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Title: Regulation of microRNA-mRNA target pairs in a model of bronchopulmonary dysplasia

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Body: Background: Bronchopulmonary dysplasia (BPD) is a chronic lung disease of premature neonates characterized by arrested pulmonary alveolar development. Objective: Because microRNAs (miRNAs) may regulate the translation of messenger RNAs (mRNAs) during normal lung organogenesis, we hypothesized that an experimental model of BPD would be characterized by the altered expression of miRNAs and their mRNA targets. Methods: Neonatal mice were exposed to 80% oxygen (O_2) or room air (RA) for either 14 or 29 days. Lung histology was assessed using standard techniques. Comprehensive miRNA and mRNA profiling was performed using lung tissue from each group. Potential direct mRNA targets of miRNAs were systematically predicted through miRNA-mRNA correlations and computational mapping in miRBase. Functional significance was investigated using Gene Ontology (GO) term enrichment analysis for miRNA regulatory networks using the DAVID and MetaCore databases. Results: At both 14 and 29 days, the lungs of O_2 mice displayed histological changes consistent with BPD. Between the two time points we identified 2,714 mRNAs and 66 miRNAs that were dynamically regulated by O_2 exposure. All but one of the miRNAs were up-regulated. We identified 581 dynamically regulated, direct mRNA targets of these miRNAs by computational mapping in miRBase. Gene ontology enrichment and pathway analysis revealed that hyperoxia modulated genes involved in a variety of lung developmental processes, including cell cycle, cell adhesion, inflammation and angiogenesis. Conclusion: A murine model of BPD is characterized by dynamic regulation of miRNAs and their computationally predicted, developmentally relevant mRNA targets.