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Healthy *versus* inflamed lung environments differentially affect mesenchymal stromal cells

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Shareable abstract (@ERSpublications)
MSCs exposed to a healthy lung environment induce an inflammatory response with increased gene/protein expression associated with self- *versus* non-self-recognition. These changes were absent or opposite in MSCs exposed to an inflamed ARDS environment. https://bit.ly/3eombO8

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Abstract

Background Despite increased interest in mesenchymal stromal cell (MSC)-based cell therapies for acute respiratory distress syndrome (ARDS), clinical investigations have not yet been successful and our understanding of the potential *in vivo* mechanisms of MSC actions in ARDS remains limited. ARDS is driven by an acute severe innate immune dysregulation, often characterised by inflammation, coagulation and cell injury. How this inflammatory microenvironment influences MSC functions remains to be determined.

Aim The aim of this study was to comparatively assess how the inflammatory environment present in ARDS lungs *versus* the lung environment present in healthy volunteers alters MSC behaviour.

Methods Clinical-grade human bone marrow-derived MSCs (hMSCs) were exposed to bronchoalveolar lavage fluid (BALF) samples obtained from ARDS patients or from healthy volunteers. Following exposure, hMSCs and their conditioned media were evaluated for a broad panel of relevant properties, including viability, levels of expression of inflammatory cytokines, gene expression, cell surface human leukocyte antigen expression, and activation of coagulation and complement pathways.

Results Pro-inflammatory, pro-coagulant and major histocompatibility complex (self-recognition) related gene expression was markedly upregulated in hMSCs exposed *ex vivo* to BALF obtained from healthy volunteers. These changes were less apparent and often opposite in hMSCs exposed to ARDS BALF samples.

Conclusion These data provide new insights into how hMSCs behave in healthy *versus* inflamed lung environments, and strongly suggest that the inflamed environment in ARDS induces hMSC responses that are potentially beneficial for cell survival and actions. This further highlights the need to understand how different disease environments affect hMSC functions.