Regulation of Steady State Dendritic Cell Migration

The intestinal immune system maintains a delicate balance between the induction of immunity to pathogens and tolerance to harmless antigens from food and intestinal microbiota. A crucial step in the induction of both immunogenic and tolerogenic responses is the CCR7-dependent migration of dendritic cells (DCs) from the intestine to the mesenteric lymph nodes (MLNs). However, while inflammation-induced DC migration has been extensively studied, comparatively little is known about the magnitude and control of steady state intestinal DC migration. Notably, it is unclear if individual DCs in the steady state migrate in response to specific signals or if this continual migration represents a stochastic process. Here we use a range of techniques, including isolation of lymph DCs and in vivo cell tracking, to reliably quantify and characterise the phenotype of migrating DCs from the intestine, lymph, and MLN. Steady state migration of intestinal DCs is highly dynamic, with between 50,000 – 100,000 DCs migrating from the mouse small intestine to the MLN each day, replacing the entire MLN migrating DC pool within 24-48h. We show that CCR7-expressing DCs represent a minor proportion of total intestinal DCs and have a phenotype reminiscent of lymph DCs, characterised by high expression of surface MHCII, upregulation of costimulatory molecules, partial downregulation of integrins and minimal BrdU incorporation. Therefore, even before leaving the intestine, CCR7-expressing DCs adopt a distinct phenotype, strongly suggesting that steady state DC migration is not a purely stochastic process, but that the DCs make a ‘decision to migrate’ in response to specific environmental signals.

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