IN BRIEF

HAEMATOPOIESIS

Adult T-cell progenitors retain myeloid potential.

Wada, H. *et al. Nature* **452**, 768–772 (2008)

The earliest thymic progenitors for T cells possess myeloid lineage potential.

Bell, J. J. & Bhandoola, A. *Nature* **452**, 764–767 (2008)

The classical model of haematopoiesis maintains that haematopoietic stem cells give rise to immune cells of all lineages via either a common lymphoid progenitor (CLP; that cannot give rise to myeloid or erythroid cells) or a common myeloid progenitor (that lacks lymphoid potential). This binary model of lineage commitment is now disputed by two new reports in *Nature* that provide evidence that early thymic progenitors (which are CLPs) can differentiate into myeloid cells in adult mice. The authors of these studies clearly demonstrate using clonal analyses that early thymic progenitors have the capacity to differentiate into macrophages or granulocytes until the double-negative 2 (KIT^+CD25^+) stage of thymocyte differentiation (after B-cell potential has been lost). *In vivo* studies confirmed the bipotent potential of early thymic progenitors and demonstrated that a significant proportion of macrophages in the thymus is derived from progenitors that can also differentiate into T cells. Although it has previously been reported that early thymic progenitors can give rise to natural killer cells, lymphoid-derived dendritic cells and more rarely B cells, their myeloid potential has not previously been confirmed. Based on this new evidence, accepted models of haematopoiesis must be reconsidered and revised.

ANTIVIRAL IMMUNITY

ISG15 inhibits Nedd4 ubiquitin E3 activity and enhances the innate antiviral response.

Malakhova, O. A. & Zhang, D. *J. Biol. Chem.* **283**, 8783–8787 (2008)

Interferons trigger a number of essential host defence pathways following virus infection. A new study has now identified a pathway that involves the interferon-inducible ubiquitin-like protein ISG15 that is important for limiting the spread of pathogens such as Ebola and rabies viruses. To promote their own spread, viruses commonly exploit host-cell intracellular pathways, including the ubiquitin pathway. Ubiquitylation of viral proteins by the host NEDD4 (neural precursor-cell expressed, developmentally downregulated gene 4) family of ubiquitin E3 ligases is an important step in the release of viruses from host cells. In this study, it was found that NEDD4 is a substrate of ISG15 activity, and that interaction between these two proteins led to a reduction in the ubiquitin E3 ligase activity of NEDD4. ISG15-mediated inhibition of NEDD4 proteins limited ubiquitylation of Ebola virus matrix protein VP40 and thereby the release of Ebola virus-like particles from host cells. Further investigation revealed that ISG15 also inhibits other NEDD4-like ubiquitin E3 ligases, illustrating the role of NEDD4 family proteins in regulating virus budding and highlighting the crucial role of ISG15 in suppressing this process.