Aufschlüsselung der immunmodulatorischen Reaktion des Stromazellkompartiments im Knochenmark

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Introduction

Recent studies have elucidated the importance of heterogeneity within the bone marrow mesenchymal stem cells (MSCs). In the context of inflammation, our group has identified a novel inflammation-responding MSC (iMSC) as a functional stromal subset [Sood et al., in preparation]. Building on this, we aim at dissecting the effect of these cells on the immune system across the stromal compartment.

Methods

To investigate the immune response of the bone marrow niche cells we performed RNA sequencing analysis on iMSCs (CD51+, PDGFRα+) 3, 24 and 72 hours post treatment with IFNα (5x106 units/kg) of C57Bl/6 mice. To quantify the functional effect of iMSCs, in vitro co-cultures, proliferation assays, immune checkpoint assays, flow cytometric analyses, qPCR and confocal imaging were performed.

Results

Sequencing analysis of iMSCs upon IFNα-treatment showed significant up-regulation of cytokine, chemokine and interleukin gene-sets within 3 hours after the start of the treatment, thus indicating an immunomodulatory role for the iMSCs in response to acute inflammatory stress. To investigate this hypothesis we next performed primary co-cultures of iMSCs with specific immune cells. Analysis of these ex vivo co-cultures indicated the capability of iMSCs to promote macrophage polarisation towards a M2 anti-inflammatory phenotype. Furthermore, the presence of iMSCs resulted in a suppression of CD4 and CD8 T cell activation and proliferation. This suppression was stronger than seen in co-cultures with other stromal cells, or known immunoregulatory cells, such as regulatory T cells.

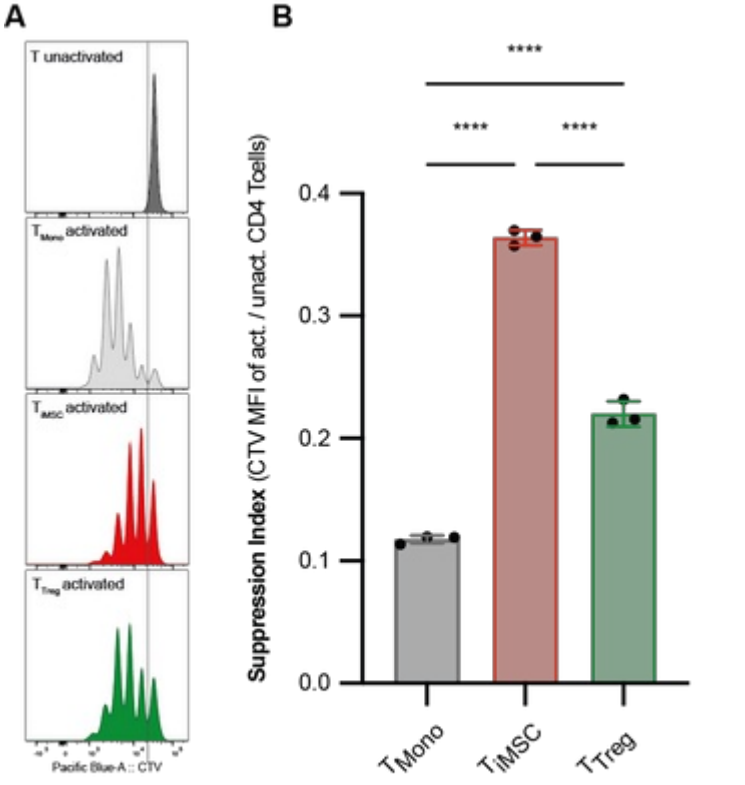

Figure 1 iMSCs show an anti-inflammatory effect
A CTV Proliferation after cd23/cd28 beads activation, **B** Suppression Index as described in Hernández-Malmierca et al., *Cell Stem Cell* 2022

Conclusion

In summary, our data suggests that within the bone marrow niche, the inflammation-responding MSCs (iMSCs) exhibit dynamic immunomodulatory function upon IFNα stimulation with functional concequencies on the immune system. Our research on the interaction between these iMSCs and the immune cell-types will help to unravel the intricacies of its induced tissue immune privilege in both homeostatic and malfunctioning states, with possible application in auto- as well as allogeneic immune diseases, malignancies and ageing.

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