B CELLS

A helping hand

Naive T cells become activated by recognizing antigen fragments that are bound to MHC complexes on the surface of dendritic cells (DCs). Naive B cells, however, are thought to primarily recognize intact protein antigens that have entered the B-cell-rich follicular area of the lymph node. Because the pattern of flow of lymph through the node means that B cells have restricted access to antigen, Hai Qi, together with his colleagues in Ronald Germain's group, asked whether the activation of B cells might also be assisted by a system of cell-aided antigen delivery. They now report in *Science* that antigen-bearing DCs can indeed activate lymph-node B cells outside the follicle.

The authors first showed that DC-associated antigen could directly induce B-cell activation in culture. They showed that hen-egg lysozyme that was endocytosed by DCs and presented on the cell surface could activate B cells *in vitro*. These findings prompted the authors to ask how naive B cells might come into contact with antigen-carrying DCs *in vivo*, considering that most DCs in the lymph nodes are found in the T-cell zone.

As B cells migrate from the blood to the lymph-node follicles, their first location in the parenchyma is the region surrounding the high endothelial venules (HEVs); this region is also rich in migrating antigen-bearing DCs. Qi *et al.* reasoned that the region around HEVs, therefore, might be where B cells survey for DC-associated antigens. Indeed, lymph-node sections stained for B cells and to delineate tissue landmarks showed areas of recently arrived B cells concentrated around the HEVs, where they colocalized with and physically contacted DCs. But were these associations resulting in B-cell activation? Using two-photon intravital microscopy, the authors showed that contact with antigen-laden DCs triggered receptor-dependent signalling in B cells in the lymph node shortly after the B cells left the areas around the HEVs, but before they migrated into the follicle.

So, Qi *et al.* found that B cells enter the lymph node and survey the local antigen-bearing DCs in the areas surrounding the HEVs. B-cell-receptor-mediated acquisition of antigen (which is a hallmark of specific B-cell activation) then occurs by direct B-cell–DC interactions in the T-cell zone, rather than by B cells associating with antigen that is spontaneously released by the DCs. Activated B cells then face temporary arrested migration, which leads to extrafollicular accumulation in the T-cell zone, before completing their migration to the follicle.

The authors suggest that antigen-specific B-cell–DC interactions might have a role in promoting T-cell-dependent antibody responses *in vivo*. Interestingly, they also propose that by presenting both T- and B-cell epitopes that are derived from the same antigen, DCs could perhaps serve as facilitators of the activation, colocalization and mutual communication of the rare antigen-specific T and B cells that form the basis of our adaptive immune system.

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ORIGINAL RESEARCH PAPER Qi, H. *et al.* Extrafollicular activation of lymph node B cells by antigen-bearing dendritic cells. *Science* **312**, 1672–1676 (2006)

In the news

AVIAN-FLU VACCINE TRIALS

PowerMed, a UK biotechnology company, has submitted plans to the Medicines and Healthcare products Regulatory Agency to conduct the first clinical trials for its experimental vaccine against the lethal H5N1 subtype of the avian influenza A virus. Several pharmaceutical companies, including GlaxoSmithKline and Sanofi-Aventis, are also in the race to produce treatments for use in the event of a pandemic.

The PowerMed trial will involve administering the vaccine to volunteers using a needle-free system. Unlike traditional vaccines that incorporate killed or weakened strains or fragments of the virus, this vaccine uses fragments of the H5N1 virus's cDNA to stimulate an immune response. DNA that encodes proteins specific for the H5N1 subtype will be coated onto microscopic gold particles and propelled into the skin at supersonic speed using a helium-powered delivery device.

The production of DNA vaccines is much faster than that of traditional influenza-virus vaccines, in which modified virus is injected into fertilized chicken eggs and allowed to replicate. "We really shouldn't rely on 50-year-old vaccine technology. It's disastrously inefficient," said John Beadle, chief medical officer at Oxford-based PowerMed (*Times Online*, 10 July 2006). The H5N1 vaccine can be created in about ten weeks and could be licensed within the next two years (*Times Online*, 10 July 2006).

PowerMed's vaccine has only been tested in animals so far, where it has been successful. Beadle commented that "… it stops the infection entirely, to the point that we can't even measure the virus in the animals afterwards." (*Guardian Unlimited*, 10 July 2006). The purpose of the proposed trials will be to determine the correct dose of vaccine required to produce an immune response in humans and to examine how long the vaccine remains effective.

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