ANTENATAL MESENCHYMAL STROMAL CELL EXTRACELLULAR VESICLE TREATMENT PRESERVES LUNG DEVELOPMENT IN A MODEL OF BRONCHOPULMONARY DYSPLASIA DUE TO CHORIOAMNIONITIS

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Abstract:

Background: Antenatal stressors such as chorioamnionitis (CA) increase the risk for bronchopulmonary dysplasia (BPD). Studies have shown that experimental BPD can be ameliorated by postnatal treatment with mesenchymal stromal cell-derived extracellular vesicles (MEx). However, the antenatal efficacy of MEx to prevent BPD is unknown. **Objective:** To determine whether antenatal MEx therapy attenuates intrauterine inflammation and preserves lung growth in a rat model of CA-induced BPD. **Methods:** At embryonic day (E)20, rat litters were treated with intra-amniotic injections of saline, endotoxin (ETX) to model chorioamnionitis, MEx, or ETX plus MEx followed by cesarean section delivery with placental harvest at E22. Placental and lung evaluations were conducted at day 0 and day 14, respectively. To assess the effects of ETX and MEx on lung growth *in vitro*, E15 lung explants were imaged for distal branching. **Results:** Placental tissues from ETX-exposed pregnancies showed increased expression of inflammatory markers NLRP-3 and IL-1ß and altered spiral artery morphology. Additionally, infant rats exposed to intrauterine ETX had reduced alveolarization and pulmonary vessel density (PVD), increased right ventricular hypertrophy (RVH), and decreased lung function. Intrauterine MEx therapy of ETX-exposed pups reduced inflammatory cytokines, normalized spiral artery architecture, and preserved distal lung growth and function. *In vitro* studies showed that MEx treatment enhanced distal lung branching and increased VEGF and SPC gene expression. **Conclusions:** Antenatal MEx treatment preserved distal lung growth and reduced intrauterine inflammation in a model of CA-induced BPD. We speculate that MEx may provide a novel therapeutic strategy to prevent BPD due to antenatal inflammation.