

➤ Genetic determinism of sperm DNA methylation in French Holstein cattle

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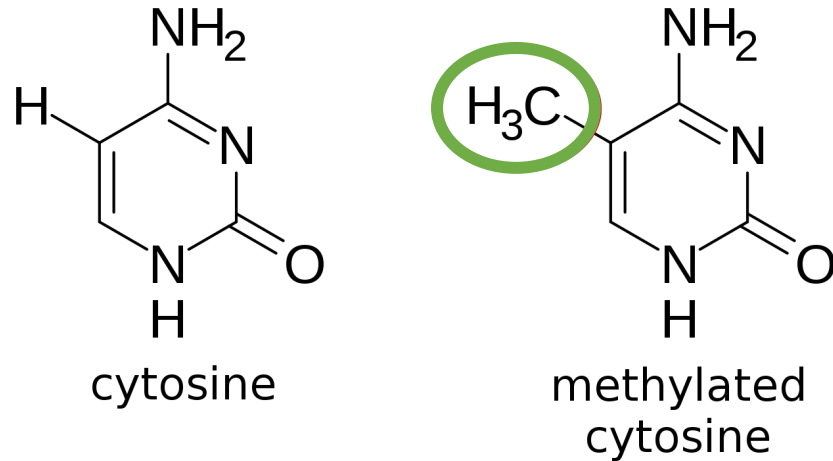
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➤ Context: Epigenetic mark - DNA methylation



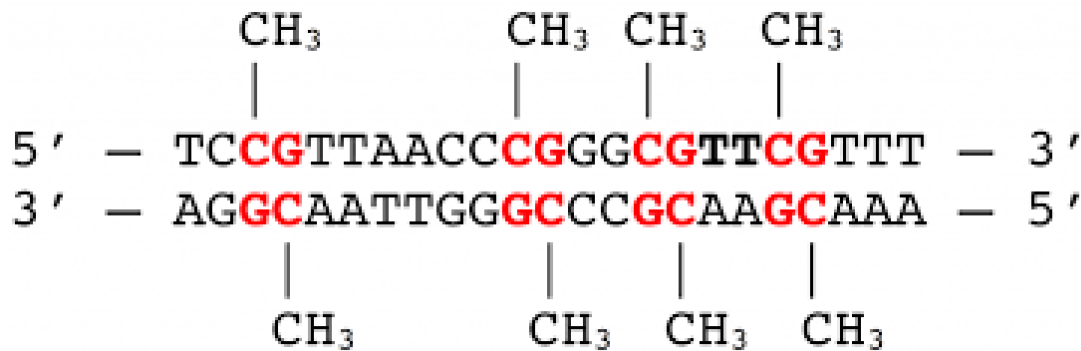
Methylation of the cytosine (C5) in the **cytosine-phosphate-guanine** groups (CpG)

DNA methylation (DNAm) :

- **Link between** the **DNA** sequence and the **phenotype**
- **Can be influenced by environmental factors**

DNAm information is envisaged to be used to better **predict phenotypic traits**

⇒ **Need** to unravel the **genetic determinism** of DNAm



➤ Aim: to study the **genetic architecture** of **DNAm** in cattle



➤ Materials and methods

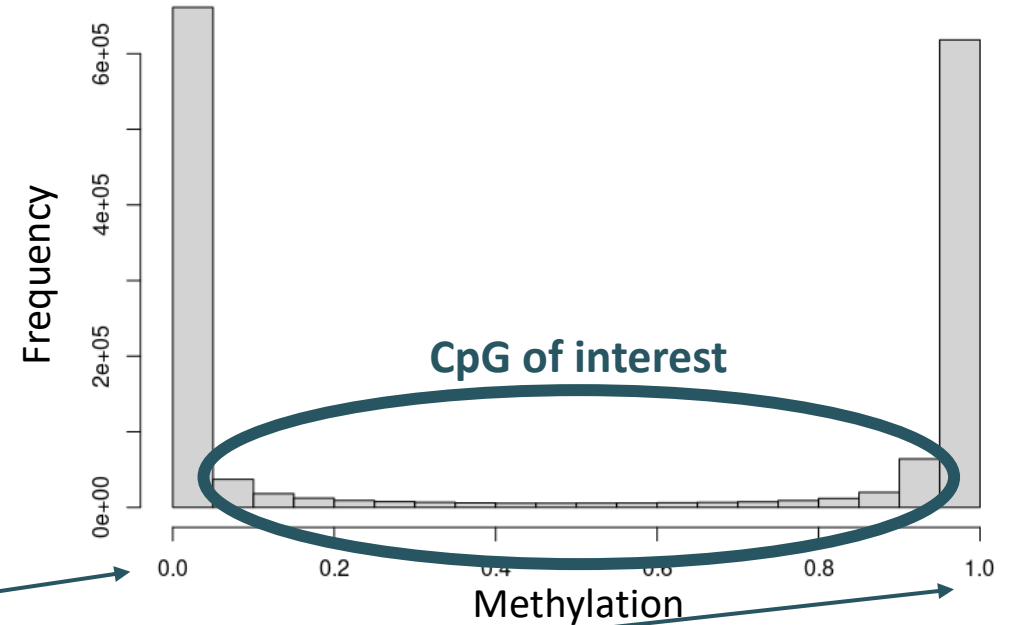
Biological material: **sperm** (262 Holstein bulls)

DNAm measured using **R**educed **R**epresentation **B**isulfite Sequencing (**RRBS**)

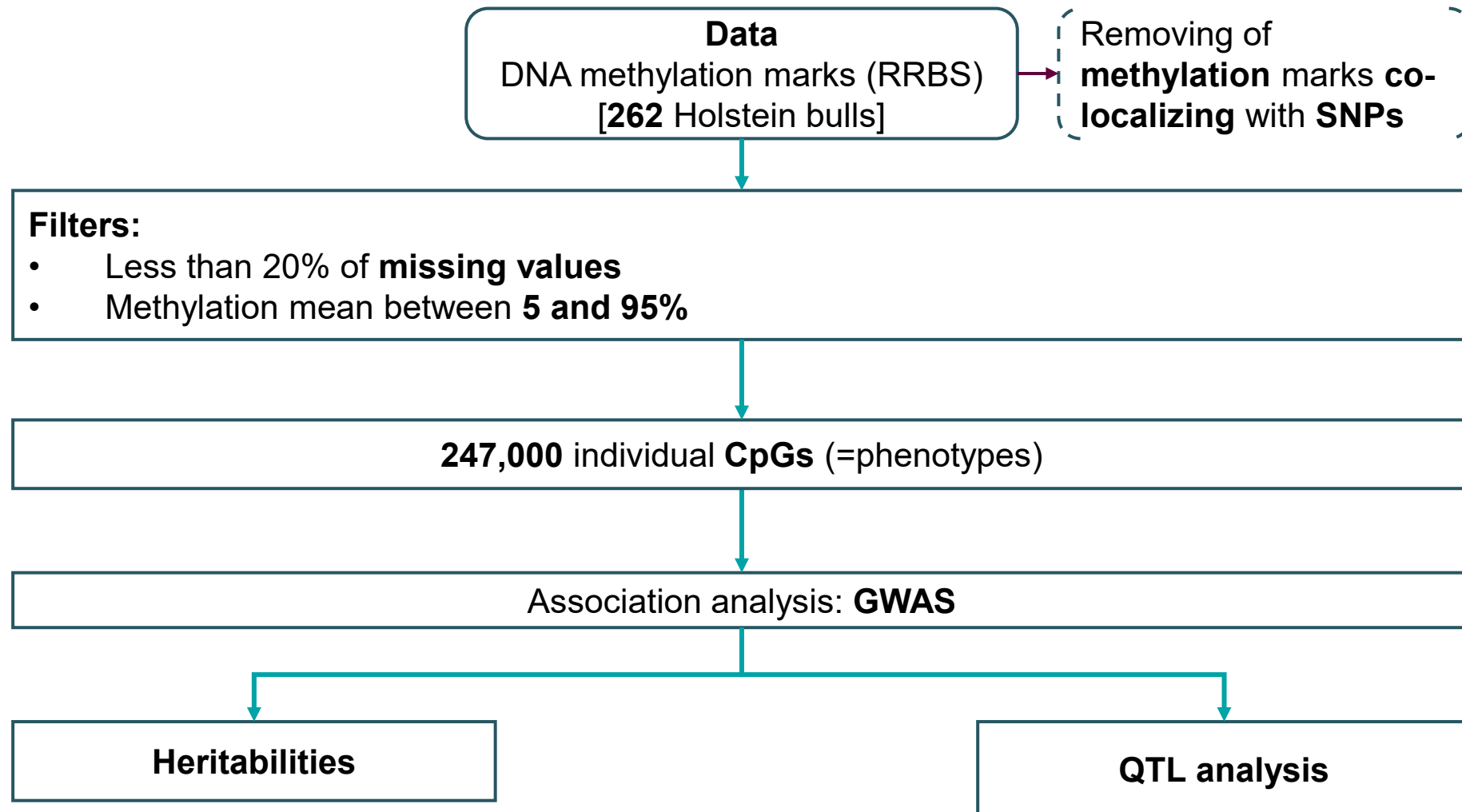
- **Methylation rate** (from a number of reads) for a given CpG-site
- **Uneven genome coverage** (beginning/end >> chromosome center)

~**2 millions** CpG-sites with **DNAm**

⇒ Most are **un-methylated** or **fully methylated** between bulls



➤ Materials and methods



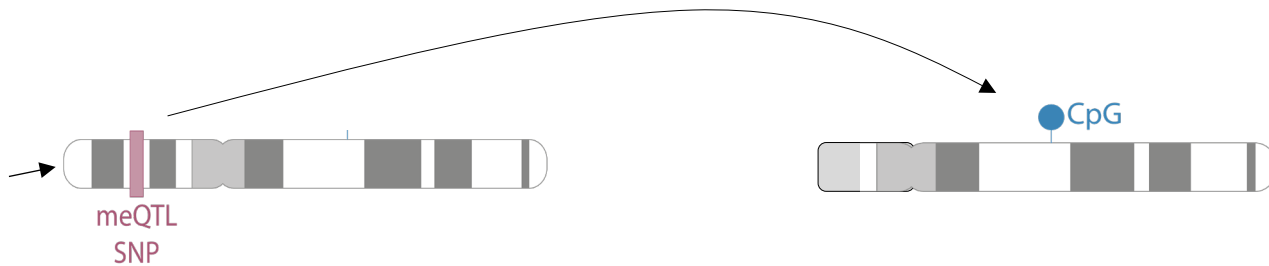
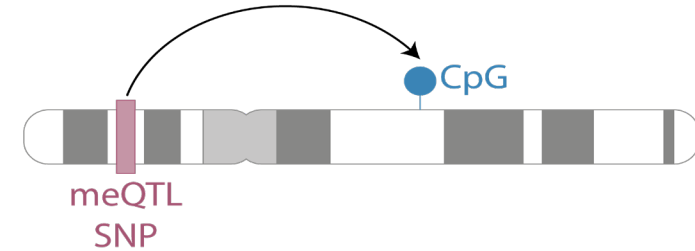
> Material & Methods

247,000 CpG-sites (phenotypes) ; **12 millions SNPs**

Software **GCTA** (Threshold: $-\log_{10}(\text{p-value}) > 7.3$)

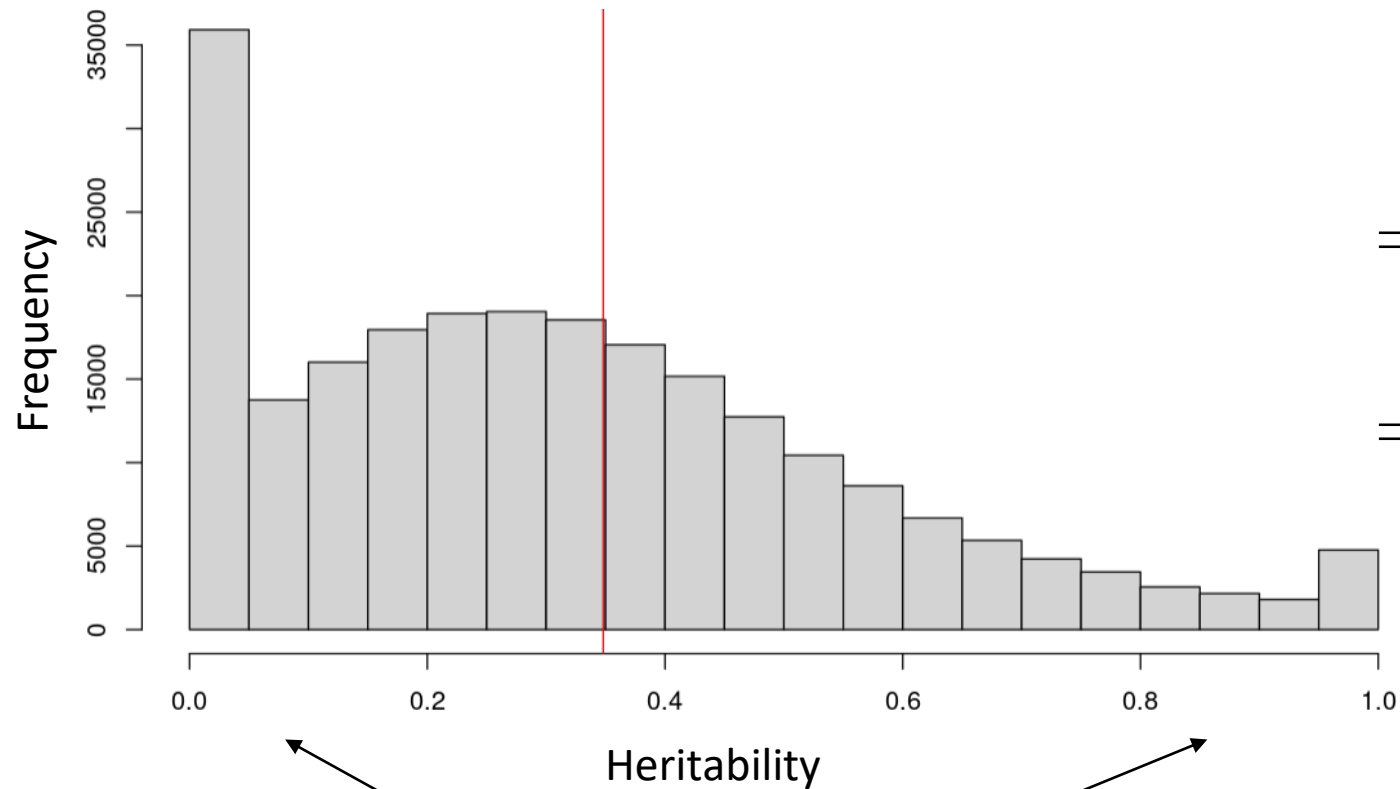
We defined (*in this presentation*) as :

- **Cis meQTL** = SNP and CpG located on the **same chromosome**
- **Trans meQTL** = SNP and CpG located on **different chromosomes**



➤ Results: Heritability

Distribution of heritabilities



⇒ Estimated with the **genetic relationship matrix**

⇒ Average (without 0 and 1): 35%

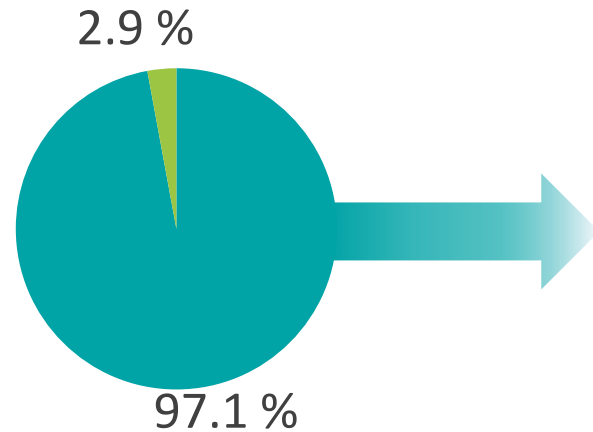
Component constrained

➤ Results: meQTL - distance between CpG-site and meQTL

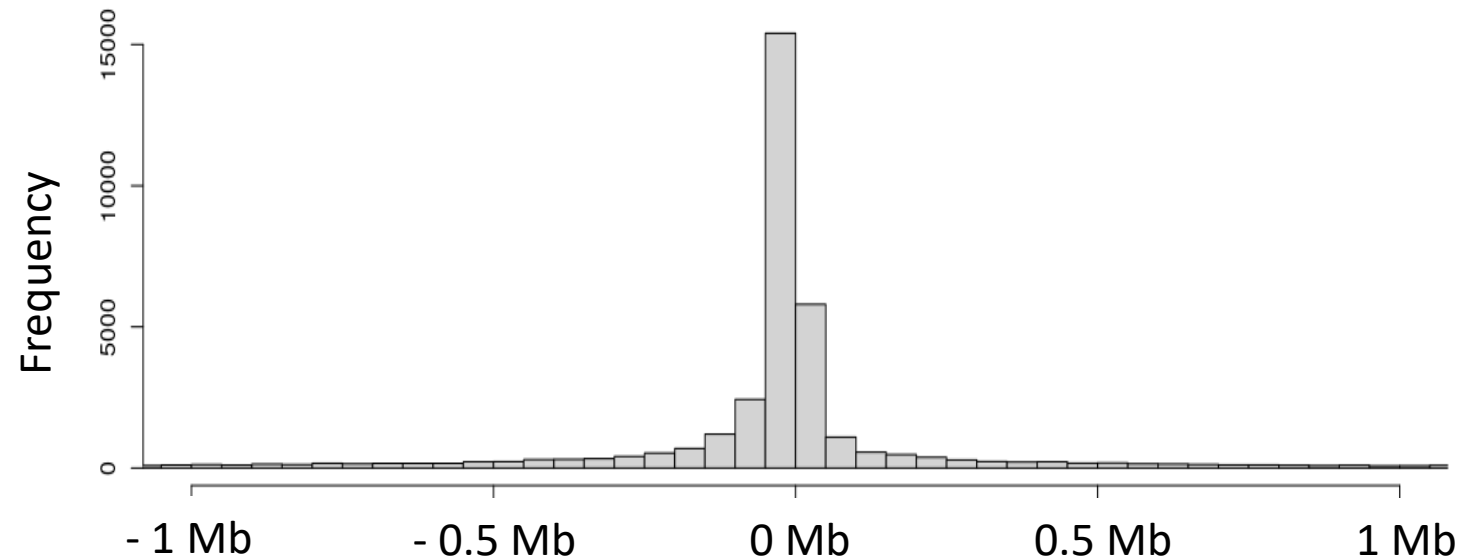
⇒ **17% of CpGs** are associated with at **least 1 SNP** ($-\log_{10}(p) > 7.3$)

Distribution of cis and trans meQTL

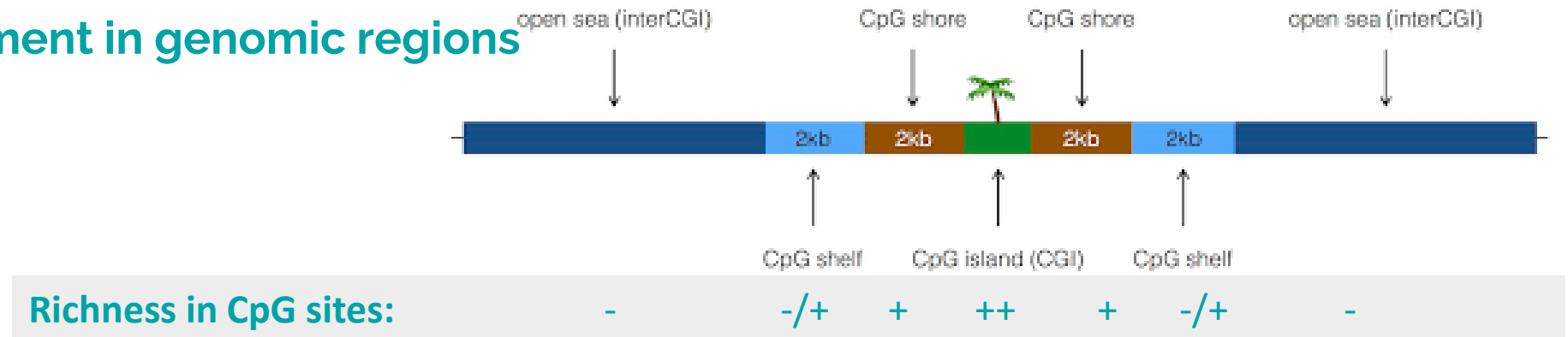
■ Cis (same CHR) ■ Trans (different CHR)



Histogram of the distance between CpG and SNP (top SNP) for cis-meQTLs



> Results: Enrichment in genomic regions

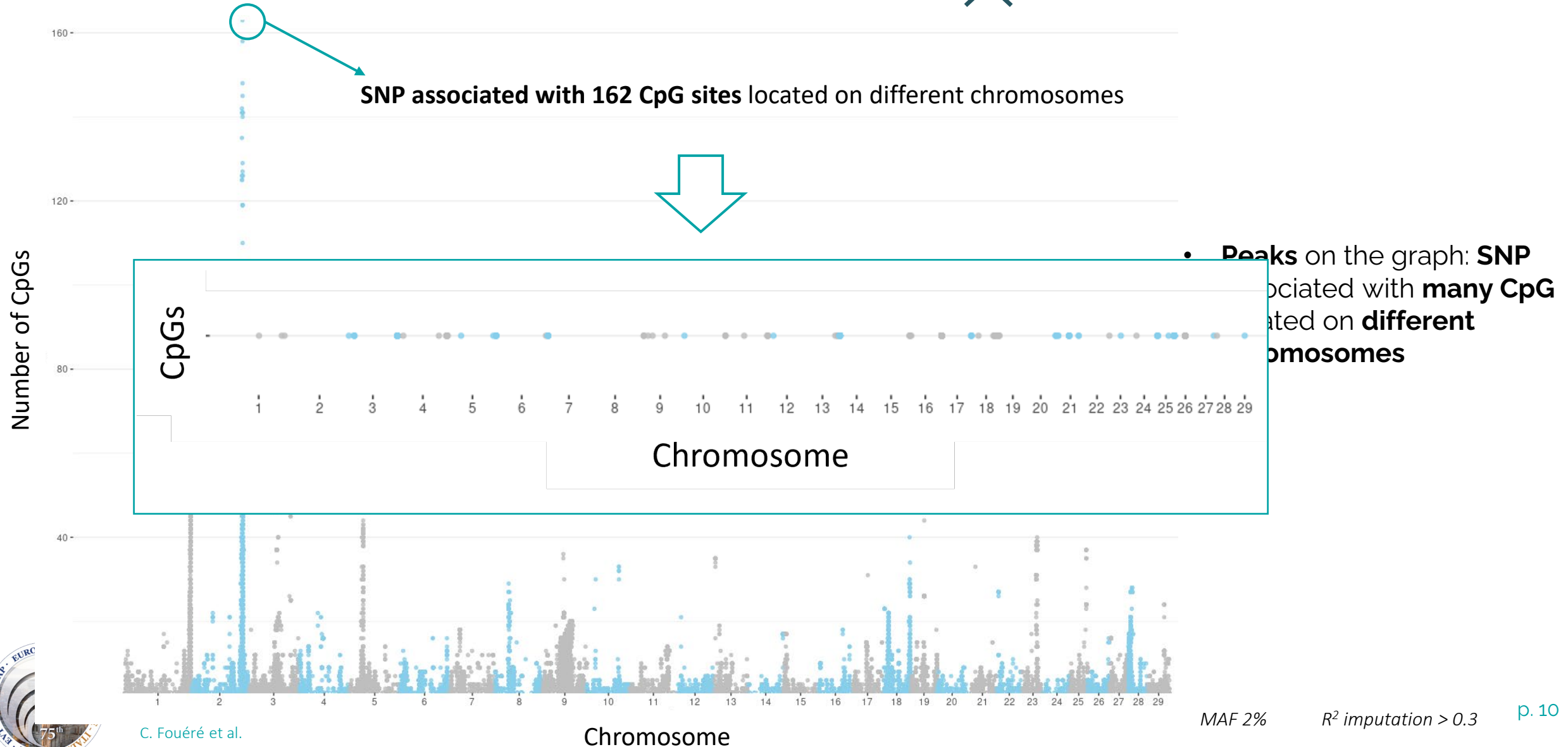


SNP

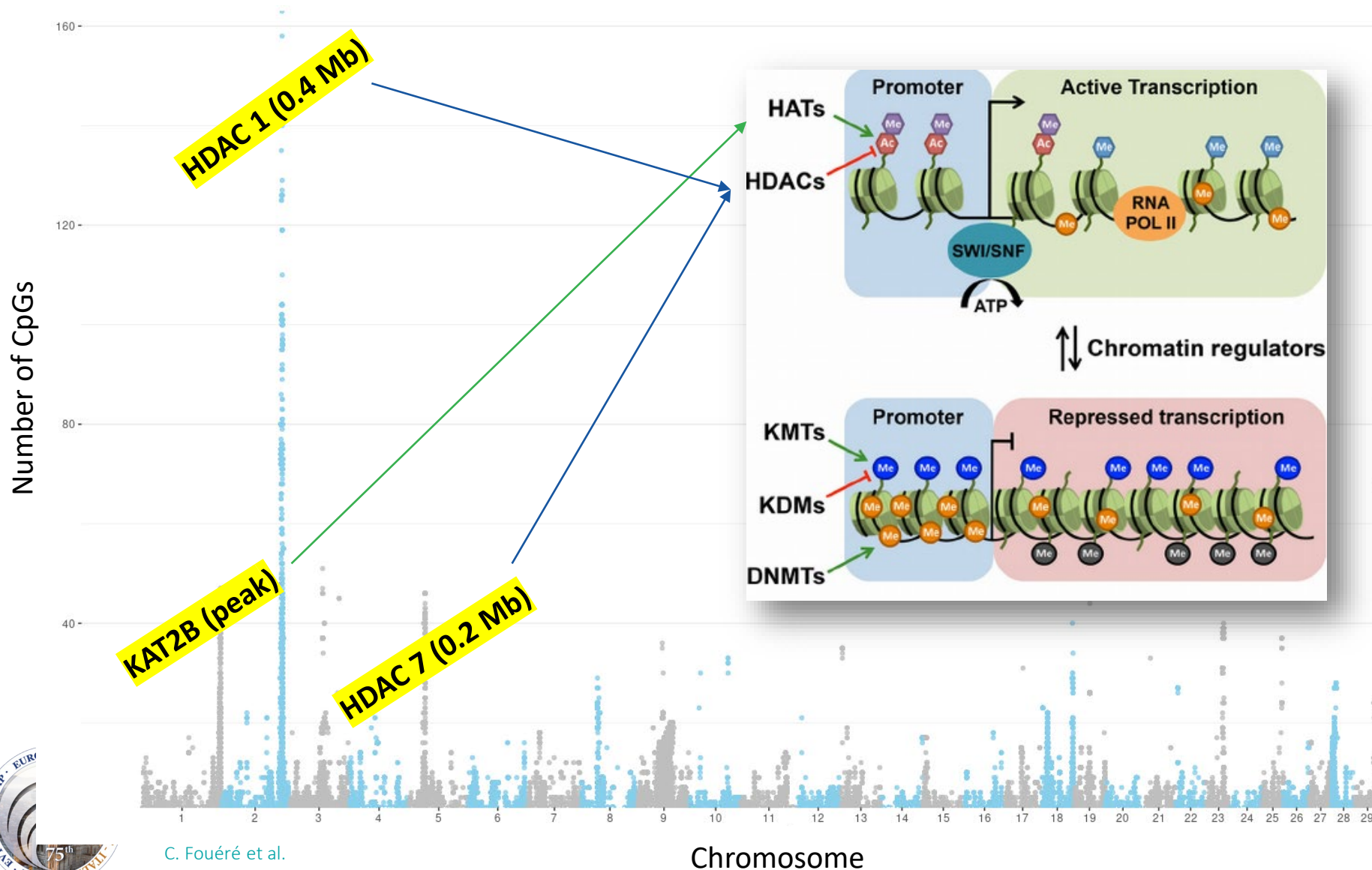
Odds Ratio (95% CI)

➤ Results: Occurrence of significant SNPs in trans

~~GWAS manhattan plot~~



➤ Results: Candidate genes



- Some **trans-meQTL** in regions with genes associated with **histone modification** (chromatin regulation)

MAF 2%

R^2 imputation > 0.3

➤ Conclusion & Perspectives

- **Interesting candidate** genes and pathways that need further investigation
- This will help to better **understand** the **relationship** between **genetics** and **epigenetics**
- Low number of animals
 - Analyses are currently running on a **larger dataset** (+40%)





TOWARDS IMPROVEMENT OF **RUMINANT** BREEDING
THROUGH **GENOMIC** AND EPIGENOMIC APPROACHES



Thank you for your attention!