Title of Abstract:

Mesenchymal Stem Cell Biomakers Prevent Bronchopulmonary Dysplasia via Suppression of Lung Inflammation

Name of Abstract Submitter:

Muhammad Aslam, MD - Neonatologist

Organization:

University of Irvine, California

Co-Author / Co-Investigators:

Meghali Singhal1, Angele Nalbandian1, Robin Lagrandeur1, Fayez Bany- Mohammed1, Cherry Uy1, Peter Donovan3, Dan Cooper2, Muhammad Aslam1

INSTITUTIONS (ALL):

1. Pediatrics, UC Irvine, Irvine, CA, United States.

2. Pediatric Pulmonology, UC Irvine, Irvine, CA, United States.

3. Molecular and Cell Biology, UC Irvine, Irvine, CA, United States.

Abstract Description:

Background: Bronchopulmonary dysplasia (BPD) is a chronic debilitating lung disease of preterm infants leading to arrested alveolar development with long term morbidity and high mortality. Current therapies lack effectiveness and cause undesirable side effects. Our work utilizing bone-marrow derived mesenchymal stem cells conditioned-media (MSC-CM) have shown protective effects in mouse BPD models. Analysis of the MSC-CM identified Osteopontin (Opn) and Macrophage colony stimulating factor 1 (Csf1), as key mediatros (biomarkers) leading to protection against BPD. Our pilot feasibility study demonstrated feasibility of detection of Opn and Csf1 in tracheal aspirate fluid (TAF) of preterm infants via immunoassay.

Objective: We hypothesized that the lack of above MSC biomarkers at birth leads to development of BPD via uncontrolled TGF-b1 activity. Our objectives were to determine the levels of Opn, Csf1, and active TGF-b1 in the TAF of preterm infants in the first week of life and correlate them with later development and severity of BPD. Design/Methods: Infants less than 32 weeks' gestational age and/or less than 1500 gms birth weight who were intubated within 24 hours of life were enrolled into the study. The first TAF sample was obtained at intubation before any exogenous surfactant administration. The second sample was obtained at extubation

or on the 4th day of life if still intubated. Levels of Opn, Csf1, TGF-b1, and secretory IgA were analyzed using immunoassay. Secretory IgA was used as control to correct for TAF volume. Infants were followed prospectively for outcome data including the development of BPD (oxygen requirement at 36 weeks' corrected gestational age).

Results: To date, 29 infants have been enrolled and TAF samples obtained. Subjects were similar in their baseline maternal and neonatal characteristics. Standard curves were used from our pilot study to analyze data. 19 of 29 subjects developed BPD. Levels of Opn and Csf1 were lower at birth for BPD infants when compared with infants who did not develop BPD (Opn 9 versus 18 ng/mL; Csf1 2010 versus 3266 pg/mL). BPD infants failed to suppress M1 macrophage surge with a higher TGF-b1 levels when compared with infants who did not develop BPD (TGF-b1 153 versus 123 pg/mL).

Conclusion(s): MSC biomarkers, Opn and Csf1, prevent BPD at birth by suppression of lung inflammation (M1 macrophage surge and active TGF-b1). Further work is underway to determine the target pathways involved in BPD protection.

Funding Acknowledgement (if applicable):

UCI Division of Neonatology Grant

UCI Neonatal-Perinatal Medicine Fellowship Grant

UCI ICTS KL2 Award

The Susan Scott Foundation