to inhibition by the viral protein Vif. Vif protects HIV from cytosine deamination by APOBEC3G by targeting it for proteasomal degradation. So, HIV produced in the presence of APOBEC3G and Vif retains infectivity. Malim and colleagues showed that in the presence of Vif and APOBEC3F, more than 90% of the HIV sequences had zero or only one mutation, whereas when Vif was removed from the system, this dropped to less than 50%. Therefore, APOBEC3F is susceptible to inhibition by Vif. By contrast, Harris and colleagues showed that Vif could only partially restore the infectivity of viruses that were produced in the presence of APOBEC3F, indicating that APOBEC3F is less susceptible to Vif than APOBEC3G. Further study is required to discover whether and how APOBEC3F might avoid Vif-mediated proteasomal degradation.

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The *Cd4* proximal enhancer normally shows high levels of histone H3-acetylation, but this was reduced in the thymus of Mi-2 β -deficient mice, probably as a result of the observed decrease in association of the histone acetyltransferase p300 with the enhancer. Subsequent analysis showed that p300 and Mi-2 β associate with the E-box-binding protein HEB. Because the *Cd4* enhancer contains E-box binding sites, the authors propose that Mi-2 β is recruited to the enhancer through its interactions with HEB. Through its ATP-dependent chromatin-modelling function, Mi-2 β stabilizes HEB binding, such that associated/recruited p300 increases local histone acetylation, locking the chromatin in an open conformation and thereby leading to *Cd4* gene expression.

This study identifies Mi-2 β as crucial for thymocyte differentiation at the transition from the DN4 to the DP stage of development and for regulation of *Cd4* gene expression in DP thymocytes. As Mi-2 β has previously been defined as a negative regulator of gene expression, this study uncovers a new role for Mi-2 β , and future studies will probably characterize more situations in which it can act positively.

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T-CELL SIGNALLING

Getting faster with experience

Like a racing driver navigating a familiar course, T cells respond faster to a second exposure to their specific antigen. But what makes an experienced T cell go faster? This study in *The Journal of Immunology* indicates that crucial differences between naive and memory T cells in terms of the formation and duration of immunological synapses might be responsible.

The immunological synapse is the region of contact between a T cell and an antigen-presenting cell (APC), consisting of a central supramolecular activation cluster (cSMAC) and a peripheral SMAC (pSMAC). Previous experiments have shown that when a naive T cell first encounters an APC presenting the antigen for which it is specific, the immature synapse that first forms contains adhesion molecules in the cSMAC and T-cell receptor (TCR)-signalling molecules in the pSMAC. This pattern then reverses as the mature synapse forms so that signal transduction occurs in the cSMAC.

Watson and Lee wanted to see if the same holds true for memory T cells. They isolated naive and memory CD4⁺ T cells from DO11.10 mice, which express a transgenic TCR specific for an ovalbumin (OVA) peptide. These were then incubated with OVA-pulsed APCs. For naive T cells, as expected, TCRs and the signalling molecule protein kinase C- θ were found in the pSMAC 5 to 15 minutes after contact with an APC, whereas the adhesion molecule lymphocyte function-associated antigen 1 (LFA1) was present in the cSMAC. This pattern had reversed by 30 minutes to form the mature synapse, but by 60 to 90 minutes, the whole synapse had dissipated. However,

for memory T cells, the mature synapse had formed by 5 to 15 minutes after initial APC contact and remained for more than 90 minutes. In the memory T cells only, TCRs were constitutively associated with lipid rafts — regions of the membrane that accumulate in the synapse — which might account for the more rapid formation of the mature synapse.

Next, they looked at the effects on TCR signalling. In naive T cells, it is known that LCK is active in the pSMAC of the immature synapse but not when the mature synapse has formed. By contrast, they showed that in memory T cells, LCK was still active when it moved into the cSMAC of the mature synapse. This might be due to the observed presence of the tyrosine phosphatase CD45 — which promotes dephosphorylation of an inhibitory tyrosine of LCK — in the cSMAC of memory but not naive T cells. CD45 was also constitutively associated with TCRs in lipid rafts in memory T cells only.

However, although Lck activity was prolonged in memory T cells, this did not affect the downstream kinase ZAP70 (ζ -chain-associated protein kinase of 70 kDa). The authors therefore suggest that prolonged LCK activity might induce alternative memory-cell-specific signalling. The downstream effects of these differences in synapse formation and composition clearly require further investigation.

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