IN BRIEF

INFLAMMATION

Host inactivation of bacterial lipopolysaccharide prevents prolonged tolerance following Gram-negative bacterial infection.

Lu, M. *et al. Cell Host Microbe* **4**, 293–302 (2008)

Endotoxin tolerance — by which the immune system undergoes transient hyporesponsiveness to the bacterial cell-wall component lipopolysaccharide (LPS; also known as endotoxin) after previous exposure to LPS — is a well-known phenomenon that protects the host against excessive inflammation. This study now describes a mechanism for recovery from this tolerant state through deacylation, and thereby deactivation, of LPS by the lipase acyloxyacyl hydrolase (AOAH). AOAH-deficient mice had a markedly prolonged state of decreased responsiveness to LPS in a model of endotoxin tolerance, which correlated with increased susceptibility to infection with *Escherichia coli* after LPS priming. Understanding this mechanism, and potentially similar mechanisms for inactivating other microbial molecules, could lead to new ways to decrease the duration of post-infection immunosuppression.

VACCINES

Superior immunogenicity of inactivated whole virus H5N1 influenza vaccine is primarily controlled by Toll-like receptor signalling.

Geeraedts, F. *et al. PLoS Pathog.* **4**, e1000138 (2008)

The ongoing threat of an influenza virus pandemic has propelled studies to improve the existing vaccines against this pathogen. This recent study helps to define what differentiates the robust immune response that is induced by an H5N1 influenza whole-virus vaccine from the response that is induced by the less-immunogenic split-virus or viral subunit vaccines. Stimulation of Toll-like receptors (TLRs) was important for the generation of protective adaptive immune responses, such as antibody production and a T-helper-1-cell response, to the H5N1 whole-virus vaccine. The finding that TLR7, which recognizes single-stranded RNA, was particularly important led the authors to suggest that intact viral nucleic acids that are present in whole-virus vaccines, but not in split-virus or viral subunit vaccines, were involved. In addition, these data strengthen the idea that the key to driving optimal adaptive immunity is through a vaccine that targets specific innate immune responses.

HIV

HIV envelope–CXCR4 signaling activates cofilin to overcome cortical actin restriction in resting CD4 T cells.

Yoder, A. *et al. Cell* **134**, 782–792 (2008)

CXC-chemokine receptor 4 (CXCR4) is used by HIV to bind and fuse with host cells, but a role for this chemokine receptor during infection was unknown. This study now shows that latent infection of resting $CD4^+$ T cells requires CXCR4-mediated signalling, which then induces changes in cortical actin. Dynamic reorganization of the actin cytoskeleton was necessary for migration of HIV to the nucleus and for viral replication, and inhibition of actin polymerization through the use of an F-actin-stabilizing agent decreased the probability of these events. Interestingly, HIV infection of resting $CD4^+$ T cells, as well as treatment with beads coated with a CXCR4-specific antibody, induced the dephosphorylation of cofilin, which is involved in actin polymerization and depolymerization. Based on these observations, the authors conclude that HIV binding to CXCR4 triggers the dephosphorylation of cofilin, which promotes the actin dynamics that are required for viral latency.