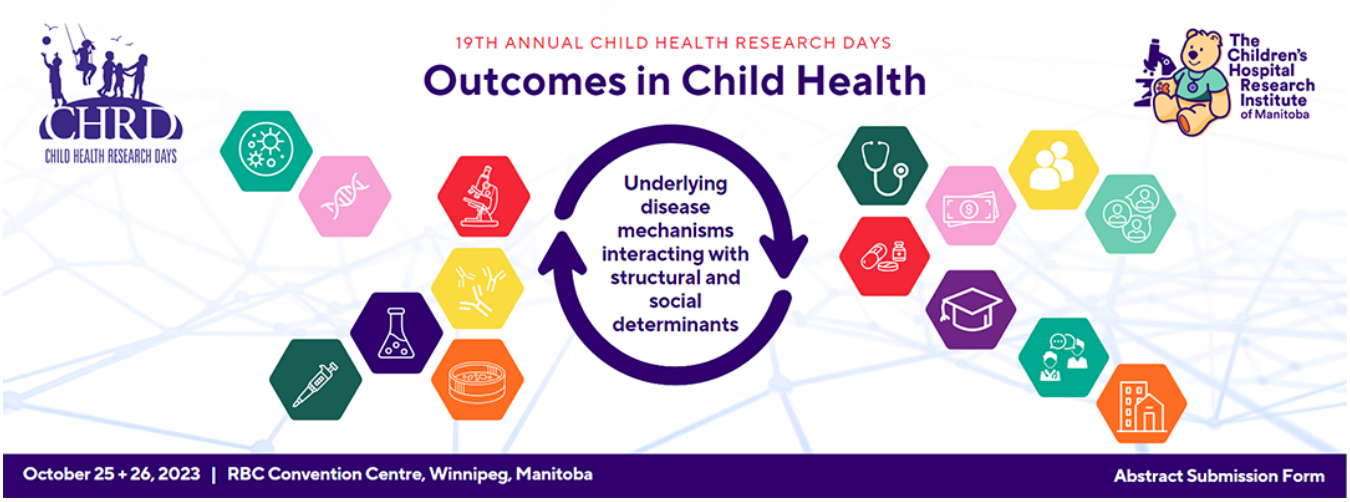

CHRD 2023: Abstract Submission Form

Submitter Name
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Presenter Name
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Presenter Status
PhD Student

Research Category
Basic Science

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Title
Male offspring exposed to cigarette smoke in early life are more likely to develop more lasting DNA methylation alterations than females

Background
Cigarette smoke (CS) exposure in early life causes long-lasting lung function defects even years after the exposure itself, and these effects may be sex-specific. Long term regulation of genes by epigenetic marks including DNA methylation (DNAm) may be one of the mechanisms maintaining the cellular memory of early life exposure.

Objective
Therefore, we investigated the effects of pregnancy, lactation or combined pregnancy and lactation (full) CS exposure on offspring lung DNAm across time, using an established mouse smoking model.

Methods
We exposed female mice to CS for 9 weeks, beginning three weeks prior to mating and ending at weaning, and cross-fostered pups at birth to generate pregnancy CS only, lactation CS only, both pregnancy and lactation CS, and control groups. We collected lungs from male and female offspring at birth, 8 and 16 weeks, and then at 63 weeks in female offspring alone. DNAm in the lungs was measured using the Illumina mouse methylation microarray, differential DNAm measured using multivariable linear regression and longitudinal data analyzed using one-way ANOVA.

Results
We found that the majority of changes in DNAm due to CS exposure were different between male and

female offspring. Only one site mapping to the Sgip1 gene was common between male and female offspring exposed to CS in the pregnancy period only. This gene has not previously been linked to smoking, but is known to be involved in maintenance of energy homeostasis, neurodevelopment, and in addiction. Our analyses also showed that CS exposure at any of the above time points is more likely to cause long-term DNAm alterations in male offspring compared to females in the same exposure group.

Conclusion
Together, these results reveal novel and sex-specific DNAm patterns established by smoke exposure in early life. The sex-specificity of our findings indicates that intervention or therapeutic development should include analysis of both sexes.

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