CHRD 2024: Abstract Submission Form

Presenter Name
Doris Onuzulu

Presenter Status
PhD Student

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Longitudinal effects of early life cigarette smoke exposure and impacts of secondary smoking in adulthood on offspring lung DNA methylation patterns established in early life

Background
Exposure to cigarette smoke (CS) in early life can cause sex-specific alterations to offspring health by perturbing numerous biological processes, some of which last well into adulthood, years after the cessation of smoke exposure. Previous research suggests that subsequent exposure to CS in later life intensifies the lung function alterations induced by early life CS exposure, a phenomenon known as priming. However, molecular mechanisms underlying these sex-specific and lasting health outcomes following early life CS exposure are unknown. In addition, the evidence for priming in mammals following repeated CS exposure remains limited, particularly concerning the role of epigenetic mechanisms like DNA methylation (DNAm) in establishing priming.

Objective
To fill these gaps, we investigated the longitudinal, sex and tissue-specific effects of early life CS exposure on offspring lung DNAm, and explored whether CS exposure in adulthood further alters DNAm patterns set by early life CS.

Methods
We exposed adult female BALB/c mice to CS for 9 weeks starting 3 weeks prior to mating, lasting throughout gestation and ending at weaning of pups (3 weeks after birth). At birth of offspring, we cross-fostered half of the offspring born to control dams with half of those born to CS-exposed dams, generating of four groups of offspring: control offspring with no CS exposure, offspring exposed to prenatal CS only, offspring exposed to postnatal CS only, and offspring exposed to both prenatal and postnatal CS. At 63 weeks of age, we further re-exposed a subset of offspring to whole body CS for 3 weeks. We collected lungs from offspring at multiple points over their lifespan: at birth, 8, 16 and 63 weeks of age. Physiological outcomes were assessed in form of lung function and lung immune cell infiltration and DNAm was measured across >200,000 CpGs in the mouse epigenome.

Results
Our results revealed distinct and sex-specific DNAm patterns in the mouse lungs, with male offspring being more likely to demonstrate long-lasting DNAm alterations than females. We also found substantially more differentially methylated sites in lungs of offspring exposed to CS both in early life and in adulthood compared to offspring exposed to CS in early life alone, suggesting priming of DNAm patterns in mouse lungs following early life CS exposure. Furthermore, we identified distinct DNAm patterns in offspring exposed to different doses of early life CS and discovered novel DNAm sites that could serve as biomarkers for prenatal CS exposure and smoking in adulthood.

Conclusion
This study establishes a framework for future research to investigate DNAm and other epigenetic mechanisms, as they offer valuable insights into the underlying mechanisms of health outcomes. It also

highlights the need for sex-specific interventions against CS and underscores the importance of distinguishing between the timing and duration of early life exposures, especially in human studies where such differentiation can be challenging.

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Authors

Name	Email	Role	Profession
Chinonye Doris Onuzulu	onuzuluc@myumanitoba.ca	Presenting Author	PhD student
Ola Salama	ola.salama@umanitoba.ca	Co Author	Data Analyst
Haziqa Kassim	haziqa.kassim@umanitoba.ca	Co Author	Laboratory Technician
Meaghan J. Jones	meaghan.jones@umanitoba.ca	Co Author	Assistant Professor