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Abstract Title

Dysregulation of Deleted in Colorectal Cancer (Dcc) and its Derived Circular RNAs in a Nitrofen-Induced Rat Model of Congenital Diaphragmatic Hernia

Authors

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Background

Deleted in colorectal cancer (Dcc) is a transmembrane receptor protein that plays a critical role in cancer, cell death and neural development. Its pattern in rat fetal lungs with congenital diaphragmatic hernia (CDH) has not been examined. Circular RNAs (circRNAs) have been implicated as biomarkers and regulators in various diseases. Two differentially expressed circRNAs originating from Dcc were identified in rat lungs following nitrofen induction using a microarray and verified in databases.

Objective

We aimed to investigate Dcc expression and its two derived circRNA isoforms (circDcc(s)) which remain elusive during lung development in the nitrofen CDH model.

Methods

Fetal lungs from control and nitrofen-treated rats on embryonic day (E) 15, E18 and E21 were collected. Gene expression was quantified by RT-qPCR. Immunofluorescence assays were performed to examine

the spatio-temporal abundance of Dcc in situ. To identify the back-splice junction (BSJ) sequences of circDcc(s), divergent primers were designed to amplify the BSJ, and PCR products were validated by Sanger sequencing. The expression profile of circDcc(s) was also investigated using BaseScope™ in situ hybridization. Biological functions of circDcc(s) were predicted in silico.

Results

Parental gene expression was upregulated in CDH lungs at E21 ($p < 0.001$) and E18 ($p = 0.002$) with no difference at E15. Dcc protein was localized in the bronchial airway epithelium and the abundance appeared higher in nitrofen groups at E21. The specific circDcc-BSJs were revealed by custom probes. Sanger sequencing confirmed the BSJ sequences of circDcc(s). In silico, biological functions of circDcc(s) were predicted, suggesting their potential involvement in lung development.

Conclusion

The Dcc gene and circDcc(s) show abnormal expression in nitrofen-induced CDH lungs with Dcc protein abundance also appearing increased. Functional assays overexpressing circDcc(s) in BEAS2B cells are currently underway to elucidate the mechanistic crosstalk between the parental gene and its circRNA isoforms.