SIgN Immunology Seminar

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The macrophage niche: in search of the tissue-specific mechanisms controlling macrophage development

Host
Dr Florent Ginhoux
Singapore Immunology Network,

Date
Monday 11 December 2017

Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Most tissue-resident macrophages are derived from embryonic precursors but, under certain circumstances, circulating monocytes can differentiate into self-maintaining tissue-resident macrophages that resemble their embryonic counterparts. We propose that distinct macrophage precursors have an almost identical potential to develop into resident macrophages but they compete for a restricted number of niches. Imprinting by the niche would be the dominant factor conferring macrophage identity and self-maintenance capacity, rather than origin. We have recently shown that circulating monocytes can efficiently differentiate into Kupffer cells (KCs), the liver-resident macrophages. Using knock-in mice that allow specific KC depletion, we found that monocytes colonize the KC niche in a single wave upon KC depletion and rapidly differentiate into self-maintaining KCs that are transcriptionally and functionally identical to embryonic KCs. This implies that: (i) access to the KC niche is tightly regulated ensuring that monocytes do not differentiate into KCs when the KC niche is full but differentiate very efficiently into KCs upon temporary niche availability, (ii) imprinting by the KC niche is the dominant factor conferring KC identity. We are now aiming at understanding which signals produced by the macrophage niche imprint the tissue-specific macrophage gene expression profile and through which transcription factors this is mediated. We utilize a research strategy that combines state-of-the-art in silico approaches and unique in vivo transgenic mouse models to tackle this challenge specifically for KCs, the most abundant macrophage in the body.