F4⁺ETEC infection elicits an IL-17 dominated mucosal and systemic immune response

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Abstract
Enterotoxigenic *Escherichia coli* (ETEC), a leading cause of post-weaning diarrhea in piglets, can possess different fimbriae of which F4 fimbriae are the most frequently associated with ETEC-induced diarrhea in piglets. These F4 fimbriae are potent oral immunogens that induce protective F4-specific IgA antibody secreting cells at intestinal tissues. Recently, Th17 cells and their hallmark cytokine IL-17A have been implicated in the protection of the host against extracellular pathogens. However, it remains unknown if Th17 effector responses are needed to clear ETEC infections.

Here, we report that F4⁺ETEC infection upregulated IL-17A, IL-17F, IL-21 and IL-23p19, but not IL-12 and IFN-γ mRNA expression in the systemic and mucosal immune system. Similarly, oral immunization with F4 fimbriae triggered a Th17 signature evidenced by an upregulated IL-17F, RORγt, IL-23p19 and IL-21 mRNA expression in the peripheral blood mononuclear cell (PBMCs) fraction. Intriguingly, IL-17A mRNA levels were unaltered, despite the ability of F4 fimbriae to elicit IL-17A mRNA expression by naïve PBMCs. The observed increase in IL-17A mRNA levels correlated with a higher IL-17A secretion by both naïve and antigen-experienced PBMCs upon F4 fimbriae stimulation. The higher frequency of CD3⁺IL-17A⁺ cells in the ileum of F4⁺ ETEC infected pigs as compared to control pigs further corroborates the role of Th17 responses in the clearance of ETEC infection.

Altogether, these data indicate a Th17 dominated response upon oral immunization with F4 fimbriae and F4⁺ ETEC infection. Our work also highlights that IL-17F may participate in the host immune response to protect against F4⁺ETEC infection. These results could contribute to the design of future ETEC vaccines.