B-CELL RESPONSES

Pass the parcel

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Initiation of an adaptive B-cell response requires contact between B cells and antigen in lymphoid tissues, but how and where this occurs within the lymph node *in vivo* is not fully understood. Now, two independent studies show that B cells encounter antigenic particles at the subcapsular sinus (SCS) and can act as antigen-transport cells.

B cells are usually found in lymphoid follicles (which are located directly beneath the SCS), but large antigen complexes cannot passively diffuse into the follicles. So, the idea of an antigen-transport cell has emerged to explain how antigen complexes gain access to the lymphoid follicles. However, the exact identity of this cell type has remained elusive. Using confocal and multiphoton microscopy, both studies tracked the deposition of large antigen particles or immune complexes in the lymph node draining the site of antigen administration. Antigen was found to be rapidly (within 1–2 hours) deposited on SCS macrophages and then, at later time points (8–24 hours), antigen accumulated on follicular dendritic cells (FDCs), which are crucial for optimal selection of B cells and are found deeper in the lymphoid follicles. Interestingly, SCS macrophages were shown to extend large processes 'decorated' with immune complexes across the sinus wall and into the follicle.

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But how does the antigen get from these SCS macrophage processes to FDCs? Nonspecific follicular B cells were shown to pick up antigen from these processes and migrate into the follicle with the antigen concentrated at the trailing uropod edge. The capture, transport and deposition of immune complexes on FDCs was impaired in lethally irradiated mice that were reconstituted with B cells deficient for complement receptor 1 (CR1) and CR2, indicating that the expression of these receptors is required for these events.

Antigen-specific follicular B cells also tended to accumulate at the SCS, where they were retained for long periods (>10 minutes), and acquired antigen cumulatively from SCS macrophages. This acquisition was dependent on the B-cell receptor and was more efficient than antigen acquisition by nonspecific B cells. Following antigen capture, these antigen-specific B cells showed a decrease in motility and upregulated the expression of co-stimulatory and MHC class II molecules. 24 hours after immunization, most of these antigen-specific B cells had relocalized to the B-cell–T-cell zone, indicating that the SCS might be a site for initiating B-cell responses.

So, the data show that follicular B cells act as antigen-transport cells for large antigen complexes in lymph nodes, by delivering antigen deposited on SCS macrophages to FDCs. In addition, cognate B cells can acquire antigen at the boundary between the follicle and the SCS and then migrate to the B-cell–T-cell zone. These studies provide important insights into the early stages of antigen transport and recognition by B cells in lymph nodes.

Olive Leavy

ORIGINAL RESEARCH PAPERS
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