Directing Traffic in Lymph Nodes

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How do the right cells get to the right place in lymph nodes? It is known that lymphocytes known as B cells (that originate in the bone marrow) migrate to follicles within the nodes, whereas T cells (that originate in the bone marrow and migrate to the thymus gland) reside in an adjacent region known as the paracortex. By combining confocal, electron, and intravital microscopy, Marc Bajénoff, Jackson Egen, Lily Koo, Jean Pierre Laugier, Frédéric Brau, Nicolas Glaichenhaus, and Ronald Germain have demonstrated a role for the stroma of the node in directing these cells to the appropriate location.[2] The stromal cells that are critical in the B cell follicles are follicular dendritic cells (FDCs) and in the paracortex it's the fibroblastic reticular cells (FRCs).

Bajénoff *et al.* employed a variety of strategies to demonstrate the movement of lymphocytes, but their primary model was a mouse chimera. These mice were genetically engineered to express ubiquitin promoter-GFP (green fluorescent protein) then the mice were irradiated to kill all the hemopoietic tissue. These mice were then injected with normal bone marrow cells and the bone marrow was allowed to reconstitute. The cells of the host mice fluoresced when properly illuminated, whereas the "new" bone marrow cells did not. Using this model, they found FRCs provide direction for T cell migration. For example, T cells changed directions along FRC fibers about 93% of the time. Also, the FRCs appeared to be arranged along blood vessels of the lymph node, including the high endothelial venules, and regulated egress of T cells to the paracortex through cell-cell junctions referred to as "exit ramps." Further studies showed that FRCs played a role in defining the border between T and B cell-occupied areas.

The movement of B cells also appeared to be influenced by FRCs, particularly as they moved through the paracortex. Their movement along the FRC network may enhance B cell stimulation as this would increase the likelihood of their encounters with antigen-laden dendritic cells. Once the B cells arrived in the follicles, their location appeared to be determined by FDCs.

The various imaging studies performed by Bajénoff *et al.* revealed that FRCs do not form an enclosed labyrinth of "corridors" that simply confine the lymphocytes, but rather they form a 3-dimensional meshwork of cell bodies and extended processes that physically interact with the lymphocytes. This provides guidance cues that direct T and B cell movement in the paracortex, and FDCs influence the B cells congregating in follicles.

A few decades ago, the stroma of an organ was generally considered the passive scaffolding that provided the spatial organization for the parenchymal cells that in turn performed the activities of the organ. Evidence has been increasing that the stroma plays more than a passive role. In an elegant series of studies using a variety of microscopic techniques, Bajénoff *et al.* have provided convincing evidence that the stroma of the lymph node plays a key guidance role in facilitating the interaction between rare antigen presenting cells and the corresponding antigen-specific lymphocytes within a densely populated lymph node. Bajénoff *et al.* hypothesized that this in turn promoted a normal immune response. ■

References

1 The authors gratefully acknowledge Drs. Ronald Germain and Marc Bajénoff for reviewing this article.

2 Bajénoff, M., J.G. Egen, L.Y. Koo, J.P. Laugier, F. Brau, N. Glaichenhaus, and R.N. Germain, Stromal cell networks regulate lymphocyte entry, migration, and territoriality in lymph nodes, *Immunity* **25**:1-13, 2006.

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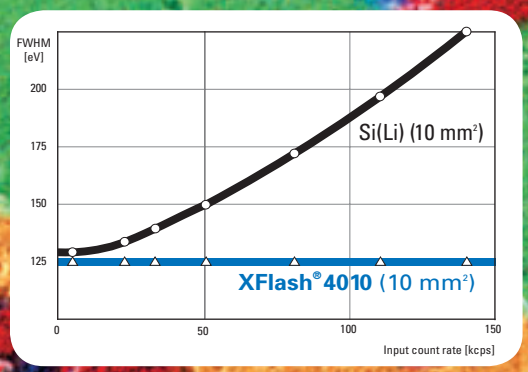

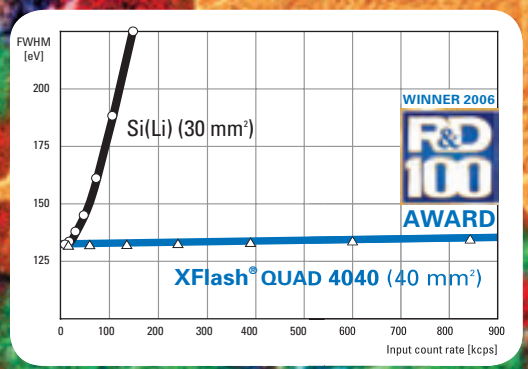

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