ImmunoTools IT-Box-139 Award 2012

Jessica Sigmans

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Unravelling interactions in the hematopoietic niche in Multiple Myeloma

Multiple myeloma (MM) is a malignant plasma cell disorder that accounts for 10% of all haematological malignancies. Despite significant improvement of prognosis in recent years, MM remains an incurable disease, with a median life-expectancy of 5-7 years. Primary MM cells depend on the bone marrow microenvironment to survive and proliferate. The interaction of the malignant plasma cells with the microenvironment in the BM among which osteoclasts results in the characteristic osteolytic bone lesions. Conversely, the bone marrow microenvironment, either directly via adhesion molecules or indirectly via the production of cytokines, chemokines and growth factors, induces proliferation and survival of the MM cells. MM cells express a wide variety of adhesion molecules and these molecules mediate homing of the MM cells to the bone marrow.

The aims of this project are to study the role of adhesion molecules, chemokines and cytokines which are assumed to be essential for homing and outgrowth of primary MM cells. For this we established a mouse model in which we can create a humanized bone marrow environment ("niche") by seeding ceramic scaffolds with culture-expanded human Mesenchymal Stromal Cells (MSC's) from human adult bone marrow. When these hybrid scaffolds are placed s.c. in immune deficient mice this leads to human bone deposition inside the scaffolds with a layer of human osteoblasts on top, thus forming a humanized bone marrow niche. By luciferase gene marking of patient derived MM cells and utilizing bioluminescent imaging, we are not only able to visualize and follow the in vivo outgrowth and homing of primary MM cells but also to quantify the effect of immuno/chemotherapy treatment. In this model we can manipulate both the MSC's as well as the MM cells for expression of adhesion molecules, cytokines and chemokines via knock-down by shRNA or via over-expression. In this way we hope to get insight in the pathology of this disease and we might be able to identify new targets to interfere with homing and outgrowth of primary MM cells, which may lead to novel targeted therapy for MM.

By using the ImmunoTools IT-box-139 we can analyze if changes will occur in the MSC's and MM cells after implantation of these cells in the mouse model. We also can verify successful knock-down or over-expression of the different adhesion molecules, cytokines and chemokines in MSC's and MM cells.

ImmunoTools IT-Box-139 for Jessica Sigmans includes 100 antibodies

FITC - conjugated anti-human CD1a, CD3, CD4, CD5, CD6, CD7, CD8, CD14, CD15, CD16, CD19, CD21, CD25, CD29, CD35, CD36, CD41a, CD42b, CD45, CD45RA, CD45RB, CD45RO, CD49d, CD53, CD57, CD61, CD63, CD80, CD86, HLA-DR, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE - conjugated anti-human CD3, CD4, CD8, CD11b, CD15, CD14, CD18, CD19, CD20, CD21, CD22, CD31, CD33, CD38, CD40, CD45, CD45RB, CD50, CD52, CD56, CD58, CD62p, CD72, CD95, CD105, CD147, CD177, CD235a, HLA-ABC, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE/Dy647 -tandem conjugated anti-human CD3, CD4, CD8, CD14, CD19, CD20, CD25, CD54

APC -conjugated anti-human CD2, CD3, CD4, CD8, CD10, CD11a, CD11c, CD14, CD16, CD27, CD37, CD42b, CD44, CD45, CD59, CD62L, CD69, CD71, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

DETAILS