Cyclooxygenase-2 in mucosal DC mediates induction of regulatory T cells in the intestine through suppression of IL-4.

Abstract:
Oral intake of protein leads to tolerance through the induction of regulatory T cells (Tr cells) in mesenteric lymph nodes (MLNs). Here we show that the inhibition of cyclooxygenase-2 (COX-2) in vivo suppressed oral tolerance and was associated with enhanced differentiation of interleukin (IL)-4-producing T cells and reduced Foxp3(+) Tr-cell differentiation in MLN. As a result, the functional suppressive capacity of these differentiated mucosal T cells was lost. IL-4 was causally related to loss of tolerance as treatment of mice with anti-IL-4 antibodies during COX-2 inhibition restored tolerance. Dendritic cells (DCs) in the MLN differentially expressed COX-2 and reductionist experiments revealed that selective inhibition of the enzyme in these cells inhibited Foxp3(+) Tr-cell differentiation in vitro. Importantly, the inhibition of COX-2 in MLN-DC caused increased GATA-3 expression and enhanced IL-4 release by T cells, which was directly related to impaired Tr-cell differentiation. These data provide crucial insights into the mechanisms driving de novo Tr-cell induction and tolerance in the intestine.

Zeitschriftentitel / Abkürzung:
Mucosal Immunol

Jahr: