

TLR5: guardian of the gut

The human gastrointestinal tract is a dynamic melting pot of commensal bacteria. Although the apical surface of intestinal epithelial cells lining the gut is constantly exposed to proinflammatory bacterial products, this rarely results in an inflammatory response. By contrast, a recent study by Gewirtz *et al.*¹ has demonstrated that exposure of the basolateral surface (but not the apical side) of intestinal epithelial cells to bacterial flagellin results in substantial upregulation of cellular nuclear factor (NF)- κ B gene expression and chemotactic interleukin (IL)-8 production.

Further analysis revealed that Toll-like receptor 5 (TLR5) is only expressed on the basolateral, but not apical, surface of model intestinal epithelium. Flagellin-mediated activation of NF- κ B was dependent both upon the extracellular leucine-rich repeats and on the intracellular Toll/IL-1 receptor homology region of TLR5, which transmits its signals through the MyD88 adaptor protein.

This indicates a mechanism by which the innate immune response of the host is triggered through TLR5 only in the event that gut-associated bacteria (or bacterial products) invade the interior of the host by crossing over to the basolateral

surface of the epithelial cell barrier of the gastrointestinal tract. Such an early defense system is likely to induce rapid recruitment of inflammatory cells, helping to prevent systemic infection from occurring.

1 Gewirtz, A.T. *et al.* (2001) Cutting edge: bacterial flagellin activates basolaterally expressed TLR5 to induce epithelial proinflammatory gene expression. *J. Immunol.* 167, 1882–1885

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Axonal transport and viral assembly

During the viral life cycle, α -herpesviruses spread in and out of the peripheral nervous system through axons. However, it was unknown where viral assembly occurred. The most recent dogma stated that viruses were first assembled in the cell body and then transported to the axon for release. This hypothesis has now been disproved by the recent work of Tomishima and Enquist¹, who have studied the mechanisms responsible for axonal transport of the viral proteins of pseudorabies virus (PRV).

Tomishima and Enquist show that the presence of a PRV protein termed Us9 is required for transport of viral membrane proteins to axons in cultured neurons. By

contrast, axonal targeting of viral capsid and tegument proteins is unaffected in neurons infected with a Us9 null mutant virus. These data imply that virus assembly must occur at or near the axon terminal. Although Us9 has no homology to other known proteins, the authors identified a di-tyrosine motif within Us9 that could interact with cytoplasmic adaptor proteins involved in intracellular trafficking in a manner analogous to YXX Φ motifs.

Viral membrane proteins that are associated with Us9 could be passively incorporated as cargo into vesicles that are specifically targeted to the axon. Viral capsid and tegument proteins presumably

use alternative mechanisms for axonal localization. The presence of separate pathways for movement ensures that assembly of mature virions is not complete until all components have reached the axon, and links the assembly process with the spread of infectious virus throughout the nervous system.

1 Tomishima, M.J. and Enquist, L.W. (2001) A conserved α -herpesvirus protein necessary for axonal localization of viral membrane proteins. *J. Cell Biol.* 154, 741–752

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In Brief

Yellow fever vaccine arrives

The first 1.4 million doses of yellow fever vaccine arrived in the Cote d'Ivoire city of Abidjan towards the end of September 2001. Six-hundred thousand doses are to follow later and a mass vaccination campaign is about to start, ensuring that the 3.5 million people living in Abidjan are protected from the disease. The WHO's urgent appeal for US\$ 2.9 million for a mass vaccination campaign in response to this outbreak has received a positive response. However, more funds are still urgently needed if the mass vaccination campaign is to be successful. *CK* <http://www.who.int>

Haemorrhagic fever in Central Asia

Cases of Crimean-Congo haemorrhagic fever along the Pakistan-Afghanistan border recently attracted media attention. However, the WHO stresses that CCHF is endemic to the region and new cases appear every year. So far over 40 cases of CCHF have been reported in Pakistan in 2001, and these numbers are typical for the region. The disease, which is primarily a zoonosis, is transmitted via ticks. As the weather cools, transmission is expected to come to a halt. *AV* http://www.who.int/disease-outbreak-news/n2001/october/CCHF_Pakistan.html

Smallpox vaccine

Acambis Plc, the British biotechnology company charged with developing a new smallpox vaccine for the USA, announced in September that it expected to begin clinical trials on the drug early next year. Attention has focused on US vulnerability to biological attack since the terrorist attacks on New York and Washington. There is now a greater urgency to manufacture a smallpox vaccine that meets modern safety standards, >20 years after the disease was officially eradicated. Acambis Chief Executive John Brown said that a major effort is under way on the contract, with