

CHRD 2024: Abstract Submission Form

Presenter Name

Marietta Jank

Presenter Status

Post-Doctoral Fellows

Role in the project

Design
Perform Experiments
Analyze Data
Write Abstract

Research Category

Basic Science

Title

circRNA EXPRESSION PROFILE TO IDENTIFY NOVEL MARKERS FOR ABNORMAL LUNG DEVELOPMENT IN THE NITROFEN MODEL FOR CONGENITAL DIAPHRAGMATIC HERNIA

Background

Circular RNAs (circRNAs) are highly stable non-coding RNAs and have a tissue- and developmental stage-specific expression; making them suitable biomarkers for congenital anomalies. Previously, we showed a unique circRNA profile in human congenital diaphragmatic hernia (CDH) lungs.

Objective

We aim to investigate circRNAs during abnormal lung development in the nitrofen rat model.

Methods

CircRNA profiles of nitrofen-induced and control lungs were compared at embryonic day (E)15 and E21 using a microarray. The results were validated with conventional PCR, amplicon sequencing, RT-qPCR and BaseScopeTM in situ hybridization. The CircRNA Function prediction Tool (CRAFT) was used to predict downstream pathways by miRNA interactions.

Results

The microarray revealed a circRNA biosignature specific for CDH, the developmental stage and sex. We validated circRNAs derived from the parental gene *Anp32e*, *Ppp3ca* and *TIAL1*. Expression of circAnp32e was increased in nitrofen-induced lungs at E21 ($p=0.004$) in both qPCR and in situ hybridization. At E15, the circAnp32e expression in total lungs did not differ between CDH and control lungs ($p=0.22$); but sex-disaggregated analysis revealed an overexpression in male pups ($p=0.034$). Further, in situ hybridization showed a distinct spatio-temporal expression pattern in early development with an increased signal for circAnp32e in the epithelium at E15. circTIAL1 showed a non-significant trend to overexpression in CDH lungs ($p=0.07$); and a statistically significant increase only in male pups ($p=0.0167$).

CircRNA::miRNA::mRNA interactions revealed pathway enrichment for inflammation/infection and neuron function/development. Furthermore, the alignment of human and rat mature circAnp32e sequences showed a 90% overlap between the two species which warrants further investigation in the pathophysiology of human CDH.

Conclusion

For the first time, we report circRNA profiling in nitrofen-induced CDH with a sex and tissue-specific expression pattern at early and late stages of abnormal lung development. Enrichment for pathways related to neuron function can guide new hypothesis formation on the pathogenesis of CDH.

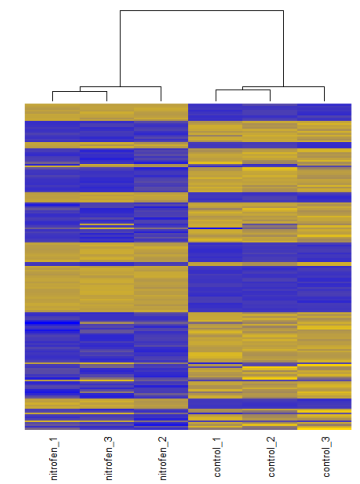
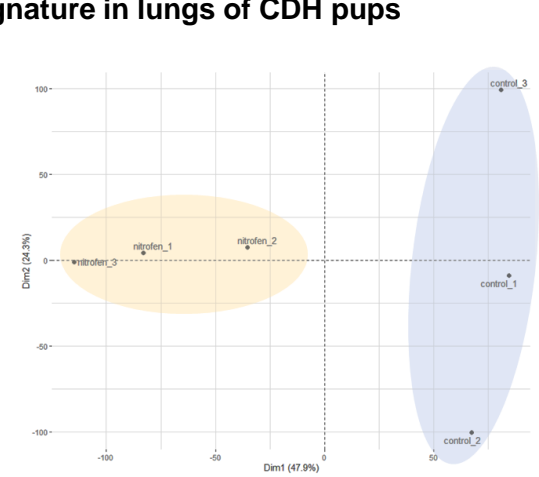
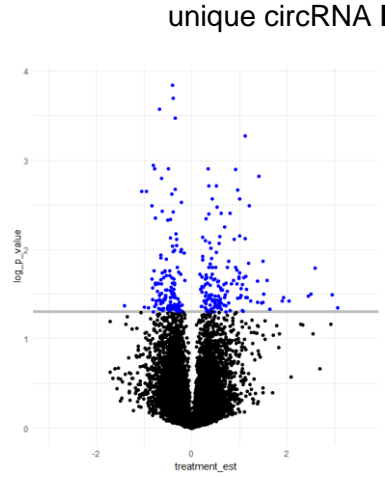
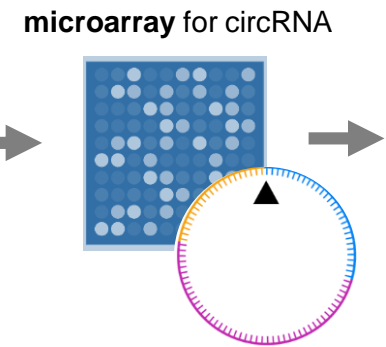
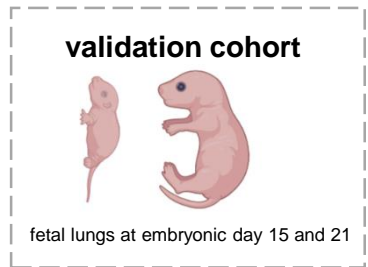
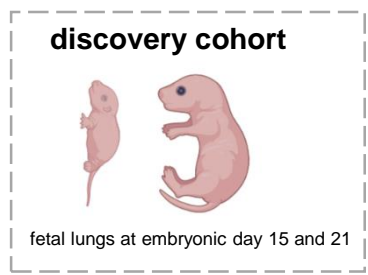
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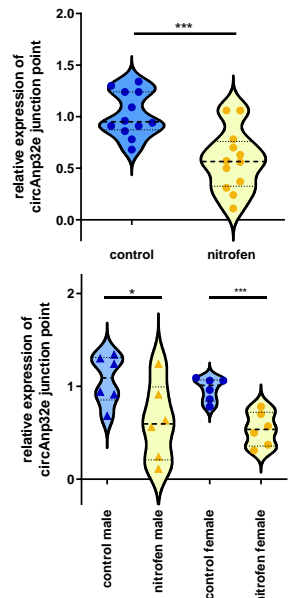
Authors

Name	Email	Role	Profession
Marietta Jank	marietta.jank@umanitoba.ca	Presenting Author	Graduate
Muntahi Mourin	muntahi.mourin@umanitoba.ca	Co Author	Graduate
Arzu Aptekmann	arzu.ozturk@umanitoba.ca	Co Author	Graduate
Nolan De Leon	deleonn@myumanitoba.ca	Co Author	Graduate
Matthew Kraljevic	matthew.kraljevic@umanitoba.ca	Co Author	Graduate
Richard Wagner	richard.wagner@medizin.uni-leipzig.de	Co Author	Graduate
Shana Kahnamoui	kahnamos@myumanitoba.ca	Co Author	Graduate
Yuichiro Miyake	yuichiro.miyake@umanitoba.ca	Co Author	Graduate
Daywin Patel	daywin.patel@umanitoba.ca	Co Author	Graduate
Wai Hei Tse	andrew.tse@umanitoba.ca	Co Author	Graduate
Michael Boettcher	michael.boettcher@umm.de	Co Author	Associate Professor
Richard LeDuc	richard.leduc@umanitoba.ca	Co Author	Associate Professor
Richard Keijzer	richard.keijzer@umanitoba.ca	Co Author	Associate Professor

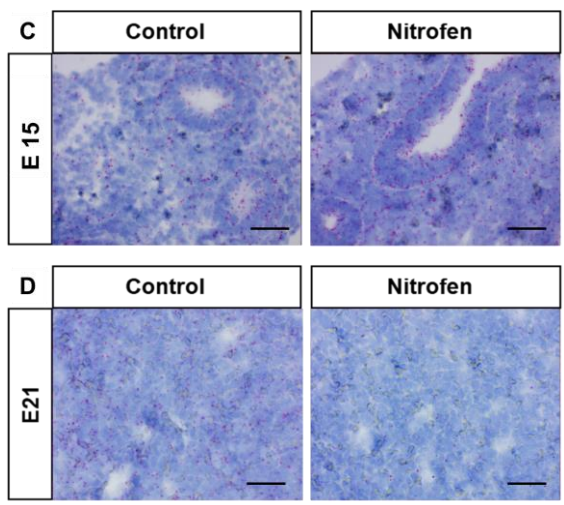
circular RNAs as novel biomarkers for abnormal lung development in Congenital Diaphragmatic Hernia



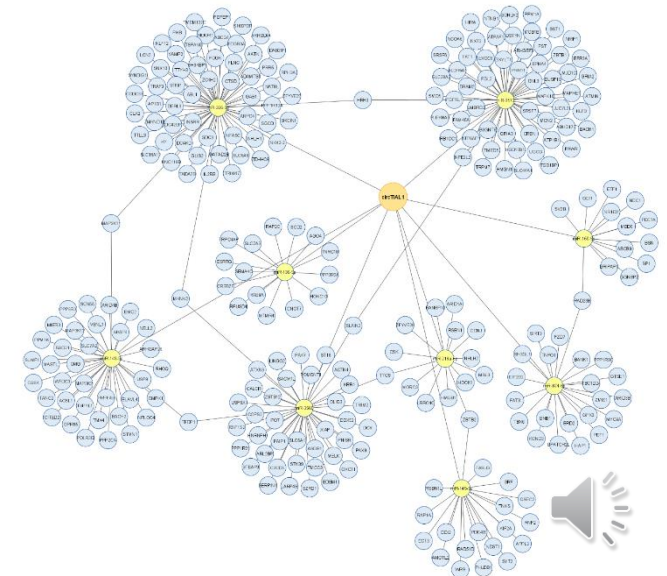
quantitative PCR



in situ hybridization



bioinformatics analysis



circRNA validation

