precipitate *in vivo* at the concentrations used in these studies and so the authors suggest, during cell death, the levels of uric acid produced locally could increase sufficiently to cause this endogenous metabolite to precipitate and promote DC maturation and activation. If the dying cell contained antigen to which the host was not tolerant then such DC activation would lead to the induction of a productive immune response to these antigens.

This study identifies uric acid as an endogenous mediator of immune activation, implicating it as crucial for surveillance by the adaptive immune system. As such, it is possible that uric acid could act as a type of adjuvant, stimulating an immune response to antigens to which the immune system was previously non-responsive, such as virus infections and tumours. Furthermore, these studies are also important to our understanding of the pathogenesis of gout — an inflammatory disease initiated by the precipitation of MSU in the joints — and raise the possibility that uric acid has a central role in the inflammatory response to tissue damage.

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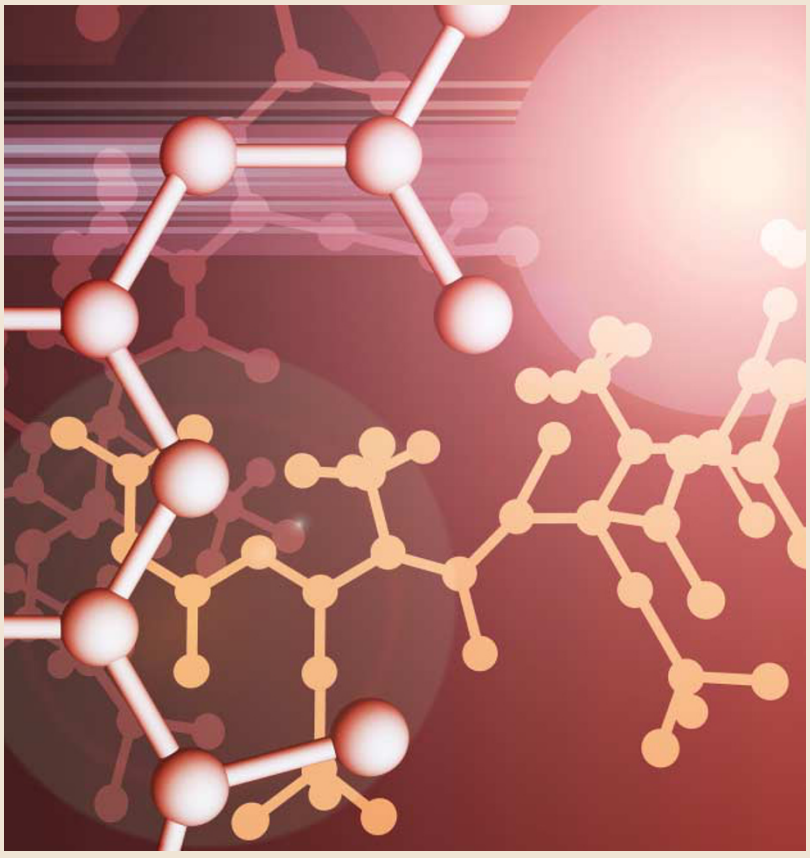
References and links

ORIGINAL RESEARCH PAPER Shi, Y. *et al*. Molecular identification of a danger signal that alerts the immune system to dying cells. *Nature* 7 September 2003 (DOI:10.1038/nature019991)
FURTHER READING Gallucci, S. & Matzinger, P. Danger signals: SOS to the immune system. *Curr. Opin. Immunol.* **13**, 114–119 (2001)



IN BRIEF

PSYCHONEUROIMMUNOLOGY

Affective style and *in vivo* immune response: neurobehavioral mechanisms.

Rosenkranz, M. A. *et al*. *Proc. Natl Acad. Sci.* USA 5 September 2003 (DOI: 10.1073/pnas.1534743100)

This study looked at the correlation between physiological measures of negative emotion and the immune response to an influenza vaccine. Individuals with high comparative levels of activation of the right-hand side of the prefrontal cortex of the brain (at baseline and in response to a negative-emotion-inducing task) experience more intense negative emotions and are more likely to suffer from depression. These individuals produce lower antibody titres in response to vaccination. Antibody titres were also correlated with the eye-blink response to a task that induced negative emotions. Individuals with a larger eye-blink response (which indicates stronger negative emotion) produced lower antibody titres in response to vaccination. These studies help to clarify the link between depression and suppressed immune function.

LYMPHOCYTE MIGRATION

The strategy of T cell–antigen-presenting cell encounter in antigen-draining lymph nodes revealed by imaging of initial T cell activation.

Bajénoff, M. *et al*. *J. Exp. Med.* **198**, 715–724 (2003)

Activated, antigen-loaded dendritic cells (DCs) migrate to the draining lymph node (LN), but how are they located by antigen-specific $CD4^+$ T cells? Bajénoff *et al.* show that DCs that acquire antigen in the periphery preferentially accumulate in the paracortical region of the LN. More specifically, the DCs were close to the high endothelial venules (HEVs), where the initial stages of T-cell activation can be observed. The authors then showed that only antigen-specific T cells are retained in the proximity of the HEVs, indicating that DCs position themselves at the site of T-cell entry into the LN to maximize the chance of an immunogenic $CD4^+$ T cell–DC interaction occurring.

VIRAL IMMUNITY

Self-inhibition of synthesis and antigen presentation by Epstein–Barr virus-encoded EBNA1.

Yin *et al*. *Science* **301**, 1371–1374 (2003)

The glycine–alanine repeat domain (GAr) of the Epstein–Barr virus-encoded protein nuclear antigen 1 (EBNA1) has been thought to prevent MHC class I presentation of EBNA1 peptides by inhibiting its proteasomal degradation. However, Yin *et al.* show that the GAr inhibits mRNA translation in cis, both *in vitro* and *in vivo*. The GAr sequence was most efficient at inhibiting translation when present at the amino-terminus of the protein, but its position did not influence its ability to inhibit proteasomal degradation, enabling the authors to show that GAr-mediated inhibition of translation and not proteasomal degradation is the mechanism by which EBNA1 evades MHC class I presentation. This is likely to prevent peptide production from defective ribosomal products (DRiPs) of EBNA1 translation — a key source of MHC class I presented peptides.