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MACROPHAGES

Breaking ranks in the lymph node

The macrophages that line the subcapsular sinus (SCS) of lymph nodes are strategically placed to prevent the systemic dissemination of pathogens. Furthermore, these cells support antibody responses by delivering intact antigen to neighbouring B cells. A new study by Facundo Batista and colleagues has found that SCS macrophages do not hold the line indefinitely; during inflammation and infection, they are displaced towards the inner follicular regions of the lymph node, temporarily impairing the immune response to subsequent infections.

The architecture of lymph nodes is highly organized to ensure that effective immune responses develop against pathogens. Infection induces remodelling of lymph nodes, but it has not been clear how the SCS macrophage layer is affected. The authors used confocal microscopy to visualize SCS macrophages in the draining lymph nodes of mice infected with *Staphylococcus aureus*. Compared with resting lymph nodes, those examined at 7 days post infection were increased in size and showed disruption of SCS macrophage organization. This change was only temporary and the SCS macrophage layer was re-established after 28 days. High-resolution imaging studies showed that inflammation led to a decrease in the number of SCS macrophages and their displacement towards the inner follicular regions of the lymph node. The organization of SCS macrophages in draining lymph nodes was similarly disrupted when mice were challenged with other bacteria, viruses or Toll-like receptor (TLR) agonists, indicating that this is a common feature of infection and inflammation.

> “disruption of the SCS macrophage layer during a primary infection can impair the B cell response to a secondary infection”

The authors found that the disruption of the SCS macrophage layer during inflammation was dependent on the expression of the TLR adaptor protein MYD88 by $CD11c^+$ cells, suggesting that migratory dendritic cells (DCs) may drive this process. In support of this, they showed that the SCS macrophage layer remained fairly intact during inflammation in mice lacking CC-chemokine receptor 7 (CCR7), which drives DC migration to lymph nodes. Additional adoptive transfer experiments using bone marrow-derived DCs showed that DC migration to the lymph node can in itself disrupt the SCS macrophage layer, even in the absence of TLR signalling.

Notably, loss of the normal organization of SCS macrophages during inflammation impaired the ability of the lymph node to support an immune response against a secondary challenge. SCS macrophages that had relocated in response to an inflammatory challenge showed decreased antigen retention, which in turn resulted in lower antigen acquisition by lymph node B cells. Furthermore, mice in which the SCS macrophage layer had been disrupted showed impaired germinal centre formation and plasma cell production in response to vaccinia virus infection.

Taken together, these data suggest that disruption of the SCS macrophage layer during a primary infection can impair the B cell response to a secondary infection. The authors suggest that the initial reorganization of SCS macrophages may enhance the response to the primary infection, possibly by facilitating the entry of lymph-borne immune cells, but this is at the cost of leaving the lymph node temporarily ‘shut down’ and refractory to subsequent pathogens.

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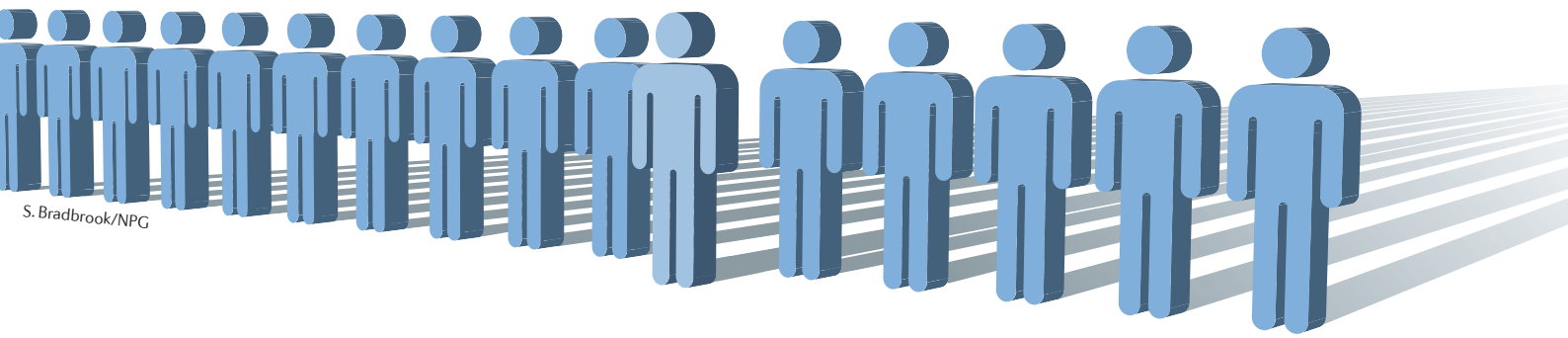
ORIGINAL RESEARCH PAPER Gaya, M. *et al.* Inflammation-induced disruption of SCS macrophages impairs B cell responses to secondary infection. *Science* **347,** 667–672 (2015)



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