THE ROLE OF HYDROXYMETHYLATION IN BRONCHOPULMONARY DYSPLASIA

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Background: Bronchopulmonary dysplasia (BPD) is one of the most frequent and important morbidities for infants born prematurely. Hyperoxia and other noxious stimuli lead to BPD but the specific cellular control leading to this pathophysiology remains unclear. DNA methylation to silence expression is the most well-known epigenetic modification with more recent studies finding hydroxymethylation through Ten-Eleven Translocation (TET) leading to increased DNA expression. The role of hydroxymethylation in the development of BPD remains unknown. We hypothesis that exposure of the developing lung to hyperoxia leads to DNA hydroxymethylation (5hmC) by ten-eleven translocation (TET), and these epigenetic changes contribute to the development of bronchopulmonary dysplasia (BPD).

Materials/Methods: Newborn C57Bl/6 mice were placed in 95% oxygen chamber for 5 days then allowed to recover in 21% O2. Mice were then sacrificed at birth, PN5, PN14, and PN42. Bronchoalveolar lavage samples were collected to compare cell counts between hyperoxia and normoxia exposed animals. Frozen samples were stained with H&E and compared used mean linear intercept and radial alveolar count. TET RNA levels will be assessed using quantitative PCR. TET protein levels will be assessed using immunohistochemistry. Global DNA hydroxymethylation signature is assessed using cytosine-5-methylenesulfonate immunoprecipitation (CMS-IP) sequencing.

Results: Results pending; currently DNA and RNA isolated, will perform global hydroxymethylation analysis on DNA and QT-PCR on mRNA for TET protein levels as well as immunohistochemistry for TET proteins; all to be completed by the time of presentation with updated results.

Conclusions: As above; to be seen with sample processing and final analysis.

Images / Graph / Table