LPS, so together with the evidence that ST2 acts as a negative regulator of signalling through TLR4 (the LPS receptor), this led them to examine whether ST2 is involved in regulating tolerance to endotoxin. Compared with wild-type macrophages, ST2-deficient macrophages produced increased levels of pro-inflammatory cytokines after LPS priming and challenge; this correlated with *in vivo* responses — only wild-type mice survived a sub-lethal dose of LPS followed by a lethal dose. So, ST2 might be involved in maintaining the balance between activation and inhibition of signalling through TLR4.

This study identifies ST2 as a negative regulator of Myd88/Mal-dependent signalling and a key regulator of endotoxin tolerance. The authors propose that ST2 sequesters Myd88 and Mal, thereby impairing signalling by receptors that require these adaptors. Further studies of the function of ST2 in various cell types should reveal the therapeutic potential of targeting this molecule during infection and autoimmune disease.

Davina Dadley-Moore

References and links

ORIGINAL RESEARCH PAPER Brint, E. *et al.* ST2 is an inhibitor of interleukin-1 receptor and Toll-like receptor 4 signaling and maintains endotoxin tolerance. *Nature Immunol.* **5**, 373–379 (2004)

FURTHER READING Dunne, A. & O'Neill, L. A. The interleukin-1 receptor/Toll-like receptor superfamily: signal transduction during inflammation and host defense. *Sci. STKE* **2003**, re3 (doi: 10.1126/stke.2003.171.re3)

WEB SITES

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http://www.gla.ac.uk/departments/immunology/people/liew.html

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interferons (IFN-α/β), as IFNα/β-receptor-deficient mice infected with LCMV Cl 13 showed normal Flt3L-induced expansion of lymphoid DC populations (although myeloid DCs remained reduced in number). Further studies are required to determine whether this mechanism is common to other immunosuppressive viruses.

Understanding more about the mechanisms of viral immunosuppression might provide new perspectives for the therapy of chronic infections.

Lucy Bird

References and links

ORIGINAL RESEARCH PAPER Sevilla, N. *et al.* Viral targeting of hematopoietic progenitors and inhibition of DC maturation as a dual strategy for immune subversion. *J. Clin. Invest.* **113**, 737–745 (2004)

IN BRIEF

MUCOSAL IMMUNOLOGY

Induction of protective IgA by intestinal dendritic cells carrying commensal bacteria.

Macpherson, A. J. & Uhr, T. *Science* **303**, 1662–1665 (2004)

This study describes a mechanism to explain why inflammatory responses to commensal bacteria in the intestines are rare, despite the fact that these bacteria share many molecular patterns with pathogenic bacteria that are recognized by the immune system. In a mouse model of intestinal challenge with *Enterobacter cloacae*, this commensal bacterium was carried in dendritic cells (DCs) to the mesenteric lymph nodes (MLNs), which confined the live commensals in DCs to the mucosal immune system and so avoided systemic priming (unlike for pathogenic bacteria). Commensal-loaded DCs induced B-cell production of IgA in the MLNs, which was shown to restrict commensal penetration of the intestinal epithelium to low levels.

IMMUNE REGULATION

Human bone-marrow stromal cells inhibit allogeneic T-cell responses by indoleamine 2,3-dioxygenase mediated tryptophan degradation.

Meisel, R. *et al*. *Blood* 4 March 2004 (doi: 10.1182/blood-2003-11-3909)

Human bone-marrow stromal cells (BMSCs) are known to inhibit allogeneic T-cell responses and are therefore being investigated to promote haematopoietic engraftment when co-transplanted with haematopoietic stem cells. Previous controversial reports have indicated that transforming growth factor-β1 and hepatocyte growth factor might be responsible for this effect. This study shows that the expression and activity of indoleamine 2,3-dioxygenase (IDO) is upregulated in BMSCs after exposure to low levels of interferon-γ, which can be generated by allogeneic T cells. IDO is responsible for the catabolism of tryptophan, which has previously been identified as a T-cell inhibitory effector mechanism. The fact that IDO is not constitutively expressed by BMSCs should enable this inhibitory mechanism to be modulated depending on the therapeutic application.

SIGNALLING

The STAT3 isoforms α and β have unique and specific functions.

Maritano, D. *et al*. *Nature Immunol*. 14 March 2004 (doi: 10.1038/ni1052)

The truncated form of signal transducer and activator of transcription 3 (STAT3β) lacks the carboxy-terminal transcriptional activation domain and is thought to be dominant negative to the full-length form STAT3α in transducing signals through cytokine receptors. But new research has shown that STAT3β can carry out the essential developmental functions of STAT3α and rescue the embryonic lethality of complete STAT3 deletion, and can also activate transcription of certain target genes, such as those encoding acute-phase proteins in the liver. However, STAT3β cannot compensate for all functions of full-length STAT3α, such as regulating signalling through the interleukin-6 receptor, indicating that the two forms are non-redundant.