crossing *Il7*$^{-/-}$ mice with *Rag2*$^{-/-}$ mice was necessary as *Il7*$^{-/-}$ thymi are arrested in γδ T-cell development, but show substantial leakiness in αβ T-cell development. Within 5 hours of IL-7 treatment, constant-region transcripts were induced in thymocytes from double-knockout mice, indicating that IL-7 signalling is directly able to open chromatin in thymocyte precursors. The authors went on to show that this IL-7-inducible chromatin opening in *Il7*$^{-/-}$*Rag2*$^{-/-}$ thymocytes was due to increased acetylation of histones within the TCRγ locus.**

**Previous work form Ikuta's group has implicated the transcription factor Stat5 in IL-7-mediated control of TCRγ locus accessibility. To see if Stat5 acts by controlling histone acetylation of this locus, ChIP assays were performed with *Il7Rα*$^{-/-}$ thymocytes cultured with or without Stat5 cDNAs. Introduction of active Stat5 restored the histone acetylation and accessibility of the TCRγ locus in *Il7Rα*$^{-/-}$ thymocytes. Ikuta and colleagues concluded that cytokine signalling results in recruitment of Stat5, which, in turn, recruits transcriptional co-activators, and controls the accessibility of the TCRγ locus by histone acetylation. These studies of the TCRγ locus are the first to directly link an extracellular stimulus to changes in chromatin structure.**

***Jenny Buckland***

**References and links**

**ORIGINAL RESEARCH PAPER** Huang, J., Durum, S. K. & Muegge, K. Histone acetylation and recombination at the TCRγ locus follows IL-7 induction. *J. Immunol.* **167**, 6073–6077 (2001) | Ye, S.K. *et al*. The IL-7 receptor controls the accessibility of the TCRγ locus by Stat5 and histone acetylation. *Immunity* **15**, 813–823 (2001)