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IN BRIEF

T-CELL DEVELOPMENT

Bone marrow-derived hemopoietic precursors commit to the T cell lineage only after arrival in the thymic microenvironment.

Heinzel, K. *et al. J. Immunol.* **178**, 858–868 (2007)

Identification of a T lineage-committed progenitor in adult blood.

Krueger, A. & von Boehmer, H. *Immunity* **26**, 105–116 (2007)

The nature of the precursor cells that enter the thymus and become T cells and where commitment to the T-cell lineage occurs are controversial issues in T-cell biology. Two recent papers further add to this controversy, with one claiming that T-cell-lineage commitment occurs after entry to the thymus, and the second claiming that T-cell-committed precursors can be isolated from adult mouse blood.

Using single-cell analysis, Heinzel *et al.* show that the earliest precursor cells in the mouse thymus retain the capacity to develop into B cells, natural killer cells and dendritic cells as well as T cells. Only when these precursors are exposed to Notch signals intrathymically do they lose their potential to develop into non-T cells. Furthermore, T-cell precursors from the bone marrow are much less sensitive to Notch-mediated signals than thymic precursors, arguing against the idea that the bone marrow is the site of T-cell-lineage commitment.

By contrast, Krueger and von Boehmer, using transgenic reporter mice, in which human CD25 is expressed under the control of the pre-T-cell-receptor promoter, were able to isolate T-cell progenitors from adult mouse blood. These cells generated T cells when cultured *in vitro* using the OP9–DL1 culture system, and *in vivo* after transfer into mice deficient in T cells and interleukin-2 (IL-12). No B cells were detected after *in vivo* transfer, and only a few were detected after *in vitro* culture. Similar frequencies of precursors were isolated from thymus-deficient and wild-type mice, which indicates that the precursors are T-cell-lineage committed prethymically rather than intrathymically.

These two studies provide further information to fuel the ongoing controversy about the nature of T-cell lineage-committed T-cell precursors.

HIV

Structural definition of a conserved neutralization epitope on HIV-1 gp120.

Zhou, T. *et al. Nature* 15 February 2007 (doi:10.1038/nature05580)

The diversity of the HIV-1 envelope proteins allows the virus to effectively evade antibody-mediated neutralization. Only two envelope glycoprotein 120 (gp120)-reactive antibodies (b12 and 2G12) with broad neutralizing reactivity against a range of primary HIV-1 isolates have been identified so far. In this study, Zhou and colleagues provide a molecular description of the interaction between b12 and gp120.

The authors generated stabilized gp120 molecules that stayed in the CD4-bound confirmation even in the absence of CD4, and used these constructs to assess the CD4-binding site, which must be conserved in order to mediate virus binding and cellular entry. CD4 and b12 were found to bind to overlapping sites on a conformationally invariant surface of gp120, which is the initial contact site for CD4 prior to the gp120 rearrangements that are necessary to mediate viral entry.