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The role of Peyer's patches in synchronizing gut IgA responses.

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Abstract

Because Peyer's patches (PP) are the main inductive sites for gut IgA responses we have focused this review on what we know about the function of PP germinal centers (GC). The vast majority of IgA gene sequences in the gut lamina propria (LP) are heavily mutated arguing for an origin in GC. Because PP GC formation is dependent on the presence of CD4 T cells, we speculate that all IgA responses in the normal gut are directly or indirectly T cell-dependent (TD). We hypothesize that the CD4 T cell involvement in gut IgA responses against the microbiota is different from that in systemic responses since cognate T-B cell interactions appear not to be required. In the absence of cognate interactions the function of CD4 follicular helper T cells (Tfh) in PP GC is unclear. However, production of IL-21 and IL-6 is more pronounced than in peripheral lymph nodes. Importantly, we discuss how multiple PP are involved in generating specific IgA responses to TD antigens given orally. Recently we found that oral immunization with NP-hapten conjugated to cholera toxin (NP-CT) stimulated a strong highly synchronized, oligoclonal and affinity matured IgA response. This was achieved through re-utilization of GC in multiple PP as GC IgA B cells emigrated into already established GC. Clonally related B cells were present in both inductive and effector lymphoid tissues in the gut and clonal trees involving multiple PP could be constructed in individual mice. Through adoptive transfer of B1-8(hi) NP-specific B cells we demonstrated that GL7(+) PP B cells could enter into pre-existing GC in PP, a process that was antigen-dependent but did not to require cognate Tfh interactions. Finally, we discuss the role of PP GC for the generation of memory B cells and long-lived plasma cells in the light of contrasting findings regarding IgA memory development to colonizing commensal bacteria versus that to oral immunization with enteropathogens or TD antigens.

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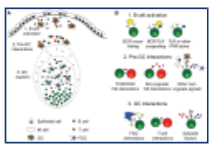
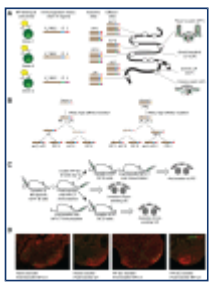

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