The relationship between mucosal IgM and IgA has recently been addressed in murine systems to investigate how IgA secreting plasma cells localise in the intestine and to determine if switching from IgM to IgA occurs in the microenvironment of the gut mucosa.

In mice the situation appears to be quite different; cells expressing IgM appear to be more strictly the precursors of IgA secreting cells. In mice, approximately 50% of intestinal IgA plasma cells are derived from IgM expressing cells in the peritoneal cavity. These cells, known as B1 cells, are a self-replenishing population, many of which express the CD5 antigen. The remaining 50% of plasma cells are derived from B cells in the organised lymphoid tissue in the Peyer’s patches and are known as B2 cells. Theoretically, the peritoneal precursors generate a rapid, although relatively low affinity response against potential pathogens while in contrast, Peyer’s patches take longer to generate a plasma cell response, but this response is of high affinity and specificity.

The relationship between mucosal IgM and IgA has recently been addressed in two murine systems in order to investigate how IgA secreting plasma cells localise in the intestine and to find out if switching from IgM to IgA occurs in the microenvironment of the gut mucosa.

One of the front lines of the immune defence is the gut mucosa, where immunoglobulin-IgA is continuously produced to react with commensal bacteria and dietary antigens. It is generally accepted that, after antigenic stimulation in the Peyer’s patches, IgA+ lymphoblasts (B220+IgA+) migrate through the lymph and blood circulation, and eventually home to the lamina propria of the intestine. Mice that lack activation-induced cytidine deaminase (AID) are defective in class switch recombination (CSR) and somatic hypermutation. CSR changes the immunoglobulin heavy chain constant region (CH) gene being expressed from Cmu to other CH genes, resulting in a switch of the immunoglobulin isotype from IgM to IgG, IgE or IgA. AID−/− mice also secrete large amounts of immunoglobulin-mu (IgM) into faeces, and accumulate B220-IgM+ plasma cells as well as B220+IgM+ cells in the gut. Here we show that lamina propria B220+IgA+ cells have just completed CSR, as they still express both AID and transcripts from circular DNA that has been “looped-out” during CSR. Lamina propria IgM+ B cells seem to be pre-committed to switching to IgA+ in vitro as well as in vivo. Culturing lamina propria IgM+ B cells together with lamina propria stromal cells enhances preferential switching and differentiation of B cells to IgA+ plasma cells. We conclude that IgA+ cells in the gut lamina propria are generated in situ from B220+IgM+ lymphocytes.
of bone marrow derived B2 cells to the murine intestine. These cells initially enter the Peyer’s patches where they switch to expressing IgA, before returning to the blood and homing to the lamina propria. This report demonstrated that the thymus expressed chemokine (TECK), which is expressed in the lamina propria of the small intestine, selectively attracts IgA+ splenic B cells but not IgM+ splenic B cells. It remains to be seen whether the IgM+ B1 cells studied by Fagarasan et al are responsive to TECK.

Not much is known about the role of TECK in B cell migration in humans. TECK expression has been observed in the crypt epithelium of the human small intestine. Only approximately 2% of freshly isolated peripheral blood CD19+ B cells migrate in vitro in response to TECK but it would be interesting to see which isotype these cells express and whether they possess any gut homing markers such as α4β7 or αEβ7.

It is not known whether B1 cells are involved in human mucosal antibody responses and it will be important to answer this question if we are to appreciate the level of relevance of these ground breaking observations in animal models to human physiology and disease. It is essential that we understand the different B cell homing and class switching mechanisms in humans because mucosal immunisation, for example, would be more difficult if a significant proportion of the effector population produces antibody with low affinity and low specificity. Similarly, in inflammatory bowel disease, it would increase our understanding of the disease process if we knew why the profile of immunoglobulin isotypes secreted by lamina propria plasma cells is altered.

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