The role of bone marrow macrophages in the HSC niche during leukaemia growth

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Acute Myeloid Leukaemia (AML) is one of the most aggressive forms of cancer. A common and lethal symptom in leukemic patients is the loss of immune cells in the blood and bone marrow (BM), also known as cytopenia. Haematopoietic stem cells (HSCs) are responsible for the maintenance of all blood cell lineages and are located in specific BM niches, where their fate is regulated by a microenvironment composed of diverse cell types, including immune cells and stromal cells. Recent work has demonstrated that competition between healthy and malignant haematopoietic cells takes place in the BM of leukemic mice, leading to the remodelling of the BM microenvironment and egress of HSCs into the blood. In addition, it has been reported that macrophages are key component of the HSC niche and regulate HSC fate by controlling CXCL12 production by mesenchymal stem cells.

Macrophages have been described to support the progression of solid cancers by promoting angiogenesis, tumor invasion and motility. Furthermore, in humans, tumour associated macrophages are linked to poor prognosis in solid tumors and lymphoma. However, the role of BM macrophages in leukaemia progression remains highly understudied. Here, we hypothesize that macrophage function is impeded by AML growth in the BM and contributes to the loss of HSC niches and egress of HSCs into the blood.

Using intravital imaging of mouse calvarium BM, we propose a unique insight on macrophage dynamics, distribution and interactions with AML. Combining this technique with advanced flow cytometry analysis, we wish to unravel one mechanism by which the BM is remodelled and HSCs are lost. Preliminary analyses have been focussing on BM macrophages localisation and migration, and whether their numbers are affected during disease development. We are currently investigating whether targeting macrophages would help restore AML-induced damage to the BM microenvironment and re-establish the signalling required to maintain healthy HSCs in the BM.

Keywords : Bone marrow, Acute Myeloid Leukaemia, Haematopoietic Stem Cells
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