

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

Claudia Chica

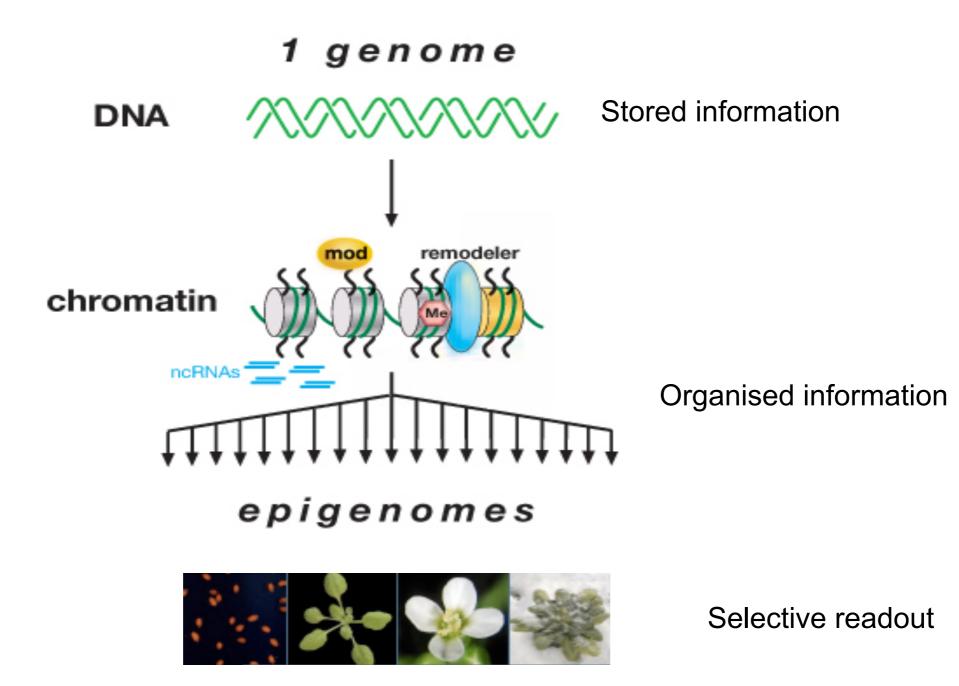
Institut Pasteur Paris Bioinformatics and Biostatistics Hub C3BI - USR 3756 IP CNRS



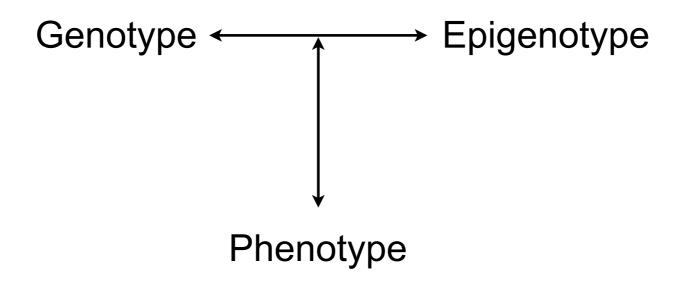
GTGC 01.07.2016 - Lyon



Chromatin is pivotal for the control of genome activity

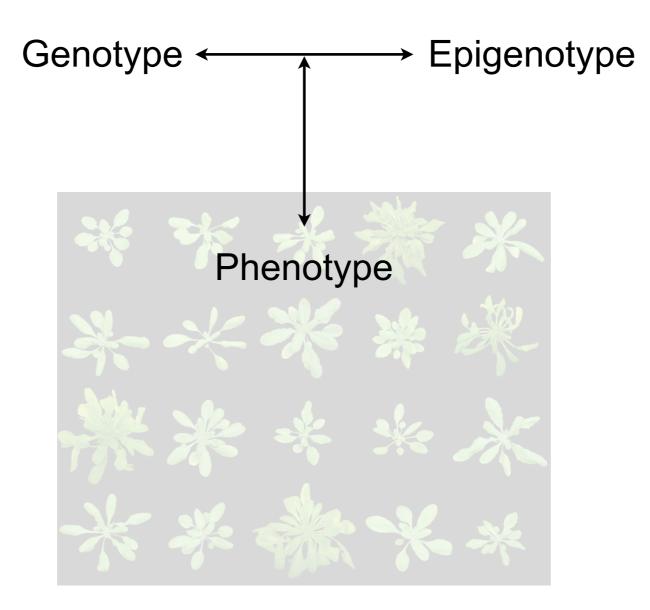


Evolutionary approach to study information transactions in biological systems



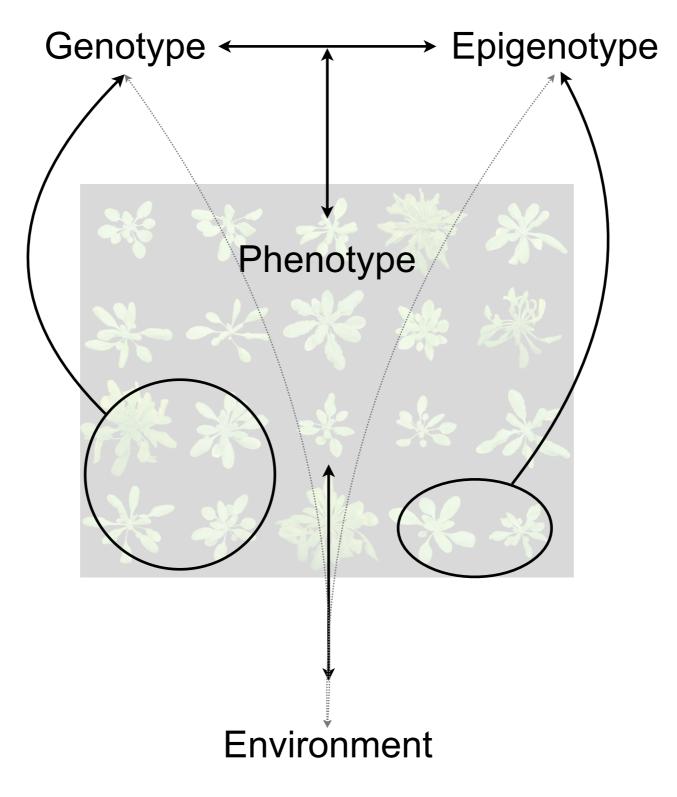
Cubas et al, *Nature* 1999 Manning et al, *Nat Genet* 2006 Cortijo S et al., *Science*, 2014 Laland K, Wray GA and Hoekstra, *Nature*, 2014

Evolutionary approach to study information transactions in biological systems



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Evolutionary approach to study information transactions in biological systems



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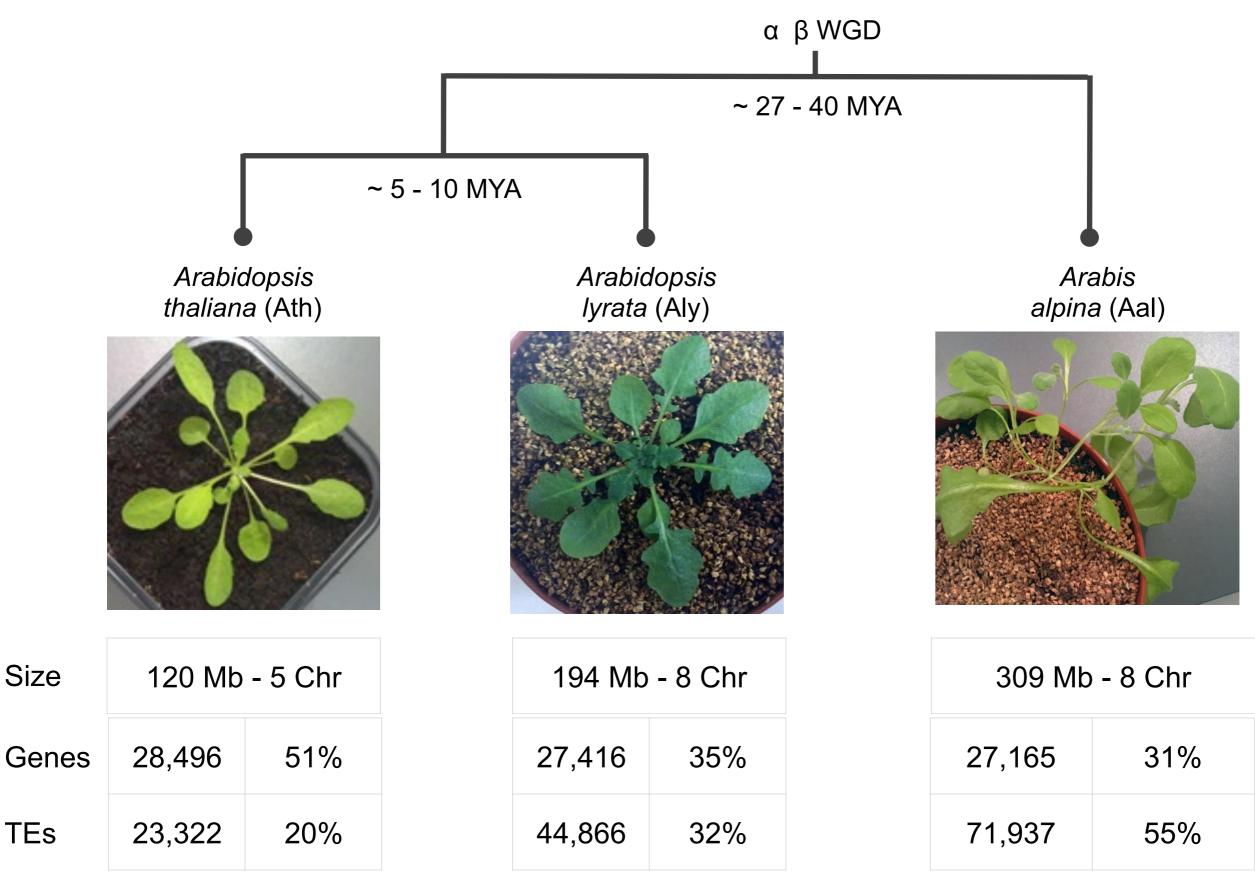
Comparative epigenomics

"I'm interested in the way time records itself into things and people" Miyako Ishiuchi

Comparative epigenomics

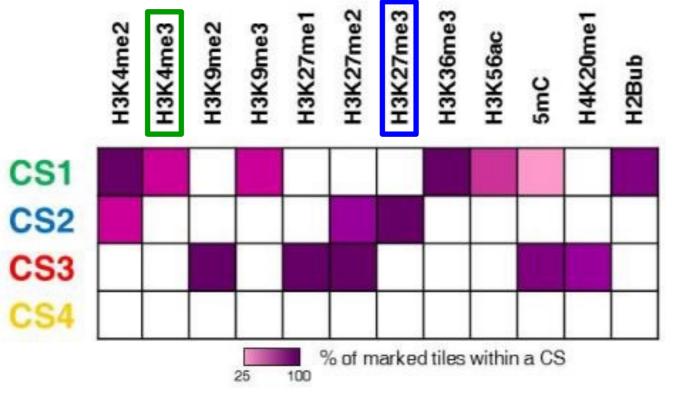
- To which extent DNA sequence and chromatin co-vary during the evolutionary process?
- How similarities and differences in chromatin marking between species inform us about the evolution of gene regulation?
- Does chromatin have an impact on the evolution of genome organisation?

Three Brassicaceae species spanning 40 MYA of divergence

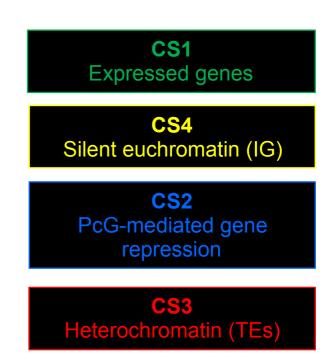


Trinational KBBE consortium. Coord. G. Coupland Willing, Rawat, Mandáková *et al.*, *Nature Plants, 2015.*

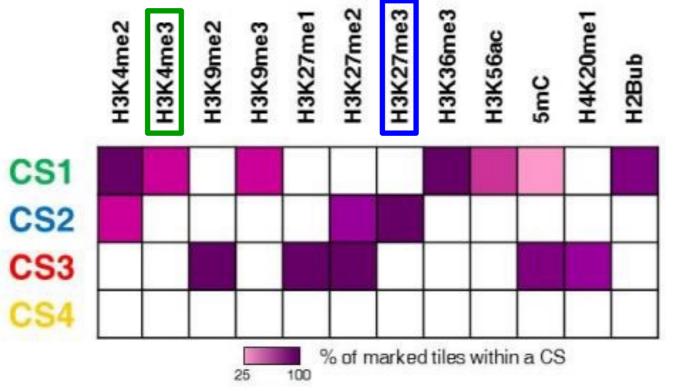
Comparing the epigenome of Ath, Aly and Aal using contrasted chromatin marks

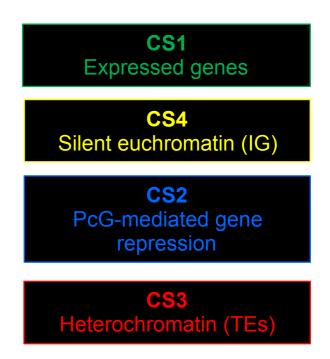


Roudier et al. EMBO J., 2011

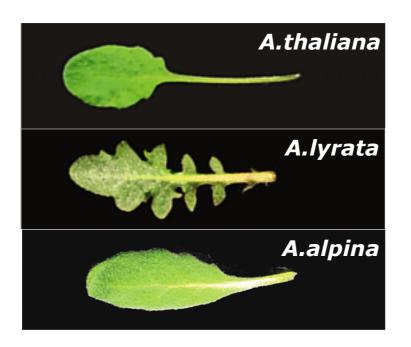


Comparing the epigenome of Ath, Aly and Aal using contrasted chromatin marks









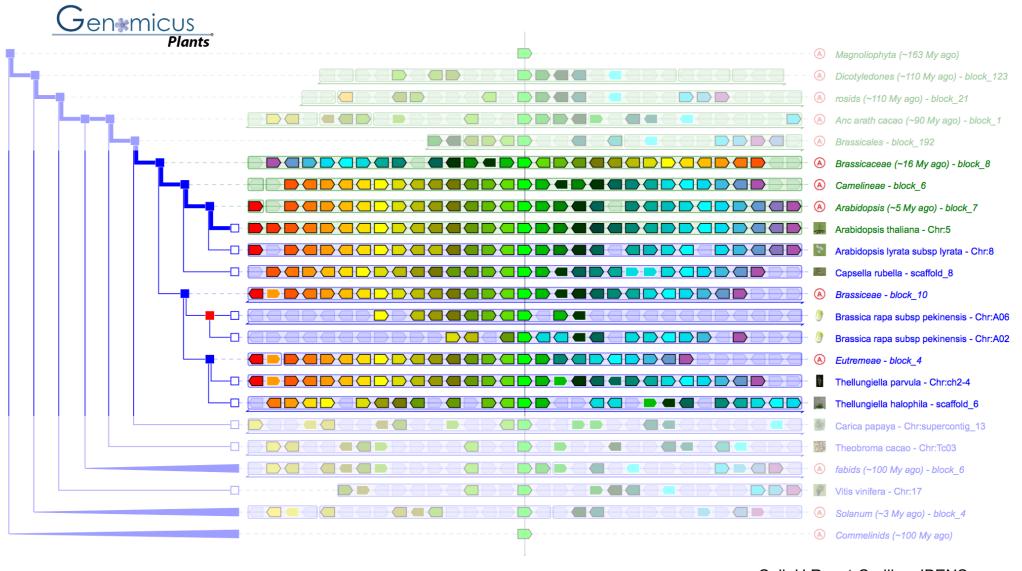
Matched samples:

 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



Genomicus — database version: 16.03 / Web-code version: 2014-03-13 — Dyogen Team

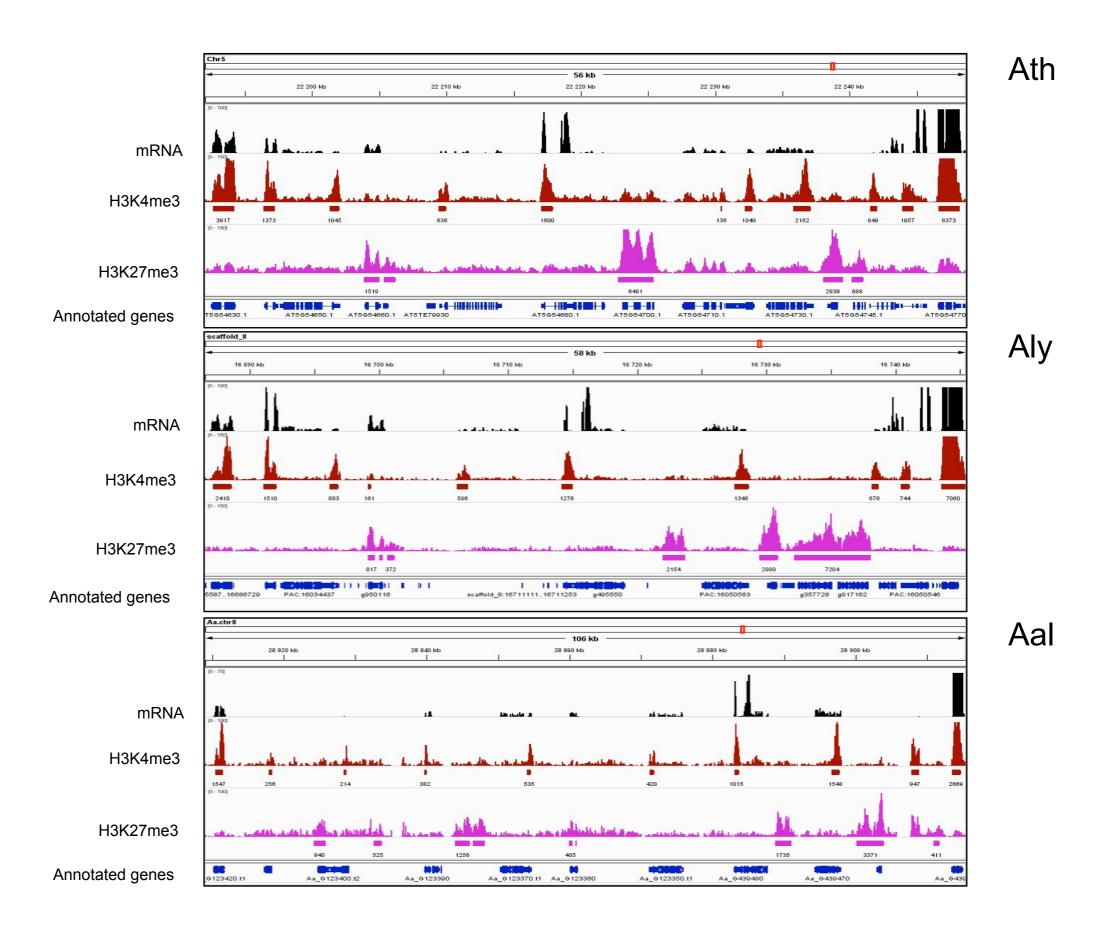
Coll. H Roest-Crollius, IBENS

26028 ancestral genes without recent duplication 13515 without gene loss

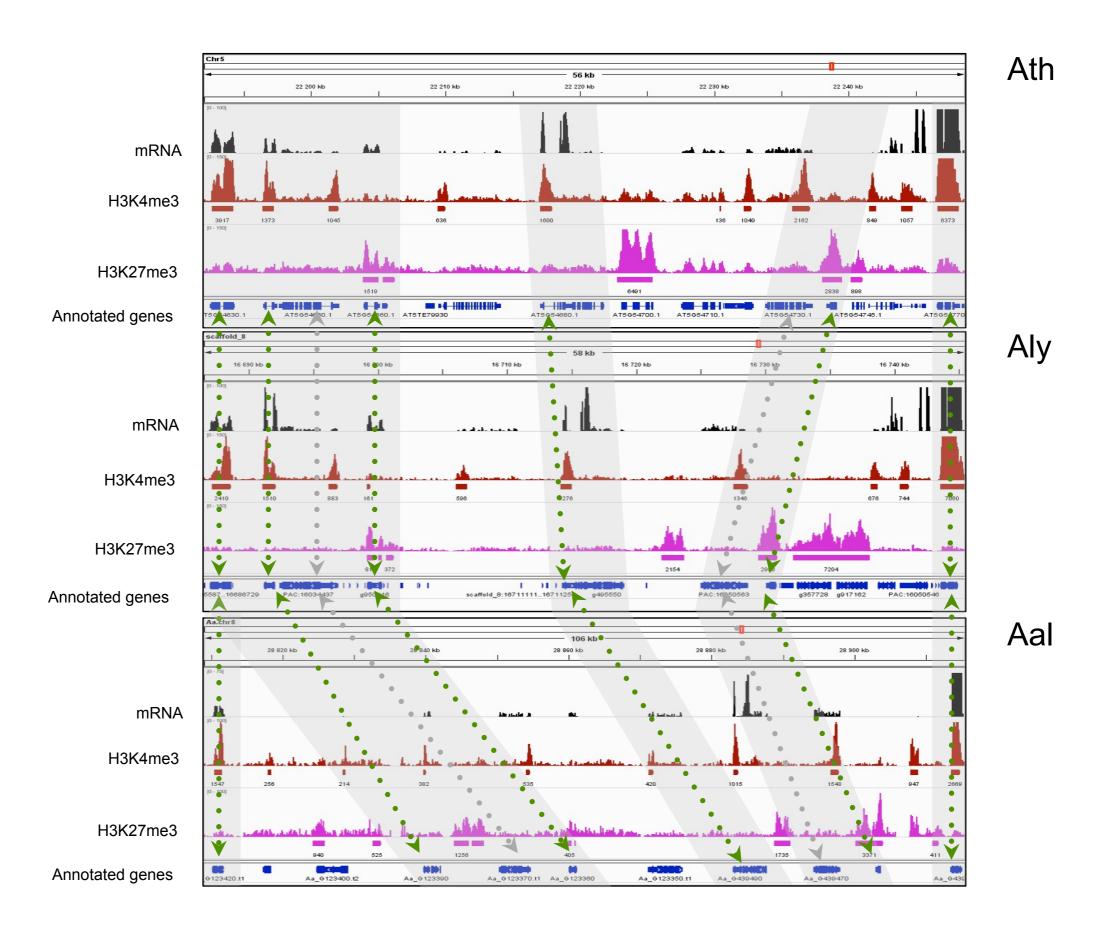
12513 gene with loss in one or two species

1316 ancestral genes that duplicated after the Brassicaceae split

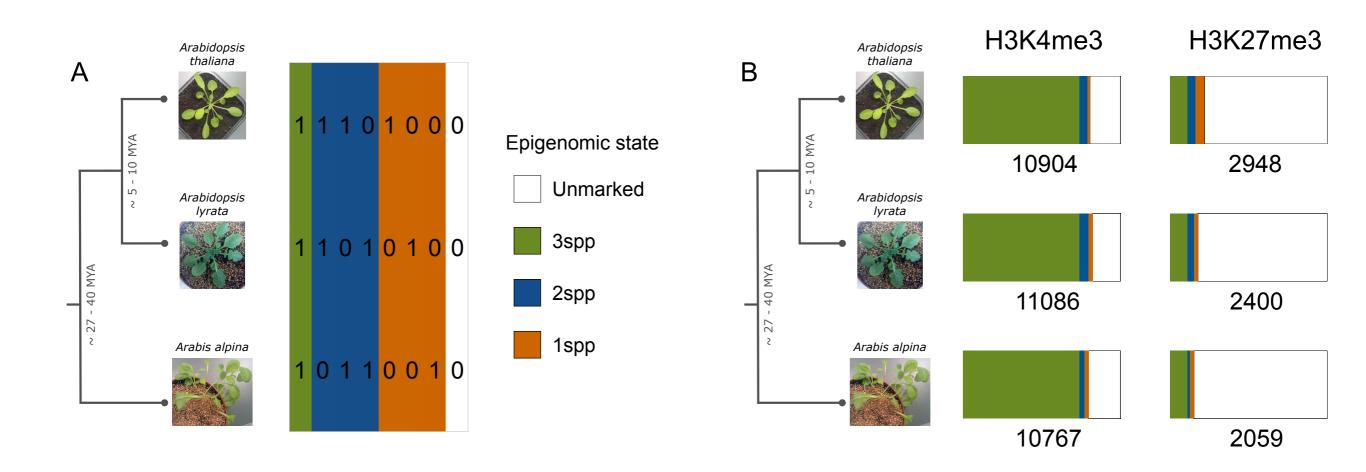
Comparative epigenomics: the raw data



Comparative epigenomics: the raw data



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



Epigenomic state distribution among marked genes

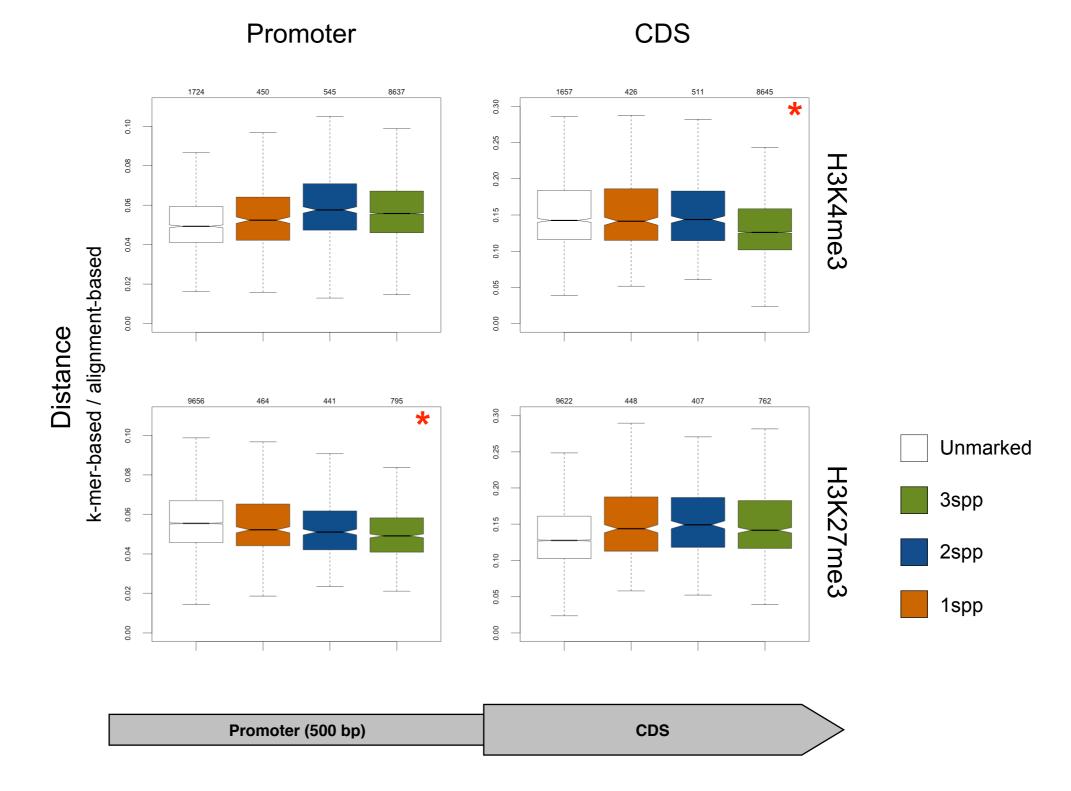
Epigenomic state	H3K27me3	H3K4me3
3spp	40 %	85 %
2spp	22 %	8 %
1spp	38 %	7 %

"I'm interested in the way time records itself into things and people" Miyako Ishiuchi

Comparative epigenomics

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Ancestrality of H3K27me3 marking is correlated with promoter conservation



Distance variance is significantly related to mark ancestrality

"I'm interested in the way time records itself into things and people" Miyako Ishiuchi

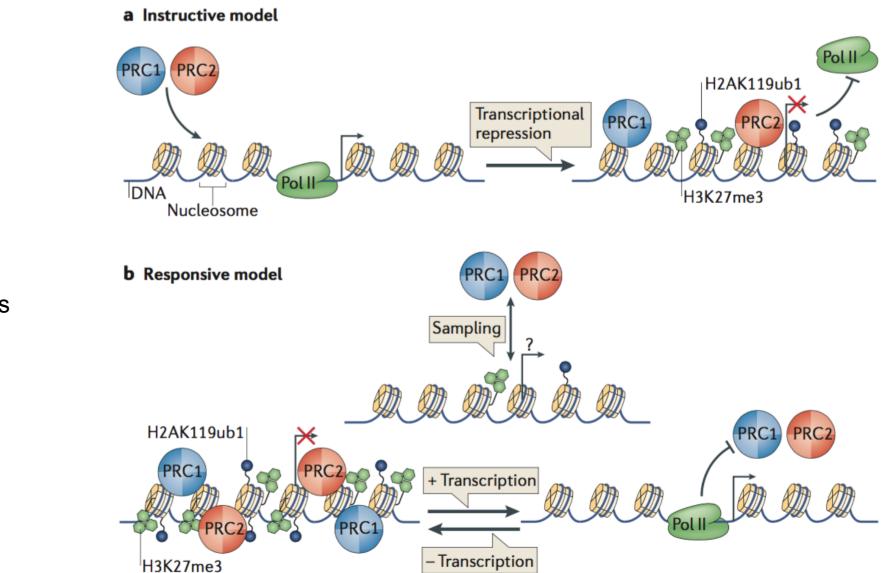
Comparative epigenomics

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Open questions about the gene regulation mediated by Polycomb systems

Complex recruitment

Gene silencing mechanisms



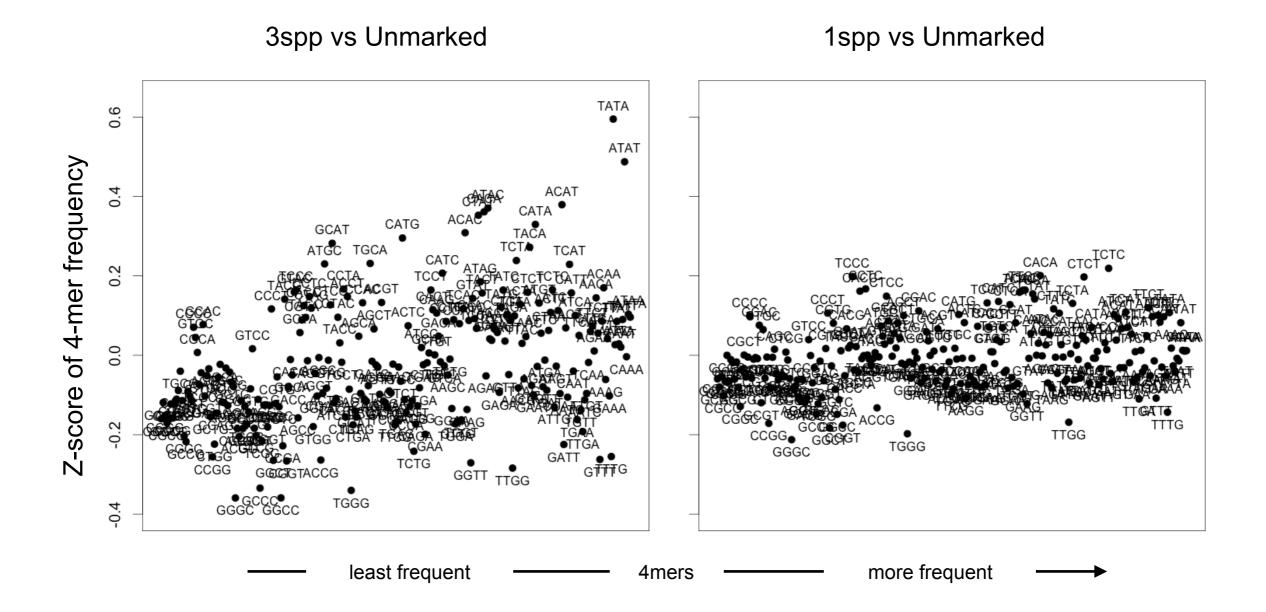
Locus-specific targetingTranscription factors

IncRNAs

Generic targeting

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

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



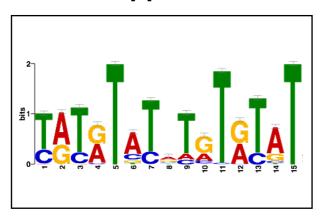
Ancestrality of PRC2 marking is associated with distinct over-represented motifs

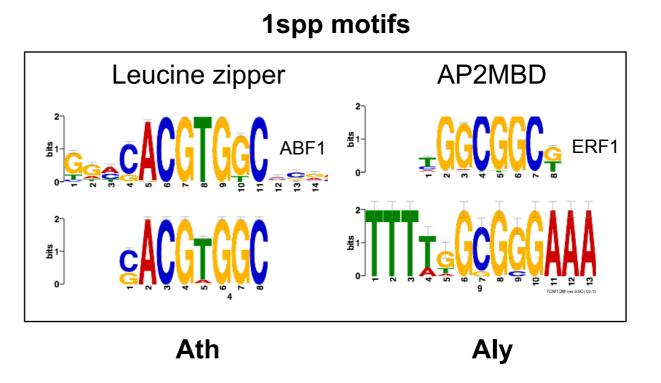
Recruitment and/or displacement of PRC2?

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

Recruitment and/or displacement of PRC2?

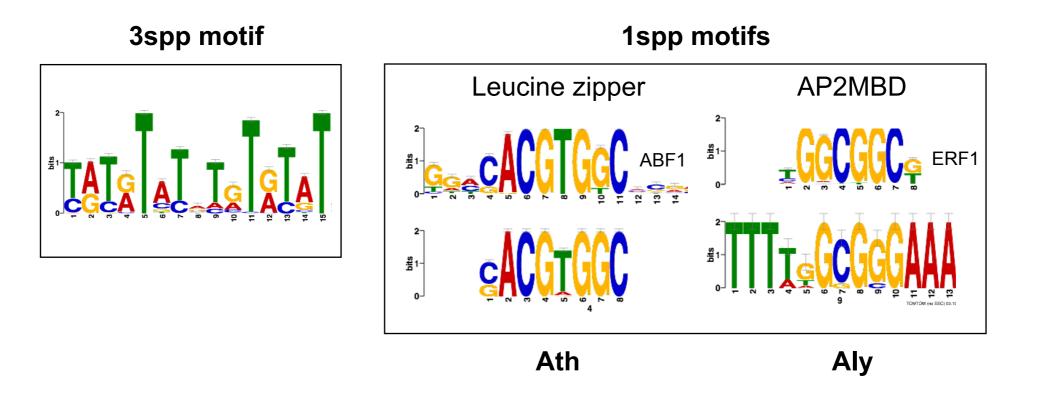
3spp motif



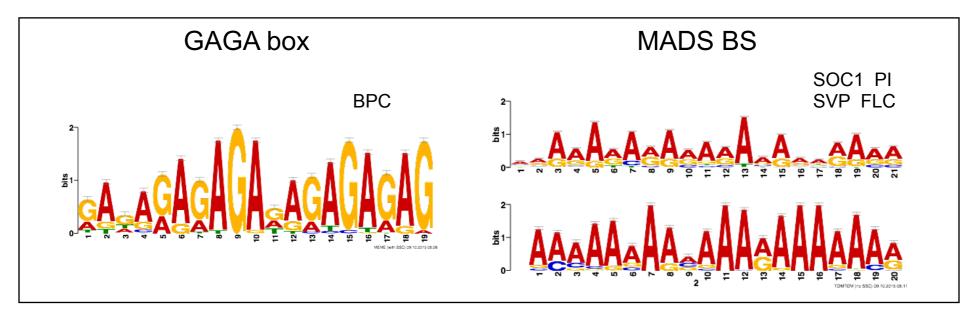


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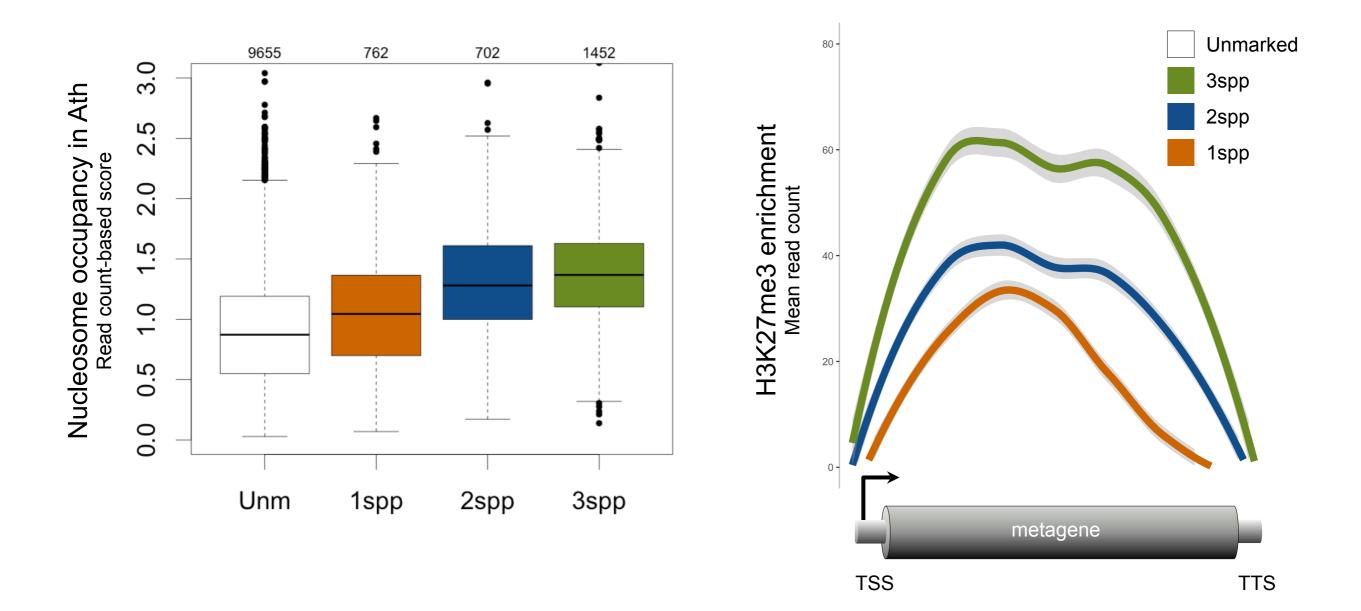
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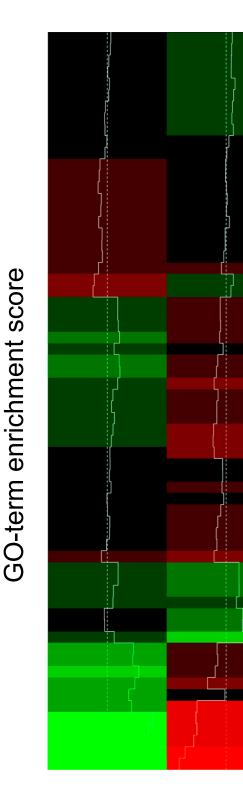
Motifs common to 3spp and 1spp gene sets



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



1spp

3spp

reproductive process reproduction anatomical structure morphogenesis multicellular organismal process homeostatic process reproductive developmental process multicellular organismal development developmental process anatomical structure development regulation of biological quality cellular developmental process transport gene expression cell differentiation localization regulation of cellular process regulation of metabolic process biological regulation establishment of localization regulation of biological process pollination transcription regulation of gene expression regulation of cellular component size regulation of anatomical structure size regulation of cell size cell growth nitrogen compound metabolic process response to biotic stimulus growth cellular macromolecule metabolic proce multi-organism process response to external stimulus cellular metabolic process macromolecule metabolic process signal transduction response to stress cellular biosynthetic process nucleic acid metabolic process biosynthetic process macromolecule biosynthetic process response to stimulus lipid metabolic process primary metabolic process cellular process metabolic process death cell death reproductive structure development post-embryonic development flower development response to endogenous stimulus embryonic development carbohydrate metabolic process response to abiotic stimulus cellular component organization catabolic process cellular amino acid and derivative meta protein metabolic process macromolecule modification protein modification process cellular protein metabolic process cell cycle generation of metabolites and energy

Cell differentiation Reproductive and developmental processes

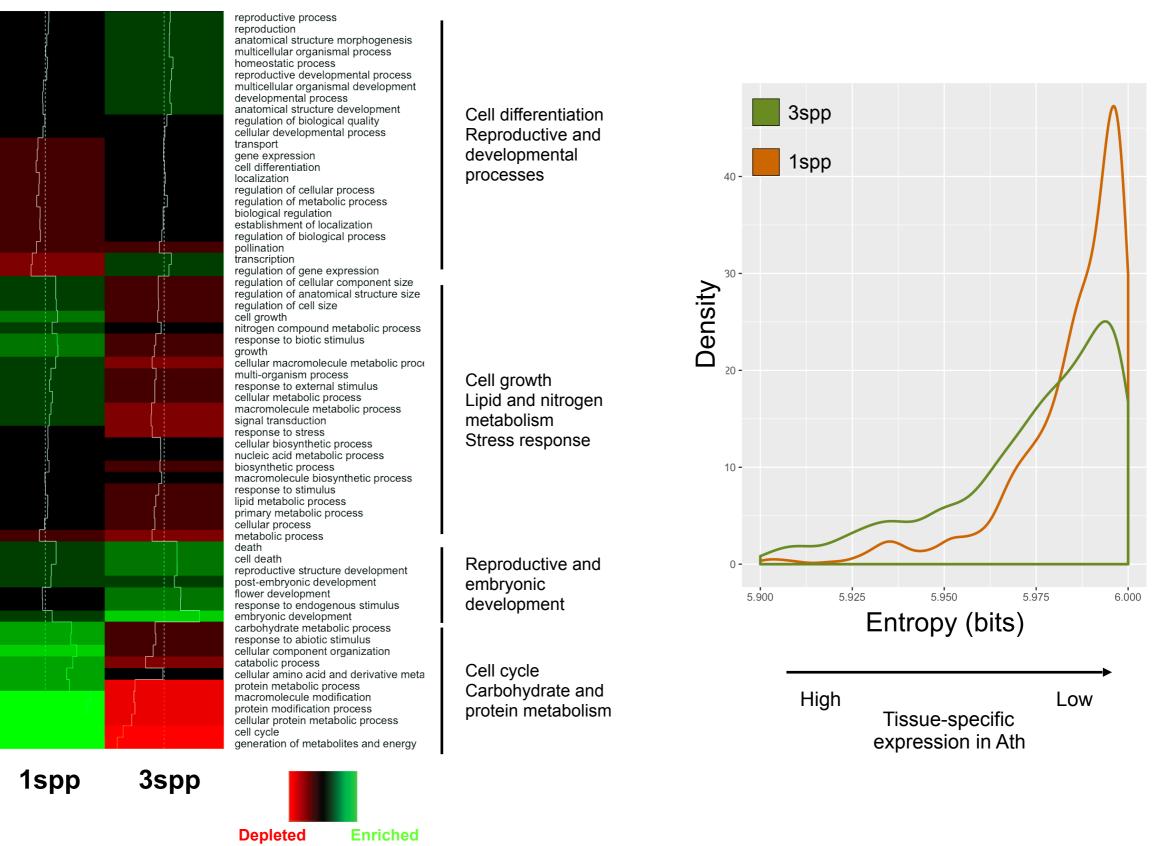
Cell growth Lipid and nitrogen metabolism Stress response

Reproductive and embryonic development

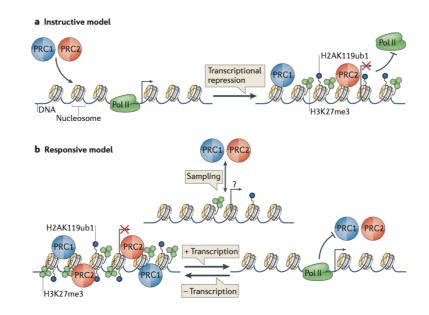
Cell cycle Carbohydrate and protein metabolism

Depleted Enriched

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)

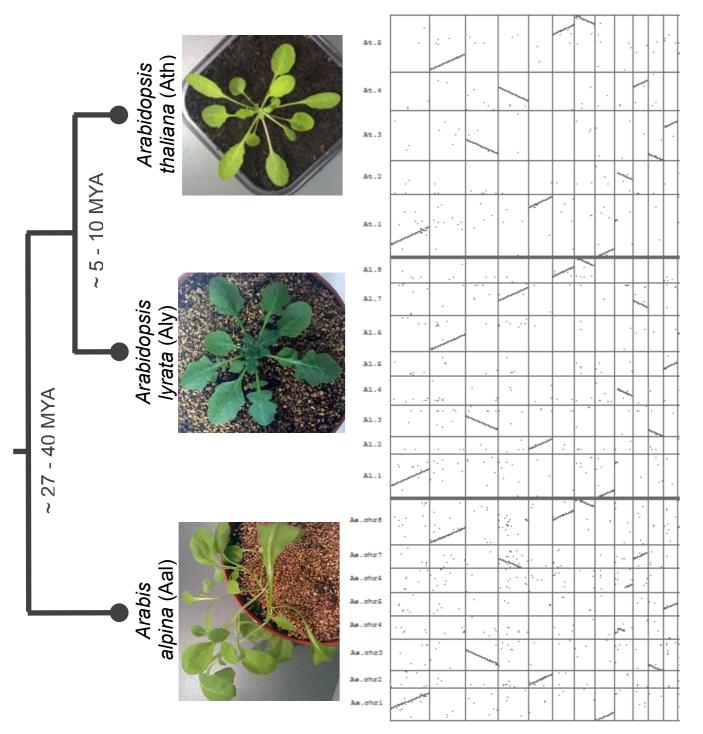
- No detectable constraints on promoter sequence
- Basal metabolism genes
- Modulated and un-specific expression profiles

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Comparative epigenomics

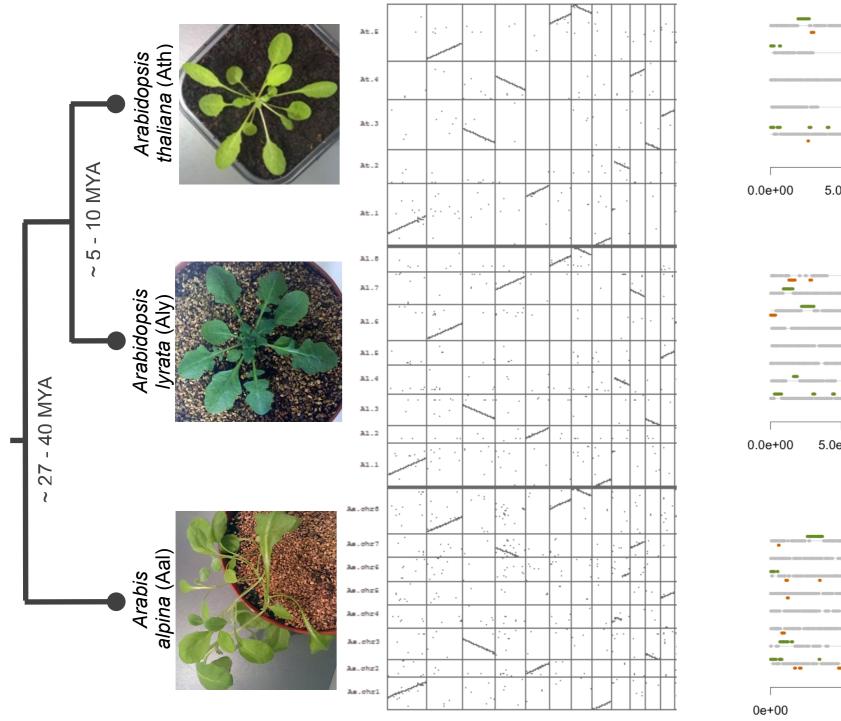
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In these highly syntenic genomes, some blocks are significantly enriched in conserved PRC2 targets

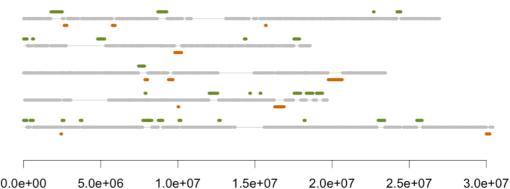


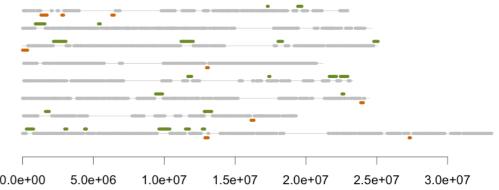
Brassicaceae reconstructed genome

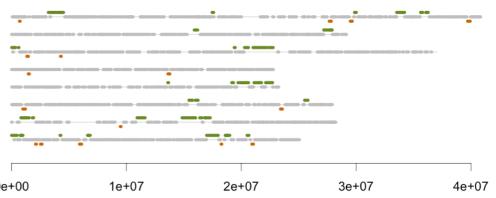
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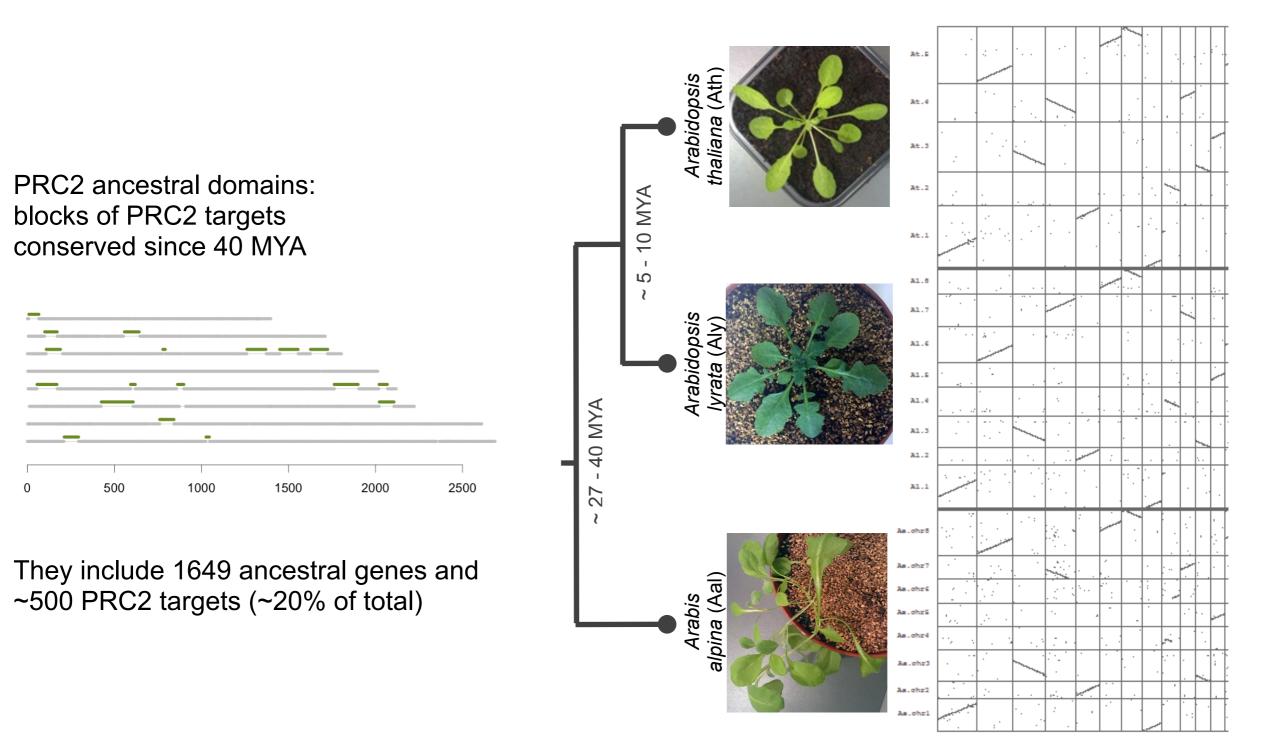
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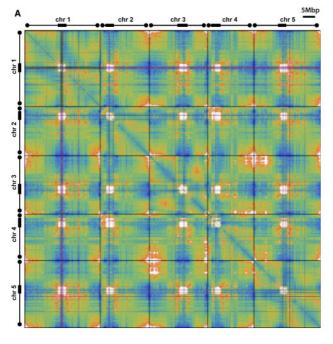


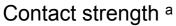
This blocks show a concerted conservation of the gene organisation and the dominant chromatin state for the last 40 MYA



Brassicaceae reconstructed genome

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

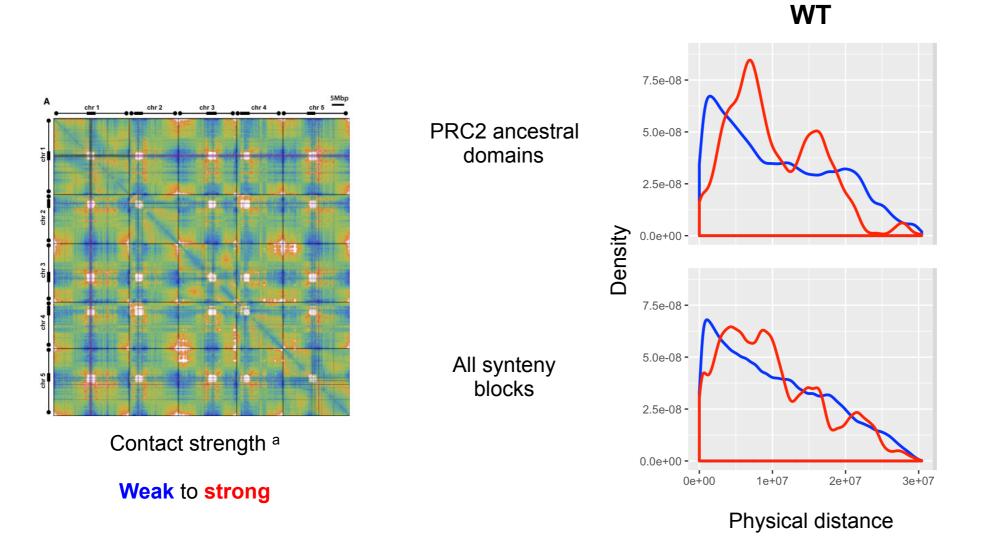




Weak to strong

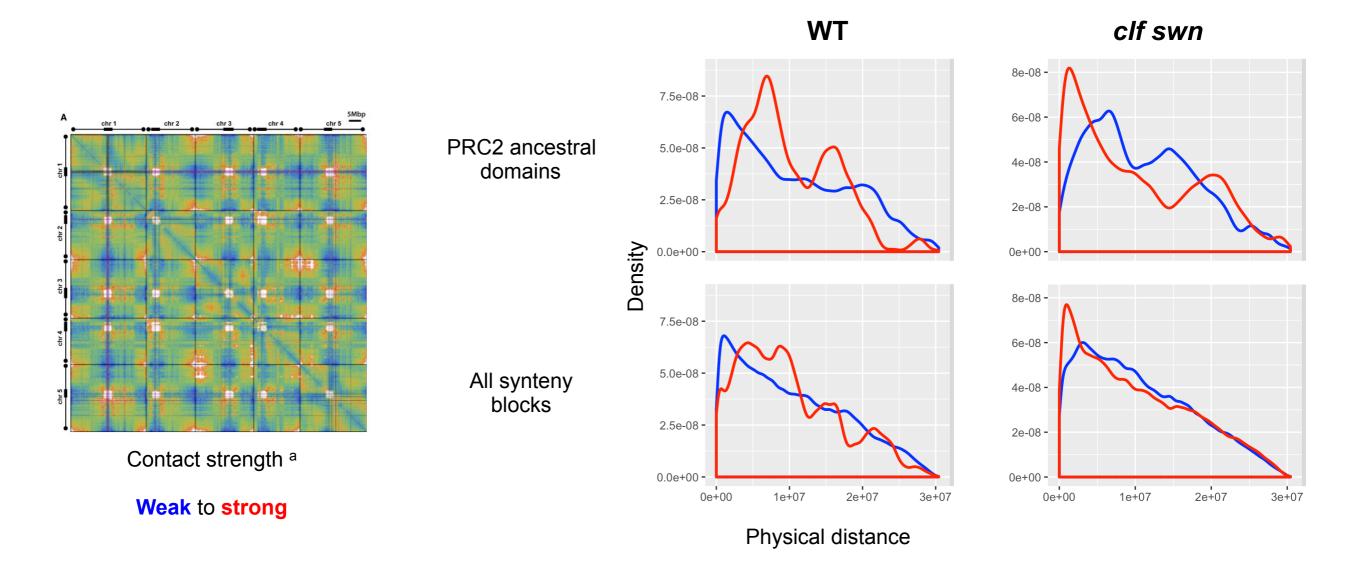
^a20 kb res Hi-C dataset from Feng, Cokus et al. *Mol. Cell,* 2014.

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

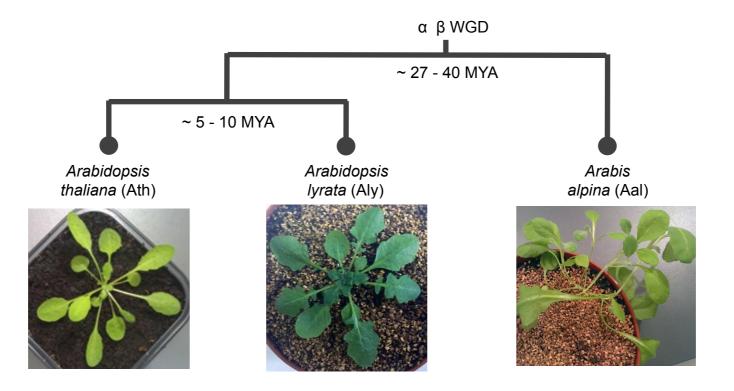


^a20 kb res Hi-C dataset from Feng, Cokus et al. *Mol. Cell*, 2014.

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



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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