6.04 Mesenchymal stromal cells attenuate immunotolerance in a model of sepsis-induced acute lung injury

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Background: Sepsis-induced acute respiratory distress syndrome (ARDS) is a secondary lung disease arising from an initial infection. Approximately 40% of sepsis patients are re-hospitalised due to an aberrant host response and increased vulnerability to subsequent infections. Commonly termed 'immunotolerance', the immune response shifts toward a refractory state, leading to immune dysfunction and impaired pathogen clearance. Mesenchymal stromal cells (MSCs) are an attractive potential therapy for ARDS, renowned for their capacity to promote resolution of inflammation and enhance repair. **Methods:** A sepsis-induced acute lung injury (ALI) preclinical model was used to investigate the role of immunotolerance in ARDS. C57BL/6 mice received 2mg/kg of LPS intratracheally followed by a single dose of hBM-MSC intravenously after 4hrs. To determine the level of immunotolerance in LPS-ALI mice, bone marrow-derived macrophage (BMDM) functionality was also investigated. **Results:** We have demonstrated that LPS-ALI mice have increased pro-inflammatory cytokines TNFα and IL-6 in the bronchoalveolar lavage fluid and MSCs significantly reduced these markers. To investigate the impact of ALI on macrophage functionality, BMDMs isolated from mice after LPS challenge demonstrated an immunotolerant phenotype in response to LPS restimulation *ex vivo*. **Conclusions:** MSCs modulate the inflammatory response associated with acute lung injury, demonstrating their potential therapeutic role to attenuate immunotolerance in a preclinical model of ALI. **Conflict of Interest**: The authors declare that they have no conflict of interest