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Basic Science

Abstract Title
PROFILING DIFFERENTIAL EXPRESSION OF DCC AND ITS DERIVED CIRCULAR RNAS IN CONGENITAL DIAPHRAGMATIC HERNIA

Background
Circular RNAs (circRNAs) are highly stable non-coding RNAs derived from protein- and non-coding genes. They have tissue- and developmental-specific expression, however their role in normal and abnormal fetal lung development is unknown. We previously showed specific circRNA expression signatures in a rat model of nitrofen-induced congenital diaphragmatic hernia (CDH). We identified differential expression (DE) of two circRNA isoforms derived from Deleted in colorectal cancer (Dcc) in embryonic day 21 (E21) nitrofen lungs in vivo. Expression of the host gene and its derived circRNAs of Dcc have not been characterized in rat and human CDH. Dcc is a transmembrane receptor protein that plays critical roles in the regulation of tumor suppression, cell death and neural development.

Objective
This study aims to define the spatio-temporal distribution of Dcc during normal and abnormal fetal lung development in nitrofen-induced CDH and compare expression of tissue specific derived circRNAs and its parental gene.

Methods
To investigate the expression of Dcc and its derived circRNAs, lungs from control and nitrofen-induced CDH rats on embryonic day 15 and 21 (E15 and E21) were isolated. The gene and back-splice junction expression of both parental genes and its circRNAs were characterized using RT-qPCR assays. BaseScope™ in situ hybridization was used to investigate circRNAs tissue expression.

Results
We demonstrated DE and distribution of Dcc between control and nitrofen-induced left lungs. It was lower in nitrofen-induced male than female lungs at E15 ($p=0.0491$). It was higher in nitrofen-induced CDH rats than controls at E21 ($p=0.0225$). The circRNAs were validated while they were not detected in the circATLAS database. Dcc circRNA expression was confirmed in fetal lung tissues using the BaseScope™ system.

Conclusion
We identified the spatio-temporal expression of circDcc variants and their parental gene expression using a CDH rat model and found that these expression patterns exhibited sex-specific differences.

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