SIgN Immunology Seminar



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Macrophage heterogeneity in liver inflammation and fibrosis – implications for future therapeutic strategies

Host
Dr Florent Ginhoux
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Date
Thursday
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Time
3pm – 4pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Hepatic macrophages are central in the pathogenesis of chronic liver injury and have been proposed as potential targets in combatting fibrosis. Recent experimental studies in animal models revealed that hepatic macrophages are a remarkably heterogeneous population of immune cells that fulfill diverse functions in homeostasis, disease progression and regression from injury. These range from clearance of pathogens or cellular debris and maintenance of immunological tolerance in steady state conditions; central roles in initiating and perpetuating inflammation in response to injury; promoting liver fibrosis via activating hepatic stellate cells in chronic liver damage; and, finally, resolution of inflammation and fibrosis by degradation of extracellular matrix and release of anti-inflammatory cytokines. Cellular heterogeneity in the liver is partly explained by the origin of macrophages. Hepatic macrophages can either arise from circulating monocytes, which are recruited to the injured liver via chemokine signals, or from self-renewing embryo-derived local macrophages, termed Kupffer cells. Kupffer cells appear essential for sensing tissue injury and initiating inflammatory responses, while infiltrating Ly-6C+ monocyte-derived macrophages are linked to chronic inflammation and fibrogenesis. In addition, proliferation of local or recruited macrophages may possibly further contribute to their accumulation in injured liver. During fibrosis regression, monocyte-derived cells differentiate into Ly-6C (Ly6C, Gr1) low expressing 'restorative' macrophages and promote resolution from injury. Understanding the mechanisms that regulate hepatic macrophage heterogeneity, either by monocyte subset recruitment, by promoting restorative macrophage polarization or by impacting distinctive macrophage effector functions, may help to develop novel macrophage subset-targeted therapies for liver injury and fibrosis.