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► **COVER:** 'Model livestock' by George Marshall, inspired by the Review on p139.



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In humans and other animals, invading pathogens are recognized by the innate immune system. Innate immune cells express pattern recognition receptors, which sense pathogen-associated molecular patterns and respond by activating a range of antimicrobial responses that aim to eliminate the pathogen and promote host survival. However, as discussed by Lautaro Diacovich and Jean-Pierre Gorvel on page 117, pathogenic intracellular bacteria employ mechanisms that protect them from the innate immune response, for example by manipulating intracellular trafficking pathways or blocking the accumulation of reactive oxygen and nitrogen species.

Pathogenic bacteria also interact with endothelial cells, which act as a key barrier to invasion by lining blood and lymphatic vessels. Endothelial cells are also actively involved during the host immune response to pathogens by producing cytokines and regulating leukocyte trafficking. On page 93, Emmanuel Lemichez and colleagues discuss the mechanisms by which pathogenic bacteria manipulate the function of endothelial cells to influence the inflammatory response and promote adhesion and breaching of endothelial barriers.

One of the strategies used by pathogenic bacteria to breach the endothelium and invade the bloodstream or tissue is the secretion of toxins. For example, enteropathogenic *Escherichia coli* secretes Shiga toxin, which induces damage to the intestinal mucosa by affecting protein biosynthesis and activating cell signalling pathways that lead to apoptosis. The Review by Ludger Johannes and Winfried Römer (page 105) summarizes what is currently known about the biology of Shiga toxins, discusses the mechanisms by which they are known to affect host cells and presents ways in which these toxins can be exploited for cancer treatment and immunotherapy.

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