**POSTER 29: Hematopoietic stem cells and Microenvironment: a conceptual approach**

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Hematopoietic stem cells (HSCs) play a fundamental role in the hematopoietic system: in physiological conditions, their differentiation produce myeloid and lymphoid cells; instead, their dysfunction can cause hematological malignancies. HSCs are not isolated but they are rather embedded in the microenvironment (ME) of the bone marrow. Despite the scientific advances, the conceptual understanding of the relation between HSCs and ME is rather limited: in healthy hematopoiesis, the main problem is to characterize how the different and heterogeneous components of the ME modulate HSCs fate; in hematological malignancies, the issue is to explain the relation between niche remodeling and HSCs mutations.

This presentation addresses two research questions: 1) how can we characterize HSCs-ME relation in healthy hematopoiesis and in hematological malignancies? 2) How does this relationship contribute to clarify the stemness of HSCs (i.e., their capacity to self-renewal and differentiate)? Through a critical review of the current scientific literature, I argue that the HSCs-ME relation changes in healthy hematopoiesis and hematological malignancies, determining a different stemness of HSCs. In the former case, HSCs and ME influence each other in an asymmetric way (reciprocity with asymmetry). In hematological malignancies, three different scenarios are possible: the asymmetric reciprocity is maintained; the asymmetry is reversed; the asymmetry is lost. These differences suggest that in physiological hematopoiesis stemness depends on the niche, whereas in hematological malignancies the dependence on the context can be lost.

In the treatment of hematological malignancies, the three scenarios suggest three different therapeutic approaches: first, when the asymmetry is maintained and altered, the objective will be to reestablish a normal regulation by targeting the altered regulation of ME. Secondly, when the asymmetry is reversed, the therapeutic target will be the HSCs, since they are the source of both the altered ME and the cancer. Finally, when the asymmetry is lost, the therapeutic strategy will be to target both the ME and the HSCs to restore the asymmetry of the healthy hematopoiesis.