

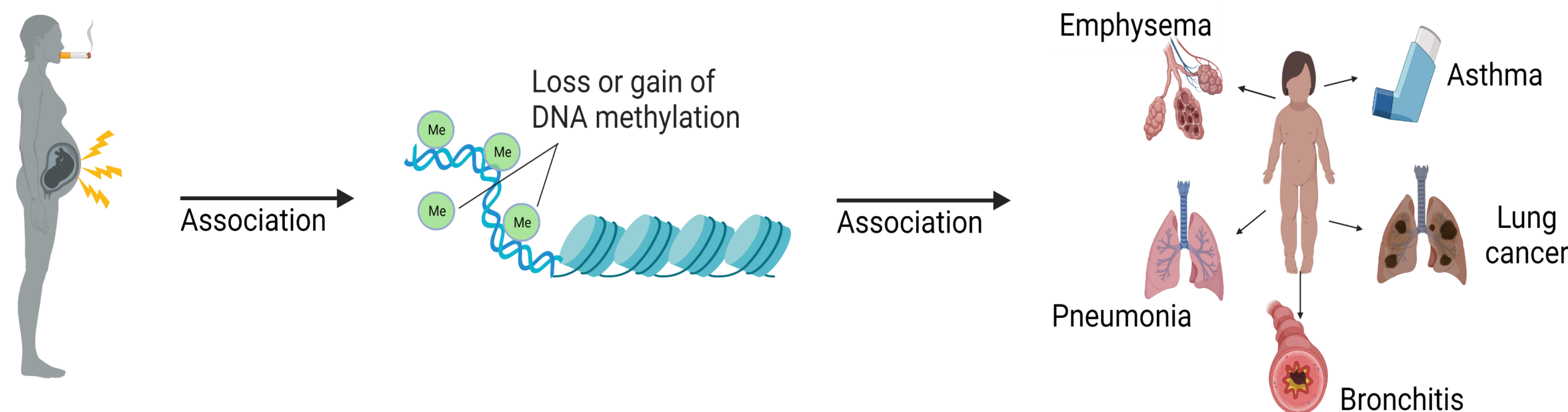
Smoking in adulthood re-establishes DNA methylation patterns set by early life cigarette smoke exposure

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INTRODUCTION

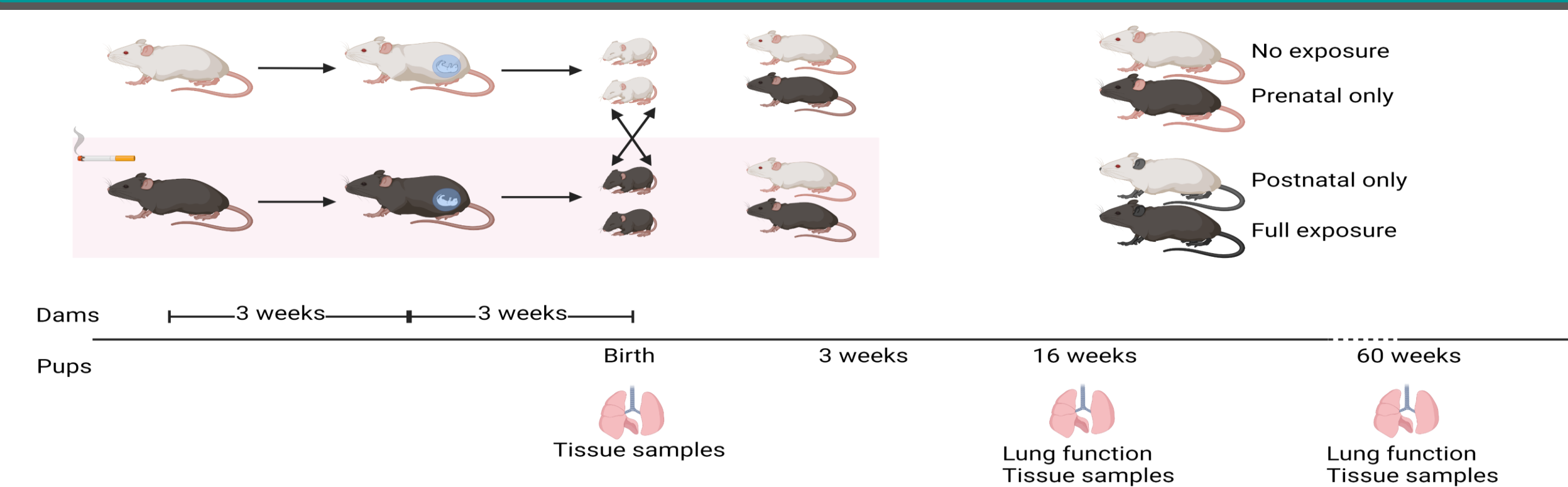
Human studies have identified association between early life cigarette smoke exposure, changes in DNA methylation in blood and peripheral tissues, and lung abnormalities



However,

- There have been no reports on effects of early life smoke exposure on offspring lung DNA methylation
- Human studies cannot completely exclude effects of postnatal smoking on offspring
- The longitudinal patterns established by early life smoke exposure remain unknown

METHODS



Dams were exposed to cigarette smoke beginning 3 weeks before mating and lasting till 3 weeks after birth. Offspring were cross-fostered at birth. Lung function and tissue collection 13 weeks after smoke exposure and at 60 weeks, after acute re-exposure to cigarette smoke.

DNA methylation measured by pyrosequencing

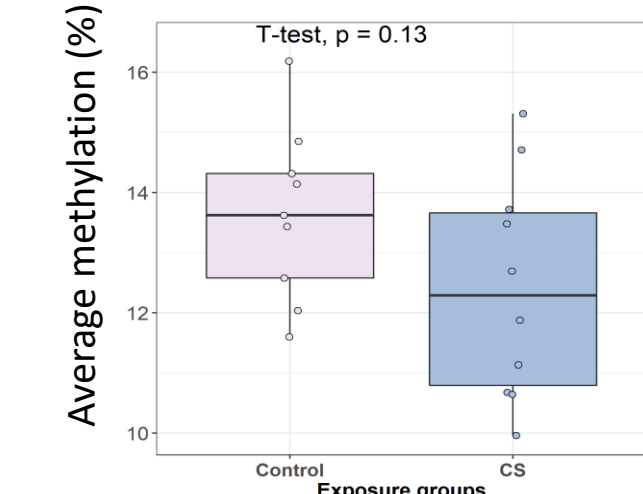
Second CS exposure

DNA methylation measured by pyrosequencing

RESULTS

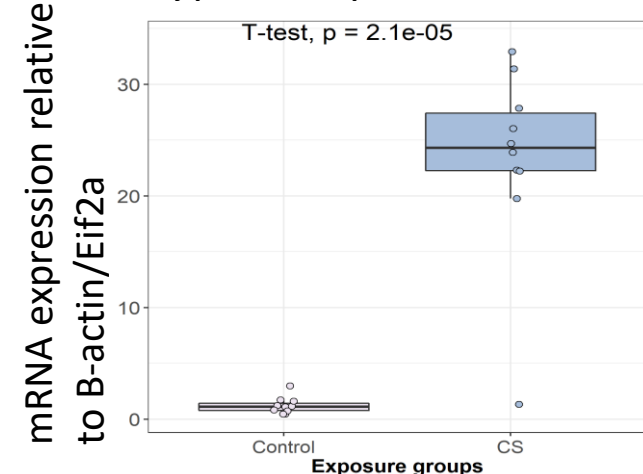
Exposure to cigarette smoke at different stages in the early life period altered offspring lung function, lung *Cyp1a1* expression and *Cyp1a1* DNA methylation in different ways

Cyp1a1 methylation at birth

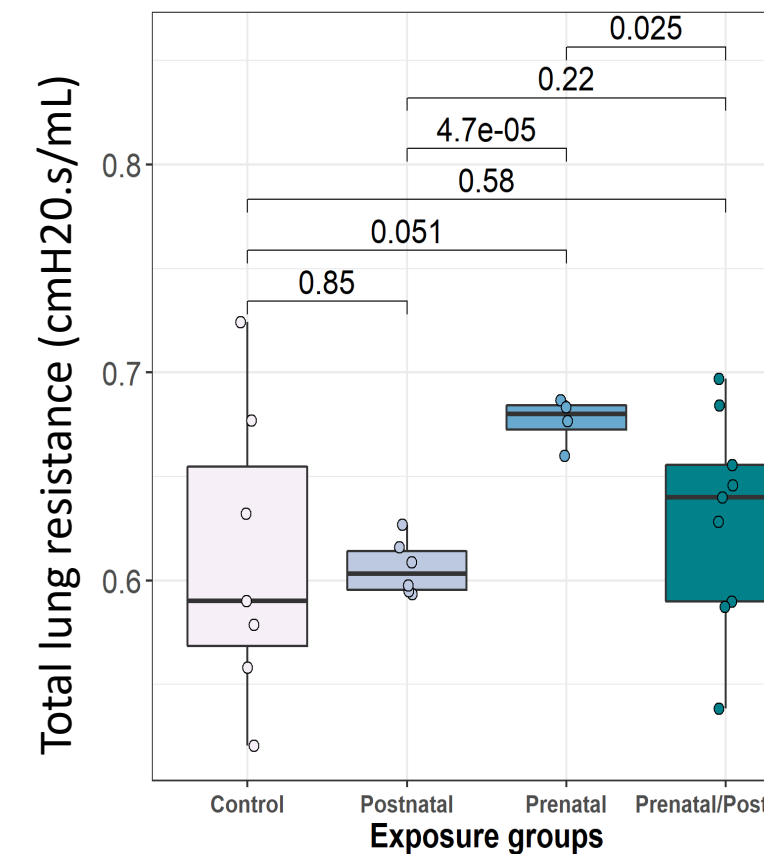


Prenatal exposure to cigarette smoke had no effect on lung *Cyp1a1* methylation at birth, but induced a significant increase in *Cyp1a1* expression at birth

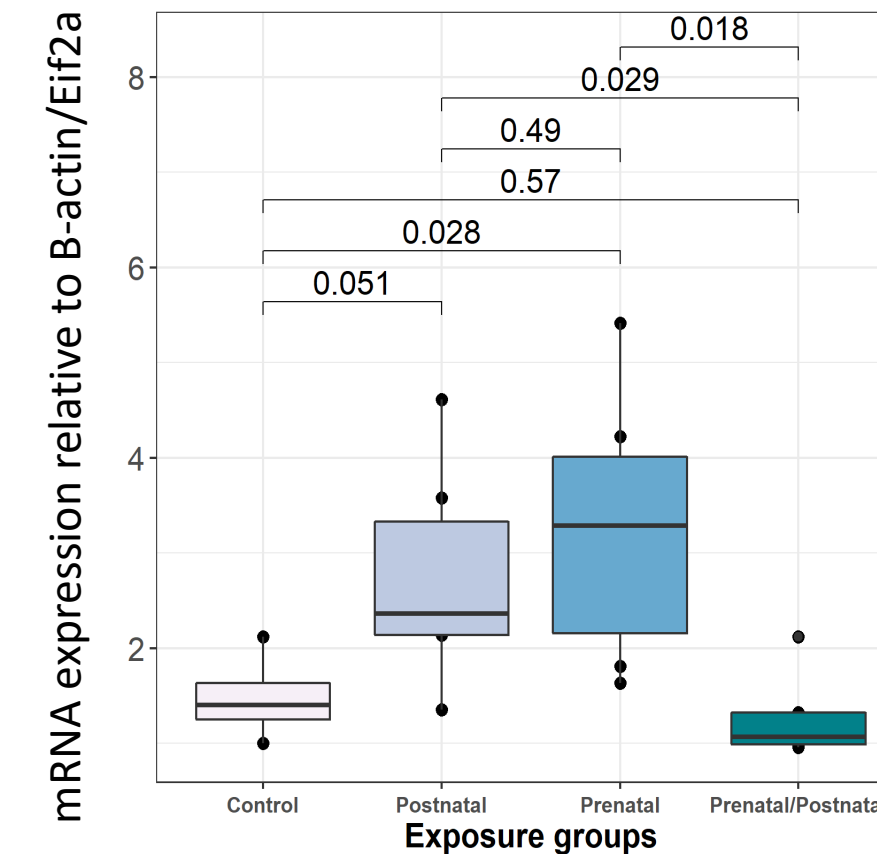
Cyp1a1 expression at birth



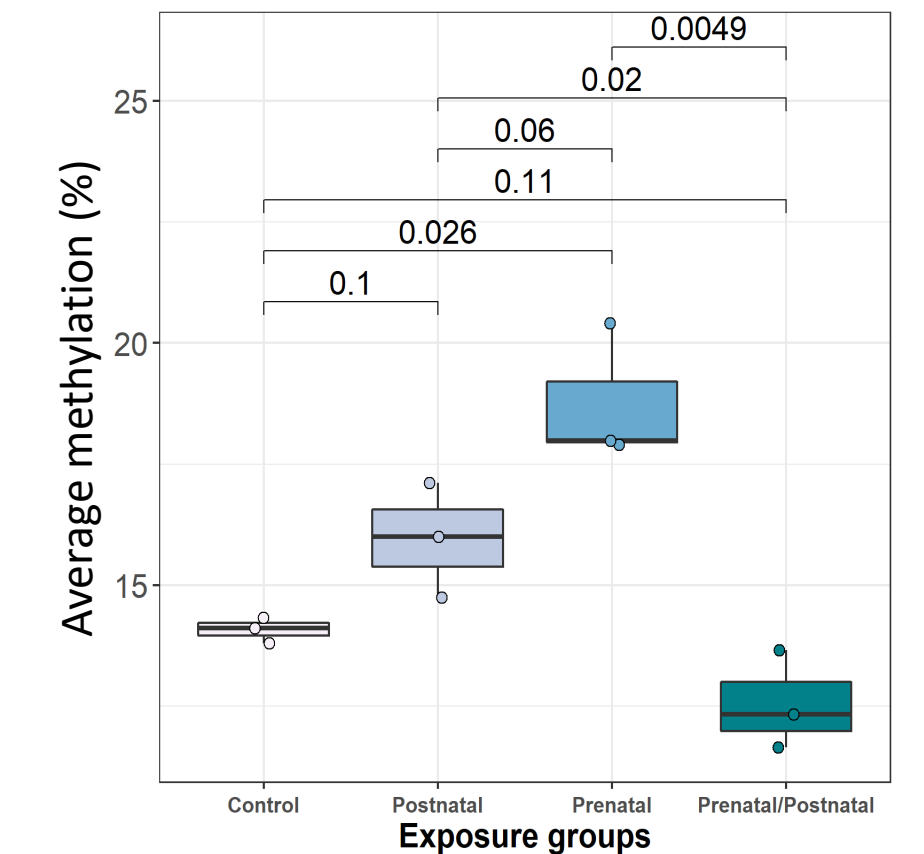
Lung function at 16 weeks



Cyp1a1 expression at 16 weeks

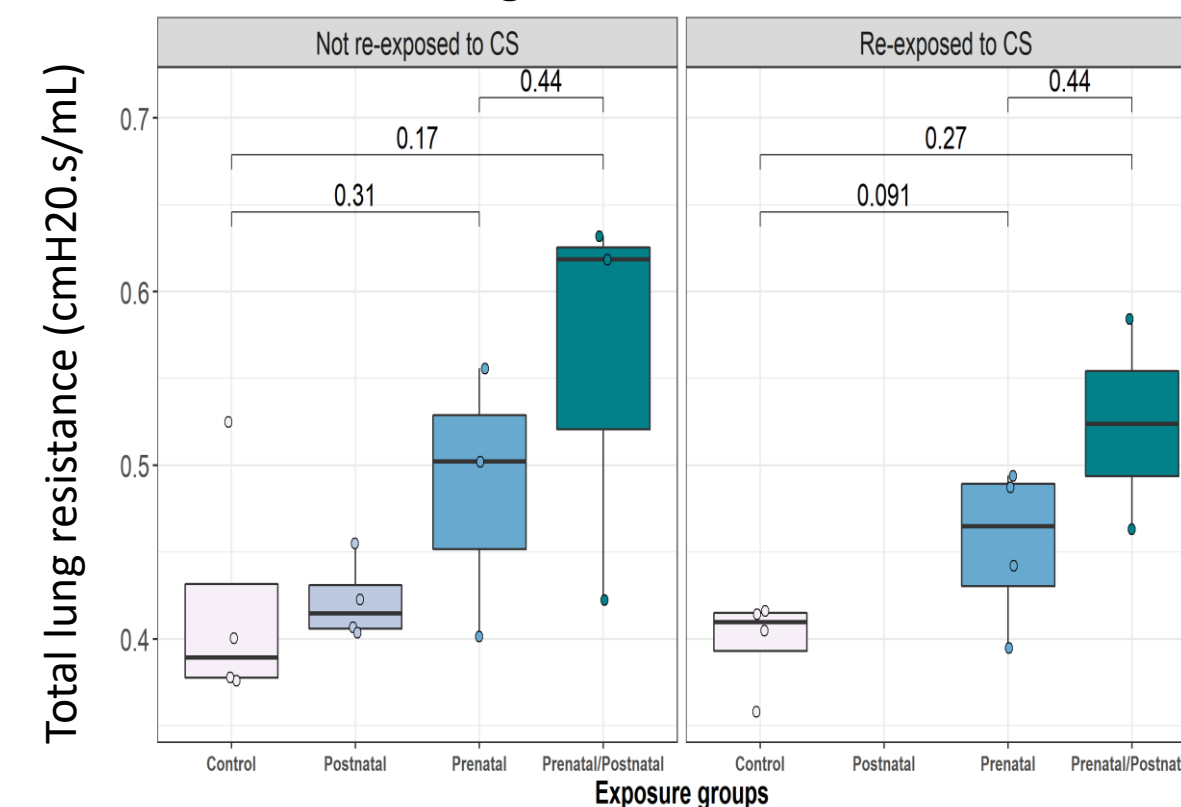


Cyp1a1 methylation at 16 weeks

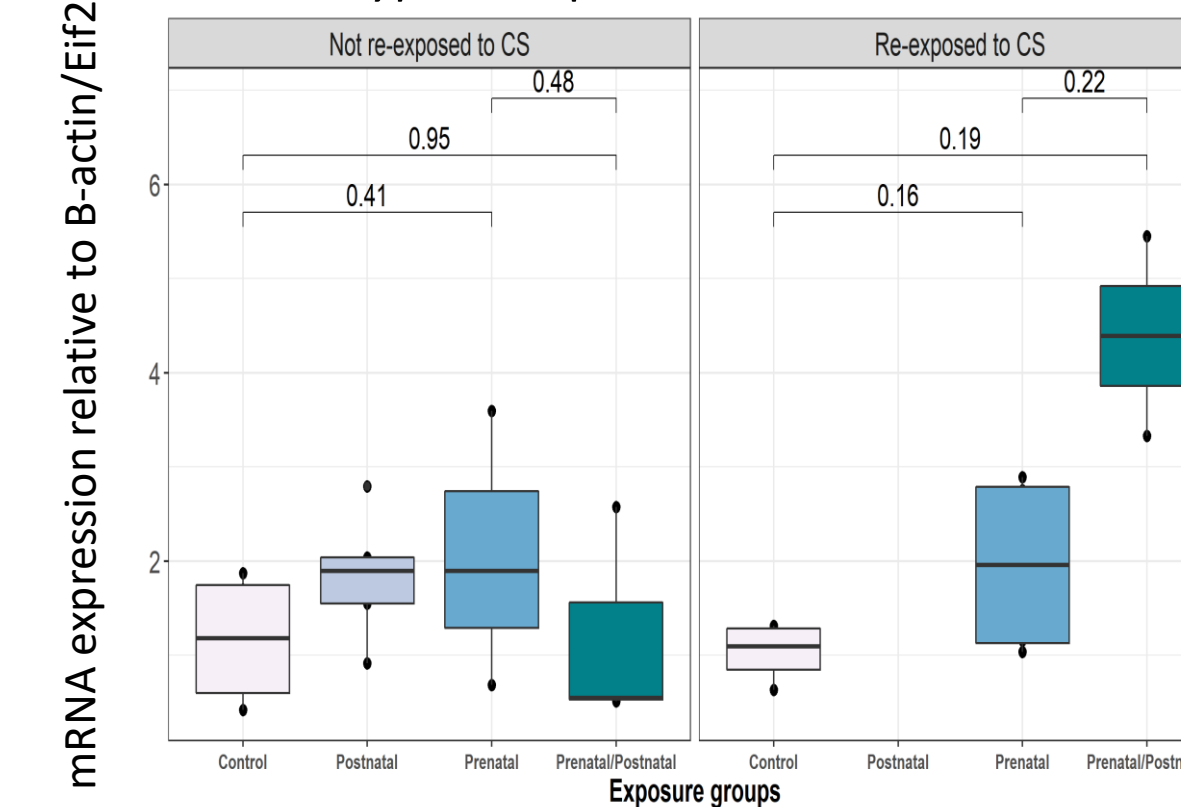


Re-exposure to cigarette smoke in adulthood decreased offspring lung function, increased lung *Cyp1a1* expression and re-established the lung *Cyp1a1* DNA methylation patterns set by early life smoke exposure

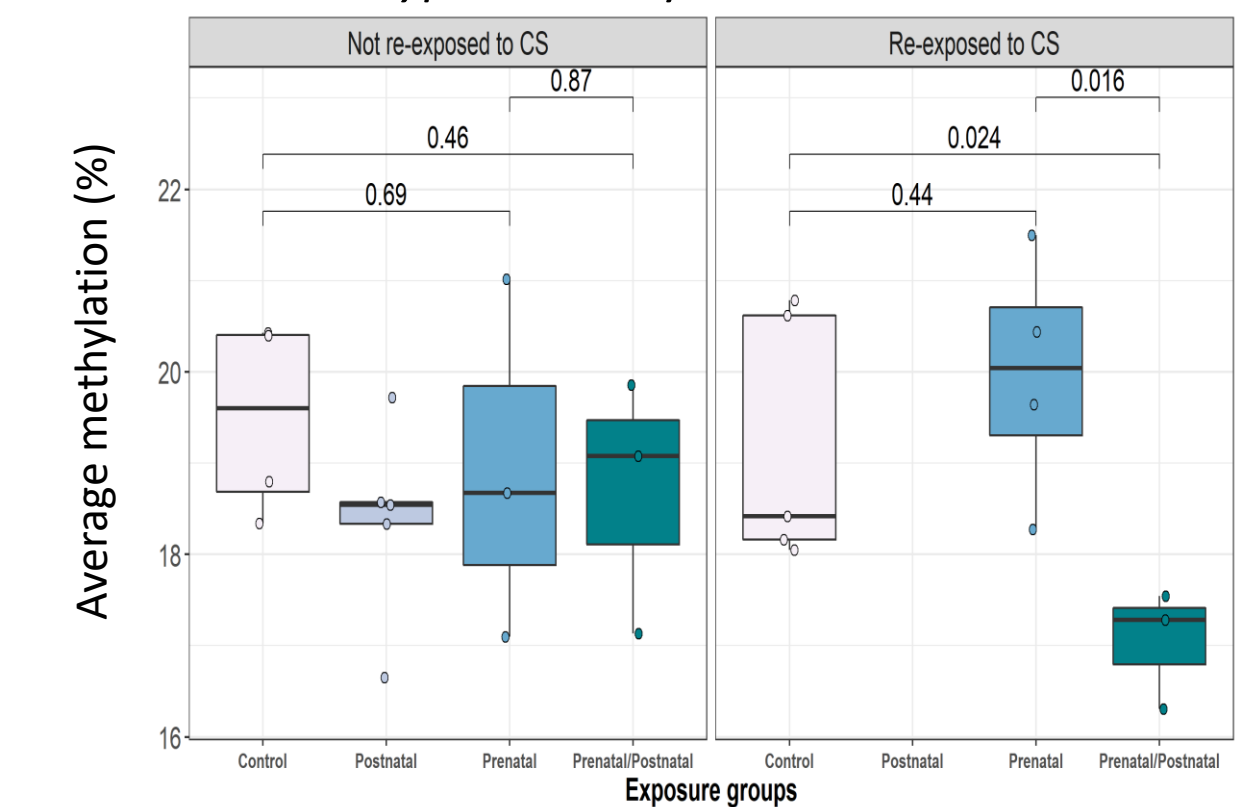
Lung function at 60 weeks



Cyp1a1 expression at 60 weeks



Cyp1a1 methylation at 60 weeks



CONCLUSION

Early-life exposure to cigarette smoke primes offspring lungs, causing phenotypic changes and transient DNA methylation changes which are easily re-established upon re-exposure to cigarette smoke in adulthood

ACKNOWLEDGEMENTS



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