CCR9 Is Not Required for the Homing of Pro-inflammatory Effector T cells, but Is Crucial for Recruitment and Expansion of FoxP3+ CD8+ Tregs in the Small Intestine

Chemokine receptor 9 (CCR9) is required for the homeostatic recruitment of T cells to the mucosa of the small intestine. Accordingly, CCR9 has been suggested as a potential target to inhibit the recruitment of proinflammatory effector T cells (Teff) in inflammatory bowel disease (IBD). Since the contribution of CCR9 to the recruitment of Teff in inflammation is not entirely clear, we aimed to address this question using IFABP-Ova mice. These mice express Ovalbumin (Ova) specifically in small intestinal epithelial cells, which allows triggering of acute inflammation following transfer of Ova-specific CD8+ T cells (OT-I cells) and adjuvant treatment. Strikingly, intestinal inflammation in IFABP-Ova mice could also be triggered following transfer of CCR9-deficient OT-I cells, demonstrating that CCR9 is not required for homing of Teff cells. Interestingly, OT-I cells transferred to IFABP-Ova mice did not only differentiate into Teff, but also into FoxP3+ CD8+ Tregs, which in contrast to Teff cells expressed high levels of CCR9. Indeed, recruitment and expansion of this regulatory subset in the small intestine was strongly dependent on CCR9. Hence, our data show that Teff and regulatory T cell subsets use distinct mechanisms for migration to the small intestine and suggest that inhibition of CCR9 in IBD could be more harmful than useful.