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# Morphological and functional characterization of IL-12 Receptor b2 chain on intestinal epithelial cells: implications for local and systemic immunoregulation

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Interaction between intestinal epithelial cells (IECs) and the underlying immune systems is critical for maintaining intestinal immune homeostasis and mounting appropriate immune responses. We have previously showed that the T helper type 1 (TH1) cytokine IL-12 plays a key role in the delicate immunological balance in the gut and the lack of appropriate levels of IL-12 had important consequences for health and disease, particularly with regard to food allergy. Here we sought to understand the role of IL-12 in the regulation of lympho-epithelial cross talk and how this interaction affects immune responses locally and systemically. Using a combination of microscopy and flow cytometry techniques we observed that freshly isolated IECs expressed an incomplete, yet functional IL-12 receptor (IL-12R) formed solely by the IL-12Rb2 chain that albeit the lack of the complementary IL-12b1 chain responded to ex-vivo challenge with IL-12. Furthermore, the expression of IL-12Rb2 on IECs is strategically located at the interface between epithelial and immune cells of the lamina propria (lp) and using in vitro co-culture models and primary intestinal organoids we showed that immune-derived signals were required for the expression of IL-12Rb2 on IECs. The in vivo biological relevance of the IEC-associated IL-12Rb2 was assessed in vivo in a mouse model of food allergy characterized by allergy-associated diminished intestinal levels of IL-12 and in chimeric mice that lack the IL-12Rb2 chain on IECs. These experimental models enabled us to show that the anti-allergic properties of orally delivered recombinant Lactococcus lactis secreting bioactive IL-12 (rLc-IL12) were reduced in mice lacking the IL-12b2 chain on IECs. Finally, we observed that the oral delivery of IL-12 was accompanied by the down-regulation of the production of the IEC-derived pro-allergic cytokine thymic stromal lymphopoietin (TSLP). However, further analysis of intestinal levels of TSLP in IL-12Rb2-/- mice suggested that this event was not directly linked to the IEC-associated IL-12Rb2 chain. We interpreted these data as showing that IEC-associated IL12Rb2 is a component of the cytokine network operating at the interface between the intestinal epithelium and immune system that plays a role in immune regulation.


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