S. typhimurium and *E. cloacae* in a TLR4-dependent manner.

So, how does the absence of this immune response in *Tlr5*$^{-/-}$ mice affect the outcome of infection with *S. typhimurium*? Surprisingly, *Tlr5*$^{-/-}$ mice survived infection with an otherwise lethal dose of *S. typhimurium*. This was probably due to the involvement of TLR5 in the transport of the bacteria from the gut to the blood and therefore in establishing lethal systemic infection, as fewer bacteria could be detected in the mesenteric lymph nodes and spleen of infected *Tlr5*$^{-/-}$ mice than infected wild-type mice.

Therefore, although selective expression of TLRs by cells in the lamina propria provides an elegant way of avoiding responses to commensal bacteria, pathogenic bacteria might have evolved ways to use this to their advantage.

Lucy Bird

ORIGINAL RESEARCH PAPER Uematsu, S. *et al.* Detection of pathogenic intestinal bacteria by Toll-like receptor 5 on intestinal CD11c^{+} lamina propria cells. *Nature Immunol.* 9 July 2006 (doi:10.1038/ni1362)

with IL-23 induced low levels of IL-17 production *in vitro*, but this was dramatically enhanced by the addition of either IL-1α or IL-1β. IL-1 alone did not directly induce cytokine production by T cells, suggesting that IL-1 synergizes with IL-23 to induce IL-17 production by T cells. TNF is involved in the development of certain T-cell-mediated autoimmune diseases and is a major target of therapeutic intervention. Here, TNF was shown to synergize with IL-23 to induce IL-17 production by splenocytes in an IL-1-dependent manner.

Together, these data suggest that IL-1 is a crucial factor in the induction of IL-17-producing antigen-specific T cells *in vivo*, which are involved in the development of experimental autoimmune disease.

Olive Leavy

ORIGINAL RESEARCH PAPER Sutton, C., Brereton, C., Keogh, B., Mills, K. H. G. & Lavelle, E. C. A crucial role for interleukin (IL)-1 in the induction of IL-17-producing T cells that mediate autoimmune encephalomyelitis. *J. Exp. Med.* **203**, 1685–1691 (2006)

APOPTOSIS

Demise of activated T cells

Apoptosis is an essential process for the control of immune responses, eliminating reactive T cells following their activation-driven expansion in response to an infectious agent. The mitochondrial apoptotic pathway is regulated by the B-cell lymphoma 2 (BCL-2) family of proteins, and BCL-2 homology 3 (BH3)-only proteins regulate the initiation stage of apoptosis. It is thought that the initiation of activated-T-cell death occurs through the activation of the BH3-only protein BIM (BCL-2-interacting mediator of cell death) at the end of the immune response. An unrelated but also important observation is that the transcription factor BCL-3 has been shown to delay the apoptosis of activated T cells in an adjuvant-dependent manner. Georg Häcker and colleagues now pull together some of these observations to help clarify how activated-T-cell death might be regulated.

Forced expression of BCL-3 prolonged the survival of activated T cells in culture, confirming that BCL-3 does have a function in the regulation of T-cell death. Subsequently, the authors compared the gene-expression patterns of activated T cells from BCL-3-deficient and wild-type mice, and found that BIM expression was slightly increased in *Bcl3*$^{-/-}$ T cells. BIM activation was also accelerated in the absence of BCL-3. Bauer *et al.* concluded that BCL-3 exerts its anti-apoptotic effect mostly, and possibly exclusively, by blocking BIM activation.

The authors conditioned activated T cells for autonomous survival by adding medium from lipopolysaccharide (LPS)-activated dendritic cells (DCs) during T-cell-receptor stimulation. They found that although the conditioned medium induced BCL-3 expression in the activated T cells, BCL-3 was not the sole mediator that promoted the survival of these cells. Because BCL-3 seemed to function by inhibiting BIM activation, could there be a BIM-independent pathway leading to activated-T-cell death?

Bauer *et al.* considered PUMA (p53-upregulated modulator of apoptosis), another BH3-only protein, to be a promising candidate because PUMA-deficient T cells survive longer in culture. Activated T cells from *Puma*$^{-/-}$ mice did show increased survival compared with wild-type T cells, although not to the same extent as *Bim*$^{-/-}$ mice. The survival of these cells, like those from *Bim*$^{-/-}$ mice, was also increased when they were activated in the presence of supernatant from LPS-stimulated DCs.

In an effort to identify candidate soluble factors in the medium from LPS-stimulated DCs, Bauer *et al.* tested individual cytokines for their ability to prime T cells for survival in the presence of mitogen. The cytokines interleukin-1 (IL-1), IL-7 and IL-15 effected this priming, even in the absence of BIM and PUMA. These findings prompted the authors to propose that a pathway(s) is activated during activated-T-cell apoptosis that can initiate the activation of BIM and PUMA, but that this pathway(s) can be inhibited by the presence of adjuvants.

These results have helped to clarify how BIM, PUMA and adjuvant-dependent stimuli interact in the activated-T-cell death pathway, and should have implications for T-cell homeostasis and autoimmunity.

Sharon Ahmad

ORIGINAL RESEARCH PAPER Bauer, A. *et al.* The NF-κB regulator Bcl-3 and the BH3-only proteins Bim and Puma control the death of activated T cells. *Proc. Natl Acad. Sci. USA* **103**, 10979–10984 (2006)