CCR2+CD103− intestinal dendritic cells develop from DC-committed precursors and induce interleukin-17 production by T cells

The identification of intestinal macrophages (mφs) and dendritic cells (DCs) is a matter of intense debate. Although CD103+ mononuclear phagocytes (MPs) appear to be genuine DCs, the nature and origins of CD103− MPs remain controversial. We show here that intestinal CD103−/CD11b+ MPs can be separated clearly into DCs and mφs based on phenotype, gene profile, and kinetics. CD64−/CD103−/CD11b+ MPs are classical DCs, being derived from Flt3 ligand-dependent, DC-committed precursors, not Ly6Chi monocytes. Surprisingly, a significant proportion of these CD103−/CD11b+ DCs express CCR2 and there is a selective decrease in CD103−/CD11b+ DCs in mice lacking this chemokine receptor. CCR2+CD103− DCs are present in both the murine and human intestine, drive interleukin (IL)-17a production by T cells in vitro, and show constitutive expression of IL-12/IL-23p40. These data highlight the heterogeneity of intestinal DCs and reveal a bona fide population of CCR2+ DCs that is involved in priming mucosal T helper type 17 (Th17) responses.