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IN BRIEF

SIGNALLING

Proinflammatory stimuli induce IKKα-mediated phosphorylation of PIAS1 to restrict inflammation and immunity.

Liu, B. *et al. Cell* **129**, 903–914 (2007)

The inhibition of signalling pathways is important to maintain balance during an immune response, but the events that restrict inflammatory gene transcription in the nucleus are poorly understood. Protein inhibitor of activated STAT1 (PIAS1) is known to block the binding of certain pro-inflammatory transcription factors to their target genes. In this study, Liu *et al.* show that phosphorylation of PIAS1 at Ser90 by IKKα (inhibitor of nuclear factor-κB (NF-κB) kinase α) in response to various immunoregulatory stimuli is necessary for the recruitment of PIAS1 to chromatin, where it blocks the binding of NF-κB to its target genes. Phosphorylation of PIAS1 by IKKα requires the small ubiquitin-like modifier (SUMO) ligase activity of PIAS1 and both Ser90 phosphorylation and SUMO ligase activity are required to repress transcription. So, this paper describes a new molecular pathway in the nucleus that is induced by various immunoregulatory stimuli to limit inflammation.

MAST CELLS

Mast cells promote atherosclerosis by releasing proinflammatory cytokines.

Sun, J. *et al. Nature Med.* **13**, 719–724 (2007)

Mast cells are known to accumulate in human atherosclerotic lesions, although their functional significance here has been unclear. Here, Sun *et al.* establish that mast cells directly participate in a mouse model of atherogenesis by releasing the pro-inflammatory cytokines interleukin-6 (IL-6) and interferon-γ (IFNγ) and promoting atheroma formation. Diet-induced atherogenesis in mice that were deficient for both the low-density lipoprotein receptor and mast cells ($Ldlr^{-/-}Kit^{W\text{-}sh/W\text{-}sh}$) was reduced owing to the absence of mast cells and mast-cell-derived IL-6 and IFNγ. Further studies suggested that these two cytokines promote atherogenesis by augmenting the expression of pro-atherogenic proteases in vascular cells and local proteolysis. This study provides new mechanistic insight into the pathogenesis of atherosclerosis.

INFLAMMATION

TRAIL limits excessive host immune responses in bacterial meningitis.

Hoffmann, O. *et al. J. Clin. Invest.* 14 June 2007 (doi:10.1172/JCI30356)

In this report, Hoffmann *et al.* provide the first evidence that tumour-necrosis-factor-related apoptosis-inducing ligand (TRAIL) can act as an anti-inflammatory cytokine in meningitis. TRAIL has important regulatory functions in the host immune response. Examining the anti-inflammatory effects of TRAIL in mice with experimental meningitis, the authors found that TRAIL-deficient mice showed prolonged acute inflammation and increased apoptosis of leukocytes in the hippocampus. These effects were reversed by the administration of recombinant TRAIL or by reconstitution of haematopoiesis with wild-type bone-marrow cells; administering recombinant TRAIL into the subarachnoid space of wild-type mice with meningitis also reduced inflammation and apoptosis. Interestingly, patients with bacterial meningitis showed increased intrathecal synthesis of TRAIL. So, TRAIL may have therapeutic potential as an anti-inflammatory agent in invasive infections.