Defining anatomical localisation and subsets of the murine mononuclear phagocyte system using integrin alpha X (ITGAX/CD11c) and colony stimulating factor 1 receptor (CSF1-R/CD115) expression fails to discriminate macrophages from dendritic cells

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Defining Anatomical Localization and Subsets of the Murine Mononuclear Phagocyte System Using Integrin Alpha X (ITGAX/CD11c) and Colony Stimulating Factor 1 Receptor (CSF1R-CD115) Expression Fails to Discriminate Macrophages from Dendritic Cells

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Introduction

The hematopoietic differentiation pathway of specific murine mononuclear phagocyte (MNP) subsets such as Dendritic cells is still a highly debated subject. Using transgenic mouse model systems we have attempted to define the expression of Itgax and CSF-1R in order to clarify the relationship between these markers, what constitutes a dendritic cell and which bone marrow precursors they differentiate from. We have combined the CSF-1R-eGFP (MacGreen) and Itgax-DTR transgenes into a compound transgenic model. Using eGFP fluorescence to identify MNPs, we can readily observe the effect of Itgax-mediated cell depletion. Adoptive bone marrow transfers of complete or fluorescence-activated cell sorted (FACS) cell populations reveal their differentiation potential.

Methods

Results: Experiment 1

Small intestinal lamina propria

Itgax-mediated depletion as visualised by Csf1r-eGFP expressing cells revealed almost all intestinal lamina propria MNPs were depleted. Residual cells were subsequently observed to be Itgax+ and actin rich.

Peyer’s patch and lung

Within the intestinal Peyer’s patch and lung, several anatomically distinct populations were depleted. Residual eGFP+ cells were subsequently shown to be both Itgax+/CD11c+ and F4/80+ (data not shown). Within the Peyer’s patch all eGFP+ cells were depleted from the germinal centre. Within the lung all bone marrow-derived MNPs were depleted while some interstitial MNPs were retained.

Spleen

Within the spleen anatomically distinct populations were lost including marginal zone macrophages, as shown by loss of Sca1 expression (Sn). Interdigitating DC were depleted from T-cell area peri-arteriolar locations. Residual eGFP+ MNPs within the splenic red pulp were observed to be Itgax+ and F4/80+.

Discussion

We have demonstrated clearly that all small intestinal lamina propria (SIP) MNPs (i.e. DC and Mφ) express both Itgax and Csf1r and also confirmed Itgax expression in numerous other anatomically distinct MP populations. Based on the implied Csf1r-dependence of these cell populations we have identified mature, multipotent and possible pluripotent progenitor populations of SIP and Peyer’s patch MNPs within murine bone marrow. We aim to further characterise and isolate these precursor populations in order to identify the full differentiation pathways of mature mucosal MNP populations.