



MORE THAN EATING AND DRINKING: THE GOURMET MACROPHAGE

SIAMON GORDON, UNIVERSITY OF OXFORD.

Macrophages and closely related cells are widely distributed throughout the body, encompassing monocytic precursors, phagocytic and non-phagocytic tissue macrophages, dendritic cells and osteoclasts. In the mouse, the F4/80 and cd68 antibodies made it possible to demonstrate the abundant presence and further microheterogeneity of macrophages in lympho-haemopoietic and other tissues. Their distribution and anatomic relationships to other cells is suggestive of broader functions than purely clearance by phagocytosis and endocytosis, for example in regulating haemopoiesis in the bone marrow and neuronal functions in the nervous system.

In blood, monocytes display heterogeneity in their response to chemokines and migration into tissues, during development, inflammation and infection. Within tissues, monocytes/macrophages are modulated by microbial stimuli and cytokines such as Interferon gamma, IL-4 and IL-13. Their phenotypic plasticity has been characterised by antigen expression, microarray and proteomic analysis, although much remains to be done in this regard, especially in humans.

Their ability to recognise and respond to diverse exogenous and endogenous ligands is broad, yet selective, influencing their gene expression and secretory activities, as well as trophic interactions with other cells. Apart from opsonic and Toll-like receptors, macrophages express a range of Scavenger and lectin-like receptors, which contribute to host defence and homeostasis, as well as tissue injury and repair.

Multinucleated giant cells arising from macrophage fusion are a characteristic, but poorly understood feature of granuloma formation associated with chronic inflammation. We have begun to analyse the fusion mechanism and functions of these cells, in vitro and in situ.

Increasing awareness of their multiple and versatile properties lend hope that future targeting of subpopulations could eliminate pathogenic properties, while preserving vital functions.