IN THE NEWS

Reverting to type

Haiti and the Dominican Republic, despite being declared polio-free in the 1980s, suffered from a surprise outbreak of poliomyelitis in 2000. Twenty-one children were infected and two of these cases were fatal. A report published on 14 March 2002 in *Scienceexpress* (the on-line, early edition of the journal *Science*) that investigated possible causes of the resurgence of this crippling disease has hit the headlines this month.

In these countries, an oral polio vaccine (OPV), which contains a live but attenuated form of poliovirus, is used to protect people from infection. As detailed in the report, and explained by Olen Kew of the US Centers for Disease Control and Prevention, Atlanta, Georgia, "In Haiti, after the wild-type poliovirus had been eradicated, the only source was through the polio vaccine." (*Associated Press*).

As summed up in an article from *Reuters*, genetic analysis of viral samples from the outbreak confirmed that the source of infection was in fact the vaccine virus itself, which had mutated back to a virulent form by swapping DNA with related viruses, known as enteroviruses, that are present in the gut. The situation might have been exacerbated by the low rates of vaccination in Haiti. "Low population immunity was the key risk factor," explained Kew.

When a person is vaccinated with OPV, the vaccine virus can mutate, be shed in faeces, spread to non-immunized individuals in the water supply and cause disease. "It's a warning that you need to have good coverage to prevent vaccines from running away like this," said Kew (*New Scientist*).

These results have obvious implications for the aims of the World Health Organisation to eradicate polio worldwide.

Jenny Buckland

IMMUNE REGULATION

A balanced response

For many decisions in life, it is important to weigh up different factors before making a decision as to the best course of action. A recent *Nature* paper from Jason Cyster's lab now shows that this is also true for B cells — antigen-stimulated B-cell migration seems to be governed by the balance of responses to the T-cell-zone chemokines CCL19 and CCL21, and the B-cell-zone chemokine CXCL13.

B cells scan for antigen by recirculating between the B-cell follicles of secondary lymphoid organs. When they encounter antigen, B cells in the B-cell zone or follicle migrate to the boundary between the T-cell and B-cell zones (T/B boundary), where they interact with T cells. However, the factors that control this migration are undefined. Genetic studies have shown that CCR7 and its ligands, CCL19 and CCL21, are important for the localization of T cells and dendritic cells to the T-cell zone. Cyster and colleagues tested whether CCR7 is also important for B-cell localization. Anti-IgM-stimulated B cells had a 2–3-fold increased expression of CCR7 and enhanced *ex vivo* chemotactic responses to CCL19 and CCL21. When transferred into new hosts, the stimulated B cells localized to the T/B boundary.

The authors wanted to test the idea that antigen-mediated relocation of B cells *in vivo* depends on the expression of CCR7 and responsiveness to CCL19 and CCL21. They transferred hen egg lysozyme (HEL)-specific transgenic B cells into *CCL19^{-/-}CCL21^{-/-}* recipients. In the absence of antigen stimulation, the B cells localized in the follicles, but antigen stimulation did not induce migration to the T/B boundary. Because these results might have been due to indirect effects downstream of T-cell-zone chemokine deficiency, similar experiments were then performed on a CCR7-deficient background, to test for an intrinsic requirement for CCR7. In CCR7-deficient mice, HEL-binding B cells did not localize to the T/B boundary, but actually migrated in the opposite direction to that observed in wild-type mice, so that the cells localized in the pole of the follicle distal to the T-cell zone.

So, CCL19 and CCL21 are important for attracting antigen-stimulated B cells towards the T-cell zone, but why do the B cells only travel as far as the T/B boundary? The authors tested whether responsiveness to the B-cell-zone chemokine CXCL13 might limit the migration of B cells into the T-cell zones. Retroviral transduction was used to upregulate the expression of CCR7 on B cells, which were then transferred into new hosts. Transduced wild-type B cells migrated to the T/B boundary as expected, but transduced cells that were deficient for CXCR5 — the receptor for CXCL13 — migrated fully into the T-cell zone and did not line up along the T/B boundary.

These results show that the precise localization of antigen-stimulated B cells in secondary lymphoid tissue is dependent on the balance of responsiveness

to chemokines that are generated in adjacent zones — CCL19 and CCL21, which attract B cells to the T-cell zone, and CXCL13, which attracts B cells to the B-cell zone.

Elaine Bell

References and links

ORIGINAL RESEARCH PAPER Reif, K. *et al.* Balanced responsiveness to chemoattractants from adjacent zones determines B-cell position. *Nature* **416**, 94–99 (2002)

FURTHER READING Kunkel, E. J. & Butcher, E. C. Chemokines and the tissue-specific migration of lymphocytes. *Immunity* **16**, 1–4 (2002)

WEB SITES

Jason Cyster's lab:
<http://itsa.ucsf.edu/~micro/Faculty/CysterSite/home.html>
 Encyclopedia of Life Sciences: <http://www.els.net/chemokines>