



# Effects of Short Term Diesel Exhaust and Allergen Exposure on DNA Methylation in Bronchial Epithelial Cells



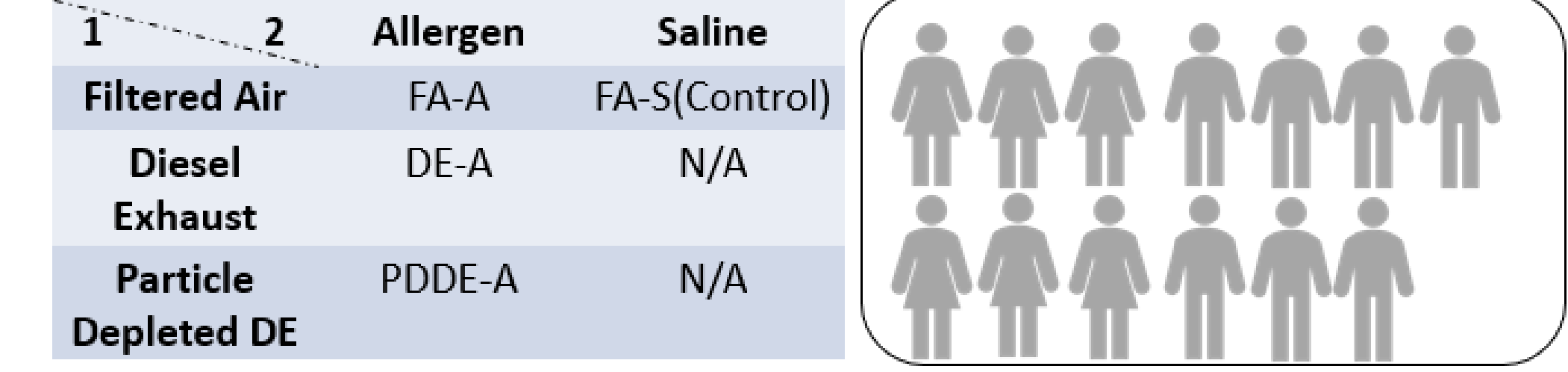
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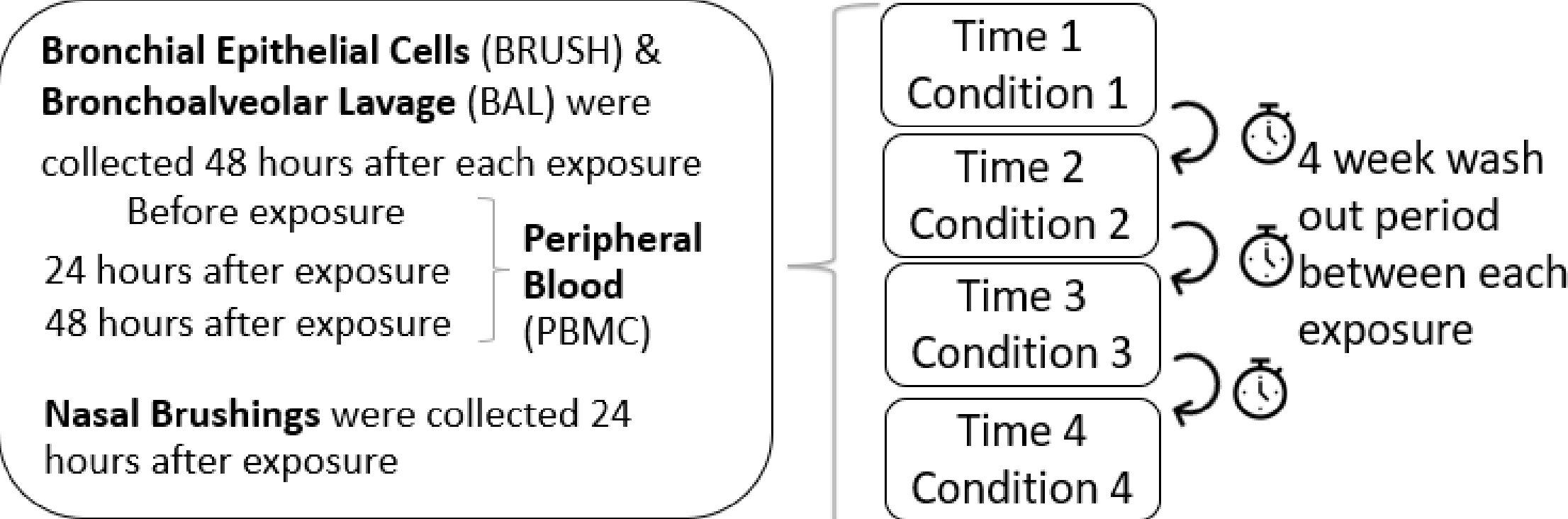
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## Introduction

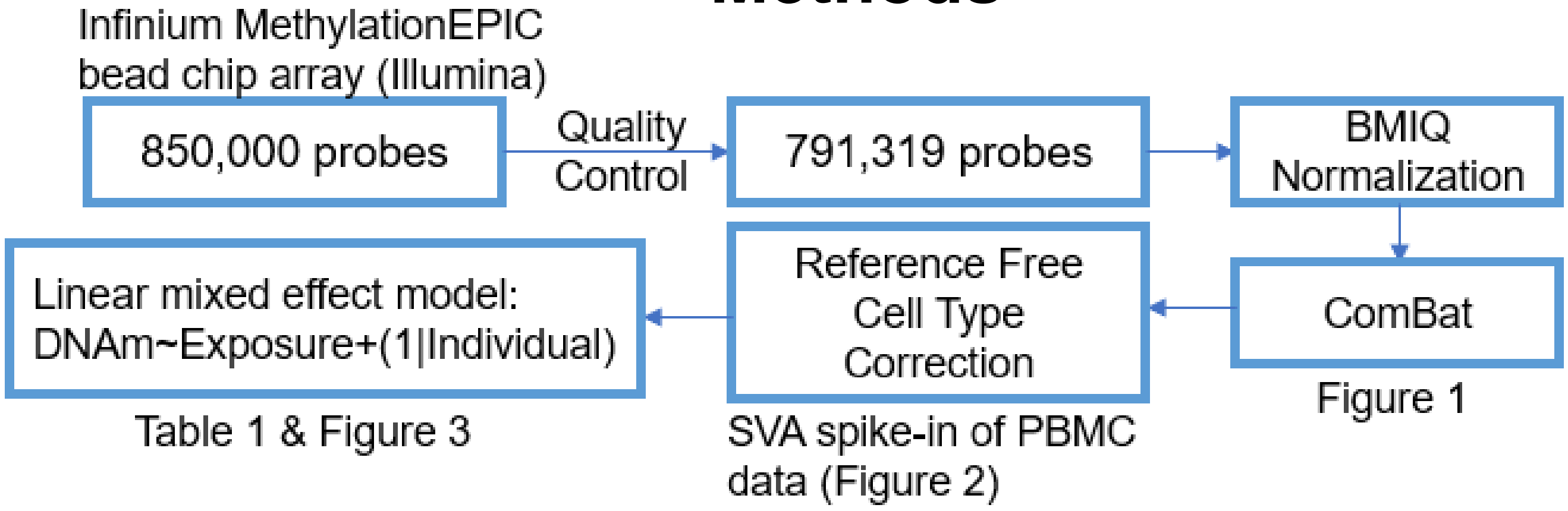
- Epigenetics is defined as the environmentally-responsive modifications to DNA and its packaging proteins that influence the accessibility of DNA to gene expression without changing the DNA sequence.
- DNA methylation (DNAm) is an important epigenetic modification widely used in epigenome-wide association studies (EWAS).
- Previous studies have shown that air pollution and allergens have significant effects on DNAm<sup>[1,2]</sup>. Diesel Exhaust (DE) emissions are a substantial component of traffic related air pollution (TRAP), but the specific mechanisms by which TRAP harms human health are not yet fully understood. We hypothesized that TRAP-induced changes in DNA methylation may contribute to worsening symptoms in asthmatics exposed to allergen.
- In this controlled randomized crossover study, we aimed to investigate the changes of DNAm after short term co-exposures of DE and Allergen. The study design is illustrated below:



The above four exposure conditions given to the 13 individuals in random orders, e.g ACBD, BCDA etc.



## Methods



## Discussion & Future Directions

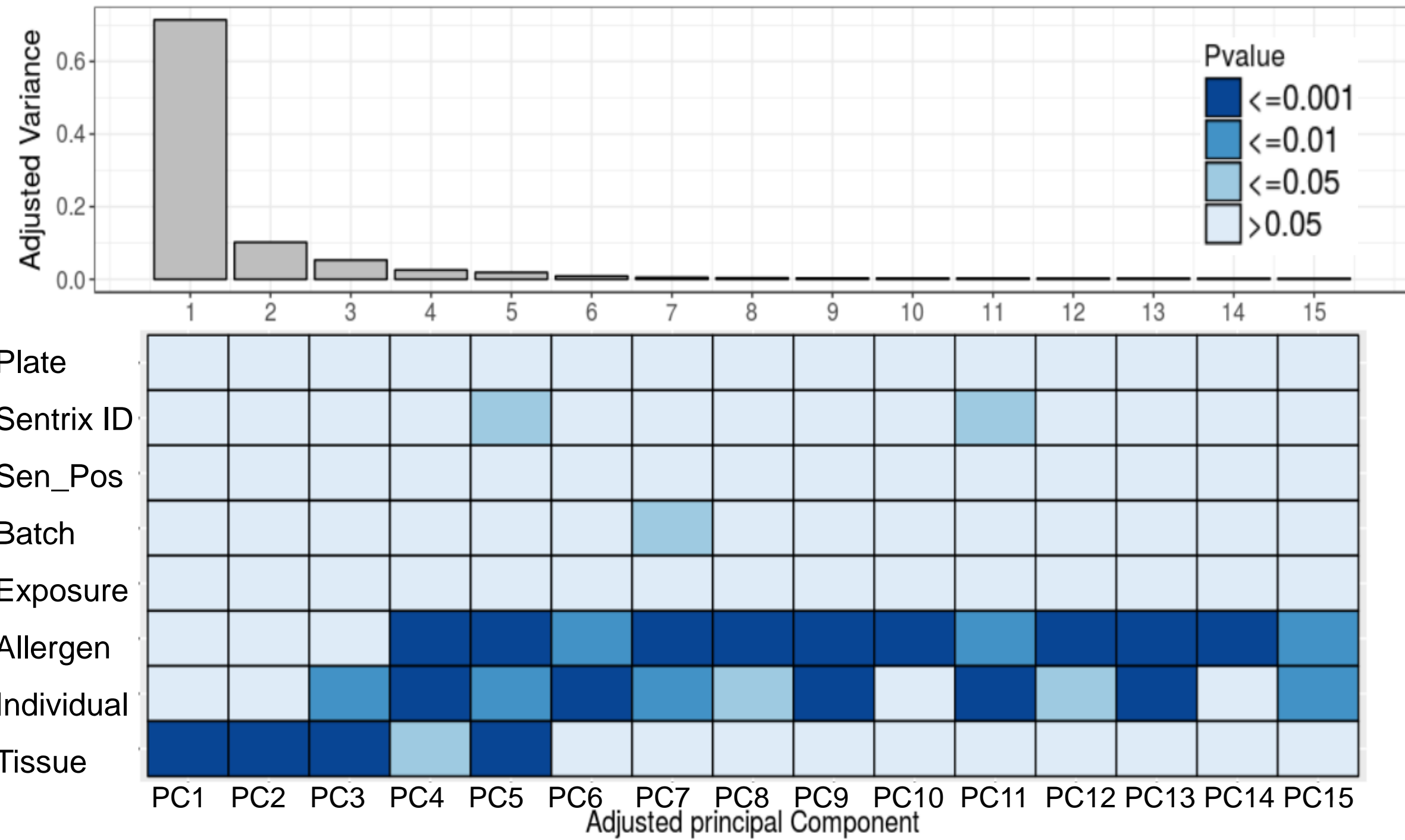
- Many studies have shown that particulate matter exposure is associated with negative effects on human health. However, few researchers have examined the effects of using active particulate depletion systems. Our examination of differences between DE and PDDE at the DNAm level make this study highly novel.
- Since we have other tissues collected from the same cohort, moving forward, it would be interesting to study how different tissues respond to the same acute exposure of diesel exhaust and allergens and whether they share the same regulation pathways.

### References

- Clifford, R. L et al. Allergy and Clinical Immunology (2017)
- Jiang, R et al. Particle and fibre toxicology (2014)

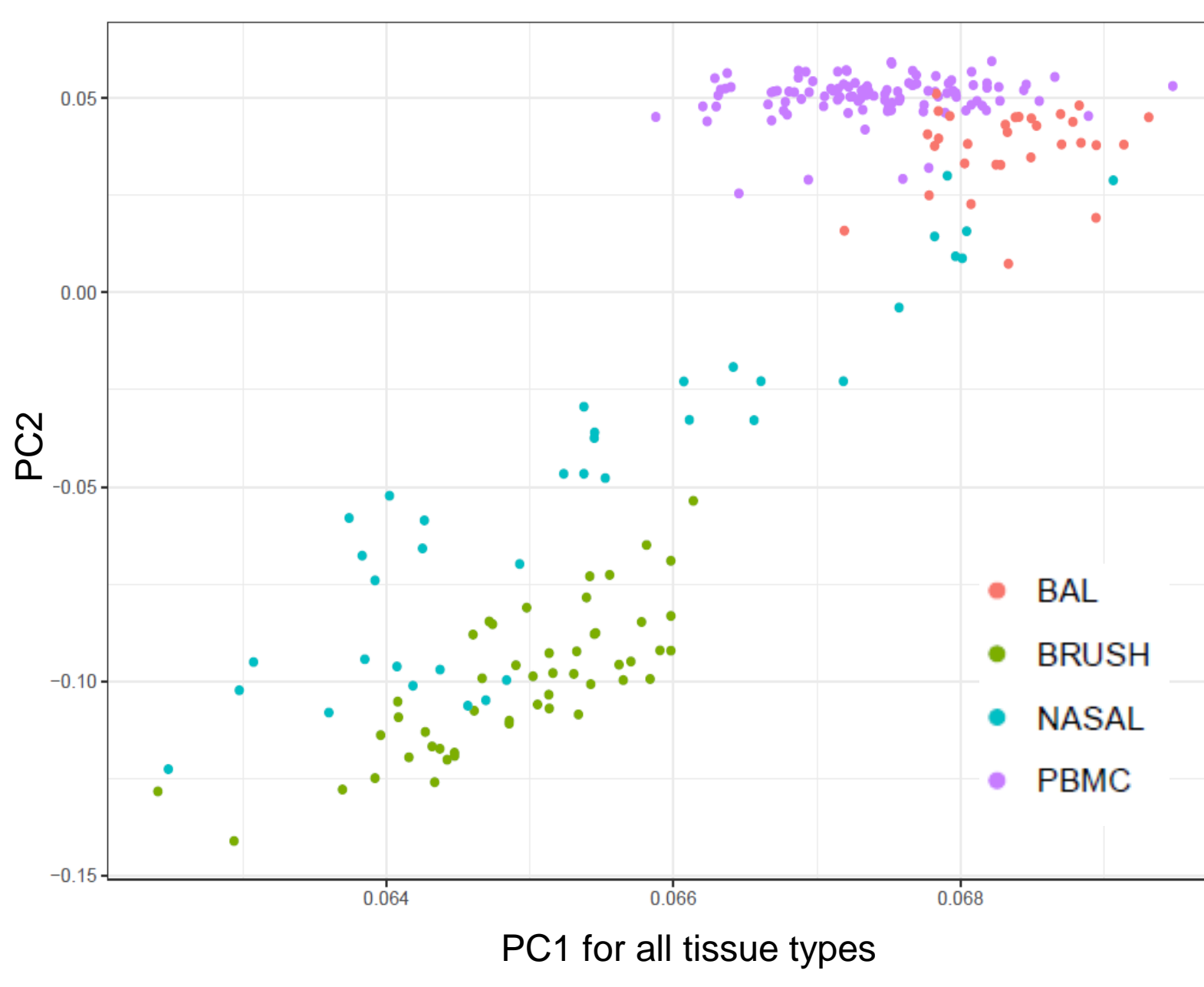
### Acknowledgements

AllerGen NCE Inc., BC Lung Association, MITACS, Michael Smith Foundation for Health Research (MSFHR), Canadian Institutes of Health Research (CIHR).



**Figure 1. Principal Component Analysis (PCA) before ComBat**  
Scree plot shows variance in methylation data accounted for by each PC. Heat map shows association between meta data variable and each PC.

## Results



**Figure 2. (Above) PC1 vs PC2 coloured by four tissue types**

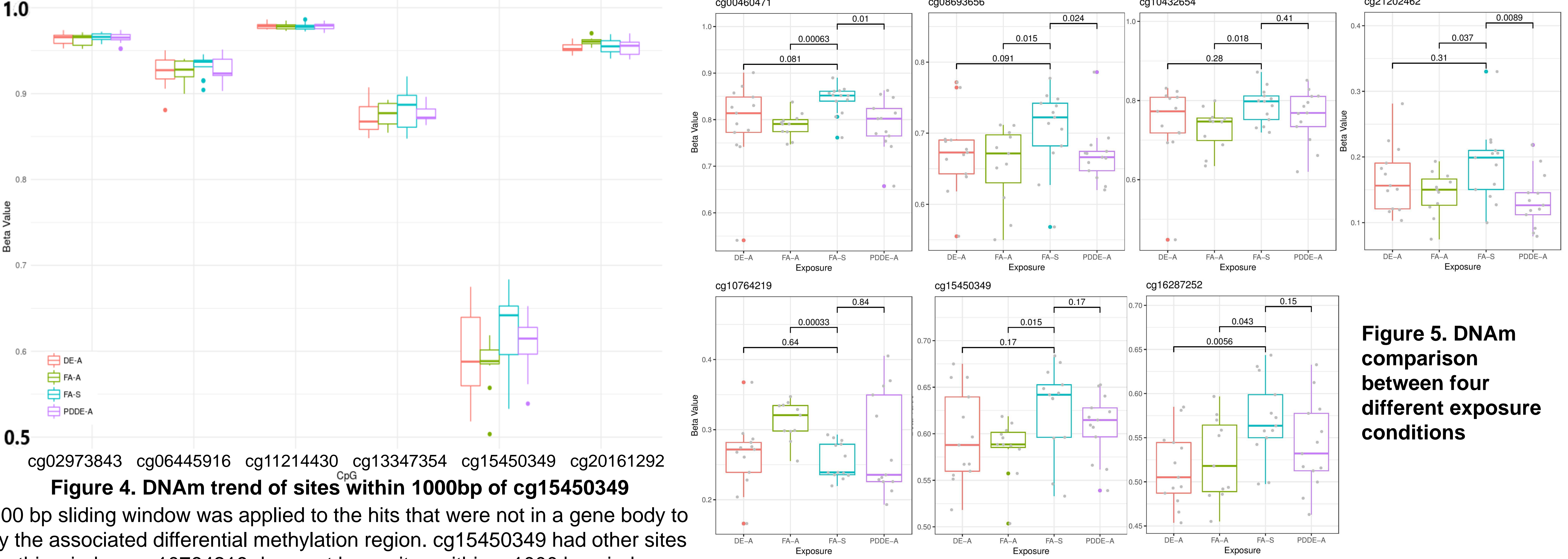
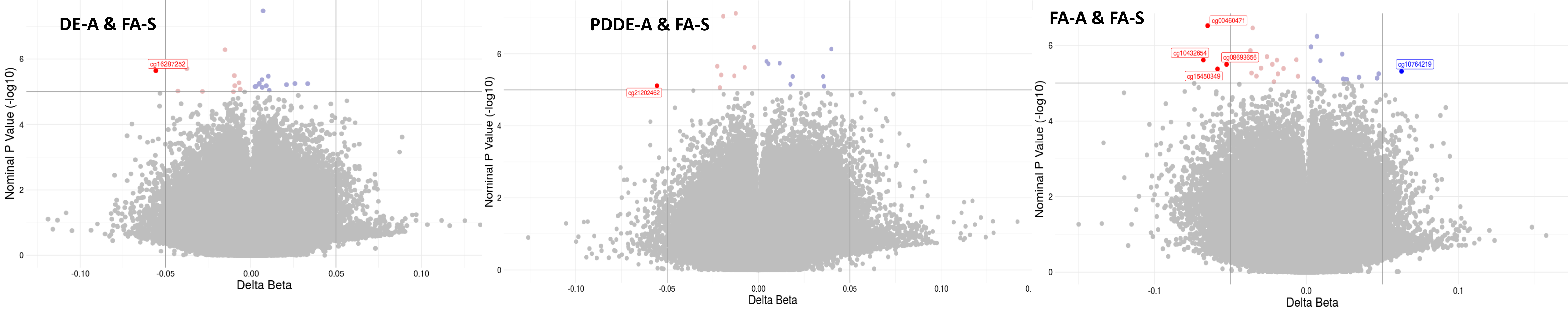
CpG	Chr	Gene(s)	Island relation	Nominal P	Delta Beta	Exposure
cg00460471	2	USP34		3e-07	-0.0650	FA-A & FA-S
cg08693656	17	SLC47A1		3.2e-06	-0.0525	FA-A & FA-S
cg10432654	7	GNA12		2.4e-06	-0.0677	FA-A & FA-S
cg10764219	8			4.9e-06	0.0627	FA-A & FA-S
cg15450349	8		S_Shore	4.2e-06	-0.0585	FA-A & FA-S
cg16287252	12	GLT1D1		2.3e-06	-0.0557	DE-A & FA-S
cg21202462	5	SSBP2		7.7e-06	-0.0556	PDDE-A&FA-S

**Table 1. Summary of probes that passed the statistically significance threshold ( $p < 0.00001$ ,  $\Delta\beta > 0.05$ )**

### Figure 3. (Below) Volcano plots

The data was split into three groups: FA-A and FA-S, DE-A and FA-S, PDDE-A and FA-S. Nominal P-value of each probe was obtained for comparing the two exposures within each group. Delta beta refers to the change in methylation level before and after the exposure.

Decreased Methylation (with Potential Biological Impact)  
Increased Methylation (with Potential Biological Impact)  
Not Significantly Different



**Figure 4. DNAm trend of sites within 1000bp of cg15450349**  
A 1000 bp sliding window was applied to the hits that were not in a gene body to study the associated differential methylation region. cg15450349 had other sites within this window, cg10764219 does not have sites within a 1000 bp window.

**Figure 5. DNAm comparison between four different exposure conditions**