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Evaluating the therapeutic potential of mesenchymal stem cells in an *in vitro* model of alveolar barrier

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Acute Respiratory Distress Syndrome (ARDS) is a form of acute lung injury that causes morbidity and mortality in ill patients. Current therapies for ARDS include lung protective ventilation and fluid clearance, but do not treat the underlying cause. Mesenchymal stem cells (MSCs) have been proposed as a promising form of therapy to treat ARDS. Currently, it is unknown which MSC type is best-suited to treat ARDS. The goals of these study were therefore three-fold: 1. Create a model of ARDS *in vitro*; 2.Identify which MSC source, bone marrow (BM) or adipose (AD)-MSC, is more suitable to treat ARDS; and 3. Evaluate the ability of MSCs to mitigate the ARDS-like injury. To accomplish this, we utlized injurious signals typically manifested in ARDS, such as low oxygen concentration (i.e., hypoxia) and lipopolysaccharide (LPS). LPS is a bacterial endotoxin that induces ARDS *in vivo* and mimics infection *in vitro*. We then subjected a co-culture system of lung epithelial and endothelial cells to these signals to induce the injury. Finally, we added MSCs to this sustem to evaluate their ability to mitigate the injury. After subjecting the co-culture system to hypoxia and LPS, we observed an increase in apoptosis as evidenced by increase in mitochondrial membrane potential and Annexin V analysis. In comparing MSC types, both BM-MSCs and AD-MSCs suppressed T-cell proliferation in a mixed lymphocyte reaction assay; however, AD-MSCs were more potent following a LPS challenge. Additionally, both cell types diminished the secretion of the pro-inflammatory cytokines IFN-γ, IL-13, IL-1α, and IL-1β; yet, unlike BM-MSCs, AD-MSCs showed a significant increase in the anti-inflammatory IL-1RA after LPS exposure. Following the addition of AD-MSCS, there was a significant decrease in protein pearmeability in the co-culture system. Taken together, in the co-culture system, we successfully established a injurios environment rmimicking an ARDS-like condition. Compared to BM-MSCs, AD-MSCs appear to be a more suitable candidate for ARDS due to their superior anti-inflammatory function. Therefore, Addition of AD-MSCs to an *in vitro* co-culture system of ARDS mitigated the injury as evidenced by reduction in membrane permeability.

Biography

Lucero Alvarado has done her B.S from The University of Texas at San Antonio 2014, she is currently pursuing her M.S. from the University of Texas at San Antonio (2017). Her research interests is developing cell –based products for use in combat casualty care and healthcare settings. She has three years experience in manurfacturing cell-derived extra-cellular matrices in a GMP setting at the San Antonio based biotechnology company, StemBioSys, Inc. Published in Stem Cell Research and Therapy and presented at RegenMed SA conference in San Antonio, TX.

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