TL1A regulates TCRγδ+ intraepithelial lymphocytes and gut microbial composition

TL1A is a proinflammatory cytokine, which is prevalent in the gut. High TL1A concentrations are present in patients with inflammatory bowel disease (IBD) and in IBD mouse models. However, the role of TL1A during steady-state conditions is relatively unknown. Here, we used TL1A knockout (KO) mice to analyse the impact of TL1A on the intestinal immune system and gut microbiota. The TL1A KO mice showed reduced amounts of small intestinal intraepithelial TCRγδ+ and CD8+ T cells, and reduced expression of the activating receptor NKG2D. Moreover, the TL1A KO mice had significantly reduced body weight and visceral adipose tissue deposits, as well as lower levels of leptin and CXCL1, compared with wild-type mice. Analysis of the gut microbial composition of TL1A KO mice revealed a reduction of caecal Clostridial cluster IV, a change in the Firmicutes/Bacteroidetes ratio in caecum and less Lactobacillus spp. in the mucosal ileum. Our results show that TL1A deficiency impacts on the gut microbial composition and the mucosal immune system, especially the intraepithelial TCRγδ+ T-cell subset, and that TL1A is involved in the establishment of adipose tissue. This research contributes to a broader understanding of TL1A inhibition, which is increasingly considered for treatment of IBD.

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