WT and LΔP mice crossed with animals expressing a T-cell receptor specific for an influenza-virus-derived peptide (F5). When transferred to Rag1-deficient mice, activated F5/LΔP T cells were more efficient at entering the PLNs than F5/WT T cells exposed to antigen, indicating that L-selectin shedding prevents the re-entry of activated T cells into the PLNs.

These studies show that the physiological role of L-selectin shedding is to shape the migration pattern of activated T cells and prevent them from re-entering PLNs.

Karen Honey

References and links

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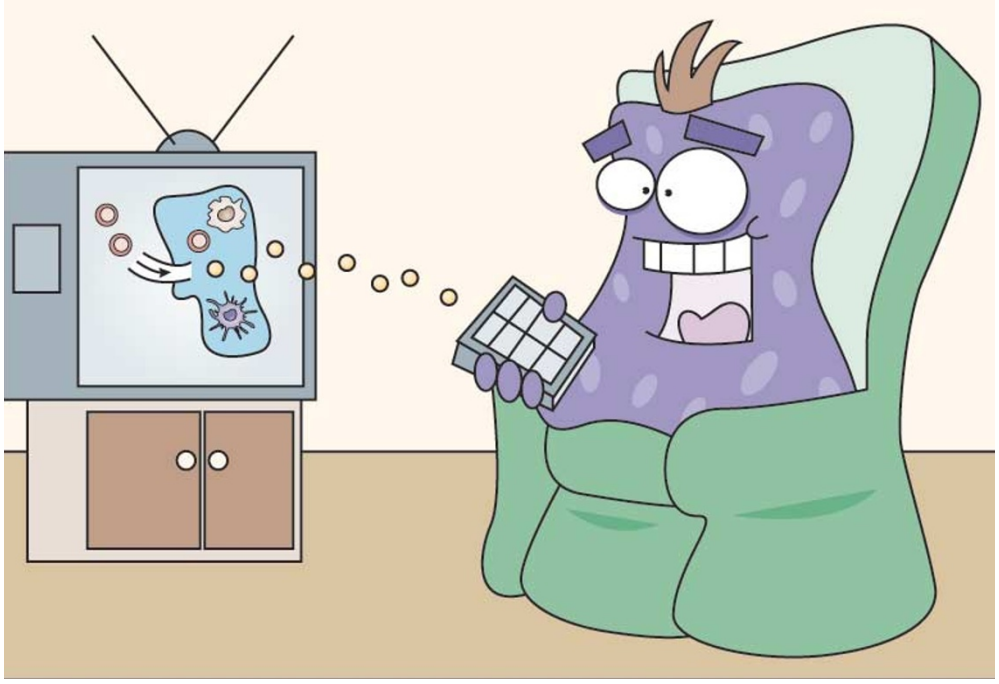
FURTHER READING Grabovsky, V., Dwir, O. & Alon, R. Endothelial chemokines destabilize L-selectin-mediated lymphocyte rolling without inducing selectin shedding. *J. Biol. Chem.* **277**, 20640–20650 (2002).



IMMUNE RESPONSES

Mast cells act by remote control

Swollen 'glands' are often one of the first signs that you have picked up a bacterial infection. This lymph-node hypertrophy results from the accumulation of circulating lymphocytes in the draining lymph nodes, which can interact with antigen-presenting cells (APCs) that are loaded with microbial antigen and so initiate an adaptive immune response. Bacterial products at the site of infection are thought to induce the emigration and maturation of APCs, but the signals that control T-cell recruitment to the lymph nodes are unknown. Work now published in *Nature Immunology* shows a central role for mast cells in this process.

Mast cells are important components of the innate immune response against bacteria, through degranulation and the release of inflammatory mediators, including tumour necrosis factor (TNF). Here, McLachlan *et al.* used a mouse model of localized infection to investigate if these cells are involved in controlling bacteria-triggered nodal hypertrophy and so have a role in the induction of adaptive immune defence.

In wild-type mice, injection of bacteria into the footpad resulted in lymph-node hypertrophy within 24 hours. However, lymph-node swelling was markedly reduced in mast-cell-deficient mice (W/W^v mice). Injection of mast cells into the footpads of W/W^v mice before bacterial challenge resulted in a similar level of lymph-node hypertrophy as seen in wild-type mice, indicating an important role for mast cells in this process. The authors confirmed this by using a specific mast-cell activator (48/80), which if injected instead of bacteria into the footpad of mice also resulted in considerable lymph-node hypertrophy.

A closer investigation of the site of infection showed that although the overall number of mast cells had not increased 4 hours after bacterial innoculation, the percentage of degranulated mast cells had. This probably indicates that mast cells act remotely to induce nodal hypertrophy and, instead of leaving the site of infection and migrating to the lymph nodes themselves, they release a product on degranulation that drains into the lymph node and signals for hypertrophy to occur.

Which mast-cell product might be involved? TNF, but not other inflammatory mediators that mast cells release, was shown to have potent hypertrophic effects, and 3 hours after infection (or mast-cell activation with 48/80), the level of TNF in the draining lymph nodes increased markedly. In addition, mast-cell activation resulted in a threefold increase in the numbers of T cells recruited to the lymph nodes.

This study indicates that, through the release of TNF, mast cells provide an essential signal early in infection to trigger, by remote control, the hypertrophy of draining lymph nodes and the initiation of an adaptive immune response.

Jenny Buckland

References and links

ORIGINAL RESEARCH PAPER McLachlan, J. B. *et al.* Mast cell-derived tumor necrosis factor induces hypertrophy of draining lymph nodes during infection. *Nature Immunol.* 2 November 2003 (doi:1038/ni1005).

WEB SITE

Soman N. Abraham's lab: http://pathology.mc.duke.edu/research/postabraham.html