CHEMOKINES / CHEMOKINE RECEPTORS
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M.42. Regulation of Intestinal Dendritic Cells and Immunity by the CCX-CKR Decoy Receptor for CCL19, 21 and 25

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Lymphocyte migration and dendritic cell (DC) homing to lymphoid tissue is governed by the chemokine receptor CCR7 and its ligands CCL19 and 21 whereas CCR9, and its ligand CCL25, direct T cell recruitment to the small intestine. We have previously identified a receptor in mice, called CCX-CKR, that binds CCL19, 21 and 25. CCX-CKR is able to mediate the sequestration and destruction of CCL19 suggesting that it may act as a "decoy" receptor, and play a regulatory role *in vivo*. Here we demonstrate that CCX-CKR regulates immune responses in the intestine, as CCX-CKR null mice have reduced numbers of CD11c+ DC in MLN, with a particular defect in plasmacytoid dendritic cells (pDC) which are known to express CCR9 in the small intestine. In parallel, there were increased numbers of CD11c+ DC within the small intestine lamina propria and the development of oral tolerance is impaired in CCX-CKR null mice, despite the presence of normal systemic immunity. These novel findings suggest that by regulating the ability of CCR7 and CCR9 ligands to control the activity of tolerogenic pDC *in vivo*, CCX-CKR may play an essential homeostatic role in mucosal immunity.

M.44. The Atypical Chemokine Receptor D6 Regulates Experimental Colitis by Modulating Intestinal γδ T Cell IL17 Production

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D6 is an atypical chemokine receptor that negatively regulates inflammation by acting as a "scavenger" for inflammatory CC-chemokines. D6 is expressed at high levels in the human intestine and we show here that it is also expressed in the resting murine colon, predominantly by non-haematopoietic cells. D6 is upregulated during DSS colitis and unexpectedly, D6 deficient mice were less susceptible to colitis, with less weight loss, colon shortening and clinical symptoms. D6 deficiency had no impact on the balance of leukocyte subsets recruited to the inflamed colon, but there was enhanced production of several inflammatory cytokines, particularly IFNγ and IL-17A. This was associated with an increase in IL-17A-producing γδ T cells in the inflamed colons of D6 deficient mice compared with WT animals and, while antibody-mediated neutralisation of IL-17A had no effect on acute colitis in D6 deficient mice, it inhibited their recovery from the disorder. Thus D6 may normally inhibit the generation of inflammatory cytokines by γδ T cells in the inflamed colon, but paradoxically, this may delay recovery from disease. These data reveal a hitherto unknown role of IL17 producing γδ T cells in intestinal homeostasis which appears to be regulated by inflammatory chemokine availability.