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ANALYSIS OF POTENTIAL BIOMARKERS OF BRONCHOPULMONARY DYSPLASIA (BPD) IN A NEWBORN RAT VENTILATION MODEL

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Background: BPD is a chronic lung disease affecting preterm infants leading to increased morbidity and mortality. Main risk factors include premature birth, mechanical ventilation (MV), hyperoxia and inflammation. A newborn rat ventilation model with reversible intubation was used to study delayed gene expression modifications to increase our understanding of its pathophysiology.

Methods: LPS was injected intraperitoneally (2mg/kg) to male rat pups on postnatal day 4 or 5 to mimic systemic inflammation. Twenty-four hours after injection they were intubated and ventilated for 6h with tidal volume of 15ml/kg and 21% or 60%O_2. After weaning from anesthesia, they were returned to their mothers for 48h. Gene expression was measured by Affymetrix®Gene-Arrays in four groups (n=9/Group) and verified by qPCR.

Results: Expression changes were mainly found in genes involved in inflammation and extracellular matrix remodeling. Among them MMP-9 and several of its regulator genes were significantly modified.

	Group I: Control	Group II: LPS	Group III: LPS+MV+21%O2	Group IV: LPS+MV+60%O2
MMP-9	1	1.39±0.22*	1.39±0.22*	1.64±0.36*
CAMP	1	2.22±0.50*	2.04±0.46*	2.78±0.68*
NGAL	1	1.84±0.08*	2.14±0.21*	2.14±0.20*
NP4	1	4.12±0.19*	3.28±0.17*	3.29±0.23*

[Table 1: qPCR fold changes]

Conclusion: MMP-9 is known to be important in lung development, angiogenesis and tissue repair. In our BPD-model, MMP-9 pathway seemed to be a central target. Several genes increasing MMP-9 activity were synergistically upregulated, highlighting its potential role in lung injury and repair. Therefore, the role of MMP-9 in the pathophysiology of BPD deserves further investigation.