Immune recognition of dietary antigens by mucosal CD4 T cells

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The adaptive immune system needs to operate at a delicate balance by responding strongly to occasional exposure to pathogenic microbes and their toxins while continuously maintaining functional tolerance to foreign antigens that are chronically present, namely, those from commensal microbiota and food. How the enteric antigens from food and commensal microbiota are tolerated by the adaptive immune system is still unclear, but this requires the participation of regulatory T cells (Tregs), especially the $CD4^+$ T cell population expressing transcription factor Foxp3. Two types of $Foxp3^+$ Tregs exist, the thymic Treg (tTreg) that develop from hematopoietic progenitors in the thymus and peripheral Treg (pTreg) that develop outside the thymus from conventional mature T cells. tTregs and pTregs are thought to have independent regulatory function, as the presence of both populations are required to prevent mortality and morbidity in Foxp3-deficient mice. pTregs are abundantly found in the intestines, with most of pTregs in the colon induced by the commensal microbes. Here, we demonstrate that antigens derived from the diet induce the bulk of pTregs in the small intestine under normal physiological conditions. These food antigen-induced pTregs have a limited lifespan, can now be distinguished from tTregs and microbiota-induced pTregs, and are required to control immune responses to orally-administrated antigens.