Abstract Title:

The Genetic Variations of WISP1 Protein in the Highly Conserved Wnt Pathway are Associated with Development of BPD in ELBWs

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Introduction: BPD is the most common pulmonary complication of ELBW infants. Twin studies have revealed genetic foundations for the susceptibility of preterm infants to BPD. Highly conserved WNT pathway is involved in early fetal lung morphogenesis. WISP1 and WIF1 genes of this pathway are tightly regulated during early lung branching morphogenesis. Disruptions of these gene expressions are associated with pulmonary dysfunctions in early postnatal life. Exogenous WISP 1 promotes proliferation of type II cells and fibroblast deposition in lung parenchyma, which is characteristic of BPD. SMAD1 is involved in pulmonary smooth muscle cell proliferation through the Wnt pathway. The downstream effects are pulmonary endothelial destruction and smooth muscle cell proliferation, also characteristic of BPD. We hypothesize that WISP1, and SMAD1 variants are associated with the progression to BPD in ELBW infants.

Methods: DNA from buccal swabs of ELBW infants (whose parents gave informed consent) was isolated and subjected to allelic discrimination by RT-PCR, using specific probes for WISP1 (rs2929973) and

SMAD1 SNP (rs763560). BPD was defined as oxygen dependence at 36 weeks PMA. ?2, t-test, and z-test were performed, with $P<0.05$ denoting statistical significance.

Results: Infants who progressed to BPD had lower birth weights ($p<0.0001$) and were more immature ($p<0.0001$) than those who did not develop BPD. The SNPs analyzed for WISP1, rs2929973 ($p=0.001$) and SMAD1, rs763560 ($p=0.032$) showed statistically significant differences between the two groups of ELBW infants.

Conclusion: Genetic variants of WISP1 and SMAD1 are associated with BPD in ELBW infants. We speculate that these genetic variants influence pulmonary and epithelial cell dysregulation following preterm birth resulting in altered morphogenesis leading to BPD.