Metabolic adaptation in the hematopoietic microenvironment during leukemic transformation

Acute myeloid leukemia (AML) is a complex heterogeneous disease, caused by a chain of events involving genetic and epigenetic changes. Although the majority of patients achieve remission, nearly half will die from disease relapse. This suggests that the current clinico-pathological and molecular evaluations are not efficient enough to predict the disease outcome. The bidirectional crosstalk with different components of the bone marrow microenvironment such as mesenchymal stromal, endothelial and immune cells has been described as critical for leukemic cell biology and therefore disease progression, treatment response, and relapse. Although investigations in pre-leukemic states like myelodysplasia suggest an increase in inflammatory reactivity of hematopoiesis and functional changes of the stromal environment, much less is known about the **inflammatory and metabolic adaptation of the marrow niche in AML**. Various metabolic mechanisms orchestrate the behaviors of immune and leukemia cells in the bone marrow microenvironment. Furthermore, leukemia cells regulate the bone marrow microenvironment through metabolism to generate an adequate supply of energy and to escape antitumor immune surveillance. **Thus, the targeting of the interaction between leukemia cells and the bone marrow microenvironment provides a new therapeutic avenue.**

In that PhD project established 2D and 3D coculture models of stromal cells with AML cell lines as well as patient samples will be used to analyze inflammation and immune signatures, energy levels and the potency of different compounds to efficiently target the leukemia supportive mechanisms and molecules.