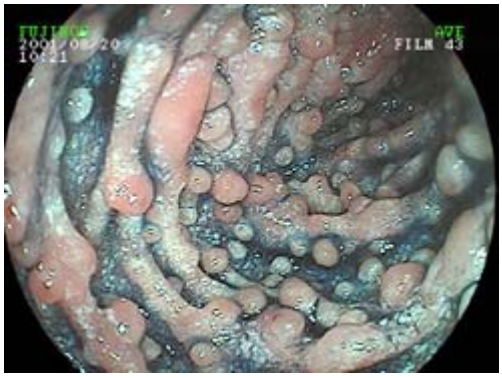
Using AID-/- mice, which have a complete absence of class switch recombination and somatic hypermutation we revealed the importance of somatically hypermutated IgA in the gut.

AID-/- small intestine with hyperplasia of ILF

Human intestine with nodular follicular hyperplasia



An animal model that appears to recapitulate the CVID pathology in human is AID-deficiency in mice. AID-/- mice develop numerous protruding follicular structures along the small intestine, which represent hypertrophia of ILF. This resembles the nodular follicular hyperplasia in humans. Furthermore, AID deficient mice have an enormous expansion of non-pathogenic but anaerobic bacteria in all segments of the small intestine. Since an appropriate antibiotic treatment against the anaerobic bacteria abolished not only the ILF hyperplasia, but also the induction of GC in all lymphoid tissues, continuous antigenic stimulation by an excessive intestinal anaerobic bacteria is probably responsible for both the local and systemic B cell activation, as well as the ILF hyperplasia and gigantic GC formation in AID-deficient mice. Thus, it appears that the IgA secreted into the gut lumen serves not only for protection against viral and bacterial pathogens, but also for the homeostasis of the gut flora, which is essential to prevent over-stimulation of the non-mucosal immune system.