Antenatal Exosome Treatment Preserves Lung Structure, Vascular Growth, and Lung Function in a Model of Bronchopulmonary Dysplasia Due to Chorioamnionitis

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Background

Bronchopulmonary Dysplasia (BPD):
- BPD is the chronic lung disease of prematurity that is characterized by early disruption of lung growth and contributes to late morbidity and mortality.
- Severe BPD is associated with many comorbidities and can cause life-long complications that significantly affect quality of life and decrease life expectancy.
- Although the etiology of BPD is multifactorial, strong evidence has shown that antenatal factors, such as chorioamnionitis (CA), are associated with an increased risk for BPD.
- Antenatal endotoxin (ETX) exposure as an experimental model of CA causes sustained disruption of lung alveolar and vascular growth, hallmark findings in BPD.

Mesenchymal Stromal Cell (MSC)
Exosomes (MEx):
- MEx are secreted membrane vesicles from MSC that modulate many cellular functions, including growth, differentiation and function in health and disease.
- Experimentally, MEx has shown promising effects in preventing or restoring lung function in models of lung disease.
- Postnatal treatment with MEx can improve lung structure in experimental BPD due to postnatal hypoxia, however, the potential efficacy of MEx for the prevention of BPD due to antenatal stress is unknown.

Study Questions

- Will intra-amniotic injection of MEx:
  - Preserve vessel and alveolar growth and improve lung structure in infant rats exposed to antenatal ETX?
  - Improve lung function in infant rats exposed to ETX?

Methods

- All animal procedures and protocols approved by the Animal Care and Use Committee at the University of Colorado Health Sciences Center.
- Timed pregnant Sprague-Dawley rats were used for this study.

Hypothesis

Antenatal MEx treatment will prevent the development of BPD in an experimental rat model of CA.

Results

Antenatal MEx Treatment Preserves Lung Alveolar Growth in BPD

Antenatal MEx Treatment Preserves Lung Vascular Growth in BPD

Summary

- Intra-amniotic ETX impairs alveolar and vascular growth and lung function in infant rats.
- Antenatal MEx injections preserve lung alveolar and vascular growth after ETX-exposure in utero.
- Antenatal MEx treatment restores lung function (as measured by resistance and compliance) to levels consistent with saline-treated controls.

Conclusion

Intra-amniotic MEx preserves lung alveolar and vascular structure and improves lung function in infant rats with experimental BPD induced by antenatal ETX.

Speculation

Early antenatal MEx treatment may prevent the development of BPD in premature infants, especially in the clinical setting of antenatal inflammation.

Disclosures

Exosomes used in these studies are provided in collaboration with the Kouroumbas lab at the Department of Neonatology at Boston Children’s Hospital, Harvard Medical School, in conjunction with United Therapeutics.