**POSTER 33: Developping the chicken embryo as a new paradigm to decipher the dialog between leukemic cells and their microenvironment *in vivo***

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The adult bone marrow is the continual seat of interactions between hematopoietic stem/progenitors cells (HSPCs) with the surrounding stromal cells which constitute their niche (NH). These interactions are crucial to ensure the correct hematopoietic homeostasis. However, during acute myeloid leukemia (AML), the NH is drastically disturbed. Despite the large amount of informations collected regarding the mechanisms of AML progression, few data are described concerning the involvement of the microenvironment. However, more and more studies indicate that the bone marrow environment plays an instrumental role in the progression of the disease, the development of resistance to treatments and potentially relapses.

We are interested in a sub-category of AML characterized by the presence of an initiating mutation in *DNMT3A* or *TET2* gene. In order to decipher the consequences of the interactions between the leukemic cells and their NH, we are developing human bone marrow organoids in a new and innovative *in vivo* model. Healthy mesenchymal stem cells (MSC) are first isolated, amplified and organized *in vitro* to generate spheroids. These structures exhibited spontaneous differentiation into adipocytes, smooth muscle cells or osteoblastic lineage after hydroxyapatite seeding. The spheroids are then grafted *in vivo* into the chorioallantoic membrane of chicken embryos. Our results showed a rapid vascularization of the graft two days after implantation. Moreover, cellular content analysis showed that the adipocyte cells population is maintained and that a sub-population of cells within the graft express Nestin, a pericyte marker. In the long term, we plan to inject healthy or leukemic cells into the embryo and evaluate the consequences of graft colonization by these cells at the cellular, molecular and transcriptomic levels.

The elaboration of such a model could not only make it possible to understand what mechanisms are involved during the dialogue between normal and pathological hematopoietic cells with the microenvironment, but also make it possible to identify new signaling pathways. These could then be disrupted in our graft system using drugs or gene editing. This implementation can be done reproducibly, quickly and at costs well below what is done in mice. In the long term, our researches could make it possible to identify new molecules useful in therapeutic strategies, particularly in the case of AML for which the relapse and mortality rates are very high.