

Hyperoxia-Induced Lung Engraftment of Human Cord Blood Monocytes in a Humanized Mouse Model of Bronchopulmonary Dysplasia

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Abstract: Bronchopulmonary dysplasia (BPD) is often characterized by chronic lung injury secondary to high levels of oxygen during the neonatal period. Previous studies have demonstrated that administration of human cord blood (CB) monocytes results in decreased alveolar damage due to hyperoxia exposure but fail to demonstrate engraftment of these cells in the lungs of the animal model. We hypothesize that administration of human CB monocytes in MISTRG humanized mice ameliorate the BPD-like phenotype after hyperoxia exposure. Cord blood was collected after delivery and processed within 36 hours. Monocytes and CD34+ cells were isolated by magnetic-activated cell sorting and intra-hepatically injected at Day 0-1 of life. Pups were then exposed to normoxia (21% oxygen) or hyperoxia (85%) for 7 days. Lungs and livers were harvested, and H&E staining and immunohistochemistry for human CD45 was performed. Alveolar count and area were measured and CD45 expression was quantified. Immunohistochemistry confirmed human CD45 expression in the liver and lung after intra-hepatic injection of CB cells. Presence of human CD45+ cells in the liver was more pronounced with CB monocytes versus CD34+ cells and in mice exposed to hyperoxia versus normoxia ($P < 0.01$). Engraftment of CD45 cells was demonstrated in lungs of mice injected with both monocytes and CD34+ cells, and in mice injected with sorted monocytes, but not in mice treated with isolated CD34+ cells. Preliminarily, CD45 positively-stained cells appeared more prominent with hyperoxia exposure, and lung histology revealed a trend towards increased alveolar number and decreased alveolar area in mice injected with sorted CB monocytes. These associations indicate that intra-hepatic delivery of CB-derived monocytes leads to engraftment of human CD45+ cells in murine lungs and attenuates alveolar simplification due to hyperoxia. Completion of the above studies will demonstrate the extent to which CB monocytes may have a protective effect on neonatal lungs exposed to hyperoxia.