

Dendritic cell migration from the periphery to lymph nodes

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The prevailing model, supported by research published so far is that DC migration from peripheral tissues to lymph nodes is regulated by signals within the periphery itself—signals that will affect maturation of DCs, expression of CCR7, and expression of its ligands by lymphatics. Given that the lymph node itself is quite a distance anatomically from the peripheral site where migration is initiated, no models have incorporated a role for the lymph node itself in regulating DC migration. Thus, naturally, considerations of how DC migration might be altered have focused on attempts to manipulate the peripheral environment where DCs are induced to enter lymphatics. For example, conditioning the periphery has been reported to increase the number of DCs that mobilize to lymph nodes.

When a robust immune response develops, lymph nodes expand in size, allowing for increased sampling between possible T cells and DC partners. During this expansion, and indeed in lymph nodes that naturally vary in size in different anatomic locations, there is a relatively constant ratio between DCs and lymphocytes. This is consistent with the possibility that activity in the lymph node could have an affect on the “upstream” peripheral environment. We show that, indeed, more DCs from the periphery enter larger, expanding lymph nodes, and this increase in DCs accumulating within lymph nodes is not an artifact that instead is caused by proliferation of migrated DCs, increased survival of migrated DCs, or increased retention of DCs in the lymph node. Data will be presented to reveal a surprising result that B cells that home to the lymph nodes regulate the magnitude of DC migration from the periphery and lymph node expansion in general during the induction of an immune response. Part of the role for B cells in this process is the production of VEGF in response to immunization that leads to the expansion of lymphatic vessels that support more efficient entry of DCs into the LN from the periphery.

Selected references:

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