Control of intestinal IgA by Th17 cells

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Mucosal surfaces serve as a protective barrier against preventing infection through the intestinal and respiratory tracts. Secretory IgA into the intestinal lumen is a significant contributor to mucosal protection, as well as the effector functions of Th17 cells. Although high amounts of IgA and Th17 cells are present constitutively in the intestine, it remains unclear whether these two systems interact to maintain intestinal homeostasis, or how they respond to pathogens. Our preliminary data revealed that mice deficient in IL-17 signaling have decreased IgA in their fecal pellets. Furthermore, repletion of Th17 cells into T cell-deficient TCRβδ-/- mice increased fecal IgA. The mechanisms by which Th17 cells influence IgA production remain unknown. B cells undergo class-switch recombination (CSR) through T cell-dependent (TD) and –independent (TI) mechanisms. TD relies on CD40 ligand contact from CD4 T cells, and the cytokine milieu to induce CSR and antibody production. Here, culture of naïve B cells with Th17 cells results in increased IgA production and differentiation into IgA-producing cells. Treatment of naïve B cells with IL-21, a prominent Th17 cytokine, greatly increased IgA CSR as well as total IgA production in conjunction with TGFβ or retinoic acid, which are present in high numbers in the intestinal tract. Furthermore, treatment of intestinal B cells with IL-17 or IL-21 greatly increased IgA production. TI occurs in the presence of BAFF or APRIL and after antigen stimulation of the B cell receptor. Our work shows that the Th17 cell cytokines, IL-17 and IL-21 are also able to function indirectly to induce IgA production by inducing the expression of BAFF and APRIL from dendritic cells, as well as intestinal epithelial cells. Collectively, these data reveal that Th17 cells contribute to intestinal IgA production directly from B cells, as well as indirectly through dendritic cells and intestinal epithelial cells.