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A Highly Dysregulated Circular RNA Profile in Lungs from Patients with Congenital Diaphragmatic Hernia could serve as a Potential Prenatal Biomarker

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Background:

Every 10 minutes, a baby is born with Congenital Diaphragmatic Hernia (CDH), a disease characterized by a hole in the diaphragm and underdeveloped lungs. Of these babies, 30 - 50 % still die. Epigenetic factors are involved in the pathogenesis. Circular RNAs are powerful epigenetic regulators of gene expression, especially in embryonic development. Their involvement in abnormal lung development is still unknown.

Objective:

We hypothesized that circular RNA profiles of human CDH lungs are dysregulated and aimed to determine if they can serve as potential biomarkers for CDH in the future.

Methods:

Lung tissues for CDH (n=6) and healthy Controls (n=6) were obtained for mid-pregnancy cases and end-pregnancy cases from deceased subjects. After total RNA isolation we profiled the circular RNA expression via circular RNA microarray (Arraystar Inc., Rockville, MD, USA). In depth statistical data analysis was performed with R Studio. Pathway analysis was accomplished with KEGG and Ingenuity Pathway Analysis (Qiagen).

Results:

CDH lungsshowed an altered circular RNA profile compared to lungs from healthy controls. Partial least squares discriminant analysis segregated clearly into two independent clusters. VIP-score analysis revealed the most important circular RNAs responsible for the profile alterations. In total, 16 circular RNAs were significantly altered (Fold change > 1.5; p-value < 0.05) at mid-pregnancy and 35 circular RNAs at end-pregnancy.

Conclusion:

Circular RNA profiling of human hypoplastic CDH lungs and healthy controls at two different developmental time points reveals significant differences between the two groups. Future studies will include prenatal circular RNA assessment of maternal plasma and thus may uncover potential non-invasive and early biomarkers for CDH.