

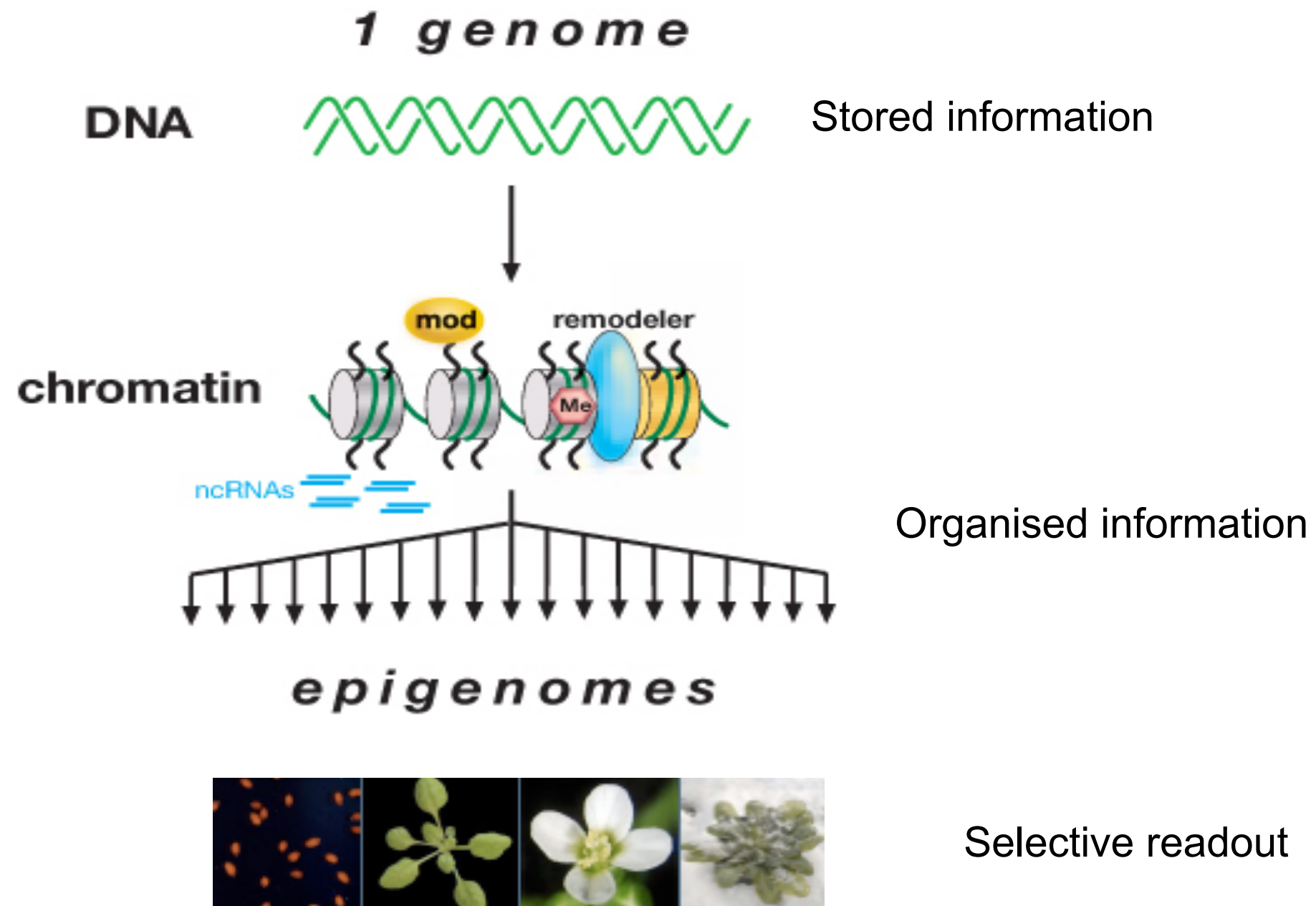


# Comparative epigenomics in Brassicaceae reveals distinct modes of PRC2-mediated gene regulation

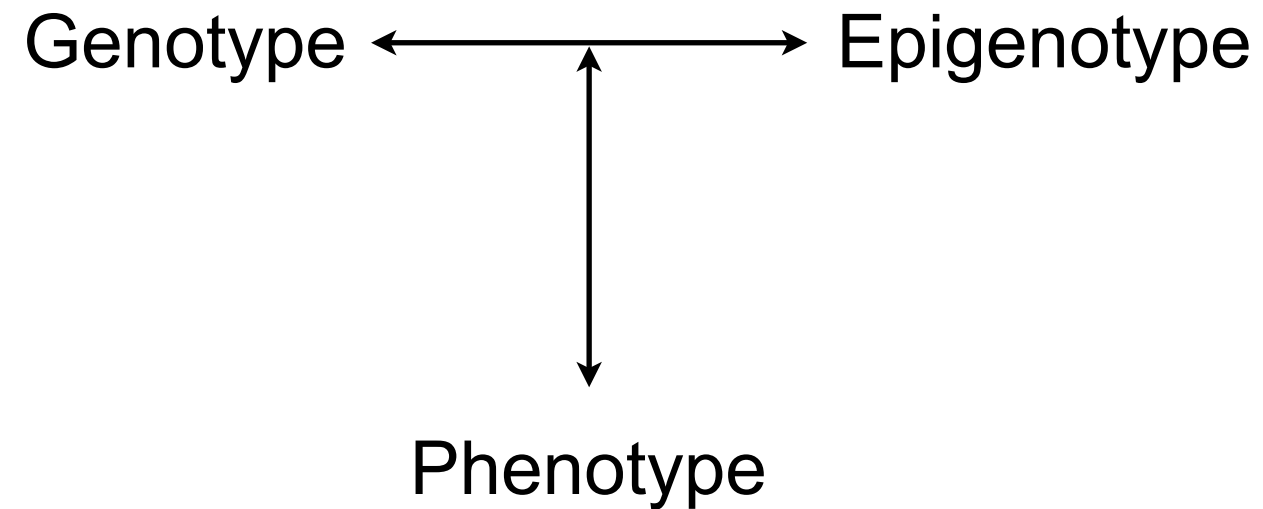
Claudia Chica

Institut Pasteur Paris  
Bioinformatics and Biostatistics Hub  
C3BI - USR 3756 IP CNRS

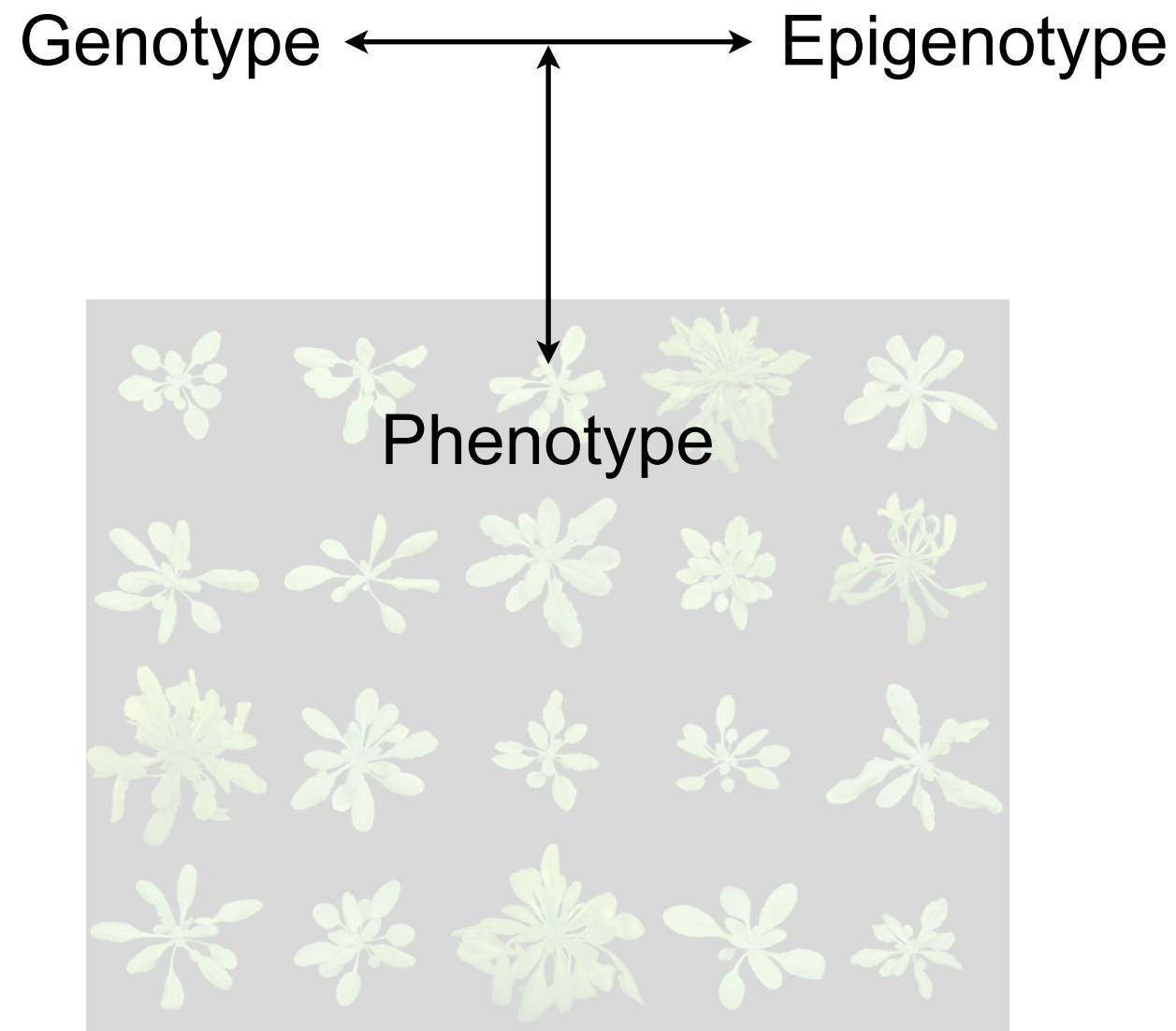
# Chromatin is pivotal for the control of genome activity



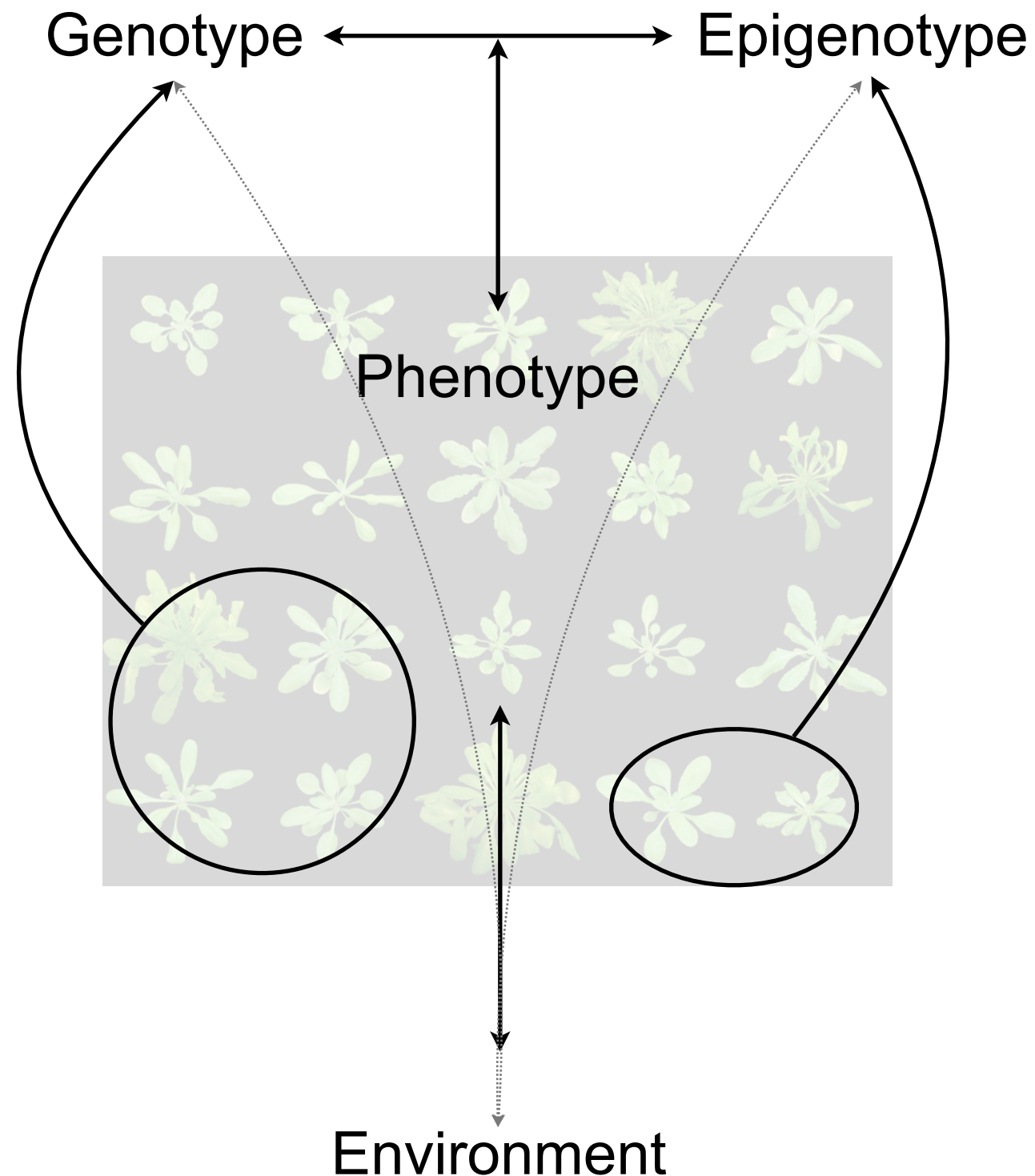
# Evolutionary approach to study information transactions in biological systems



# Evolutionary approach to study information transactions in biological systems



# Evolutionary approach to study information transactions in biological systems







“I’m interested in the way time records itself into things and people”

Miyako Ishiuchi

## **Comparative epigenomics**

“I’m interested in the way time records itself into things and people”

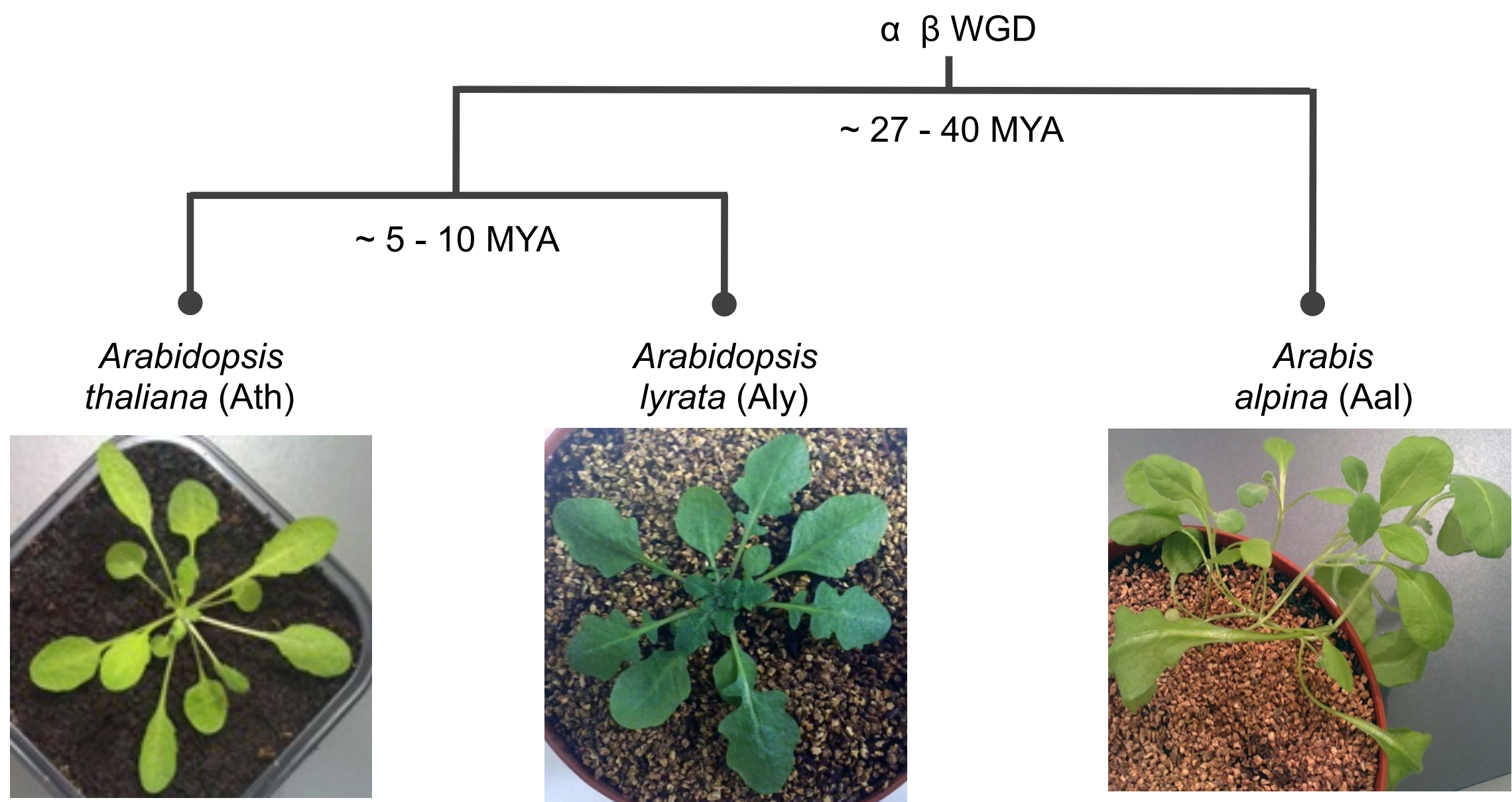
Miyako Ishiuchi

## **Comparative epigenomics**

- To which extent DNA sequence and chromatin co-vary during the evolutionary process?
- How similarities and differences in chromatin marking between species inform us about the evolution of gene regulation?
- Does chromatin have an impact on the evolution of genome organisation?



# Three Brassicaceae species spanning 40 MYA of divergence



Size

120 Mb - 5 Chr

Genes

28,496      51%

TEs

23,322      20%

194 Mb - 8 Chr

27,416      35%

44,866      32%

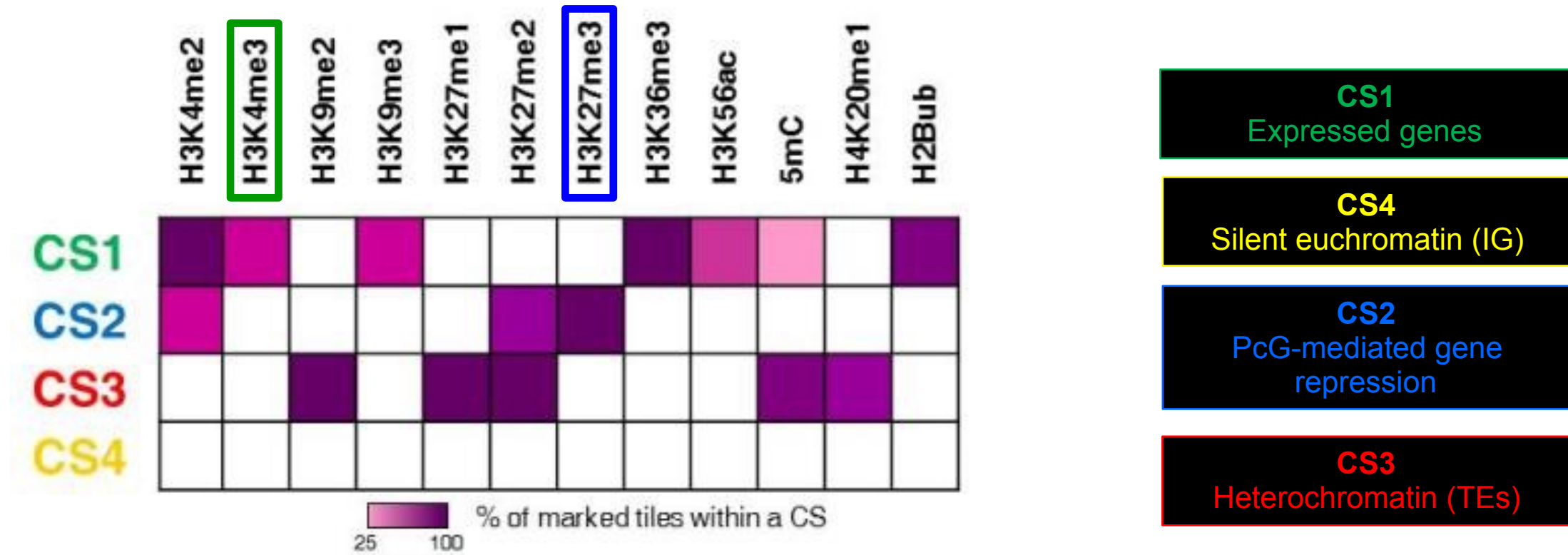
309 Mb - 8 Chr

27,165      31%

71,937      55%

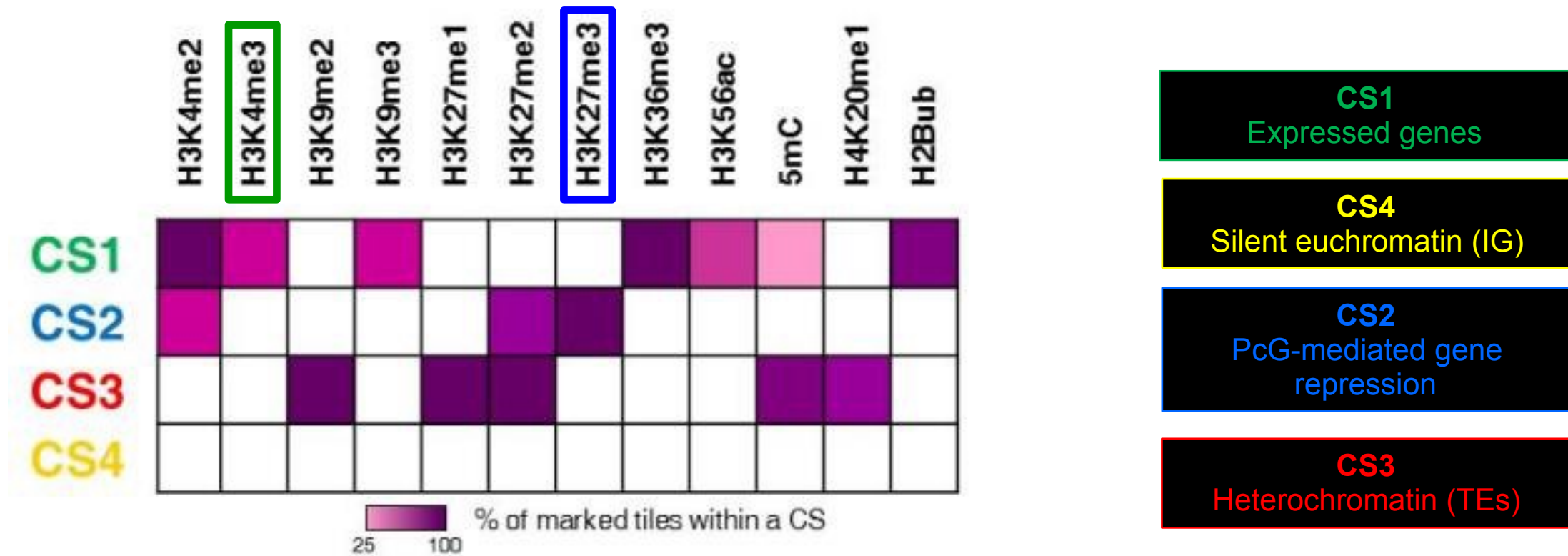


# Comparing the epigenome of Ath, Aly and Aal using contrasted chromatin marks

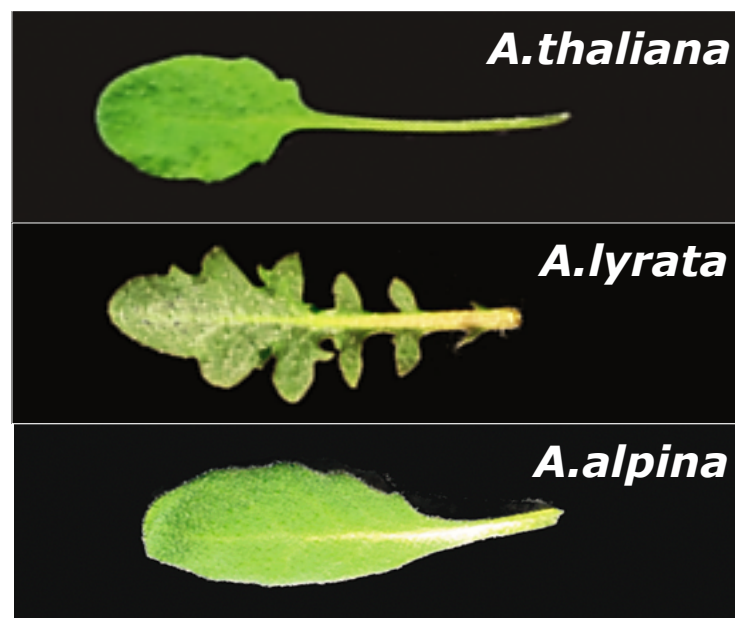


Roudier et al. *EMBO J.*, 2011

# Comparing the epigenome of Ath, Aly and Aal using contrasted chromatin marks



Roudier et al. *EMBO J.*, 2011



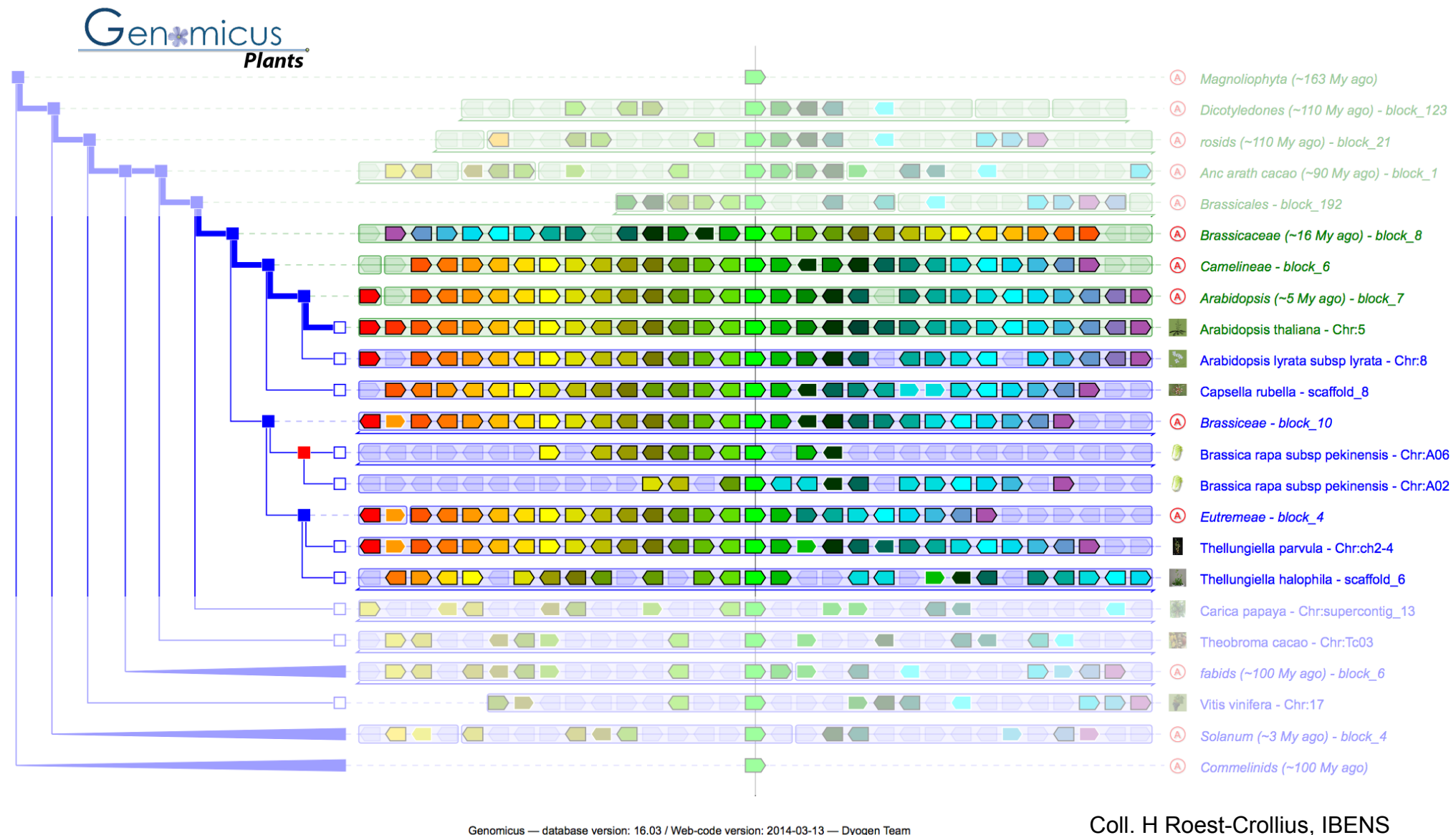
Matched samples:

- fully expanded leaves (RNA-seq Pearson correlation 0.89)

Chromatin and expression profiling:

- ChIP-seq H3K27me3 - H3K4me3
- RNA-seq
- 2 biological replicates

# Defining a robust set of homologous genes using the reconstructed Brassicaceae ancestral genome



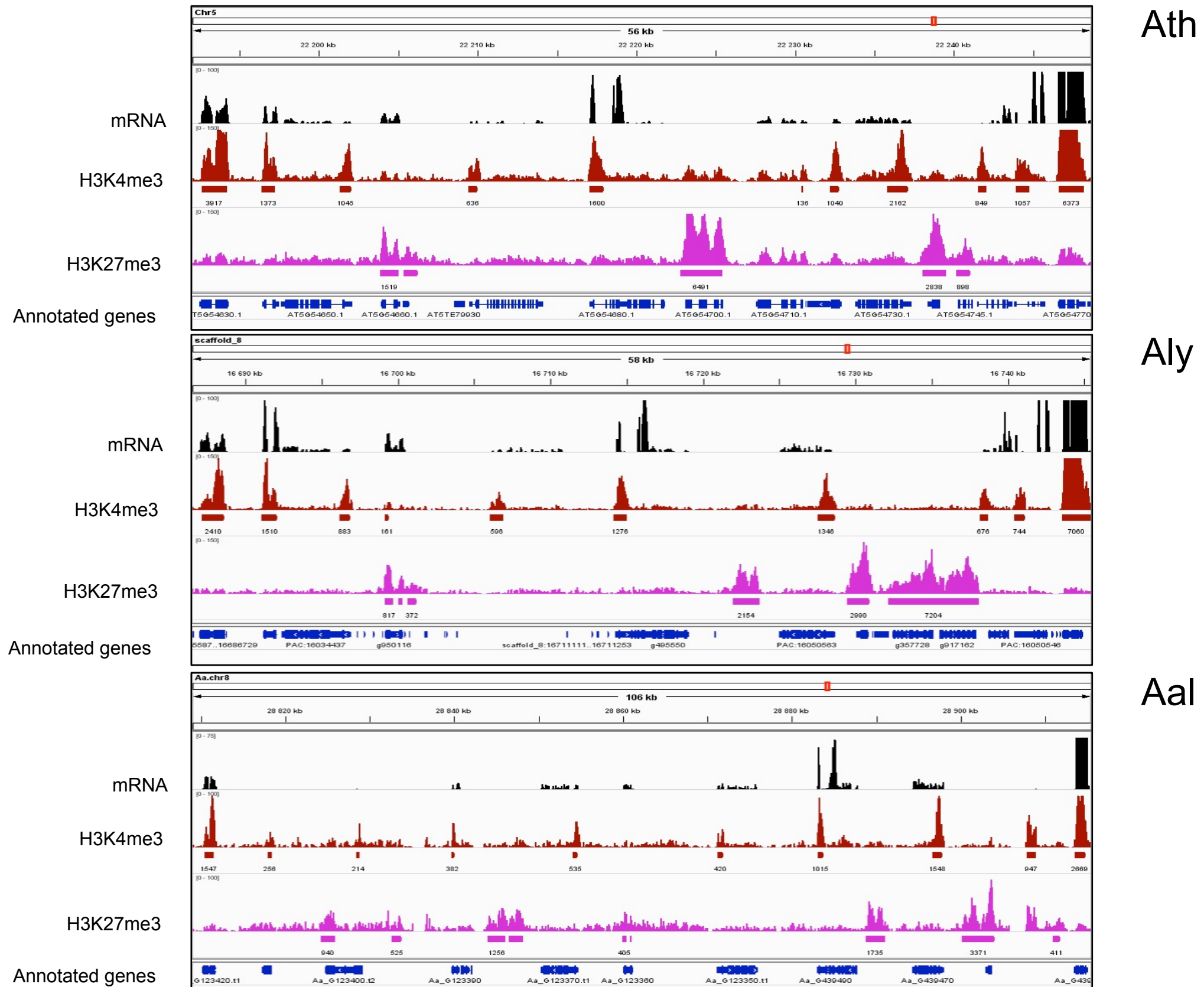
26028 ancestral genes without recent duplication

13515 without gene loss

12513 gene with loss in one or two species

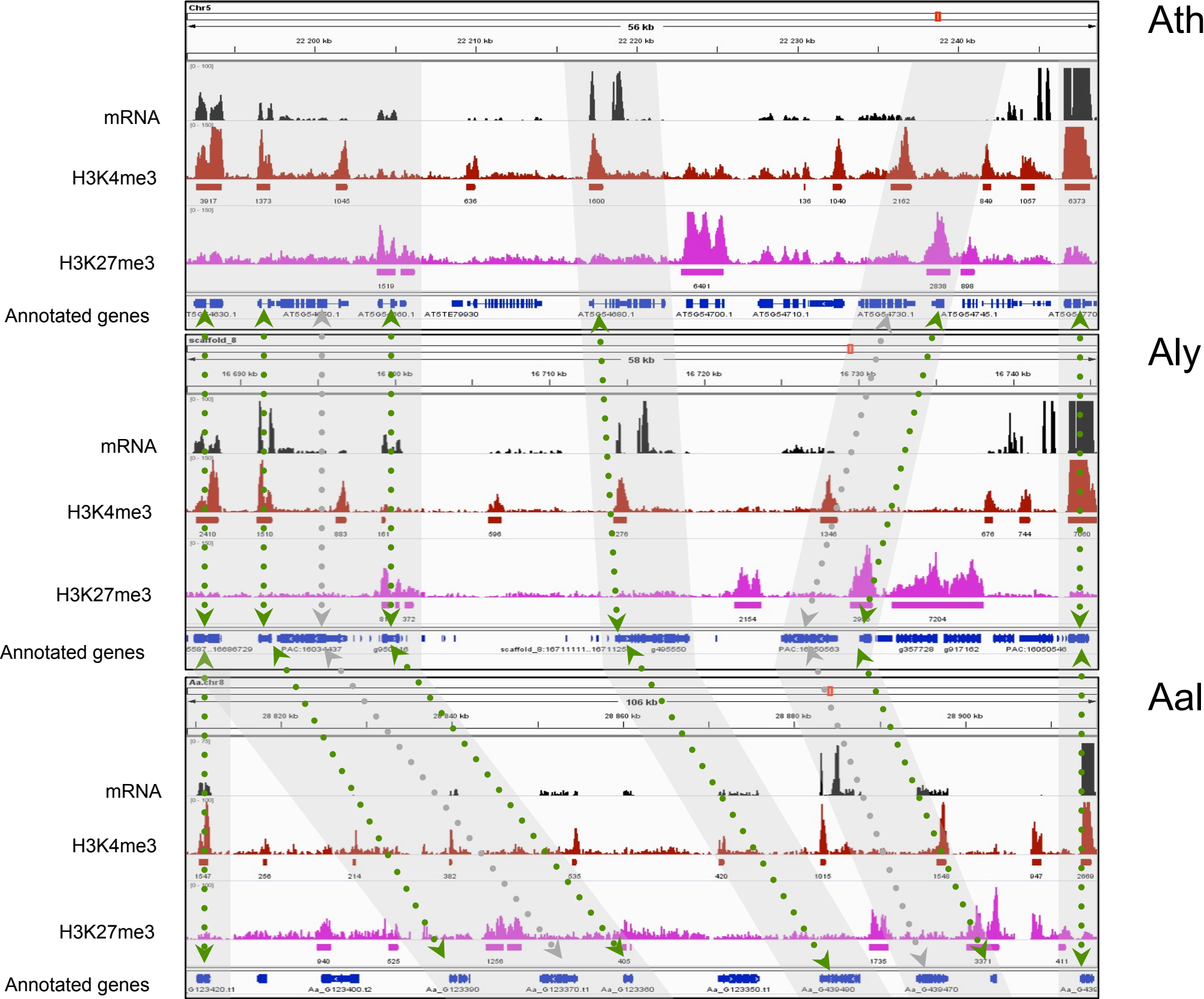
1316 ancestral genes that duplicated after the Brassicaceae split

# Comparative epigenomics: the raw data

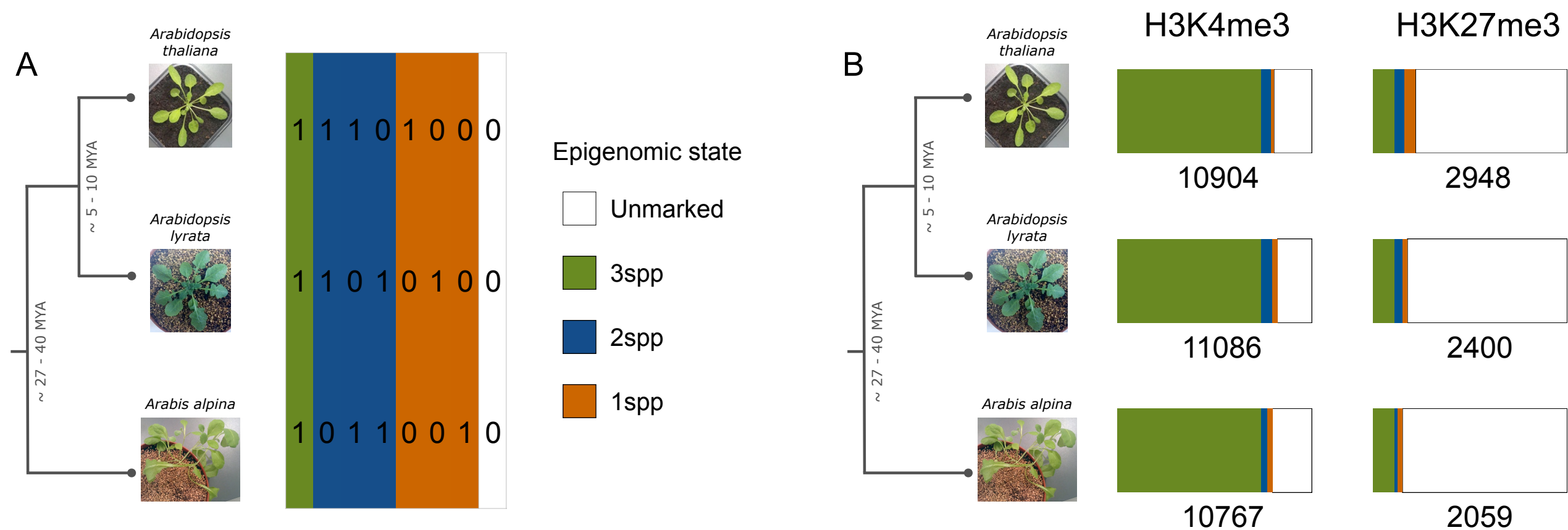




# Comparative epigenomics: the raw data



# H3K4me3 marking is highly similar between species whereas H3K27me3 marking shows some variation



Epigenomic state distribution among marked genes

Epigenomic state	H3K27me3	H3K4me3
3spp	40 %	85 %
2spp	22 %	8 %
1spp	38 %	7 %

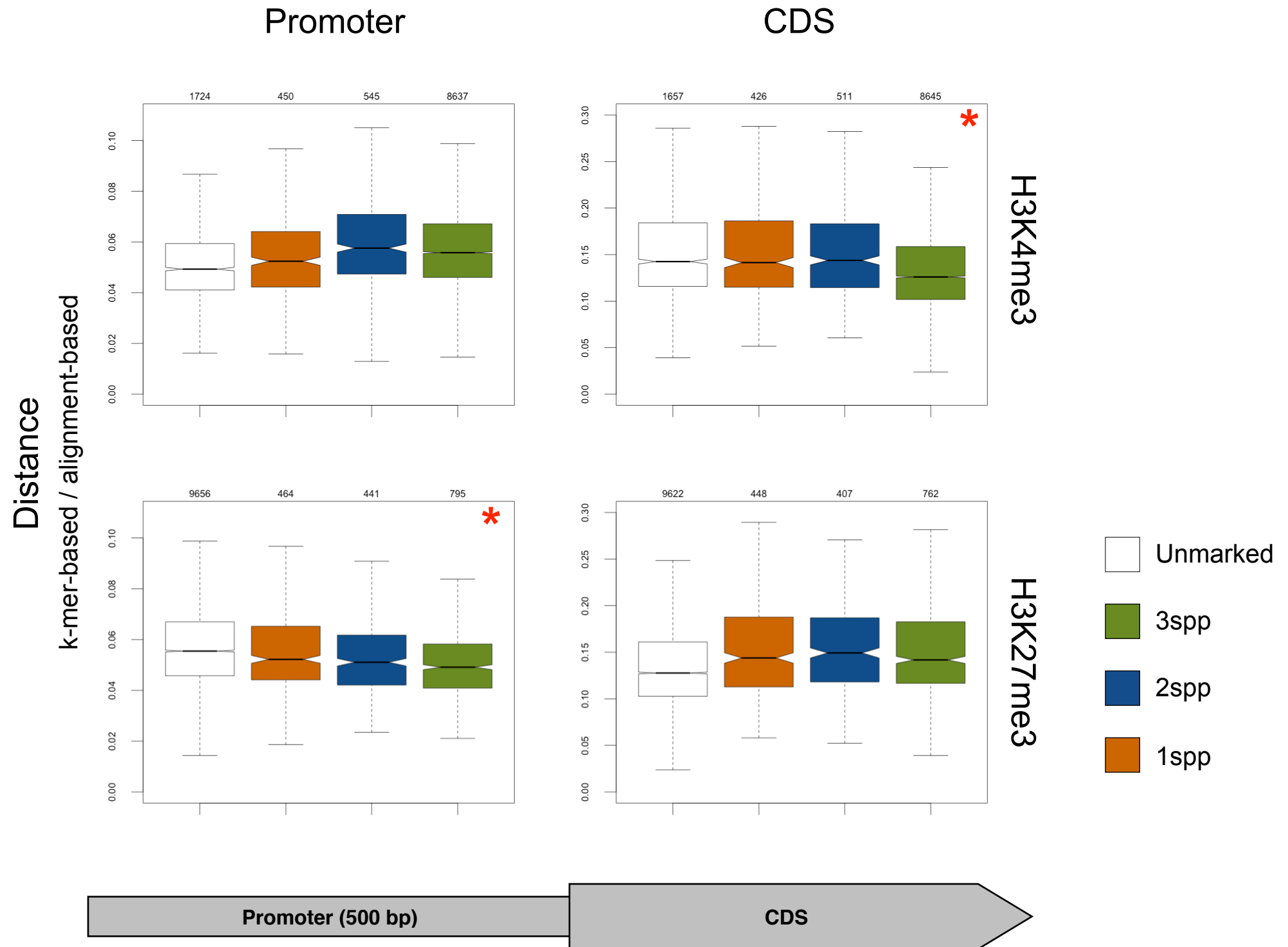
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## **Comparative epigenomics**

- To which extent DNA sequence and chromatin co-vary during the evolutionary process?
- How similarities and differences in chromatin marking between species inform us about the evolution of gene regulation?
- Does chromatin have an impact on the evolution of genome organisation?

# Ancestrality of H3K27me3 marking is correlated with promoter conservation



Distance variance is significantly related to mark ancestry



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## **Comparative epigenomics**

- To which extent DNA sequence and chromatin co-vary during the evolutionary process?
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# Open questions about the gene regulation mediated by Polycomb systems

## Complex recruitment

### Locus-specific targeting

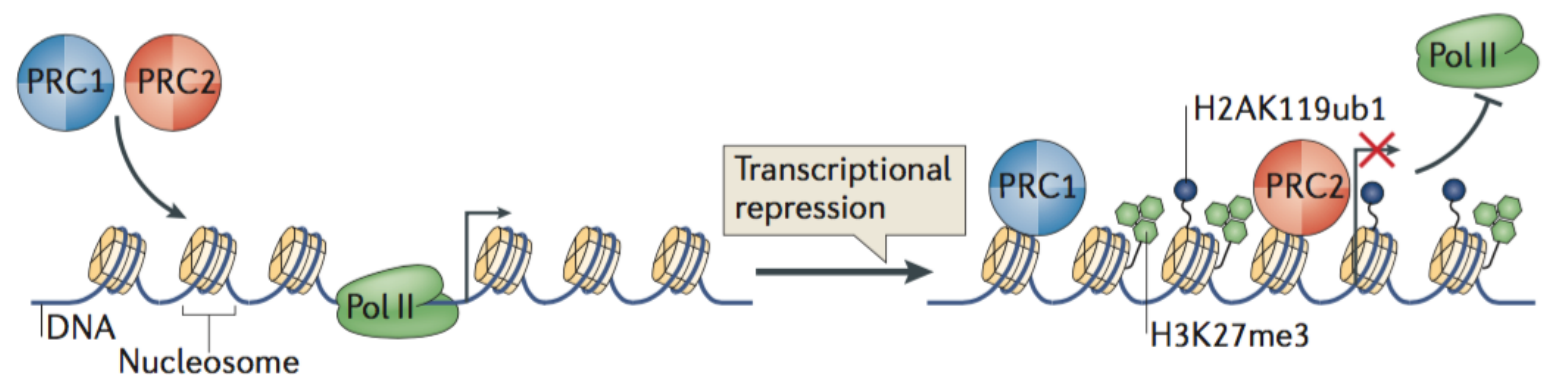
- Transcription factors
- lncRNAs

### Generic targeting

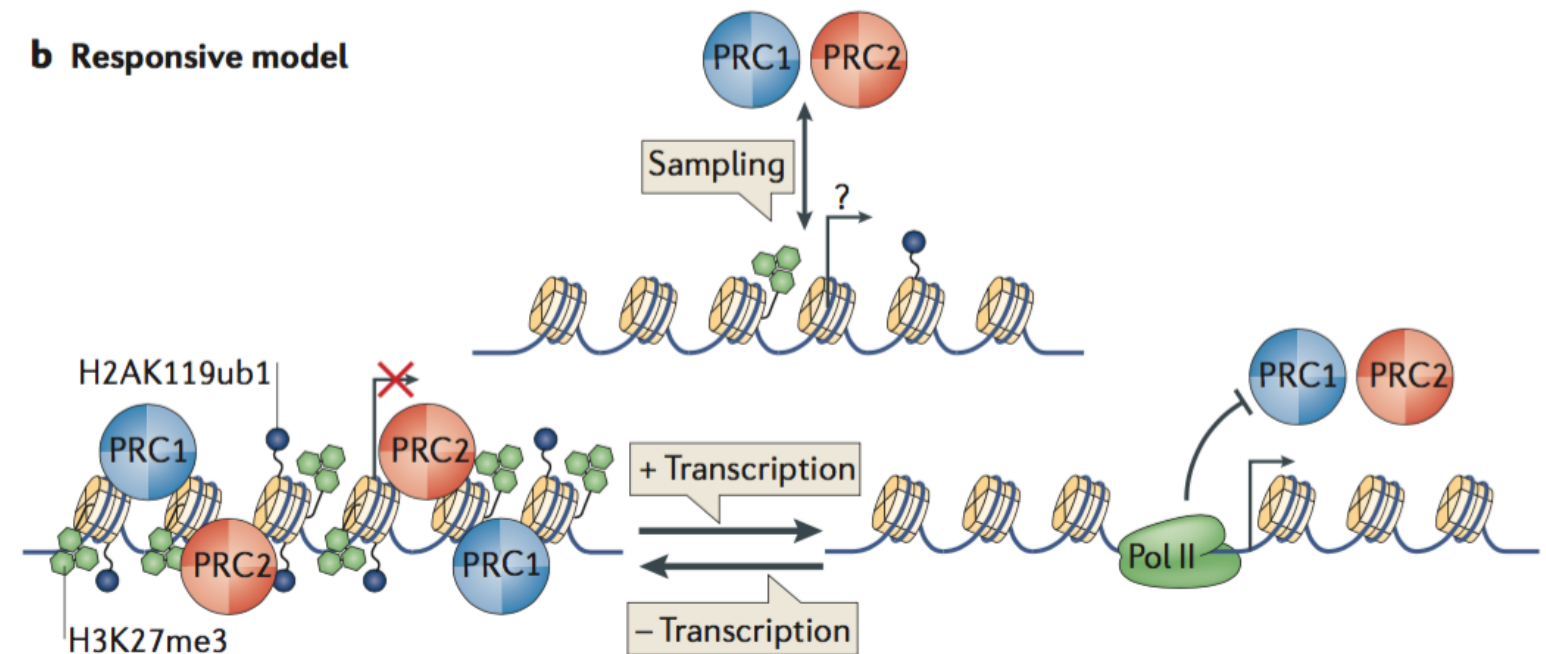
- un-methylated CpG islands
- Nascent transcripts
- Pre-existing histone modifications

## Gene silencing mechanisms

**a Instructive model**

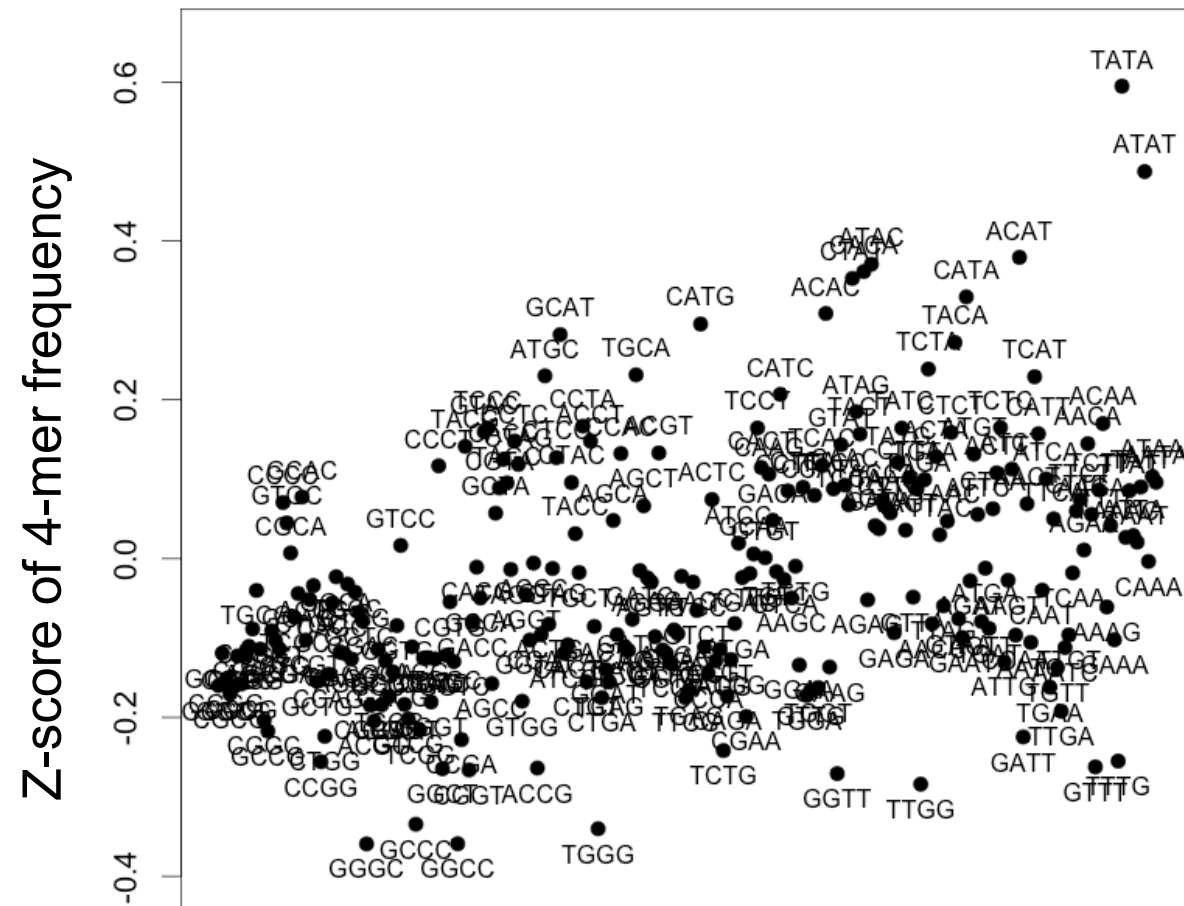


**b Responsive model**

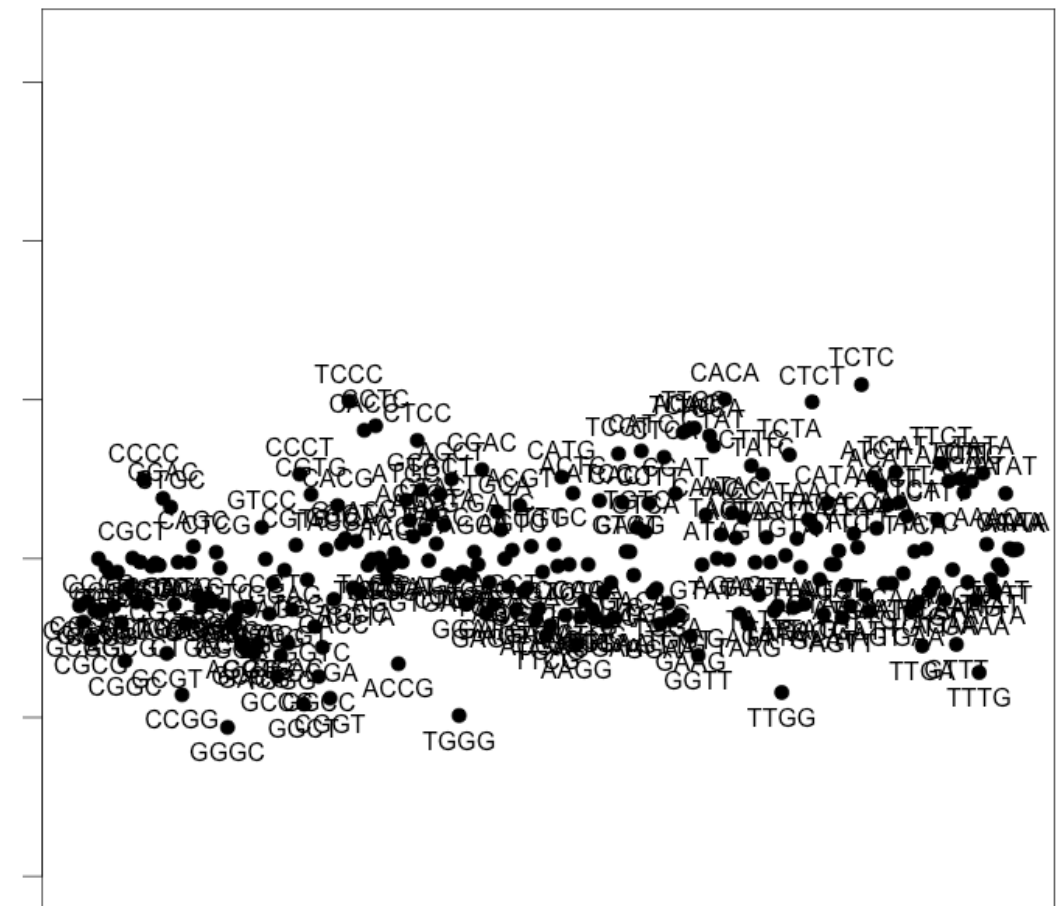


# Promoter conservation at PRC2 targets is associated with high frequency of 4-mers rich in AT/TA/AC/CA

## 3spp vs Unmarked



## 1spp vs Unmarked



— least frequent      — 4mers      — more frequent      →

# **Ancestrality of PRC2 marking is associated with distinct over-represented motifs**

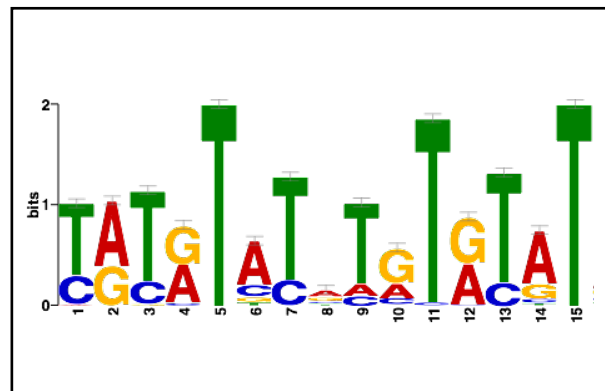
Recruitment and/or displacement of PRC2?



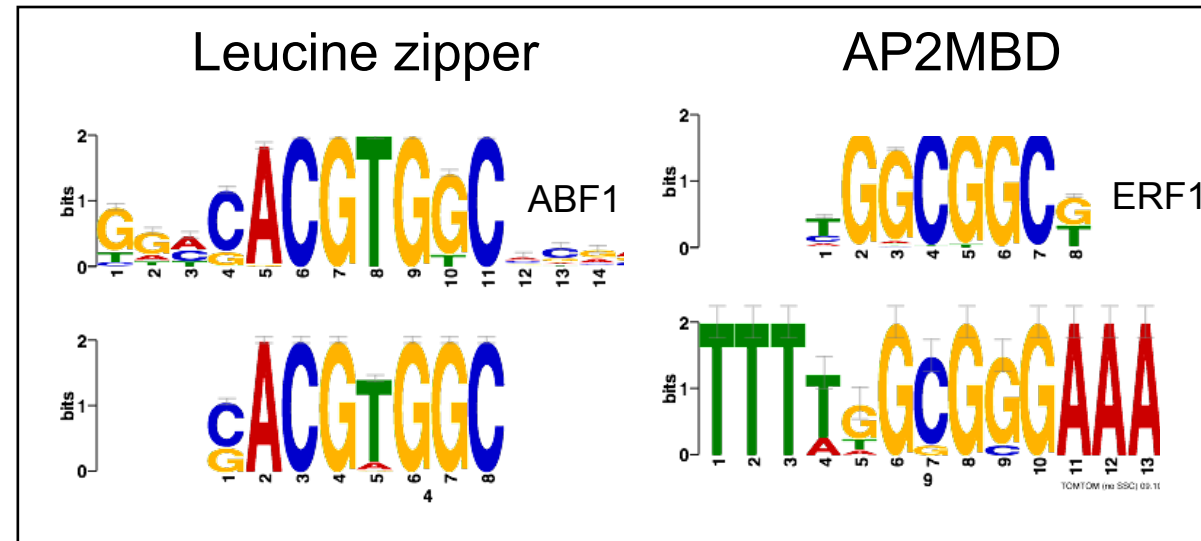
# Ancestrality of PRC2 marking is associated with distinct over-represented motifs

Recruitment and/or displacement of PRC2?

3spp motif

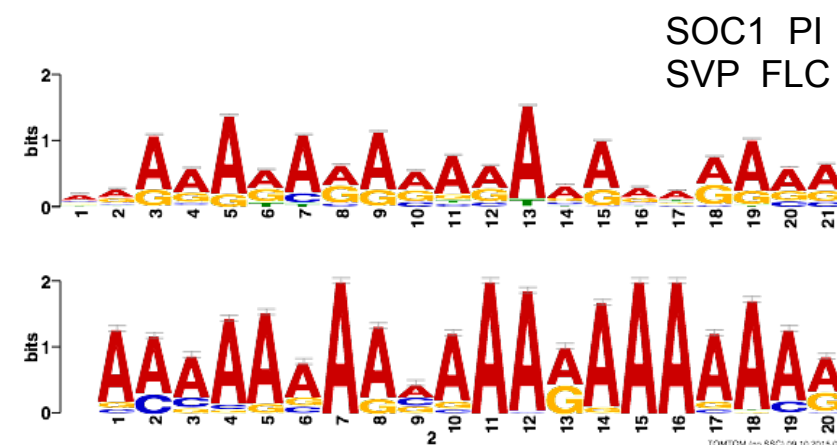


1spp motifs

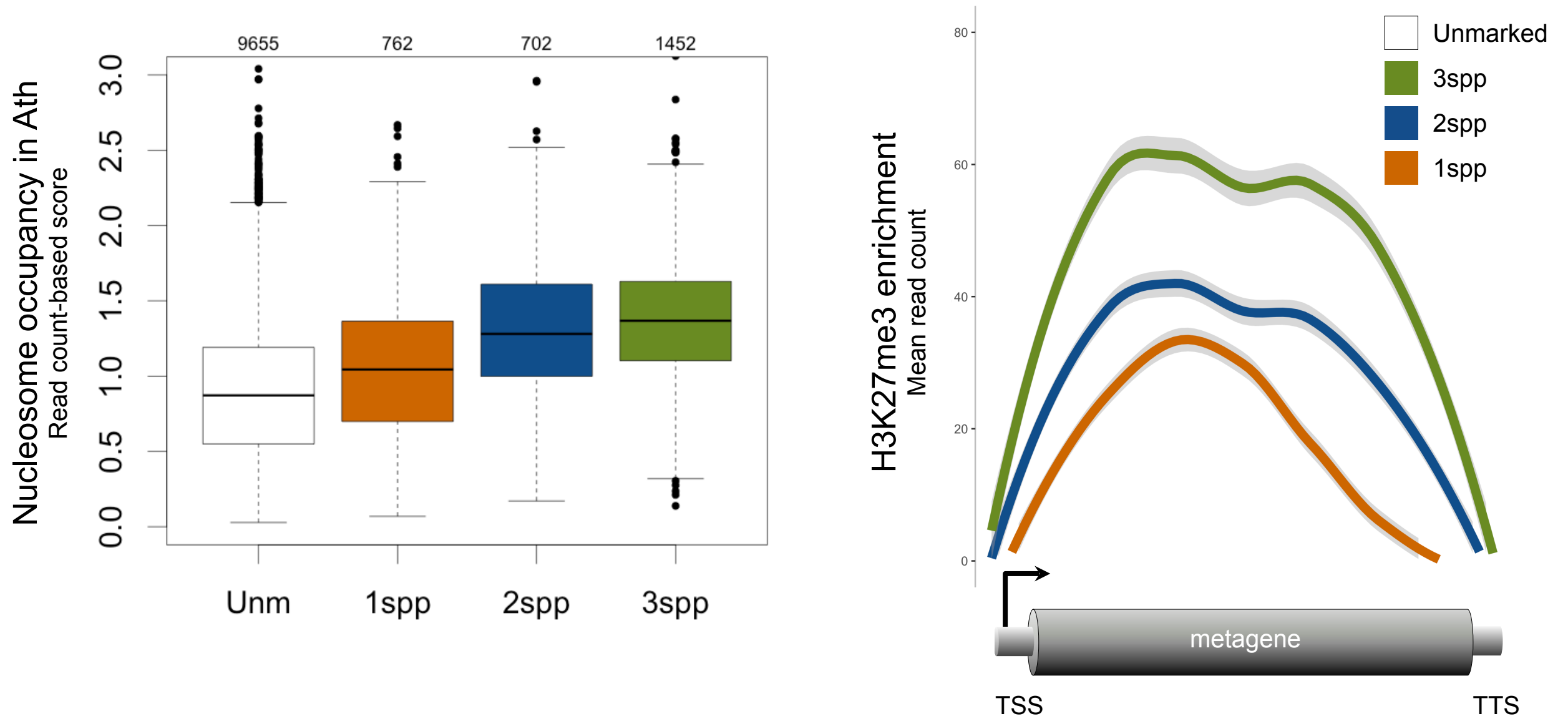


Ath

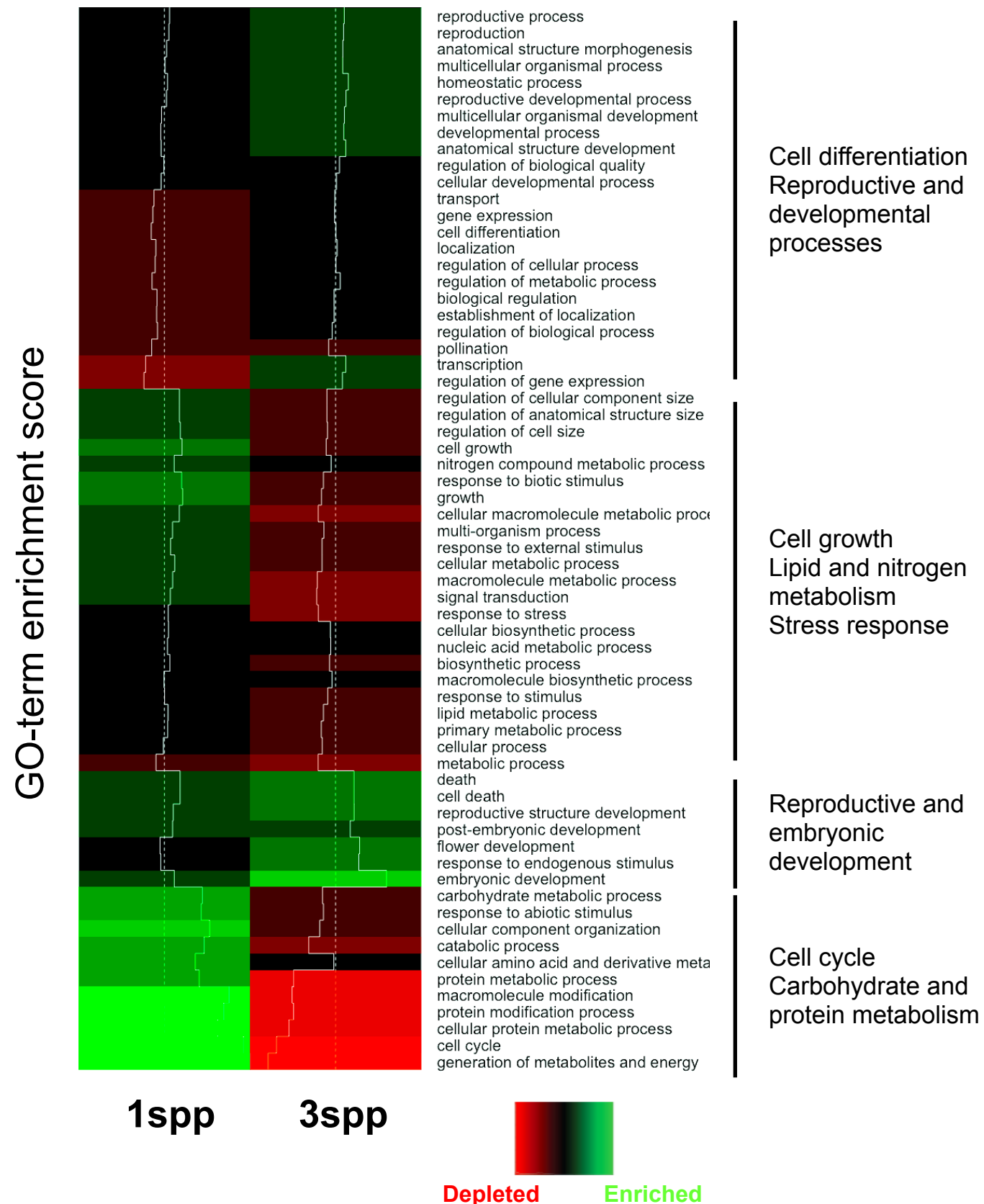
Aly



# Conservation of the promoter sequence of PRC2 targets is associated with higher nucleosome occupancy and H3K27me3 enrichment level

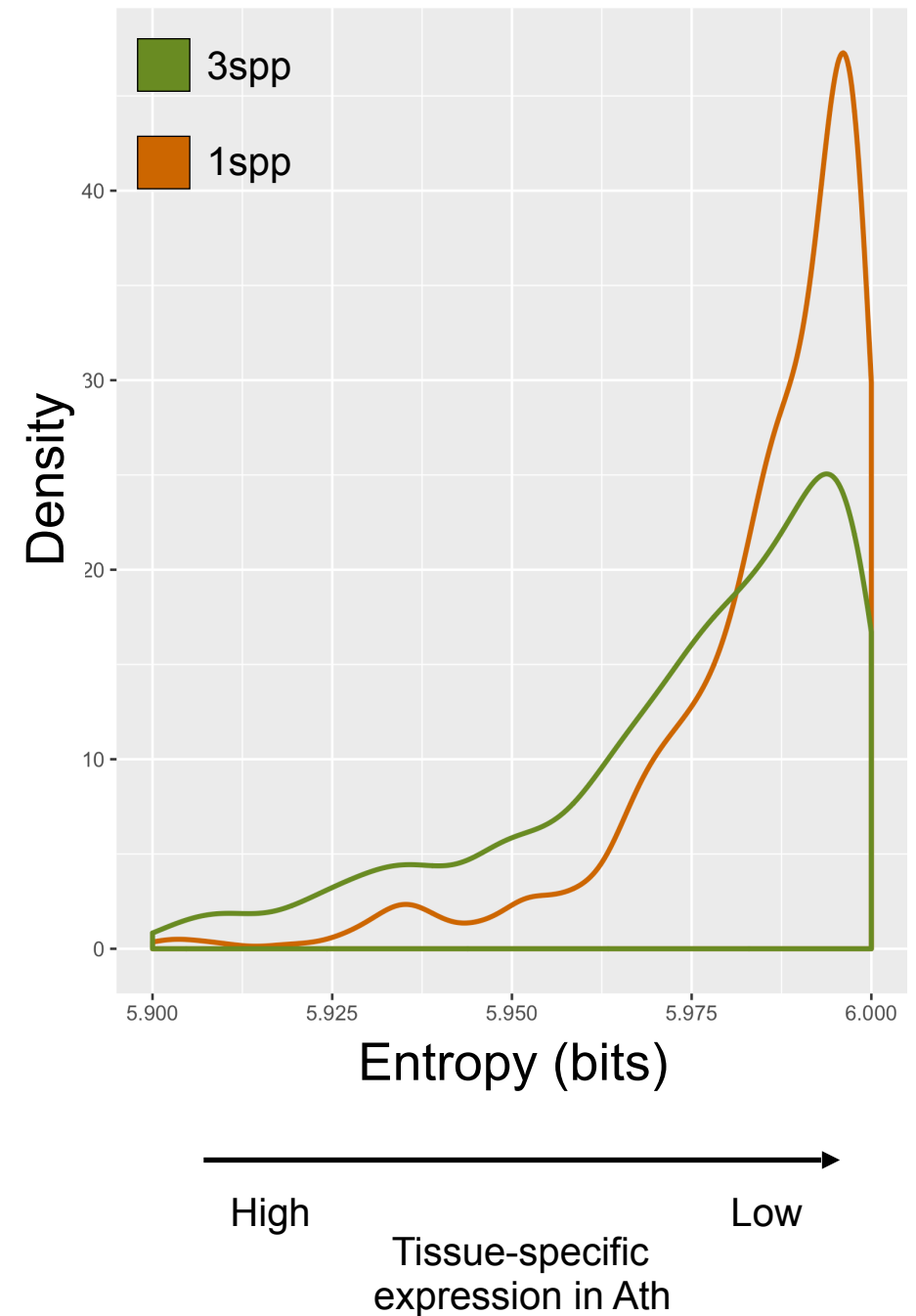
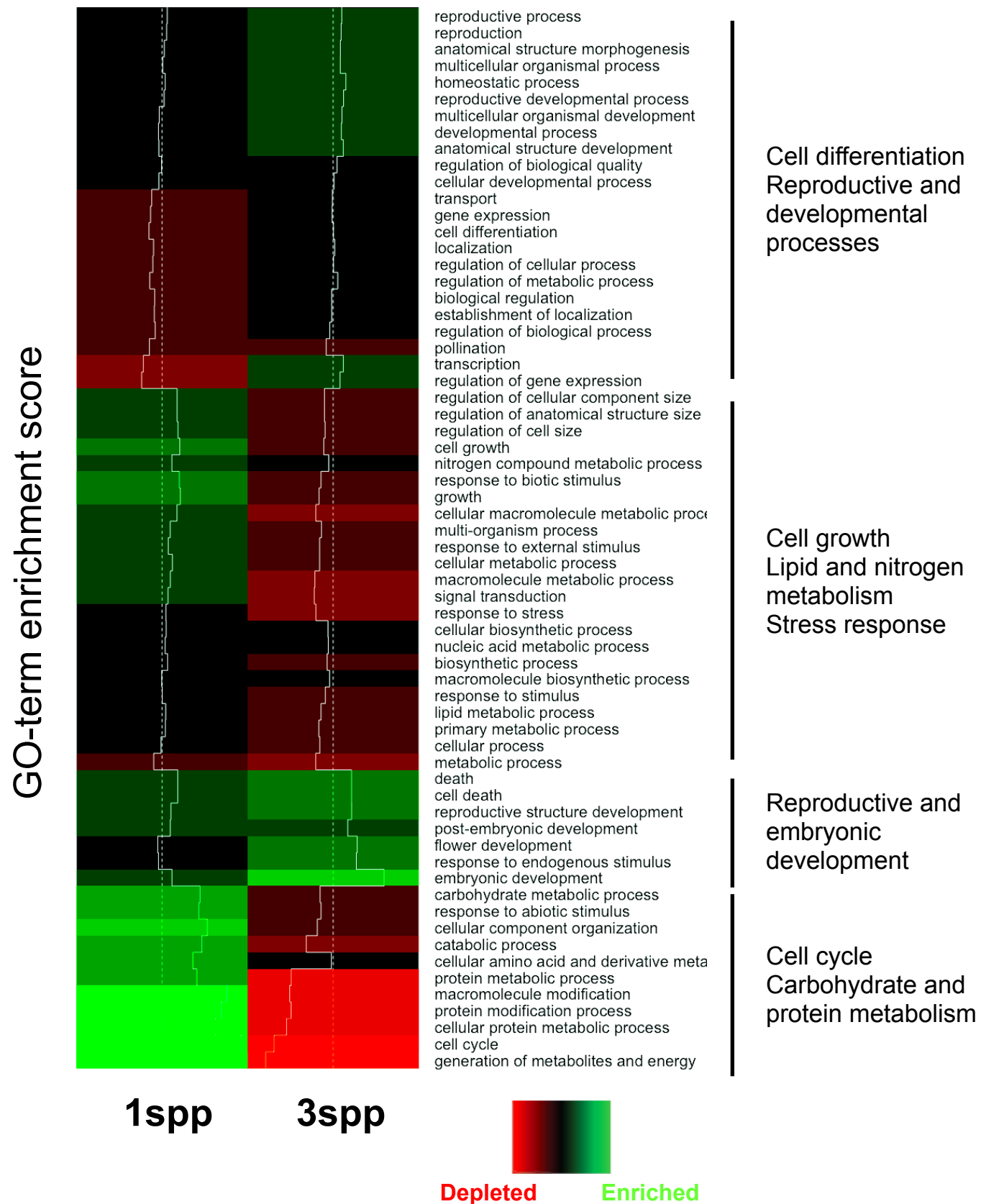


# PRC2 evolutionary dynamics correlates with distinct functions and expression patterns

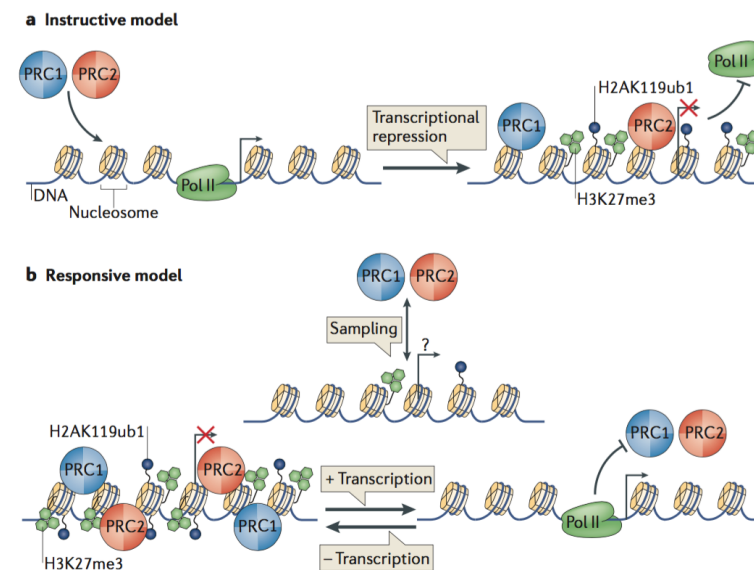




# PRC2 evolutionary dynamics correlates with distinct functions and expression patterns



# Evolutionary epigenomics suggests distinct modes of PRC2-mediated gene repression



## Conserved H3K27me3 marking (3spp)

- Conserved promoter features that favour PRC2 repression
- Developmental genes
- Sharp and tissue-specific expression profiles

## Variable H3K27me3 marking (1spp)

- No detectable constraints on promoter sequence
- Basal metabolism genes
- Modulated and un-specific expression profiles

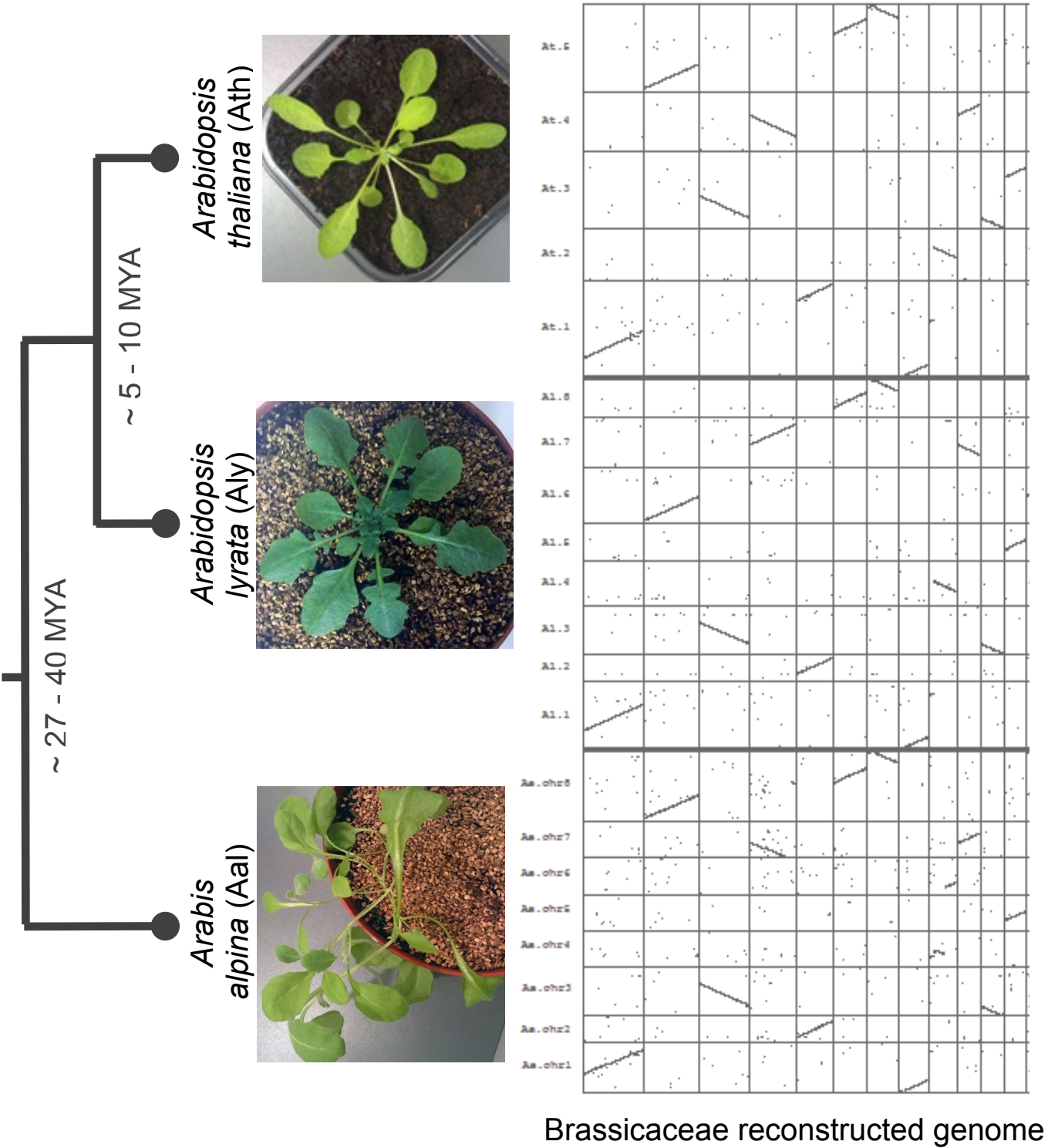
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## **Comparative epigenomics**

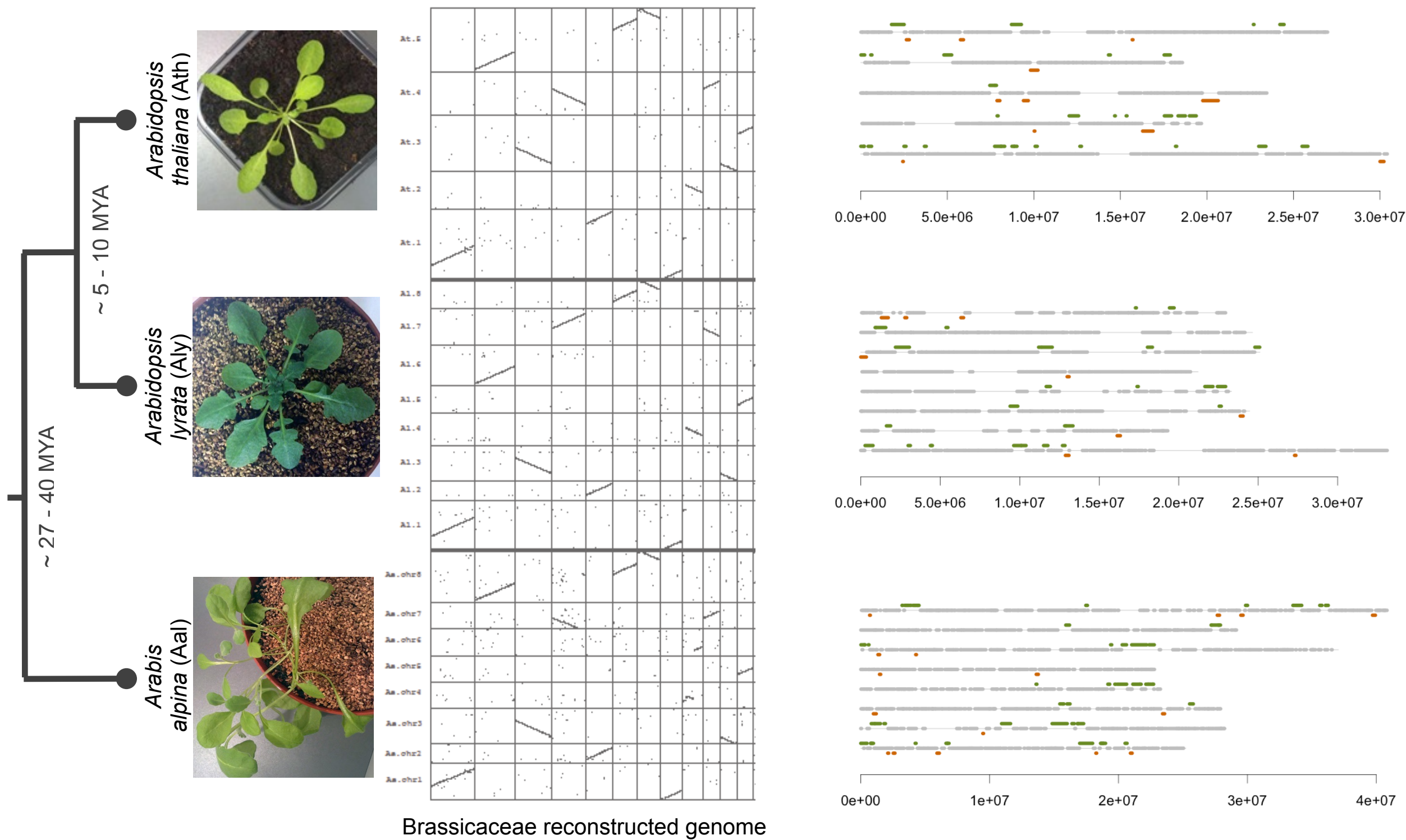
- To which extent DNA sequence and chromatin co-vary during the evolutionary process?
- How similarities and differences in chromatin marking between species inform us about the evolution of gene regulation?
- Does chromatin have an impact on the evolution of genome organisation?

In these highly syntenic genomes, some blocks are significantly enriched in conserved PRC2 targets



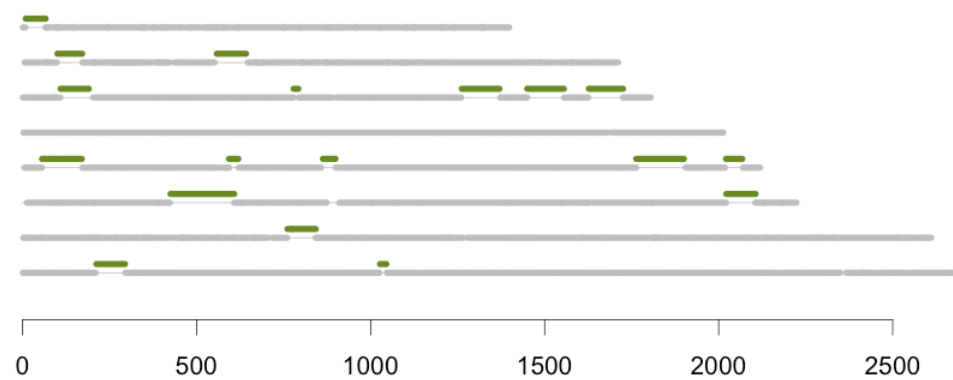


# In these highly syntenic genomes, some blocks are significantly enriched in conserved PRC2 targets

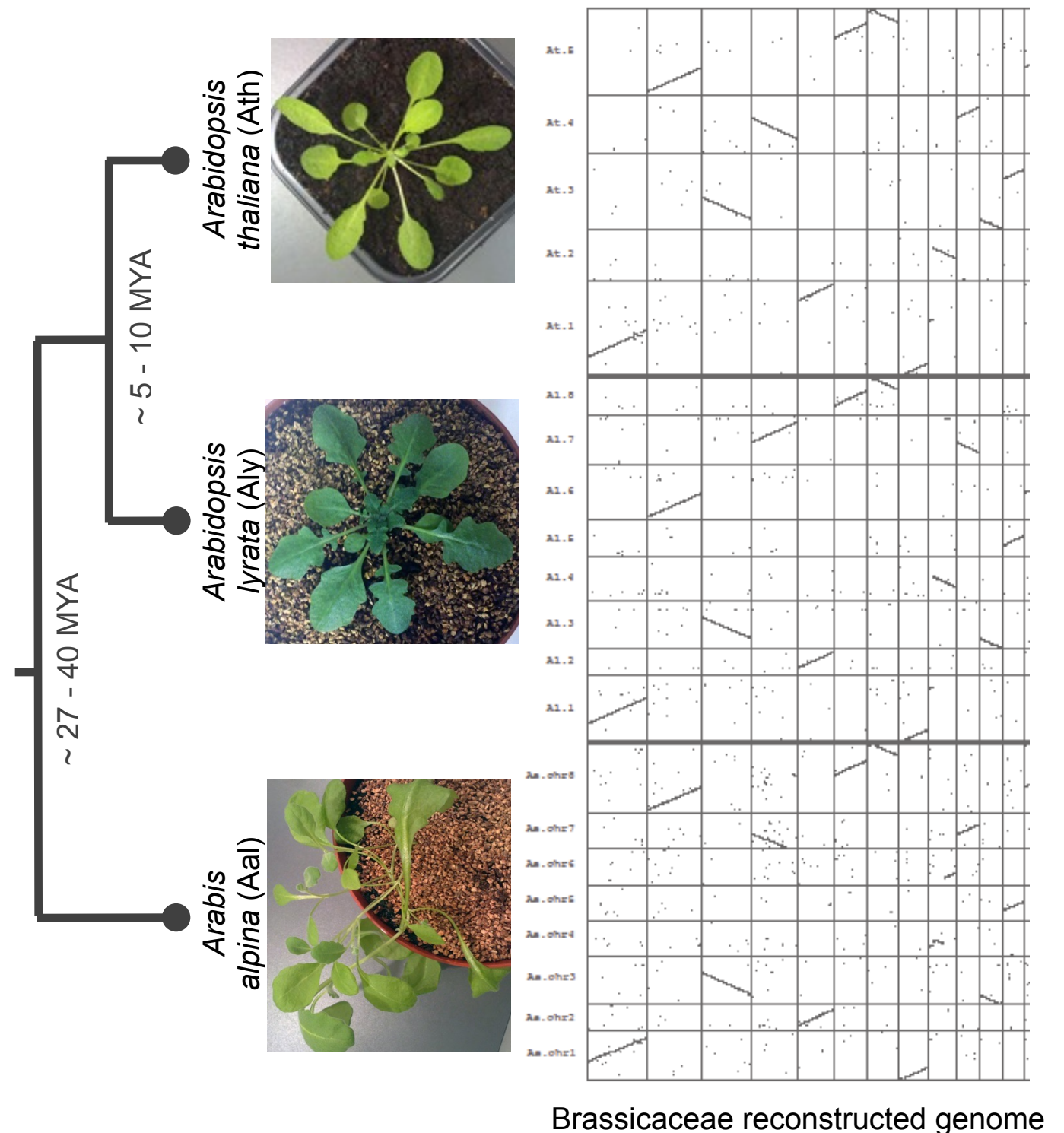


# This blocks show a concerted conservation of the gene organisation and the dominant chromatin state for the last 40 MYA

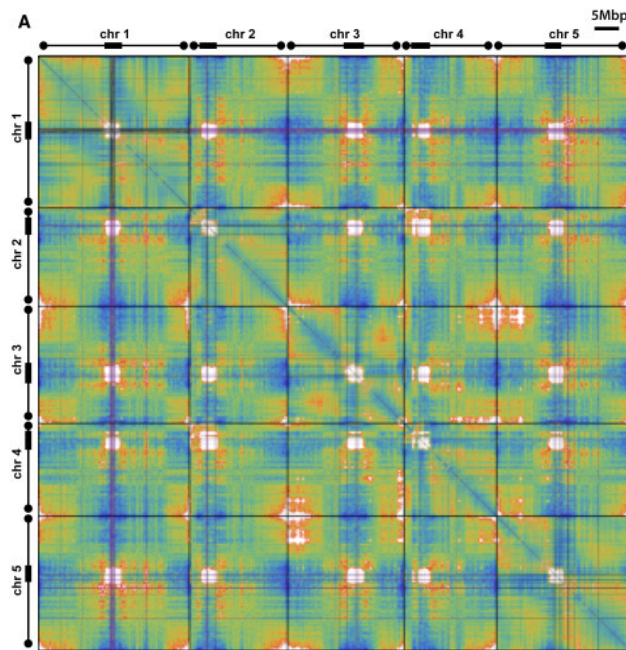
PRC2 ancestral domains:  
blocks of PRC2 targets  
conserved since 40 MYA



They include 1649 ancestral genes and  
~500 PRC2 targets (~20% of total)



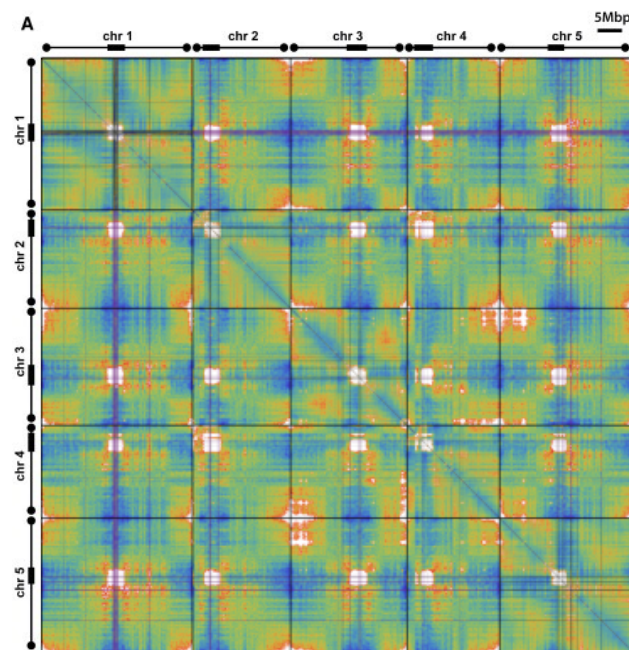
# PRC2 ancestral domains are important determinants of strong intra-chromosomal contacts



Contact strength <sup>a</sup>

Weak to strong

# PRC2 ancestral domains are important determinants of strong intra-chromosomal contacts



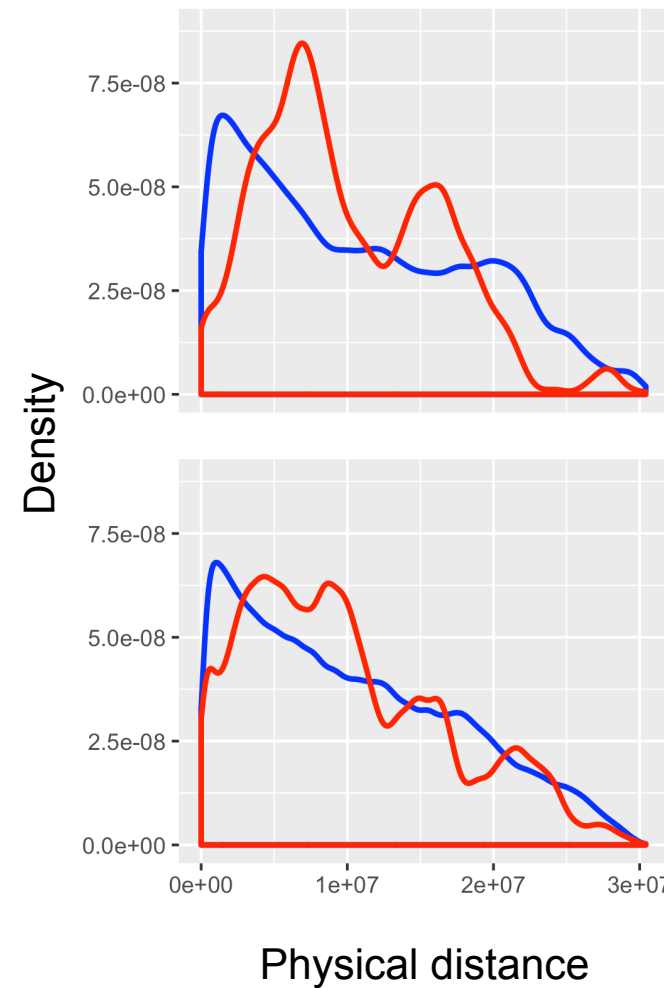
Contact strength <sup>a</sup>

Weak to strong

PRC2 ancestral  
domains

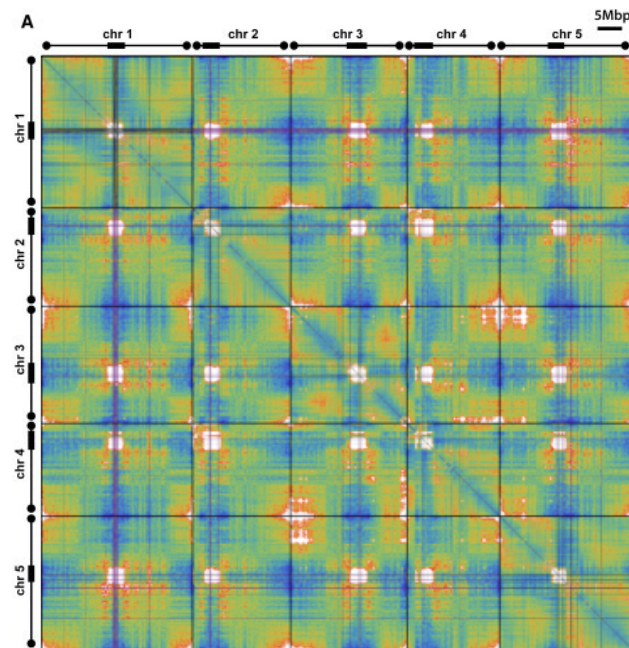
All syntenic  
blocks

**WT**





# PRC2 ancestral domains are important determinants of strong intra-chromosomal contacts



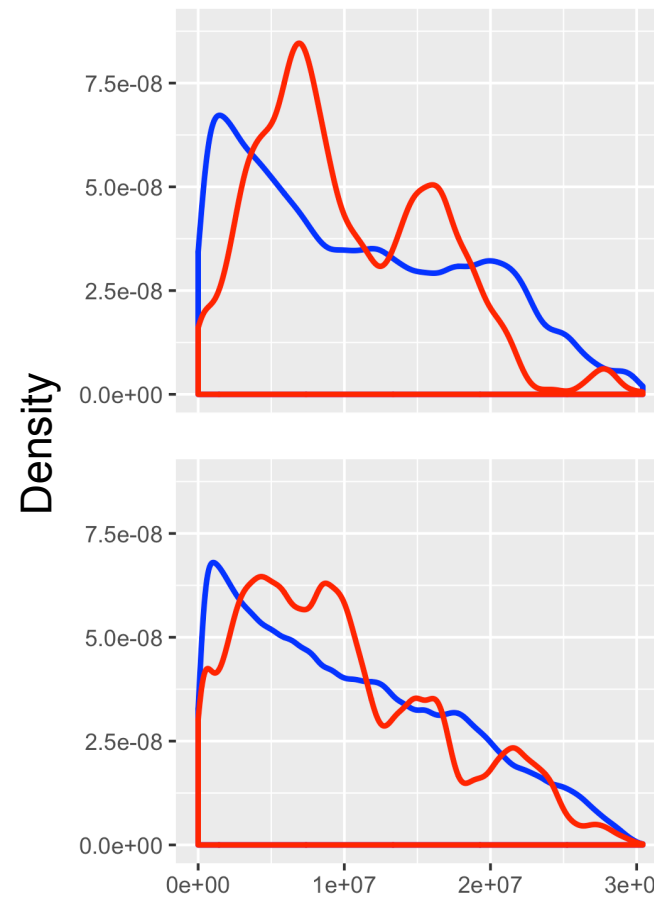
Contact strength <sup>a</sup>

Weak to strong

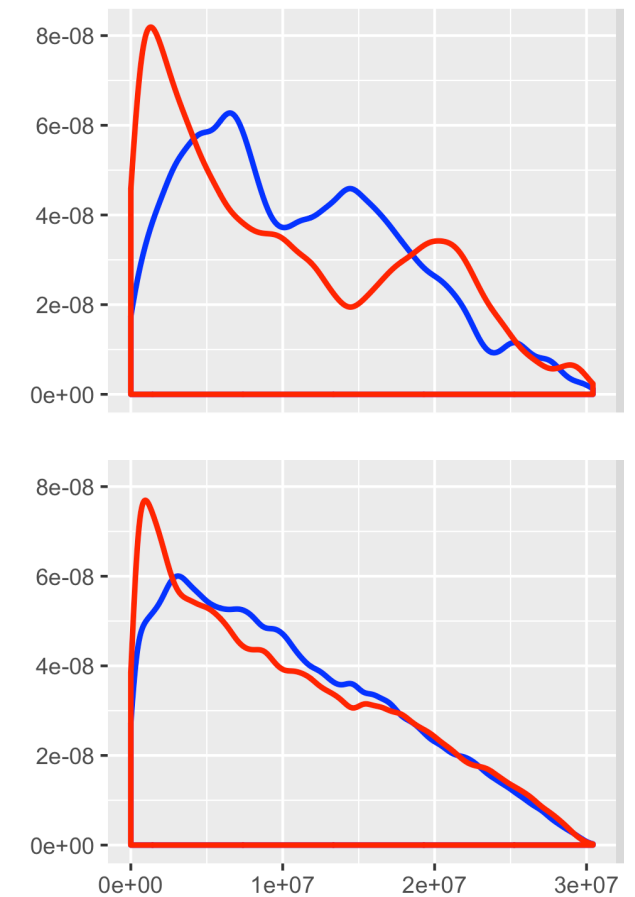
PRC2 ancestral  
domains

All syntenic  
blocks

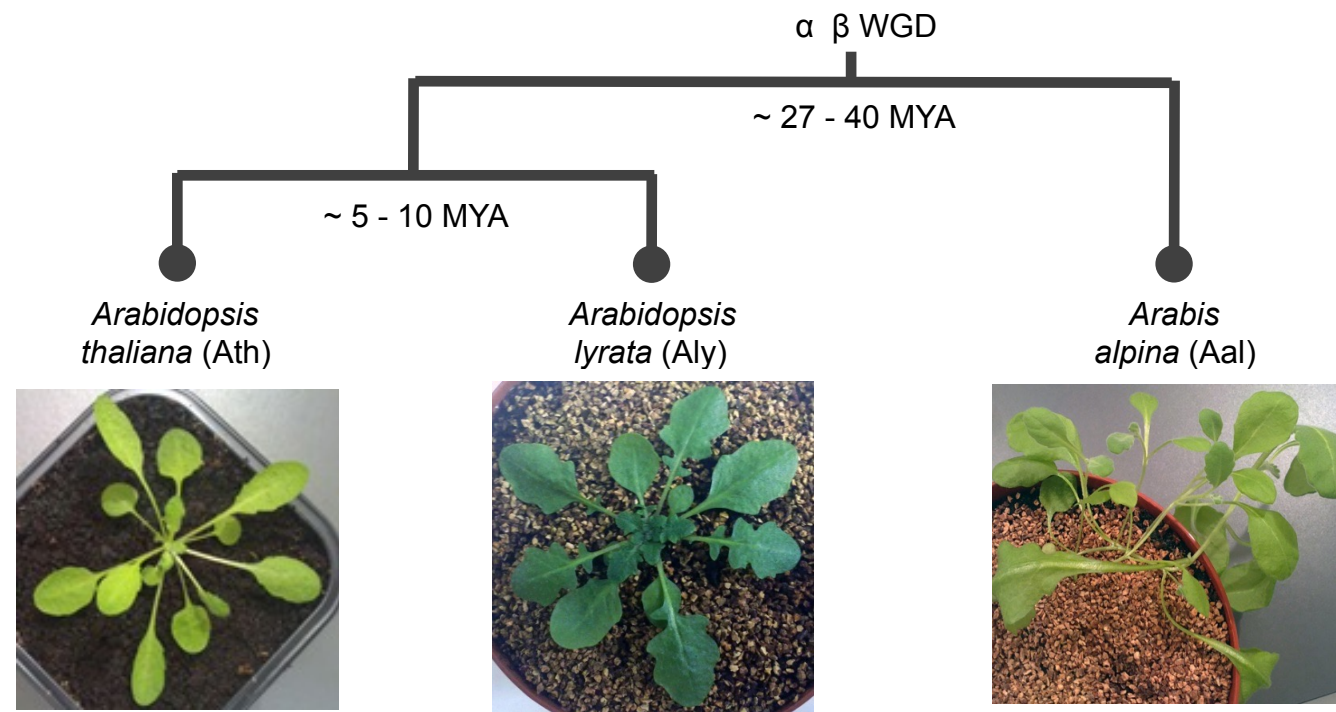
**WT**



***clf swm***



# Comparative epigenomics reveals that PRC2 regulation is subject to different types of evolutionary constraints



## Conserved H3K27me3 marking (~60%)

- Conserved promoter features that favour PRC2 repression
- Developmental genes
- Sharp and tissue-specific expression profiles
- PRC2 ancestral domains that shape intra-chromosomal interactions

## Variable H3K27me3 marking (~40%)

- No detectable constraints on promoter sequence
- Basal metabolism genes
- Modulated and un-specific expression profiles

# Acknowledgements

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Detlef WEIGEL



Institut Pasteur



C3BI - USR 3756

**IBENS**

Institut de Biologie de l'Ecole Normale Supérieure

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**Epigenesys**

**MEMO  
LABEX  
LIFE**