LYMPHOID ARCHITECTURE

Restoration project

The generation of secondary lymphoid organs (SLOs) during embryonic development and the early postnatal period is orchestrated by the interaction of lymphoid-tissue inducer (LTi) cells with stromal lymphoid-tissue organizer cells. But, if the structural integrity of the SLOs is compromised later in life, for example by infection, are these interactions also responsible for restoring the lymphoid architecture in adults? Scandella *et al.* now show that disruption of lymphoid organization following infection with lymphocytic choriomeningitis virus (LCMV) is repaired by an accumulation of LTi cells during the acute phase of infection and productive crosstalk with the stromal cells of the T-cell zone, known as fibroblastic reticular cells (FRCs).

LCMV infection, which has a strong tropism for SLOs, is controlled by antiviral cytotoxic T lymphocytes (CTLs). Using immunofluorescence analysis, the authors found that infection with LCMV resulted in a complete loss of the white-pulp structure of the spleen at the peak of the ensuing CTL response but that the structural integrity of the SLO was restored following viral clearance. FRCs, which can be infected by LCMV, were particularly susceptible to CTL-mediated killing, resulting in a loss of the FRC network.

FRCs constitutively produce chemokines involved in shaping the T-cell zone of SLOs, so the authors next examined the expression of these chemokines during LCMV infection. As expected, a transient loss in the expression of these chemokines was observed, which correlated with the disruption and subsequent restoration of the FRC network. By contrast, an increase in the expression of genes known to be involved in the development of lymphoid tissues (and in the crosstalk between LTi cells and stromal lymphoid-tissue organizer cells during development) was observed, the peak of which correlated with that of the antiviral cellular immune response. In addition, LTi cells accumulated in SLOs during this peak phase through increased proliferation.

So, is there a role for LTi cells in the restoration of lymphoid architecture following LCMV infection? Using a chimeric mouse model, the authors showed that adult mice lacking LTi cells rebuilt their FRC network and restored the SLO architecture following LCMV infection less efficiently than control mice. In addition, blocking the lymphotoxin-β receptor, which is expressed by stromal cells and interacts with lymphotoxin-$\alpha_1\beta_2$ expressed by LTi cells, significantly delayed the reorganization of FRCs following infection in wild-type mice, indicating that this signalling pathway might have an important role in the restoration of lymphoid architecture. Additional *in vitro* studies confirmed a productive interaction between these two cell types.

So, the data indicate that crosstalk between LTi cells and stromal cells continues into adulthood and functions to restore the FRC network and architectural integrity of the SLO following LCMV infection.

Olive Leavy

ORIGINAL RESEARCH PAPER Scandella, E. *et al.* Restoration of lymphoid organ integrity through the interaction of lymphoid tissue-inducer cells with stroma of the T cell zone. *Nature Immunol.* 20 April 2008 (doi:10.1038/ni.1605)