Further analysis of the cloned antibodies showed that more than half of the antibodies produced from early B-cell compartments were polyreactive, in that they bound to more than one antigen in a defined panel of antigens tested, but most of these polyreactive antibodies were removed from the repertoire by the immature B-cell stage.

This study shows that a large percentage of developing B cells produce autoreactive antibodies. Although these cells are removed from the population at two distinct checkpoints, ~20% of mature B cells still produce autoantibodies with the potential to contribute to autoimmune disease.

Elaine Bell

References and links

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WEB SITE

Michel Nussenzweig's lab:
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INNATE IMMUNITY

DCs 'tip' off the innate immune system

The role of dendritic cells (DCs) in adaptive immune responses is well established, but do these cells have a direct role in innate immune defence? A recent study, published in *Immunity*, identified a subset of DCs termed Tip-DCs (tumour-necrosis factor (TNF)/inducible nitric oxide synthase (iNOS)-producing DCs) that are essential for host defence against bacterial infections.

To investigate which cells are involved in the clearance of bacteria, Serbina and colleagues infected wild-type mice and mice that lacked expression of the chemokine receptor CCR2 with *Listeria monocytogenes*. Previous studies have shown that CCR2 targets monocytes to sites of inflammation and that *Ccr2*^{-/-} mice are unable to control bacterial infections *in vivo*. Initially, the numbers of *L. monocytogenes* were similar in the wild-type and *Ccr2*^{-/-} mice, but after 48 hours, the wild-type mice had begun to clear the infection, whereas the bacterial load kept increasing in the *Ccr2*^{-/-} mice.

Immunohistological examination of the spleens from these mutant mice showed normal localization of *L. monocytogenes* and Mac3⁺ (a marker expressed by some DCs and activated macrophages) cells to T-cell areas of the spleen, and the pattern of DEC205⁺ DCs was also similar to that seen in wild-type mice.

However, the *Ccr2*^{-/-} mice lacked a population of cells with intermediate expression of CD11b and CD11c that was present in their wild-type counterparts.

What role do these CD11b^{mid}CD11c^{mid} cells have in the clearance of bacterial infections? T-cell responses to *L. monocytogenes* seemed to be normal in the *Ccr2*^{-/-} mice, showing that the central role of these cells is not in T-cell priming. Further experiments showed that the CD11b^{mid}CD11c^{mid} DCs that are lacking in *Ccr2*^{-/-} mice are the main sources of TNF and iNOS (which catalyses the synthesis of NO, a central mediator of bacterial killing) within the first 48 hours of bacterial infections, hence their name of Tip-DCs.

Early control of *L. monocytogenes* infection, therefore, requires the presence of Tip-DCs, which are probably recruited to the spleen by CCR2 signalling, so confirming a direct role for DCs in innate immune responses against microbial pathogens.

Jenny Buckland

References and links

ORIGINAL RESEARCH PAPER Serbina, N. V. *et al.* TNF/iNOS-producing dendritic cells mediate innate immune defense against bacterial infection. *Immunity* 19, 59–70 (2003)

WEB SITE

Eric Pamer's lab: <http://www.mskcc.org/mskcc/html/11109.cfm>