IMPROVEMENT OF PERIPHERAL BLOOD STEM CELL MOBILIZATION USING HUMAN CHORIONIC GONADOTROPIN IN ADDITION TO CURRENT MOBILIZATION APPROACHES WITH GRANUOCYTE-COLONY STIMULATING FACTOR

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1. BACKGROUND

•The mobilization technique currently represents an essential step in PBSCT and post chemotherapy granulocytopenia.

• Insufficient mobilization represents one of the most important limitations of the standard approach with G-CSF.

• MSCs offer a structural (stromal) and functional (paracrine) support for the physiology and homeostasis of the hematopoietic system.

• MSCs continue to express gonadotropin receptors in the adulthood.

• Our preliminary results *in-vitro* have shown that HCG treatment leads to the selection of more primitive and potent MSCs from the bone marrow. (fig.1)

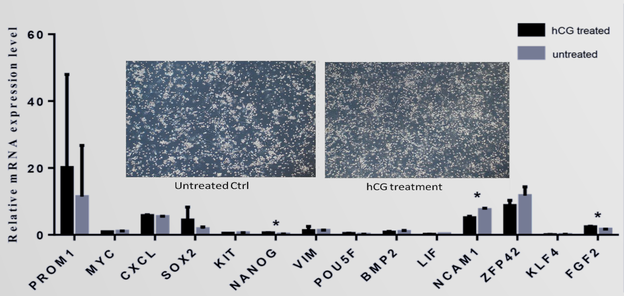

Figure 1. Proliferation in culture evaluated by optical microscopy and stemness gene expression evaluated by RT-qPCR after HCG treatment.

•MSCs stimulation could have relevant implications for the current mobilization strategies.

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2. MATERIALS AND METHODS

• We evaluated HCG as a complementary approach for peripheral blood stem cell mobilization on a rat model. (fig.2)

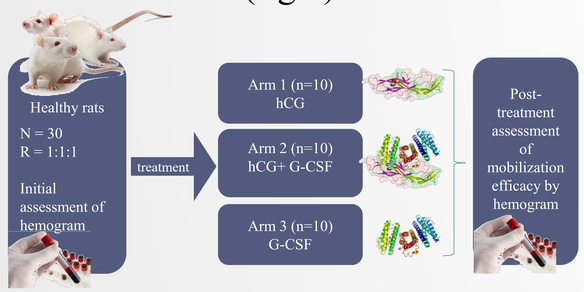

Figure 2. *In-vivo* study workflow on the rat model

•To validate the additional mobilization capability of HCG obtained in the rat model, we validated the effect on a mouse model where we evaluated cell surface markers before and after the addition of HCG to G-CSF (fig.3)

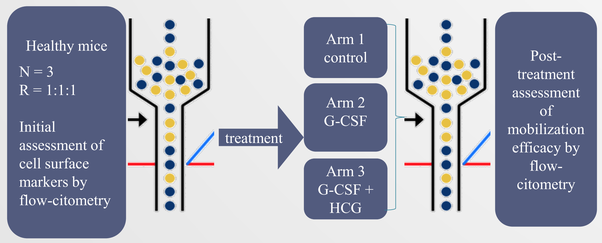

Figure 3. *In-vivo* study workflow on the mouse model

•We evaluated CD34 and SCA1 expressed on hematopoietic stem cells, CD29 widely expressed on monocytes and lymphocytes, CD31 expressed on endothelial cells, CD11b expressed on immune cells and CD44 a negative marker for MSCs.

3. RESULTS

• Our approach showed a superior mobilization capability of HCG+G-CSF than G-CSF alone for the number of monocytes and lymphocytes in the rat model.(fig.4)

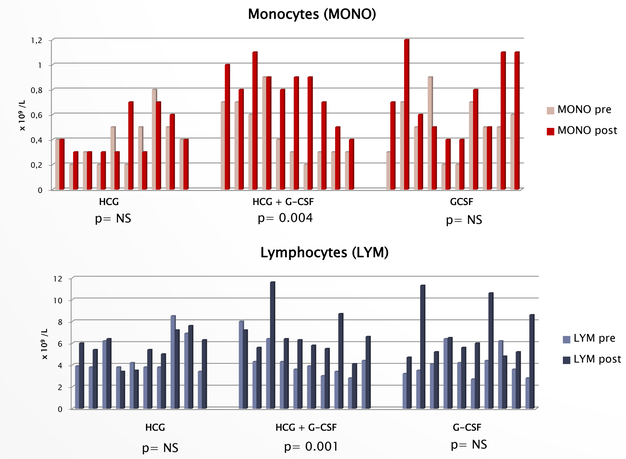

Figure 4. Graphic representation of the effect of the treatment on the number of MONO and LYM.

•The effect of the combination in the mouse model showed a 9.3% increase in CD34 expression and a 21% increase in CD29 expression, with solely minor effects for the other markers. (fig.5)

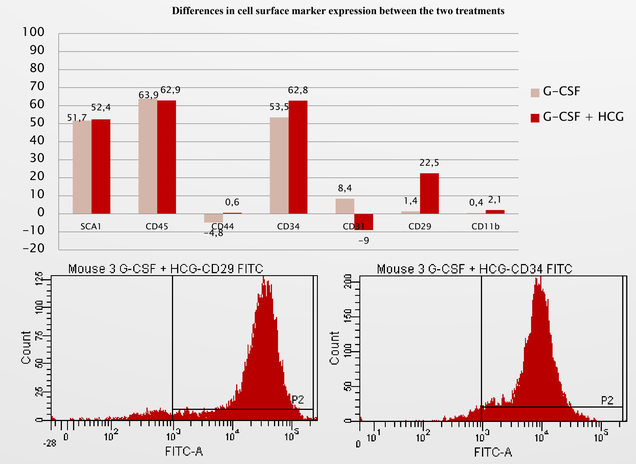

Figure 5. Graphic representation of the effect of the treatment on the expression of cell surface markers.

4. CONCLUSIONS

•The study confirms the capability of HCG to stimulate the additional mobilization of hematopoietic stem cells, monocytes and lymphocytes.

•Our findings (unpublished) have relevant clinical implications residing in the potential of improving the outcomes of PBSCT by increasing the mobilization of hematopoietic stem cells and also for reducing hematologic toxicity of chemotherapy by mobilizing monocytes and lymphocytes more efficiently.

•This prompts for the validation of the mobilization capability of HCG+G-CSF combination in a proof-of-principle feasibility clinical trial.

5. REFERENCES

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