

## Will Mesenchymal Stromal Cells become tools for immunomodulation in Myasthenia Gravis ?

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### *Background and aims*

Myasthenia Gravis (MG) is due to auto-antibodies directed against the neuromuscular endplate. Mesenchymal Stromal/Stem Cells (MSC) can modulate the immune system via soluble mediators and cell-cell contacts. Research grade (RG-) MSC conditioned by peripheral blood mononucleated cells (PBMC) improved the clinical outcomes in a humanized mouse model of MG (*Sudres et al., JCI Insight 2017*). In a clinical perspective, we characterized the phenotype and functional capacities of resting and conditioned MSC of clinical grade (CG-MSC), as compared to RG-MSC.

### *Methods*

RG- and CG-MSC were derived from adipose tissue. They were conditioned by PBMC, monocytes, or activated by IFN- $\gamma$ , or left untreated. Their phenotype was assessed by flow cytometry (61 antibodies), and mass cytometry (CyTOF) (31 antibodies). Immunomodulating capacities of CG-MSC were evaluated by PBMC inhibition assay, and quantifications of cytokines (IL-6, TGF- $\beta$ , IDO and PGE2).

### *Results*

(1) RG- and CG-MSC showed close phenotypes despite some differences in growth kinetics. However the strongest correlations were obtained in comparing CG cultures from different donors between them, or RG cultures between them. (2) Some markers were modulated by all conditioning treatments, while others exclusively by one of them, thus conferring

conditioning signatures. (3) Both resting and conditioned CG-MSC blocked the proliferation of activated PBMC in vitro. (4) The conditioning treatments enhanced the secretion of immunomodulatory molecules by MSC, but they differed in their molecular footprint.

#### *Conclusion*

RG- and CG-MSC show similarities and differences ; CG-MSC present immunomodulation capacities and the different treatments result in phenotypic and functional signatures.