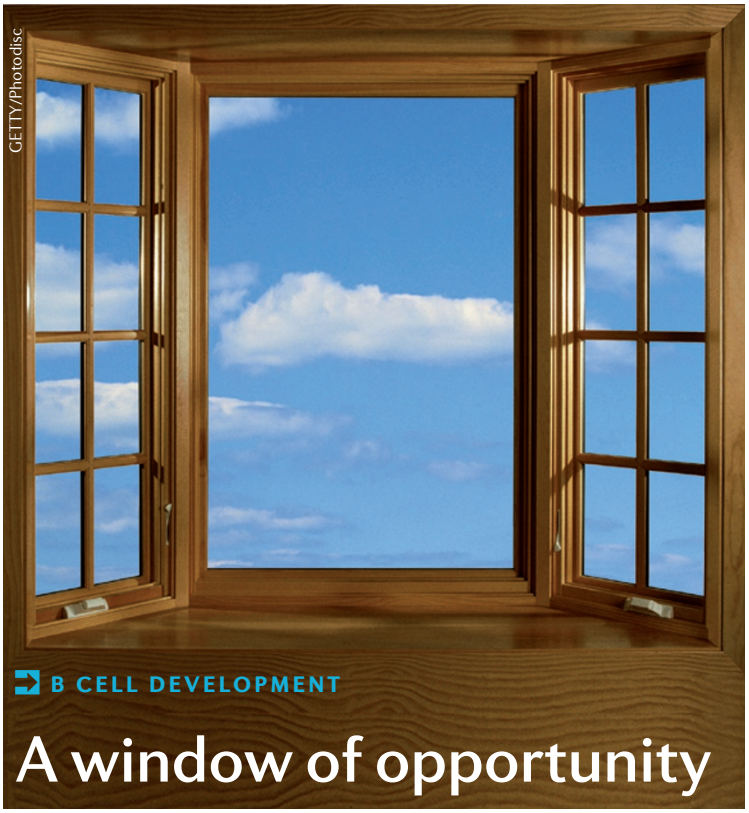

B CELL DEVELOPMENT

A window of opportunity

> B cell development and diversification can occur in the intestinal mucosa in response to colonization of the intestinal microbiota

The textbook tenet is that B cells arise in the bone marrow. But Fred Alt, Duane Wesemann and their colleagues now show that B cells can also develop in the mouse gut for a short time period after birth.

The authors used recombination activating gene 2 (*Rag2*)-reporter mice, in which the *Rag2* gene is fused to the gene that encodes green fluorescent protein (GFP), to mark immature B cells undergoing RAG2-mediated generation of B cell receptor repertoires. Analysis of these mice showed that approximately 3% of total CD19$^+$ B cells in the small intestinal lamina propria expressed RAG2–GFP. The RAG2$^+$ B lineage cells were mainly located near to the bases of the villi, whereas mature B cells were distributed throughout the lamina propria but were not found in the mesenteric lymph nodes or among intraepithelial lymphocytes and only in very low frequencies in the large intestinal lamina propria. Interestingly, the numbers of lamina propria RAG2$^+$ B lineage cells gradually increased after birth, peaking at about 18–23 days, before decreasing to undetectable levels by postnatal day 35.

The RAG$^+$ B lineage cell populations in the bone marrow comprise pro-B cells (Igμ$^-$Igκ$^-$), pre-B cells (Igμ$^+$Igκ$^-$) and immature B cells undergoing receptor editing (Igμ$^+$Igκ$^+$). Similar relative levels of these three subsets were found in the gut and the bone marrow. Further investigation of repertoire diversity indicated that the immunoglobulin heavy chain (IgH) repertoires of the gut and the bone marrow cells were indistinguishable, but the immunoglobulin light chain (IgL) repertoires were distinctive. The authors proposed that the lamina propria IgL repertoires were generated by receptor editing in RAG2$^+$ immature B cells in response to commensal microorganisms. In support of this idea, colonization of germ-free mice with commensal microorganisms led to increases in RAG1 and RAG2 expression and increased the percentages of pro-B cells relative to total B cells in the gut and the bone marrow. Moreover, there was a commensal bacteria-dependent increase in Igλ usage — a marker of receptor editing — specifically in the lamina propria.

So, B cell development and diversification can occur in the intestinal mucosa in response to colonization of the intestinal microbiota at weaning. Whether this process enhances overall antibody diversity or whether it helps to eliminate antibody reactivity to commensal bacteria and self antigens will require further study.

Lucy Bird

ORIGINAL RESEARCH PAPER Wesemann, D. R. *et al.* Microbial colonization influences early B-lineage development in the gut lamina propria. *Nature* **501**, 112–115 (2013)
FURTHER READING Schlissel, M. B cell development in the gut. *Nature* **501**, 42–43 (2013)