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Deep phenotyping of the human bone marrow microenvironment in acute myeloid leukaemia by CODEX highly multiplexed microscopy

Abstract

Acute myeloid leukaemia (AML) cells actively interact and remodel the bone marrow (BM) niche in order to support their needs. The BM microenvironment consists of various cell types such as mesenchymal stromal cells, endothelial cells, osteoblastic cells and multiple immune cell types.

Recent studies have shown that leukaemia can create and maintain a leukaemia-supporting BM microenvironment, and vice versa, a dysfunctional BM microenvironment can contribute to leukaemia development and progression. However, the bone marrow microenvironment and its remodelling during AML progression has not been deeply studied.

In this collaboration project, I propose to use CO-Detection by antibody indEXing (CODEX), a multiplex immunofluorescence microscopy technique, on AML BM trephines to understand in a detailed manner the BM microenvironment and how it is affected by AML development. Spatial and functional information is preserved using this immunofluorescence technique.

I will use markers to detect various BM niche components, immune populations, AML cells and functional markers. The results will be used in an integrated computational pipeline, appropriately built for high-dimensional data, in order to generate an interrelationship map of the bone marrow microenvironment (including immune cells) and AML.

This will improve our understanding of the BM niche remodelling as well as its role in the AML progression. The data generated will potentially identify new therapeutic targets. In conclusion, the proposed project will improve our understanding of the mechanisms by which AML reprogrammes its microenvironment and may form the basis for novel therapeutic strategies including immunotherapies.