Transgenerational epigenetics in quail: whole genome DNA methylation analysis

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Transgenerational epigenetics in quail: whole genome DNA methylation analysis

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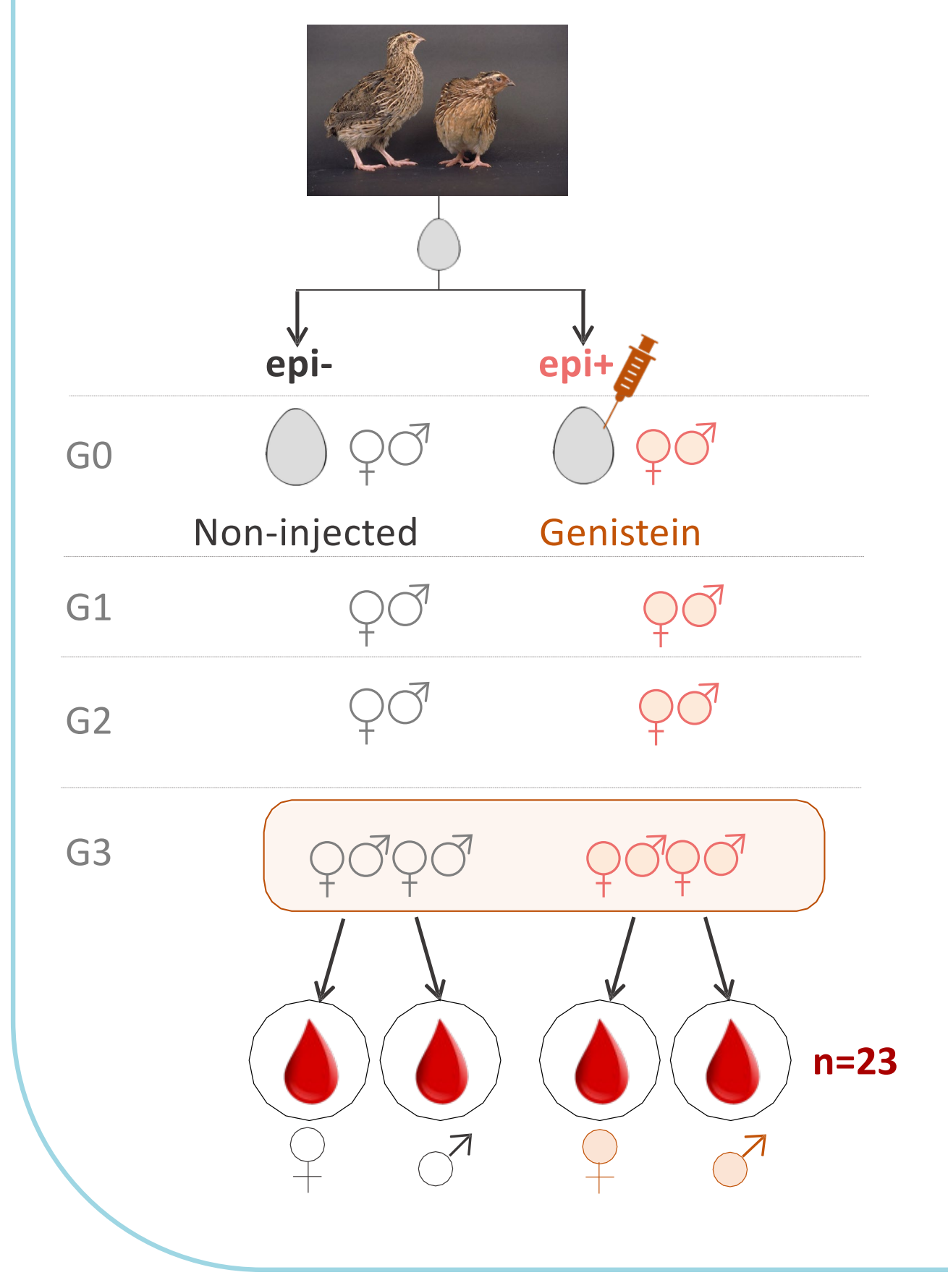
Introduction

The influence of the prenatal environment on the adult phenotype development is partially mediated by epigenetic phenomena. An increasing number of studies highlight the transmission of epigenetic marks between generations following an environmental exposure. However, there is much debate about their acquired transmission beyond the exposed individuals. Recent studies revealed that non-genetic inheritance was probably present in avian species. In one of them, fertilized eggs were injected with an endocrine disruptor (genistein) and after three generations without any other injection, several traits were impacted by the ancestor treatment such as the reproduction and the behavior. Here we analyse the DNA methylation between control and treated lines of the third generation.

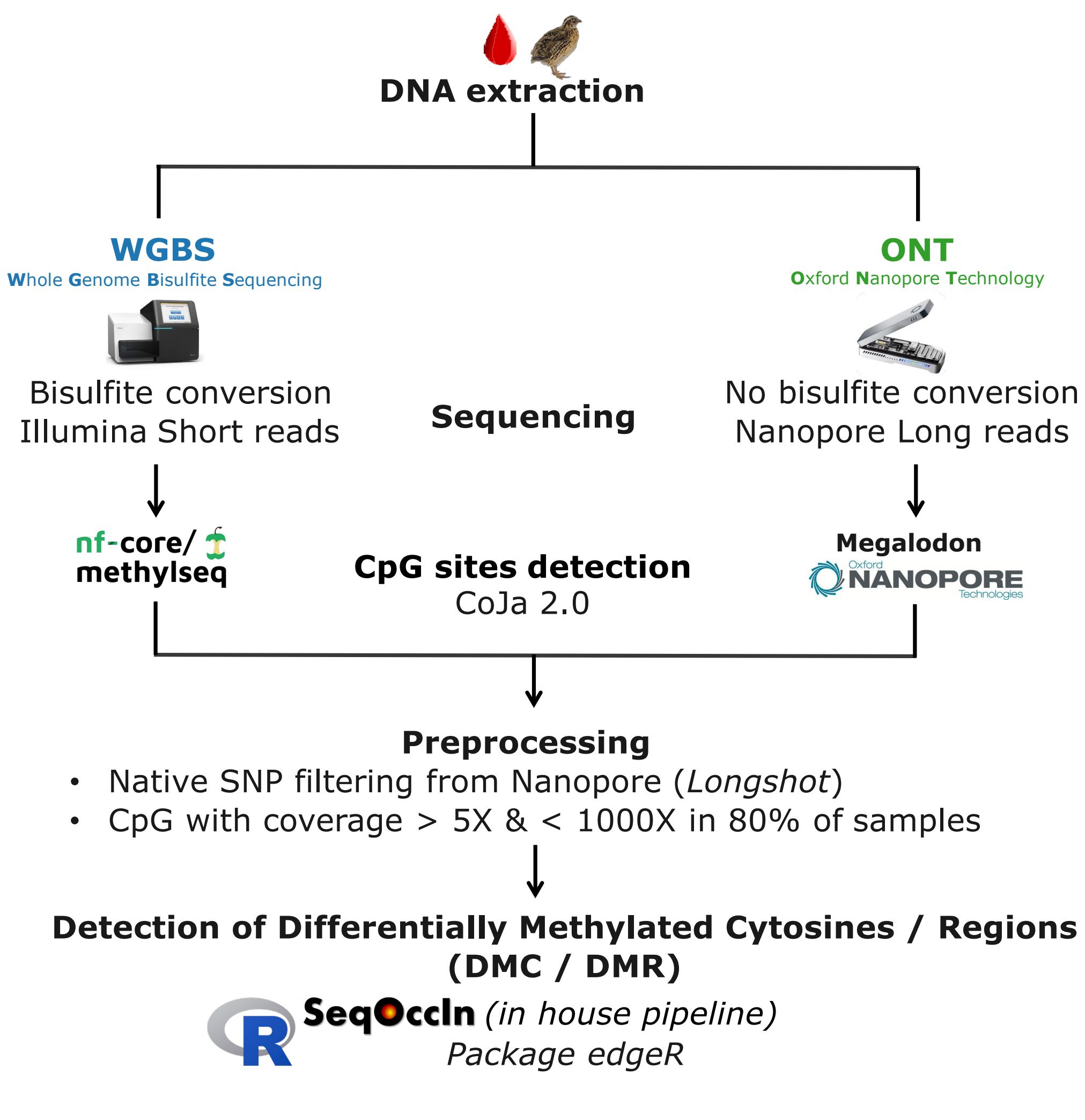
Experimental design



Mirror crossing, with parallel pedigrees between both groups, was set up so that both groups have the same expected genetic contribution from their founders

→ **WGBS**
→ **ONT**

Methods



DNA extraction

WGBS
Whole **G**enome **B**isulfite **S**equencing

ONT
Oxford **N**anopore **T**echnology

Sequencing

Bisulfite conversion
Illumina Short reads

No bisulfite conversion
Nanopore Long reads

nf-core/ methylseq

CpG sites detection
CoJa 2.0

Megalodon
Oxford NANOPORE Technologies

Preprocessing

- Native SNP filtering from Nanopore (*Longshot*)
- CpG with coverage > 5X & < 1000X in 80% of samples

Detection of Differentially Methylated Cytosines / Regions (DMC / DMR)

SeqOccIn *(in house pipeline)*
Package edgeR

Genetic analyses
Allele frequency comparison between epilines (*plink / R*)

Conclusion

ONT vs **WGBS**: comparable results but best detection of differential methylation from ONT data

Thousands of **DMCs detected** between epilines: **transgenerational effects** of **genistein** on **DNA methylation level**

Most of the **methylation level variability** seems to **correlated with genetic variability**

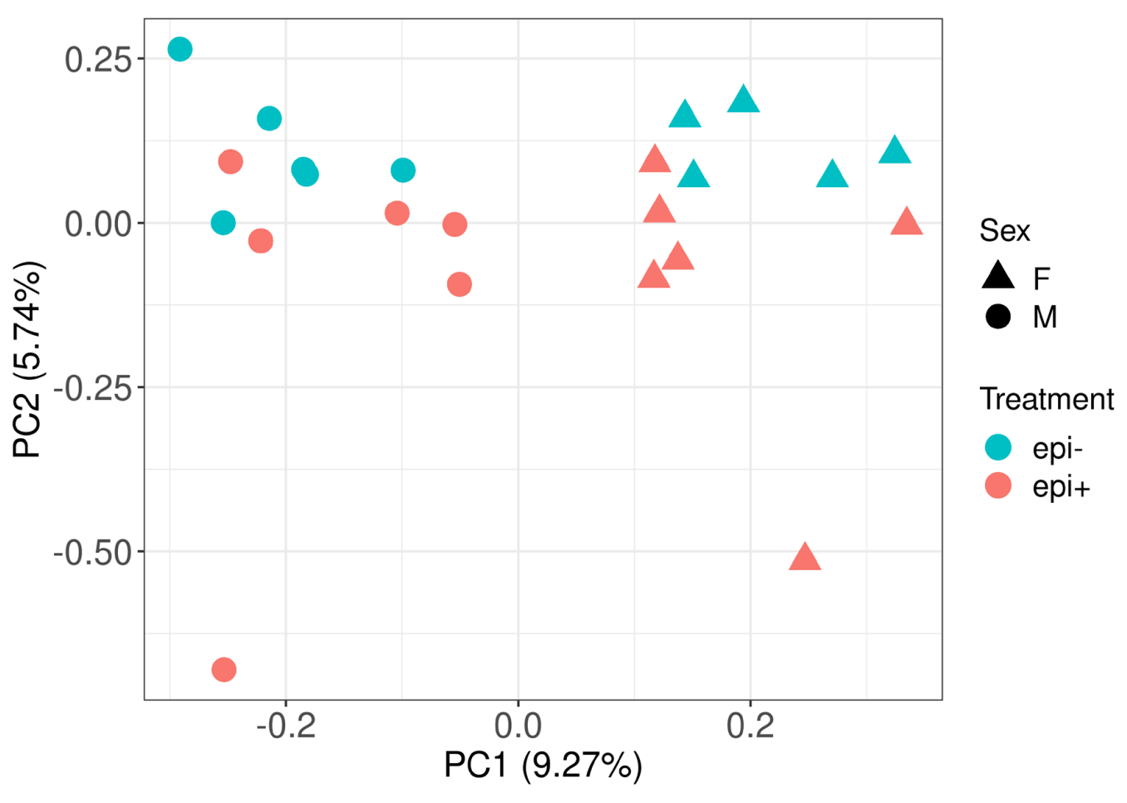
Several candidate regions will be further analysed

Results

WGBS | **ONT**

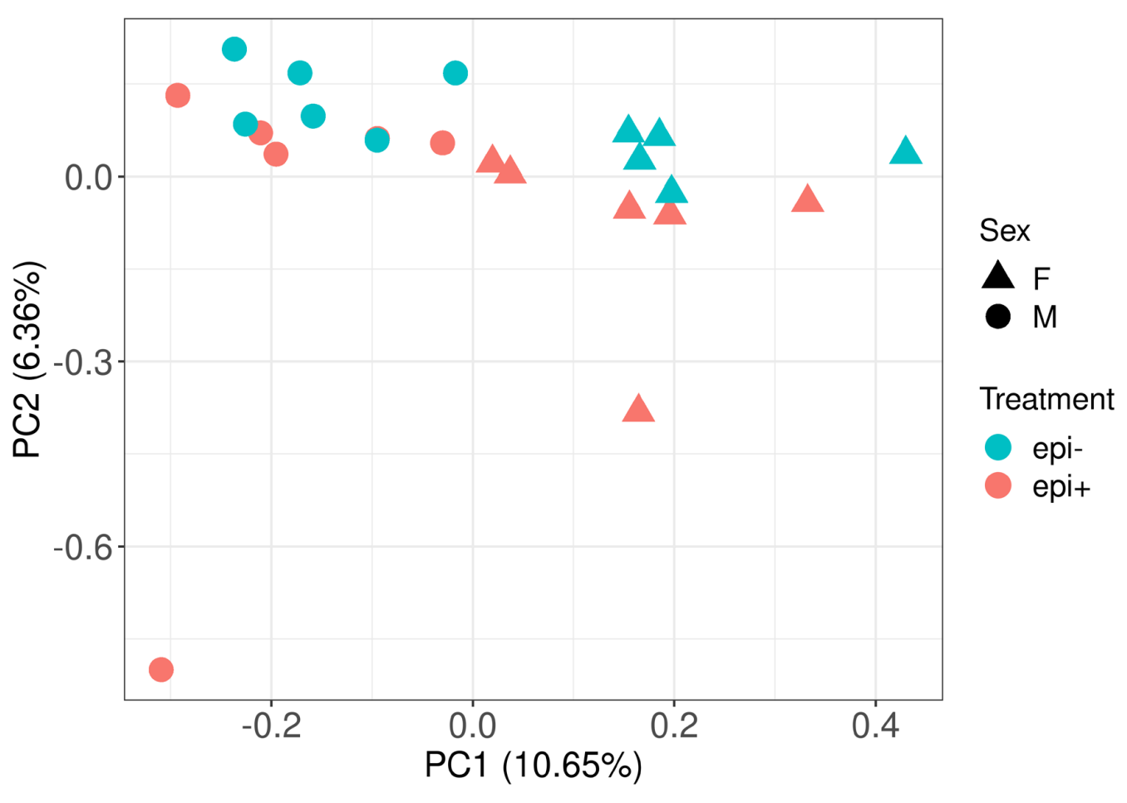
Methylation profile of CpG sites

5,881,815 common CpG



mCpG : 0.56 ± 0.3
coverage CpG: 20.5 ± 20.4

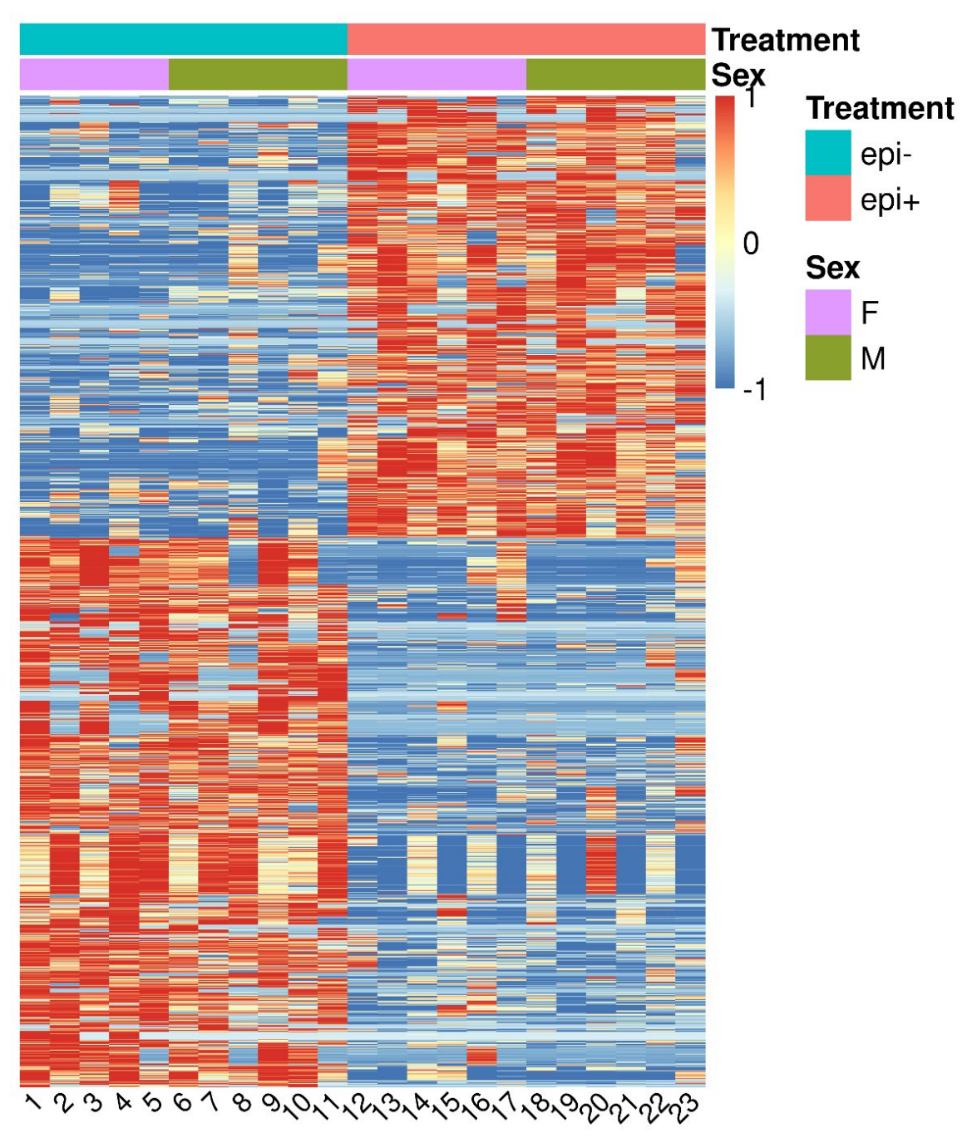
7,537,007 common CpG

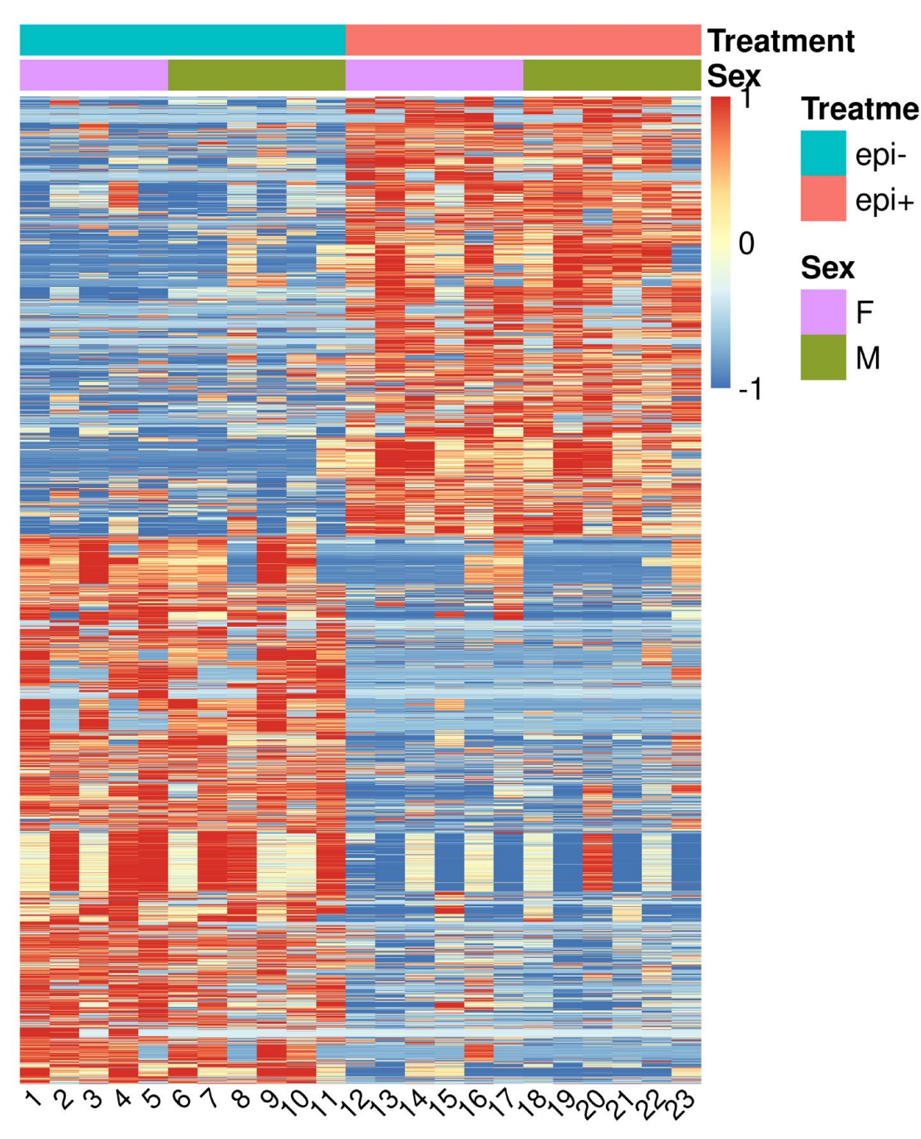


mCpG : 0.46 ± 0.3
coverage CpG: 38.7 ± 16.7

Methylation level: separation per sex and epiline

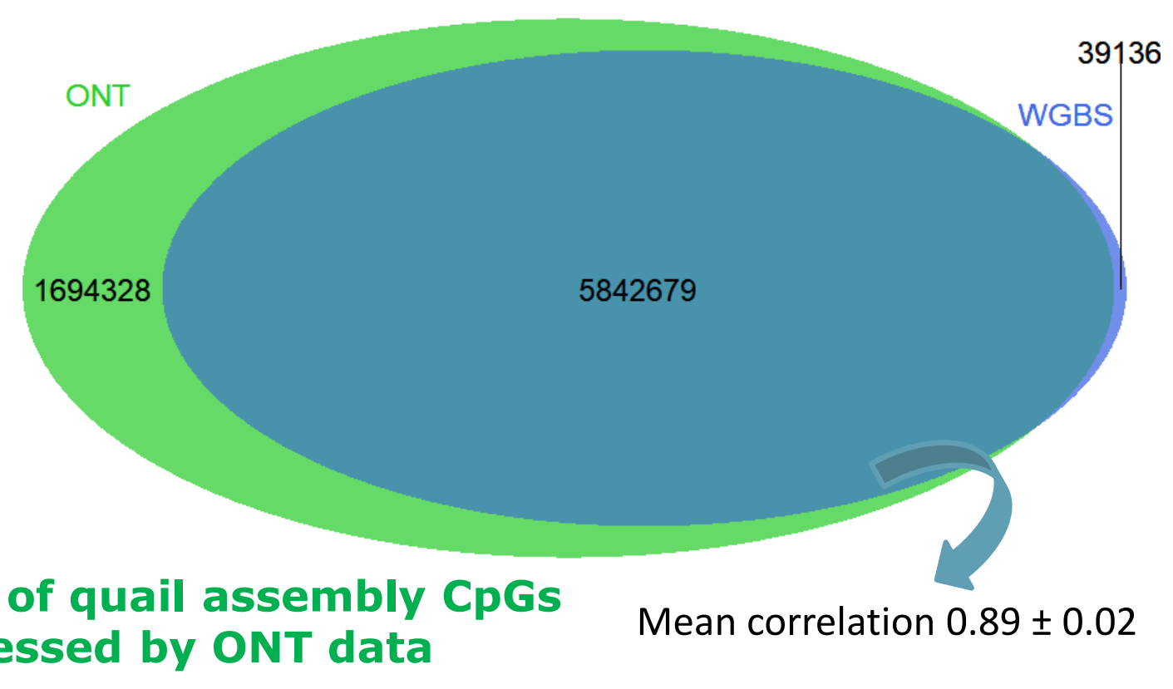
Heatmap of methylation rate of 10,000 DMCs epiline





Similar methylation profiles between technologies

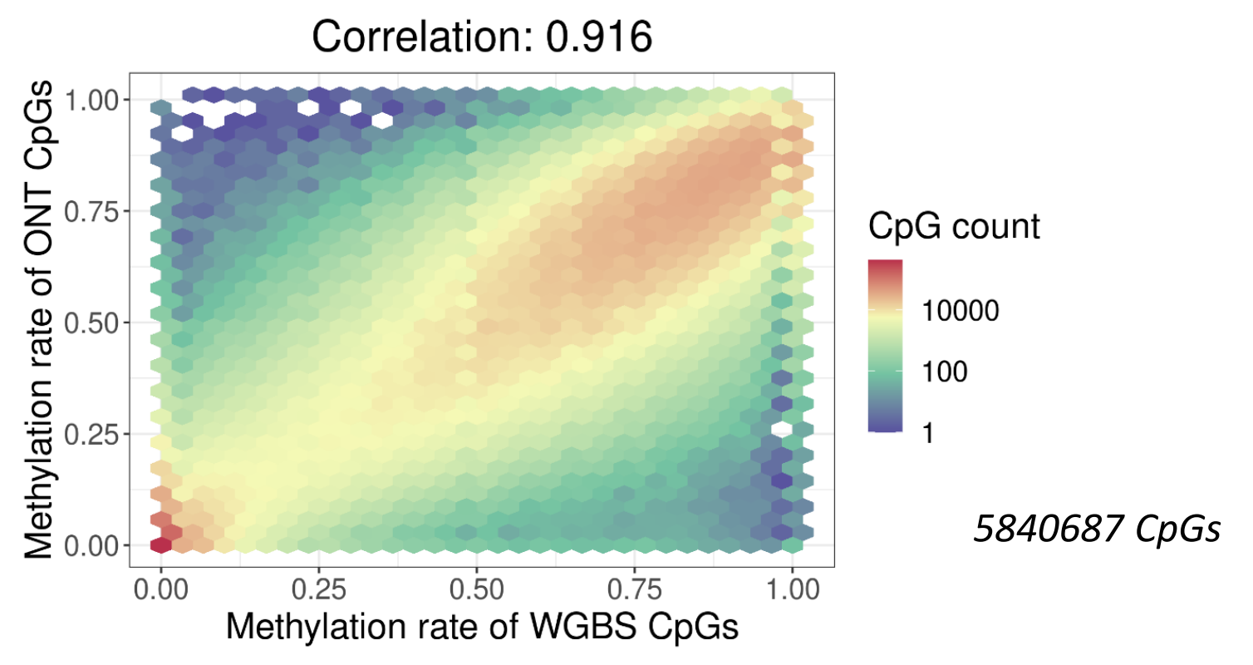
Number of CpG sites measured



84% of quail assembly CpGs addressed by ONT data

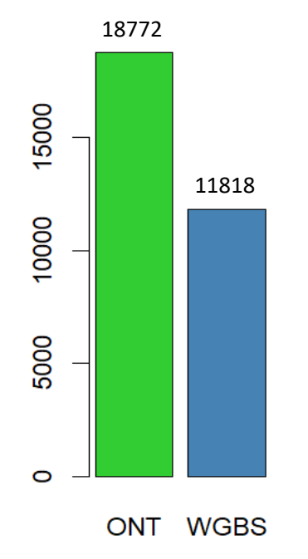
Mean correlation 0.89 ± 0.02

99% WGBS CpG found in ONT data

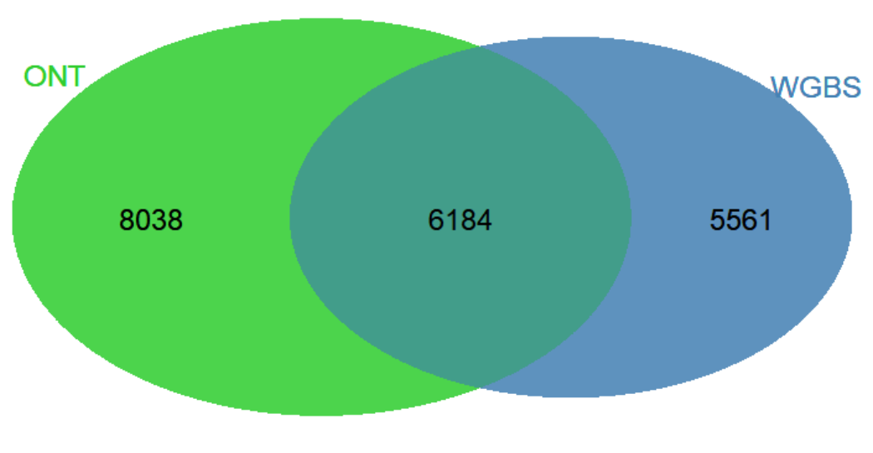


5840687 CpGs

Number of significant DMCs observed



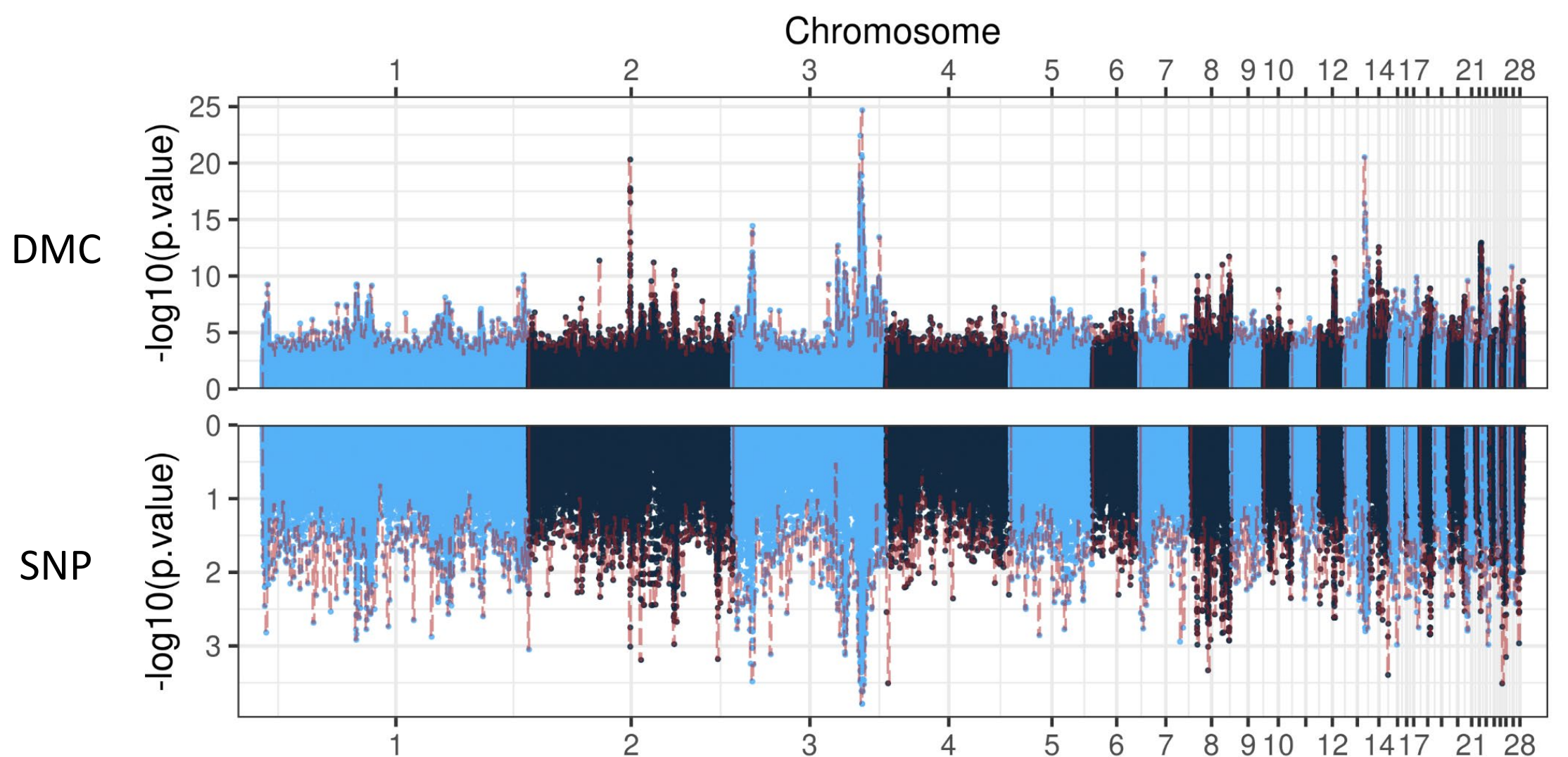
Total number of DMCs per technology

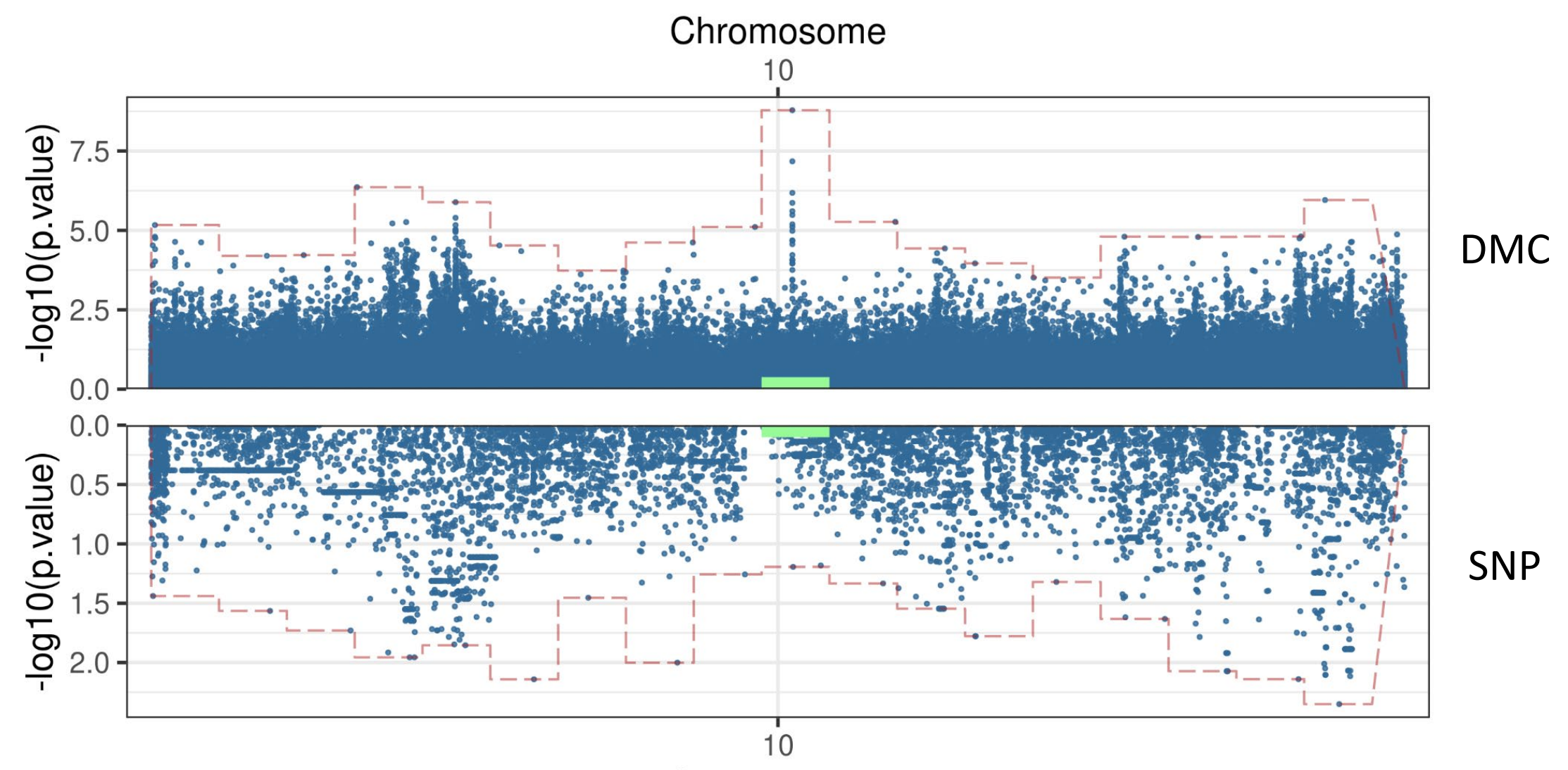


Distribution of DMCs from common CpGs

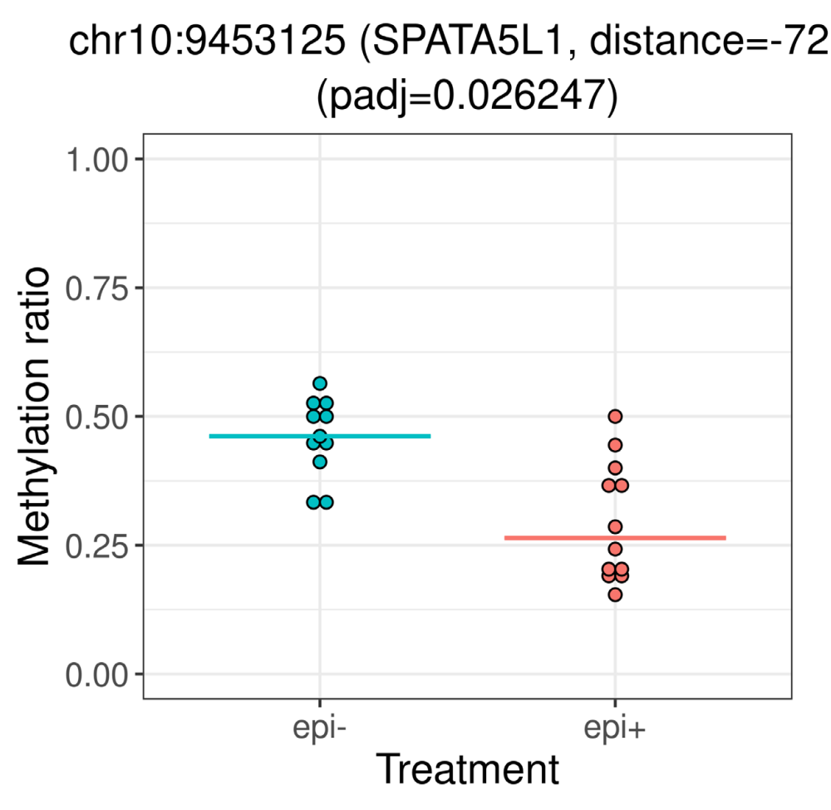
Thousands DMCs detected by both technologies

Taking SNPs into account

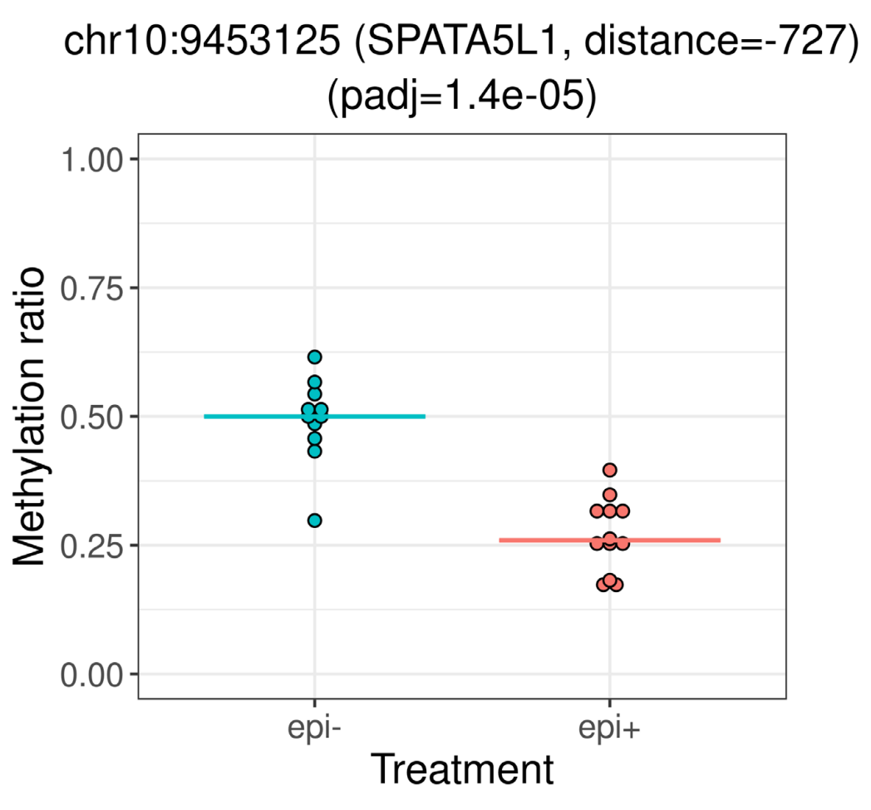




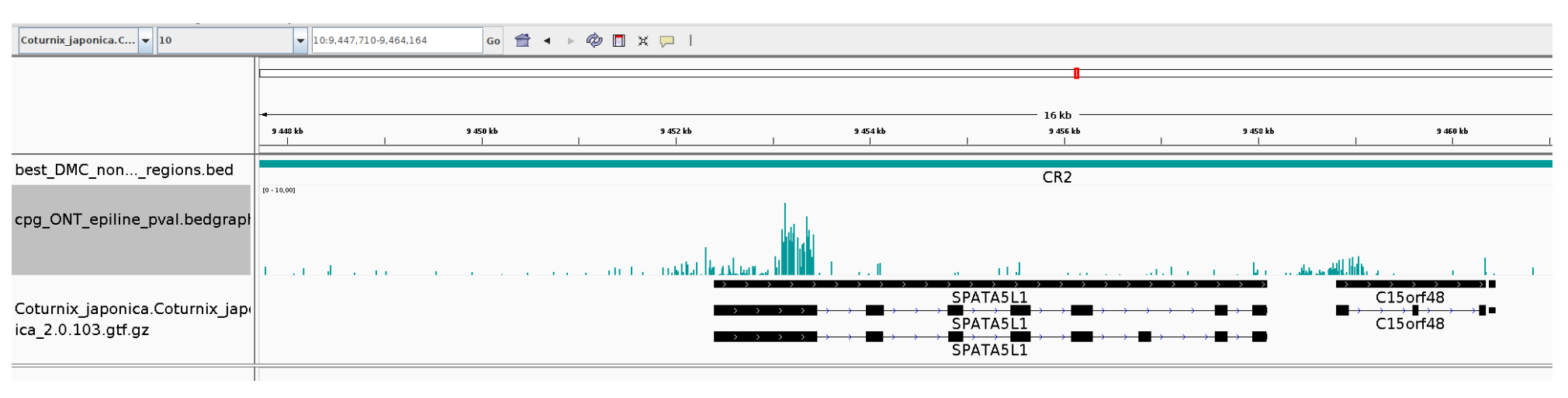
Comparable genetic and epigenetic differential patterns between epilines, but several interesting regions



WGBS



ONT



SPATA5L1 (Spermatogenesis-Associated Protein 5-Like Protein 1) = AFG2B (AFG2 AAA ATPase Homolog B), involved in ribosome biogenesis

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