HAEMATOPOIESIS

# SLAM-dunk decider

Finding a simple method for the reliable identification of haematopoietic stem cells (HSCs) has proved elusive. Now, a report in *Cell* shows that, in mice, long-term-reconstituting HSCs (LT-HSCs) — which have extensive self-renewal capacity (a hallmark of stem cells) — can be precisely distinguished from closely related haematopoietic progenitors by their cell-surface expression of members of the signalling lymphocytic activation molecule (SLAM) family.

At present, mouse HSCs are identified on the basis of their expression of a complex combination of cell-surface markers, many of which are strain specific or activation dependent. Furthermore, using the most common combination of markers, only ~20% of the cells isolated have self-renewal capacity and thereby allow long-term reconstitution of all haematopoietic-cell lineages following transplantation. So, Kiel and colleagues set out to improve our ability to reliably identify LT-HSCs.

They first carried out gene-expression profiling of highly purified populations of LT-HSCs and multipotent progenitors (MPPs); MPPs give rise to multiple haematopoietic-cell lineages but do so only transiently, as they do not have self-renewal capacity. Of the 27 genes that were identified to be upregulated in LT-HSCs compared with MPPs, the SLAM-family member CD150 (also known as SLAM) was a good candidate for identifying LT-HSCs because of its cell-surface expression. Next, the authors transplanted $CD150^+$ or $CD150^-$ bone-marrow cells into irradiated mice. The $CD150^+$ cell population provided long-term reconstitution of multiple haematopoietic-cell lineages, whereas the $CD150^-$ cell population could do so only transiently.

On subsequently examining the expression of other SLAM-family molecules, the authors found that three members were differentially expressed by progenitors with different capacities for reconstitution — LT-HSCs were $CD48^-CD150^+CD244^-$, MPPs were $CD48^-CD150^-CD244^+$, and most restricted progenitors were $CD48^+CD150^-CD244^+$ — and this expression pattern was conserved across different mouse strains.

SLAM-family members are known to regulate the activation and proliferation of lymphocytes, but they have not previously been shown to be expressed by haematopoietic progenitors. The ability to identify populations of haematopoietic progenitors on the basis of the combination of SLAM-family molecules that they express provides a simple, broadly applicable tool for isolating LT-HSCs and for studying their regulation and anatomical localization. If this differential expression is conserved across species, then it has potential for improving the success of HSC transplantation in humans.

*Davina Dadley-Moore*

**References and links**

**ORIGINAL RESEARCH PAPER** Kiel, M. J. *et al.* SLAM family receptors distinguish hematopoietic stem and progenitor cells and reveal endothelial niche s for stem cells. *Cell* **121**, 1109–1121 (2005)

## IN BRIEF

REGULATORY T CELLS

### IL-12 induces $CD4^+CD25^-$ T cell activation in the presence of T regulatory cells.

King, I. L. & Segal, B. M. *J. Immunol.* **175**, 641–645 (2005)

This study provides another explanation for the pro-inflammatory, T-helper-1-cell-inducing effects on $CD4^+$ T cells of interleukin-12 (IL-12) produced by myeloid cells. $CD4^+$ T cells can escape suppression mediated by $CD4^+CD25^+$ regulatory T ($T_{Reg}$) cells in *in vitro* co-cultures through IL-12-mediated support of activation, proliferation and cytokine production. This effect was not reproduced by the related family member IL-23 or by indirect effects on interferon-γ production, and it required expression of the IL-12 receptor by the effector T cells but not by the $T_{Reg}$ cells. The authors suggest that, in an inflamed microenvironment, IL-12 blocks immunoregulation by $T_{Reg}$ cells to allow an effective immune response.

ASTHMA AND ALLERGY

### Disruption of *Nrf2* enhances susceptibility to severe airway inflammation and asthma in mice.

Rangasamy, T. *et al. J. Exp. Med.* **202**, 47–59 (2005)

Oxidative stress as a result of inflammation is thought to be involved in asthma pathogenesis, but until now, there has been little direct evidence that a defect in anti-oxidant pathways might contribute to disease. This paper shows that mice with disruption of the *Nrf2* gene — which encodes a redox-sensitive transcriptional regulator of anti-oxidant genes — have increased allergen-driven airway inflammation associated with increased levels of oxidative-stress markers. Future studies looking for an association between variation in the *NRF2* response and asthma susceptibility in humans will help to determine the general importance of maintaining an oxidant–anti-oxidant balance in the lungs.

HIV

### Macrophages archive HIV-1 virions for dissemination *in trans*.

Sharova, N. *et al. EMBO J.* **24**, 2481–2489 (2005)

Most research has focused on understanding the mechanisms of HIV-1 persistence in $CD4^+$ T cells; however, macrophages can also function as cellular reservoirs of the virus. Sharova *et al.* found that, after a single cycle of HIV-1 infection, macrophages could sustain *de novo* production of virions that were able to infect lymphocytes *in trans*. If macrophage production of virus was blocked using a protease inhibitor, the level of infectious virus produced by the macrophages decreased rapidly for the first week after treatment. However, after this time, the decrease in the level of infectious virus was much slower, and infectious virions could be detected 5 weeks after exposure to the protease inhibitors. This study indicates that some virions are relatively stable in macrophages, leading the authors to suggest that macrophages contribute to HIV-1 persistence in the host.