Mesenchymal Stem Cells: Innovations in Infection and Inflammation Therapy

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Background: Mesenchymal stem cells secrete anti-inflammatory and antimicrobial products. Cystic Fibrosis is a disease that results in infection with P. aeruginosa (PA) S. pneumoniae (ST) or S. aureus (SA). Hypothesis: 1) MSCs and their secreted products (Sups) impact bacterial growth and resolve inflammation and 2) MSCs and Sups with blocked CFTR will have altered abilities. Aims: Determine if 1) Sups alter bacterial growth and kinetics 2) Sups improve antibiotic efficacy and 3) MSCs make chemokines to aide in cell recruitment and 4) this is impacted by CFTR blockage. Methods: Sups were derived from bone marrow aspirates. Bacterial growth was measured by colony forming units and ATP production. For chemokine studies, MSC pellets were cultured with CFTR inhibitor and lipopolysaccharide (LPS) stimulation to mimic bacterial response. Pellets were processed for and analyzed by PCR for chemokines CCL2, IL6, MIP1a, SCF and IL8. Secreted chemokines were analyzed using Luminex. PBMCS were cultured with Sups and followed for cell recruitment. Results: Sups decreased bacterial growth. Blocking CFTR created MSCs that weren't effective at producing CCL2 or IL6. Blocking MSC CFTR enhanced production of chemokine IL8 and MIP1a. Luminex and gene expression data were consistent. Conclusions: 1) Sups lower PA, ST and SA CFUs and kinetics 2) Sups enhance antibiotic efficacy; 3) PBMCS and Sups recruit higher levels of lymphocytes 4) MSCs and Sups make chemokines which aide inflammatory cell recruitment necessary to resolve infection and inflammation and, 5) MSCs and Sups with blocked CFTR are defective at making chemokines. Summary: MSCs may be a possible new or augmented therapeutic treatment for patients with CF.

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