3.13 The importance of ARDS patient stratification prior to MSC-based therapy: and the notable impact of MSC-licensing

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Background: Clinical trials investigating the potential of mesenchymal stromal cells (MSCs) in the treatment of acute respiratory distress syndrome (ARDS), have shown underwhelming results; with <50% of patients responding to treatment. MSCs are an alternative option for the treatment of ARDS, due to their immunomodulatory and cytoprotective capacity in response to inflammatory stimuli. ARDS-phenotyping shows that patients can be stratified into hypo- and hyper-inflammatory sub-groups; with $ARDS_{Hyper}$ having augmented levels of inflammation. We hypothesised that MSCs may be more efficacious in the treatment of $ARDS_{Hyper}$, due to the known impact of inflammatory signals on MSC-activation/licensing. **Methods:** MSCs were exposed to 20% ARDS patient serum, or healthy control, for 24hrs; before replacing the media with serum-free media. The MSC-secretome was then screened *in vitro* and *in vivo*. **Results:** Hyper-licensed MSCs had the capacity to significantly reduce lung permeability. This was assessed in CALU-3 lung epithelial cells through the execution of a TEER assay as a functional readout of barrier integrity *in vitro*. This was further confirmed in a pre-clinical model of acute lung inflammation, through the use of Evan's Blue permeability dye. **Conclusion:** Hyper-licensed MSCs show enhanced therapeutic efficacy; highlighting the importance of MSC-licensing, and the need for patient stratification. **Conflict of Interest:** The authors declare that they have no conflict of interest.