Transcriptome analysis in a preterm rabbit model of hyperoxia-induced lung injury to identify novel therapeutic targets

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Objective

Bronchopulmonary dysplasia (BPD) remains an important complication of preterm birth. At the molecular level, BPD is not yet completely understood. In this study we applied whole transcriptome sequencing, on tissues harvested in the hyperoxia-induced preterm rabbit model for BPD. Our primary goal was to identify pathways involved in BPD, which eventually may lead to novel therapeutic targets for prevention or treatment of BPD.

Methods

Transcriptome analysis by mRNA sequencing was done on lungs from 4 preterm rabbit pups (28 of 31 days of gestation, early saccular stage), incubated in hyperoxia (95% O2) for 7 days, and on a control group of 4 preterm pups kept in normoxia (21% O2). Transcriptomic data were analysed using array studio (OmicSoft) and ingenuity pathway analysis. Upstream analysis was used to identify upstream expression regulators responsible for the expression changes observed in the hyperoxia group.

Results

Clear consistent gene-expression differences were observed. We identified 2216 significantly dysregulated transcripts following hyperoxia. As expected some were coding for inflammatory mediators (IL8, CCL2, MMP3…), or lung development (ACE, PPARγ…) and vasculogenesis (VEGF, angiopoetin2…), consistent with what has been previously reported using different tools. Our findings support a beneficiary role for clinically or experimentally used therapies for BPD (vitamin A, corticosteroids, caffeine…) yet also suggest some new targets.

Conclusion

We first used whole transcriptome analysis on hyperoxia-induced, preterm rabbit lung tissue. It enabled to confirm known pathways involved in BPD, and supported the use of current treatments, yet also identified a number of potential new targets.