**POSTER 30: Exploring Nat8L involvement in HSC self-renewal/expansion processes upon stress**

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Introduction: Hematopoietic homeostasis within the blood compartment is maintained in the bone marrow (BM) by a rare population of hematopoietic stem cells (HSCs) that have the ability to self-renew, differentiate and expand to meet the organism’s needs. To gain a better understanding of the mechanisms governing the expansion and self-renewal of HSCs, we are studying several physiological expansion situations: HSC expansion during embryonic development in the fetal liver before BM migration, and HSC response to hematopoietic stress caused by infections or myeloablative treatments. Metabolomic analysis in our laboratory revealed that N-Acetyl-L-Aspartate (NAA) in fetal liver HSCs was up to ten-fold higher than in quiescent BM HSCs. This finding suggests a potential role of NAA in HSC expansion. NAA is a metabolite found mainly in the brain, with no previously described role in hematopoiesis.

Method: To investigate the function of NAA in hematopoiesis, a transgenic mouse model deficient for *Nat8l* gene (*Nat8l*-KO), which encodes for the enzyme responsible for NAA synthesis, was used.

Results: Functional and phenotypic analyses were conducted to characterize HSC and multipotent progenitor populations from adult *Nat8l*-KO mice. However, these analyses did not show any effects on hematopoiesis under basal conditions between control and mutant animals suggesting NAA could be specifically used during hematopoietic expansion, such as embryogenesis or after stress exposure. To study the impact of NAA loss in a hematopoietic stress context, analyses were conducted after serial injections of LPS or 5-FU in *Nat8l*-KO mice. We showed that *Nat8l* deficiency impairs mice survival upon 5-FU treatment and primitive hematopoietic compartments characterization revealed a slight expansion. Cell cycle alterations in these same populations were also noted.

These results encourage further investigation into the role of NAA in stress-induced hematopoiesis.