

Formation and transmission of human Robertsonian chromosomes

Andrea Guaraccino and Jennifer Gerton

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Centromeres
p arms acrocentrics



Stowers
Institute

Gerton team



Tamara Potapova



Leonardo Gomes de Lima

Chris Seidel
Sean McKinney
Kate Hall
Michael Peterson



Sergey Koren (NHGRI)



Adam Phillippy (NHGRI)

Garrison team

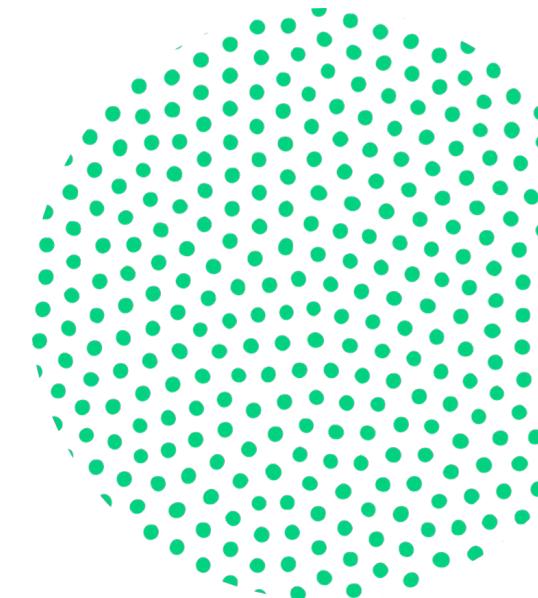


Erik Garrison (UTHSC) Andrea Guaracino (UTHSC)

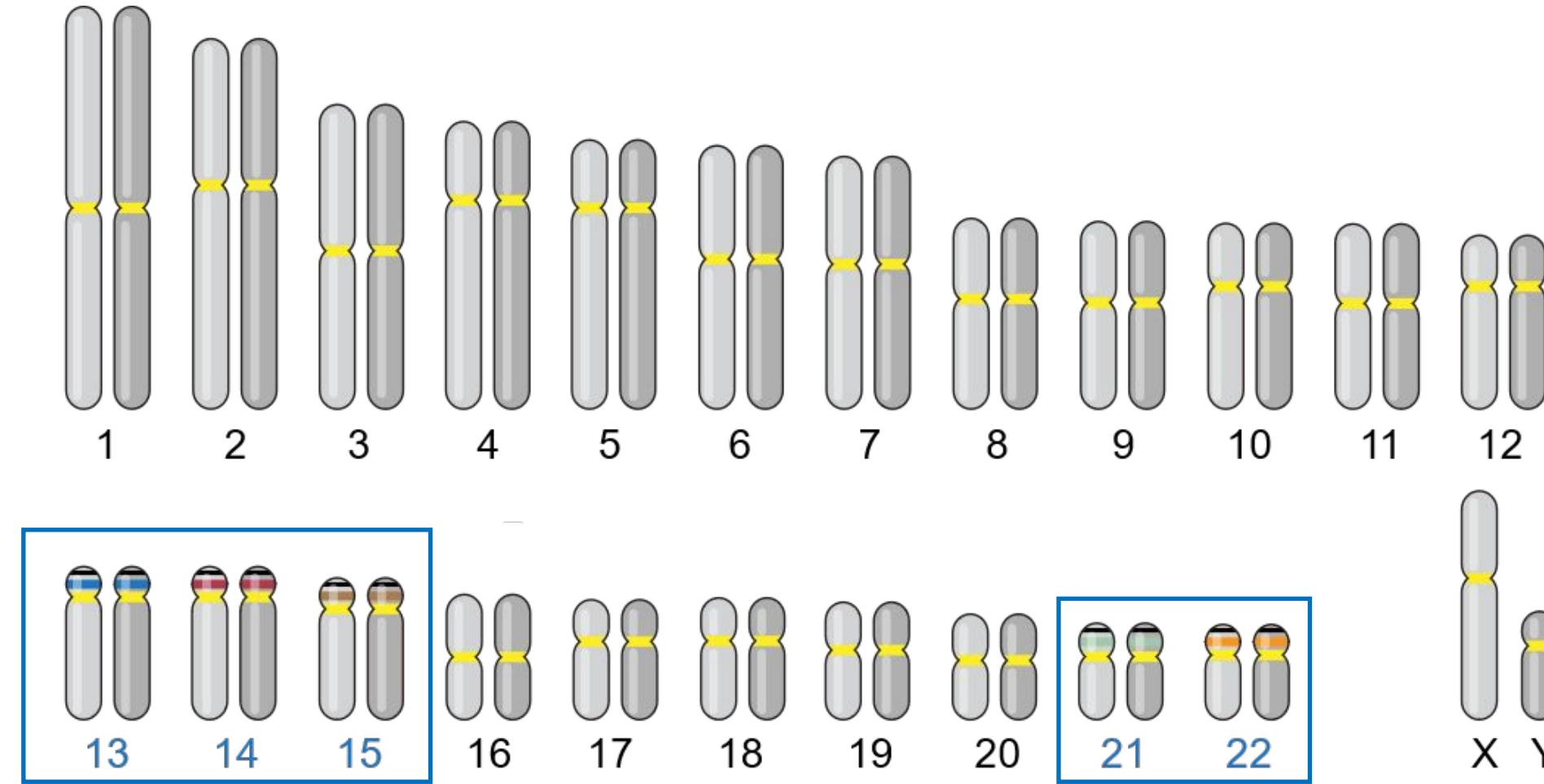


Phillippy team

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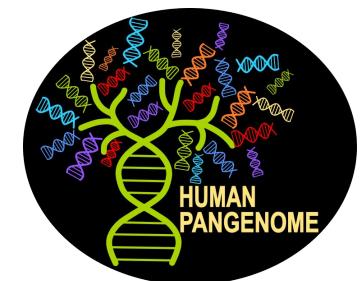


Human acrocentric chromosome short arms, assembled 2022

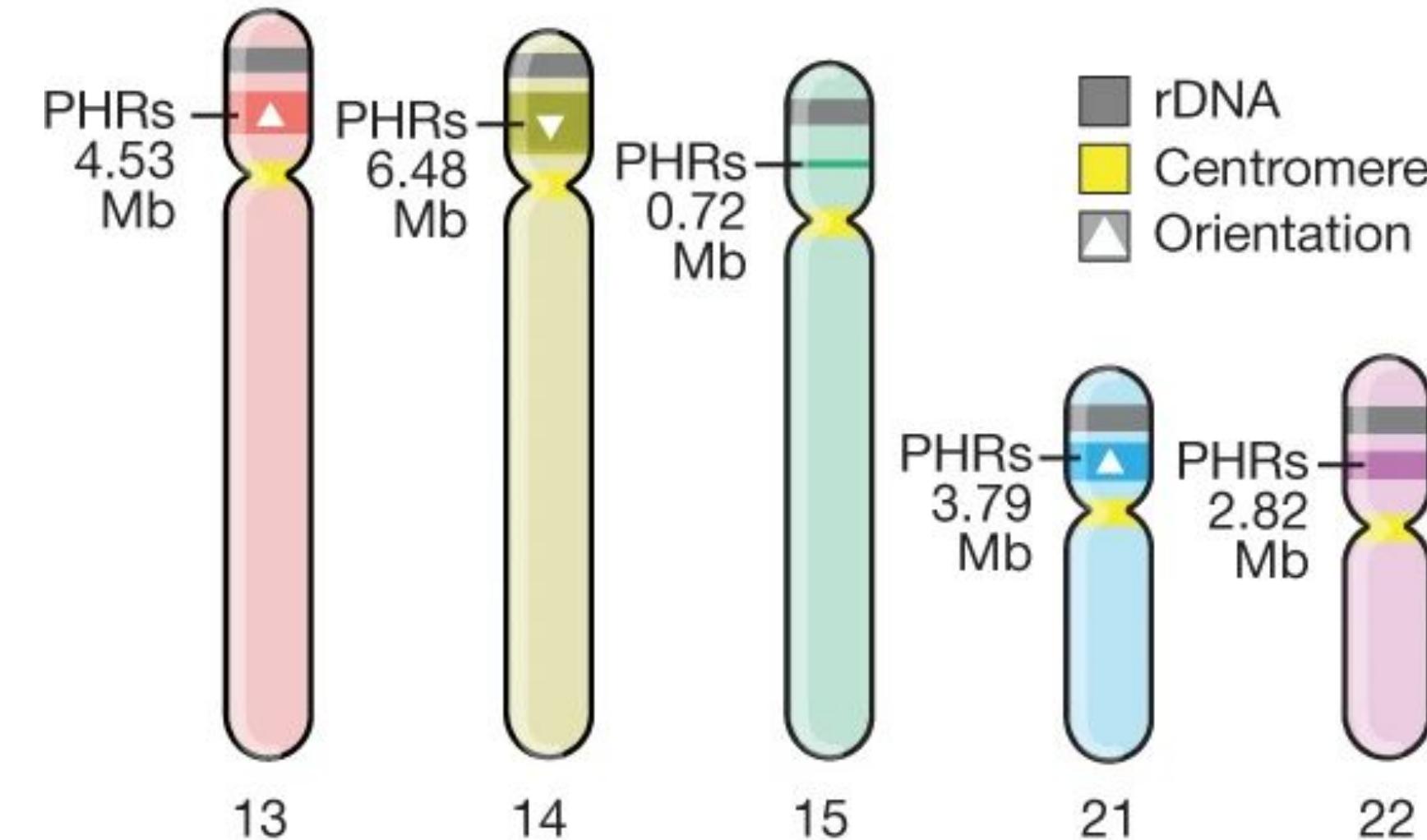


Guarracino et al, 2023, Pangenome acrocentrics, *Nature*

Nurk et al, 2022, CHM13 genome (acro p arms), *Science*



Pseudohomolog regions in acrocentric chromosomes



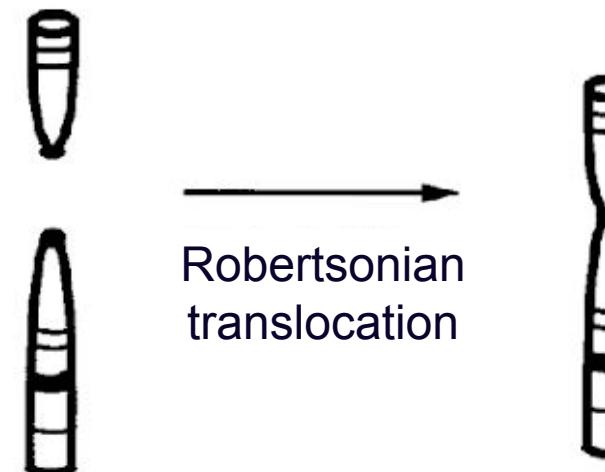
Andrea Guerracino Erik Garrison



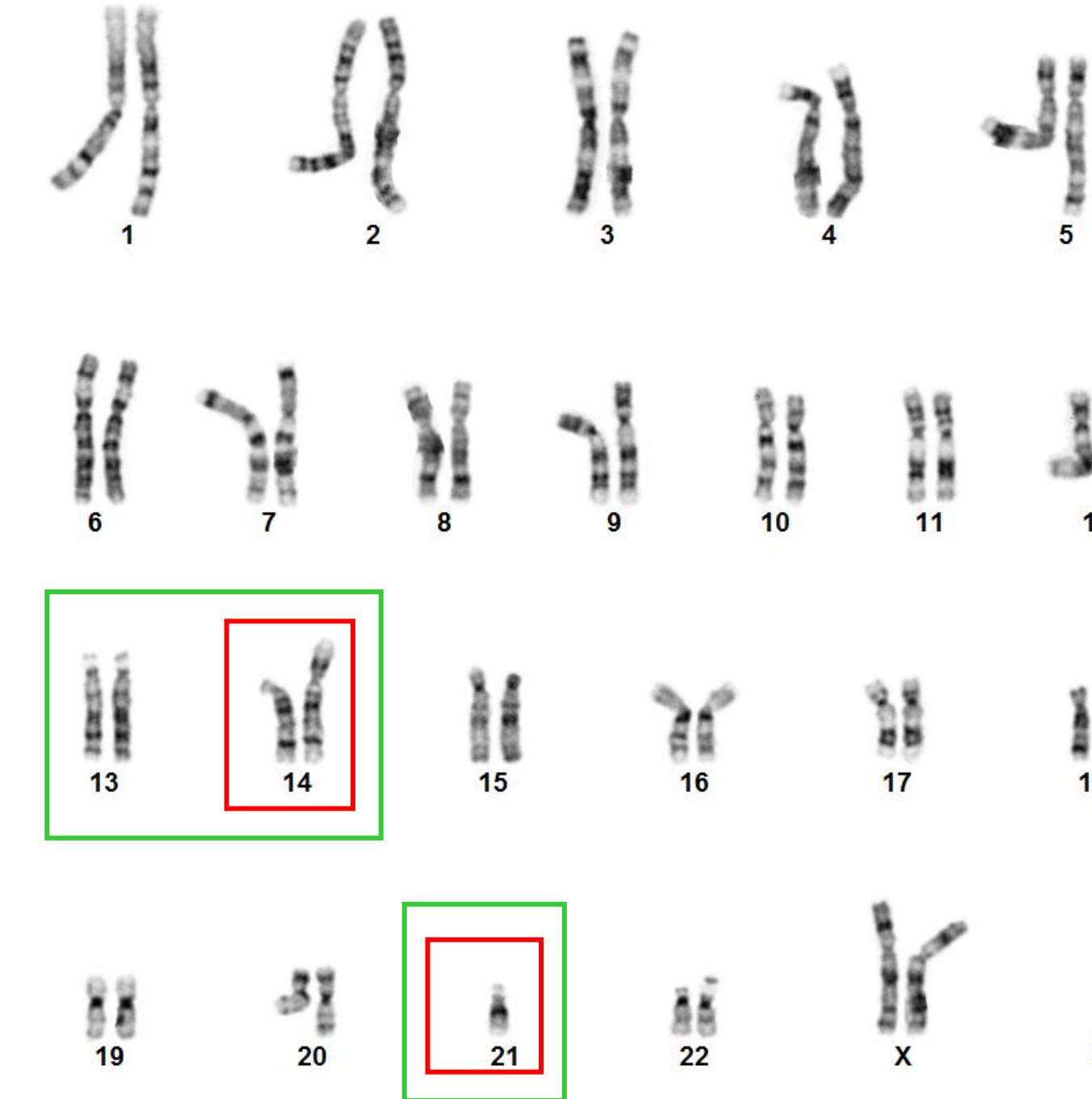
Guerracino et al., *Nature*, 2023
Jarmuz-Szymczak et al., 2014

Robertsonian chromosomes are common in nature-WHY?

William Rees Brebner Robertson 1881- 1941
American zoologist and early cytogeneticist

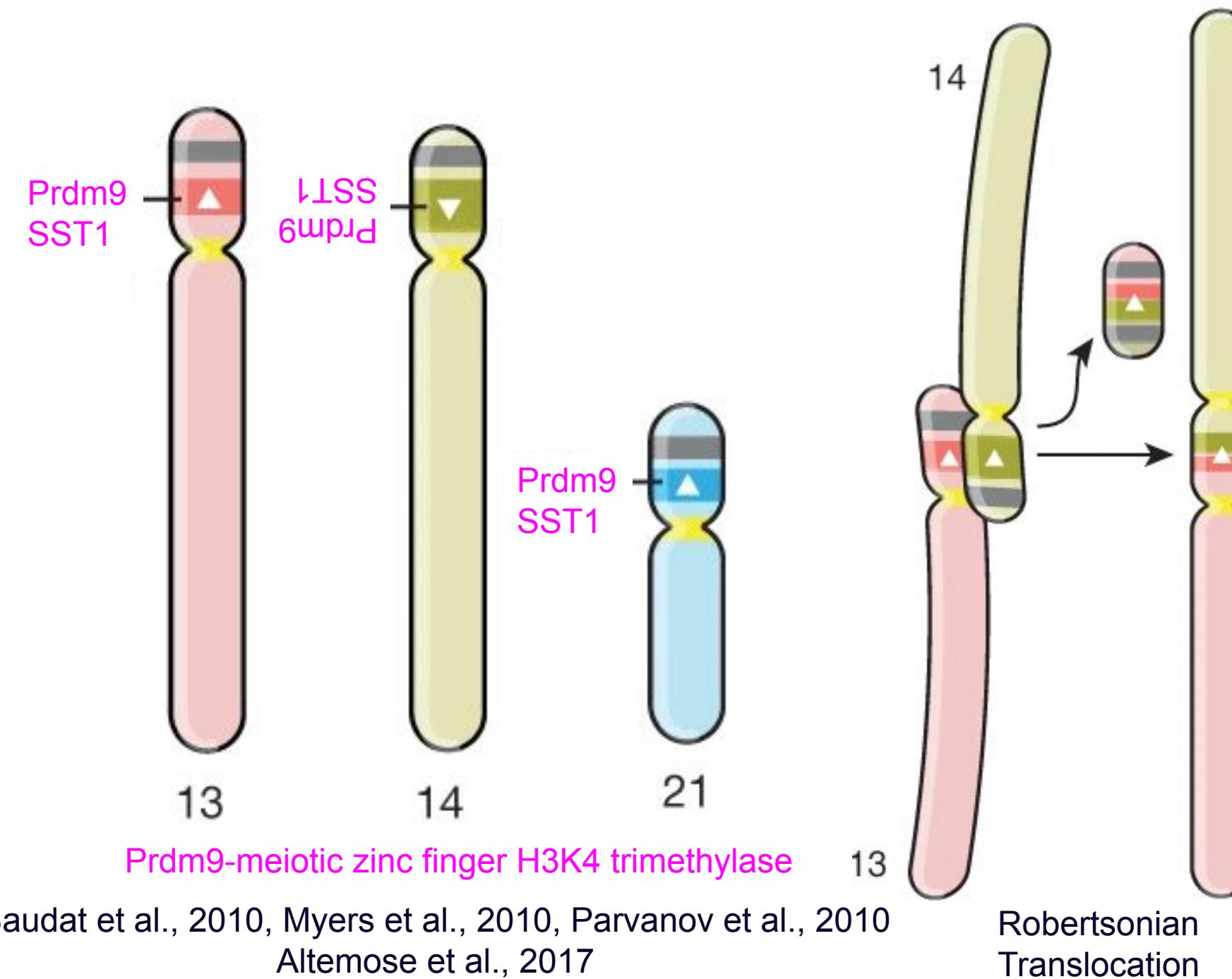


- Karyotype evolution
- Speciation



- 85% involve 14
- Female meiosis
- 1 in 800
- Sub/infertility
- Aneuploidy
- Cancer Incidence

Recombination between acrocentric chromosomes



Andrea Guarracino

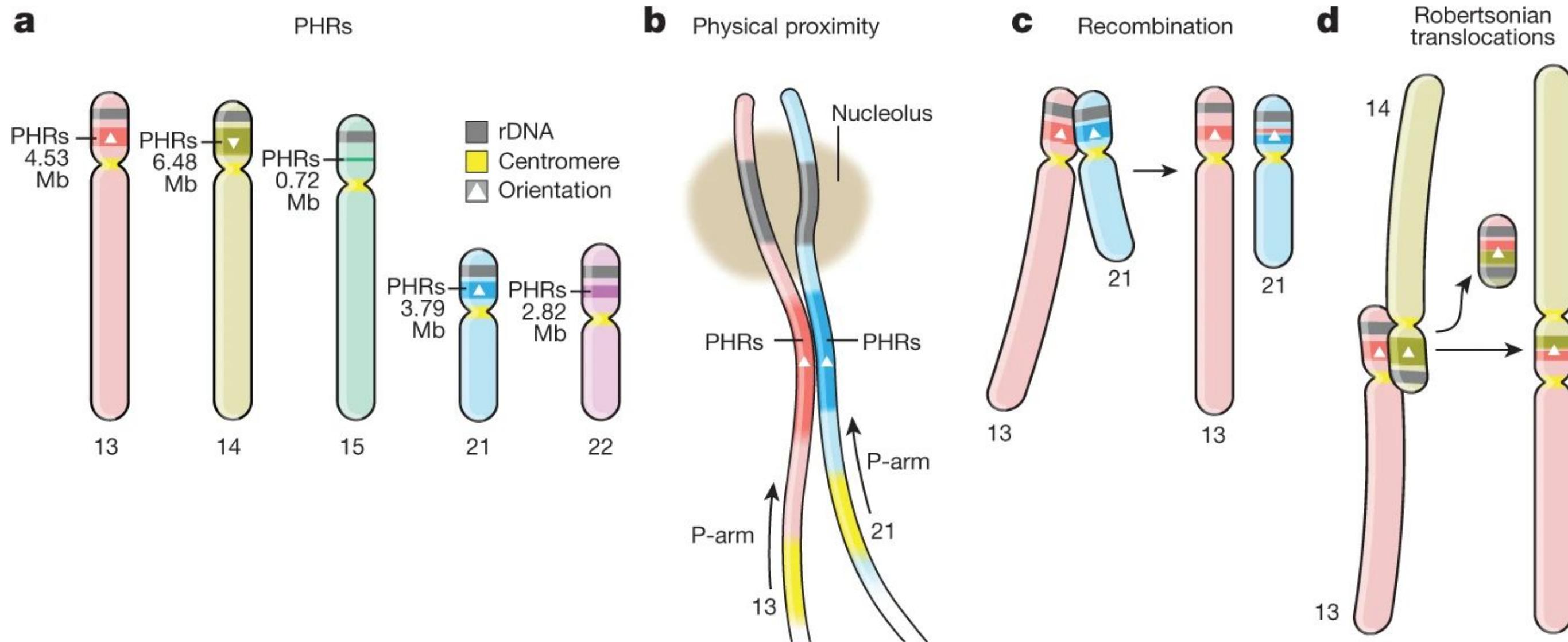


Leo Gomes de Lima



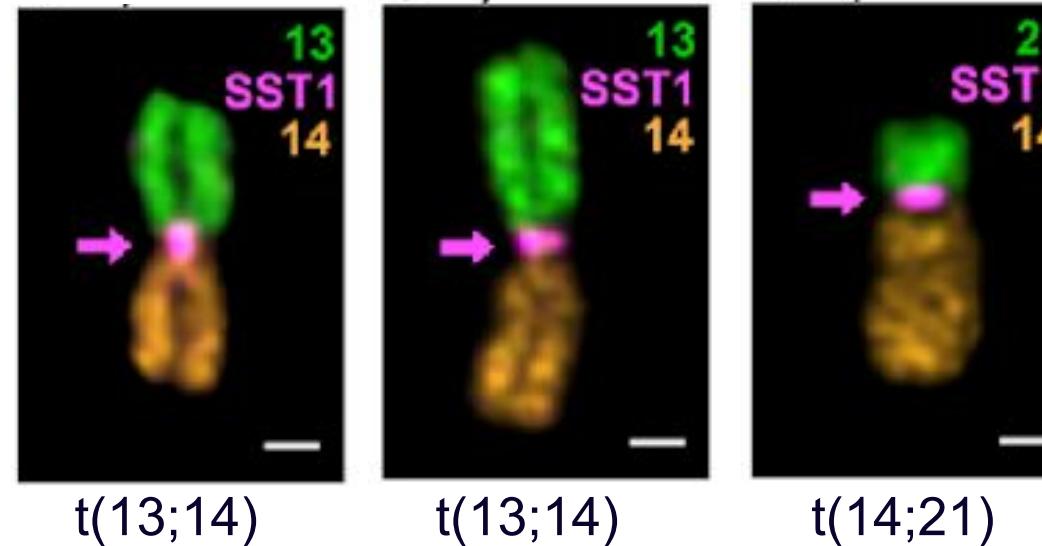
Guarracino et al., *Nature*, 2023

Model for the formation of Robertsonian translocations



Robertsonian chromosomes-three predictions

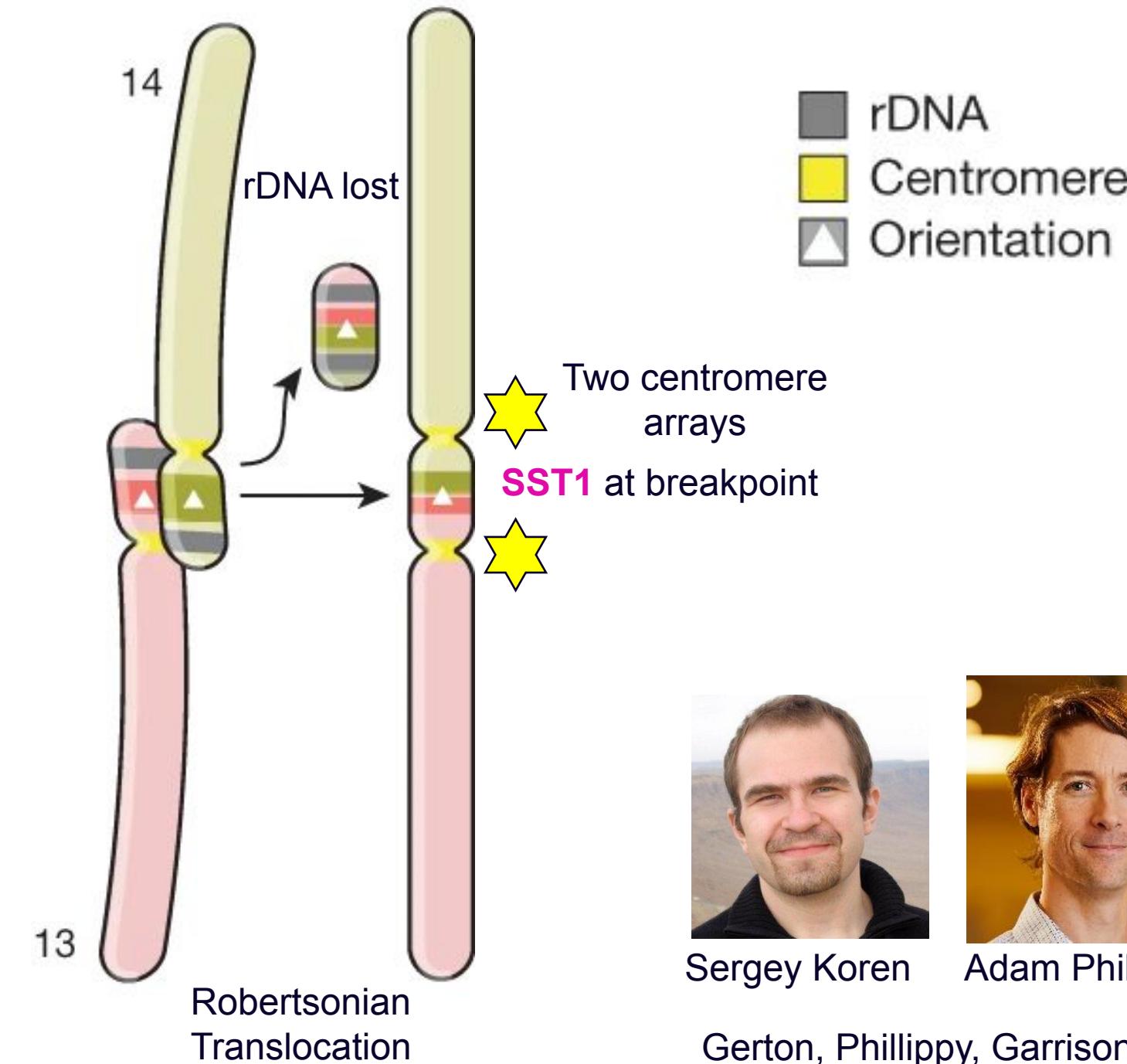
3 ROB lines



T. Potapova



- ONT, PacBio HiFi, HiC
- DNA methylation
- Cytogenetics
- Super-resolution imaging
- Phylogenetics



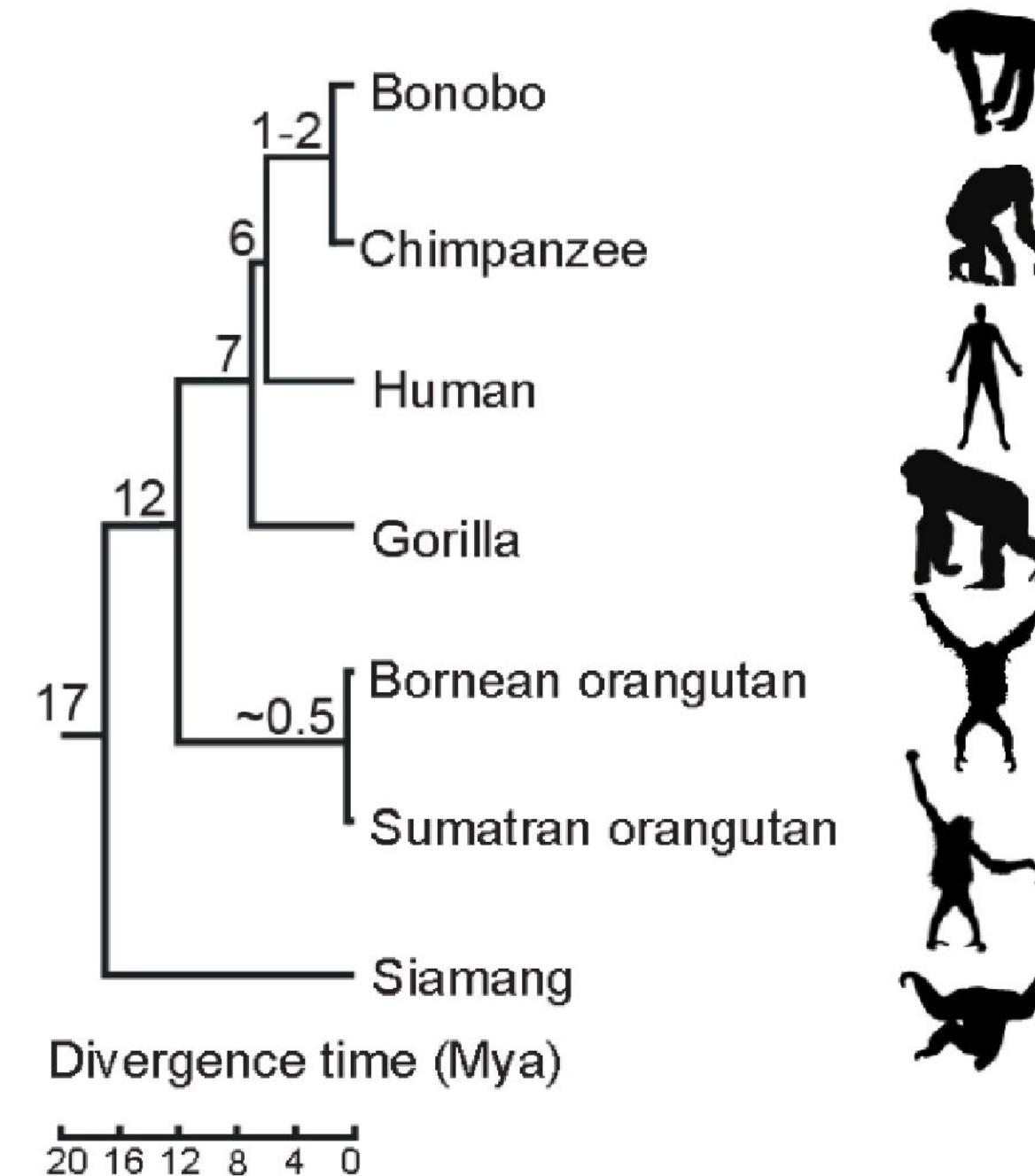
Sergey Koren



Adam Phillippy

Gerton, Phillippy, Garrison, in prep

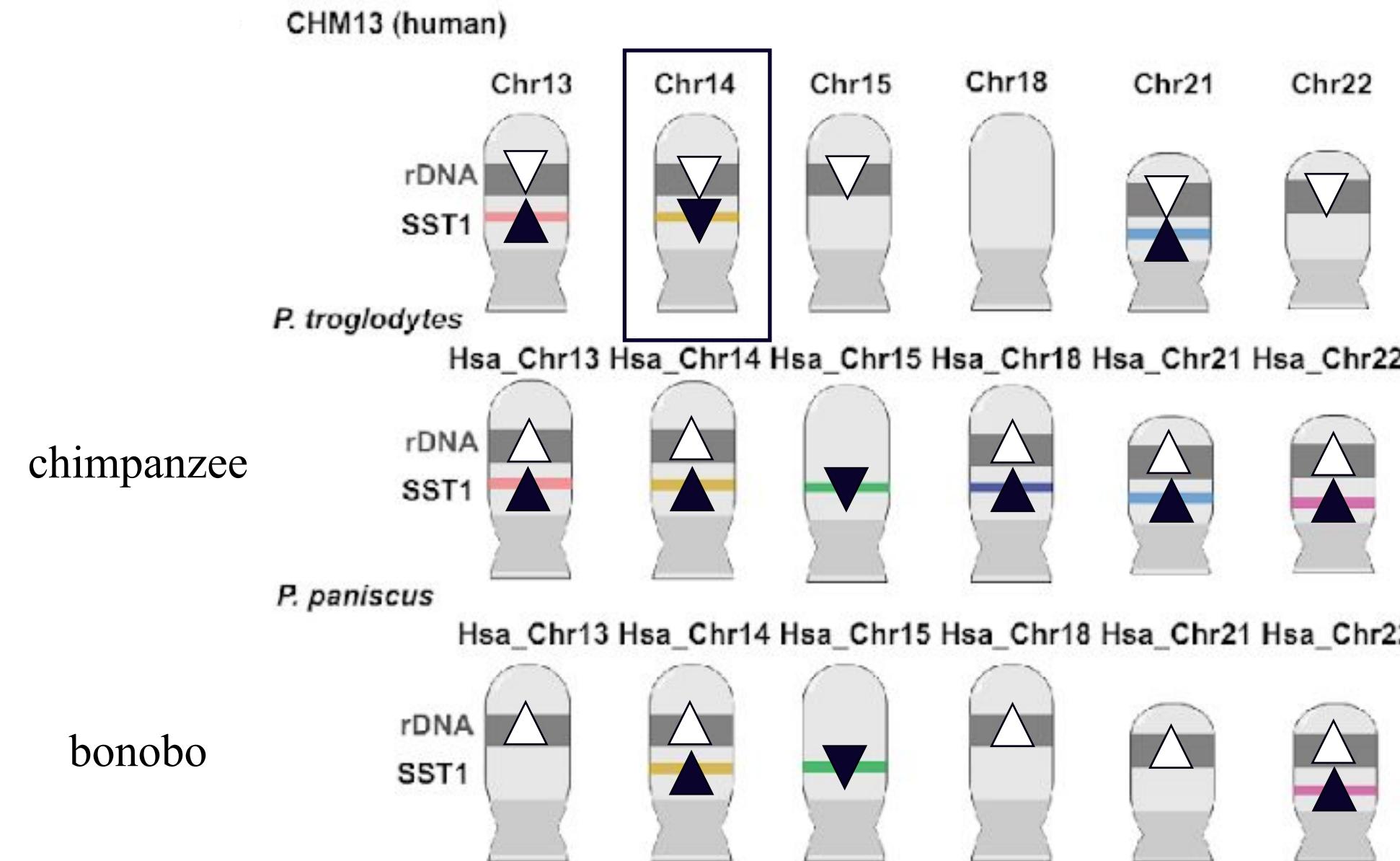
New primate assemblies enable evolutionary insights



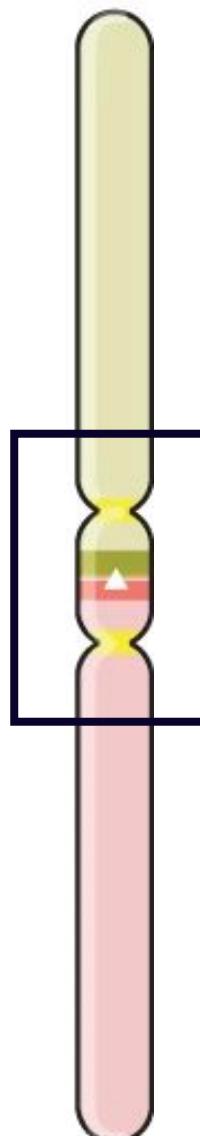
Eichler et al, 2024, Primate autosome assemblies, submitted



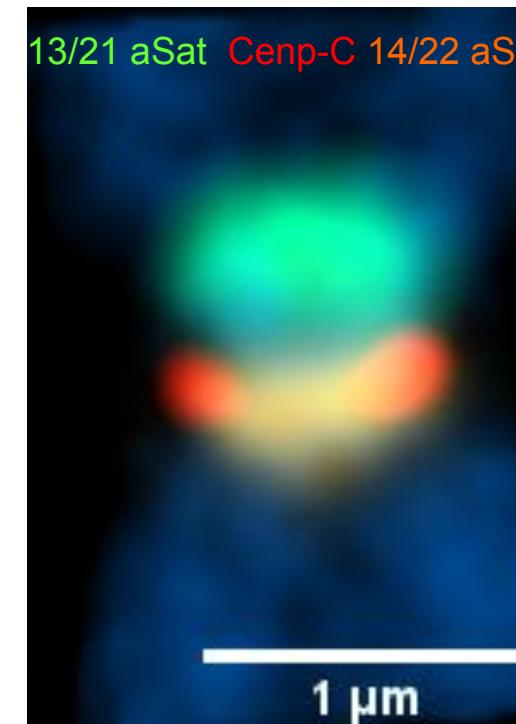
Inversion of SST1 + rDNA array-unique to human genome!



ROBs-epigenetic alterations at centromeres enable stable chromosome transmission

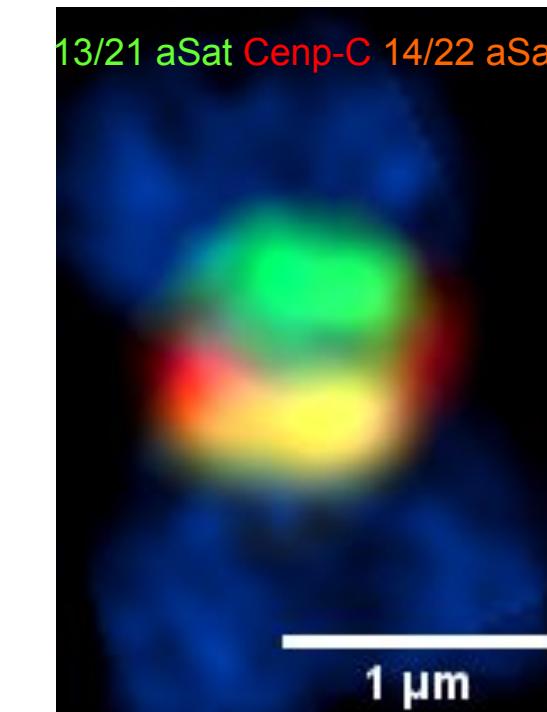


$t(13;14)$



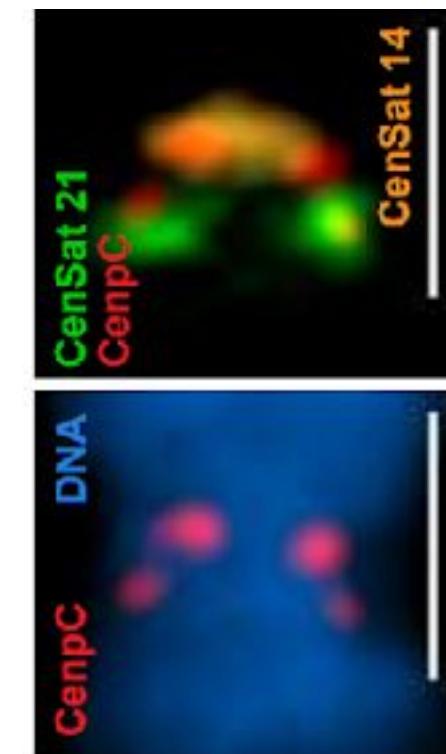
Averaged image 11 ROB chromosomes, GM08490

$t(14;21)$



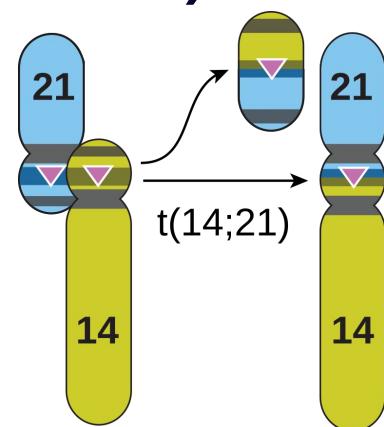
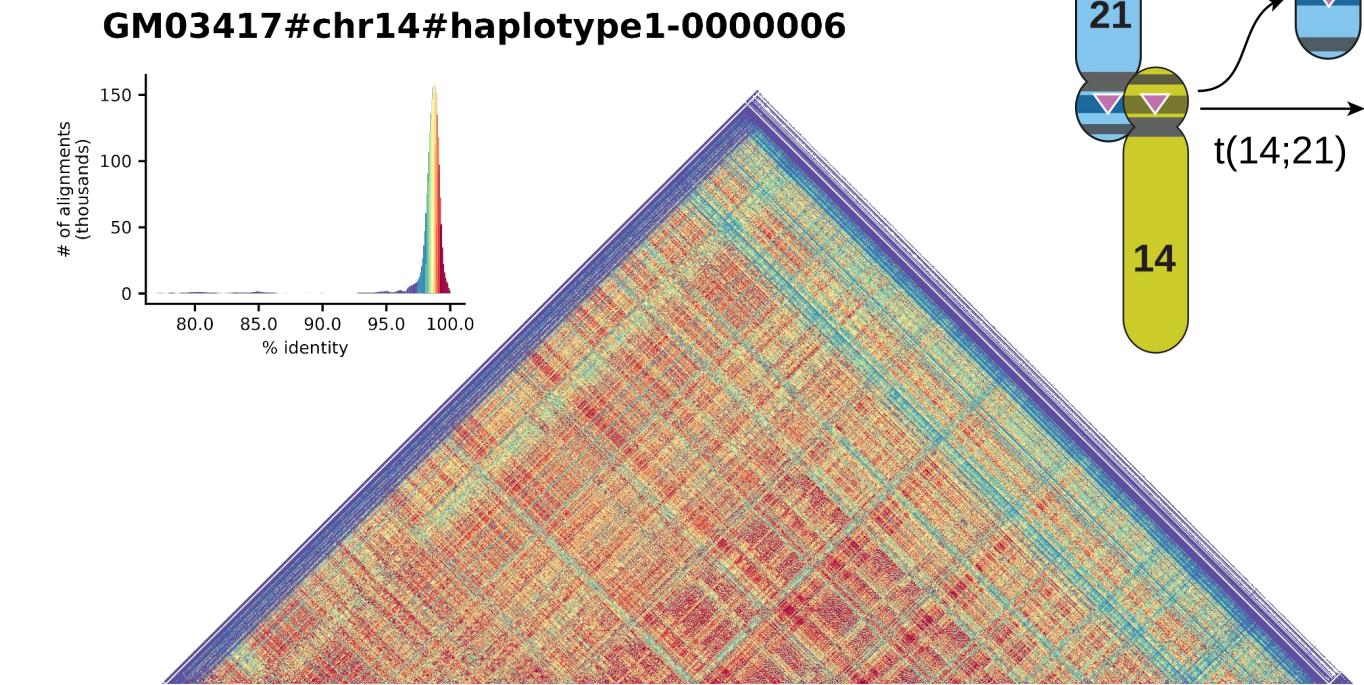
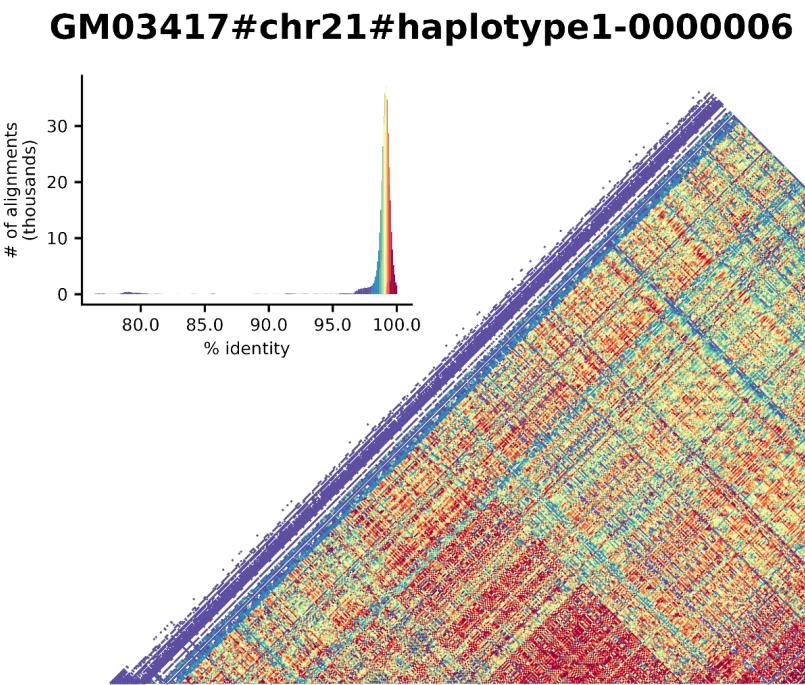
Averaged image 10 ROB chromosomes, GM03417

Cen14 wins
Sullivan et al., 1994

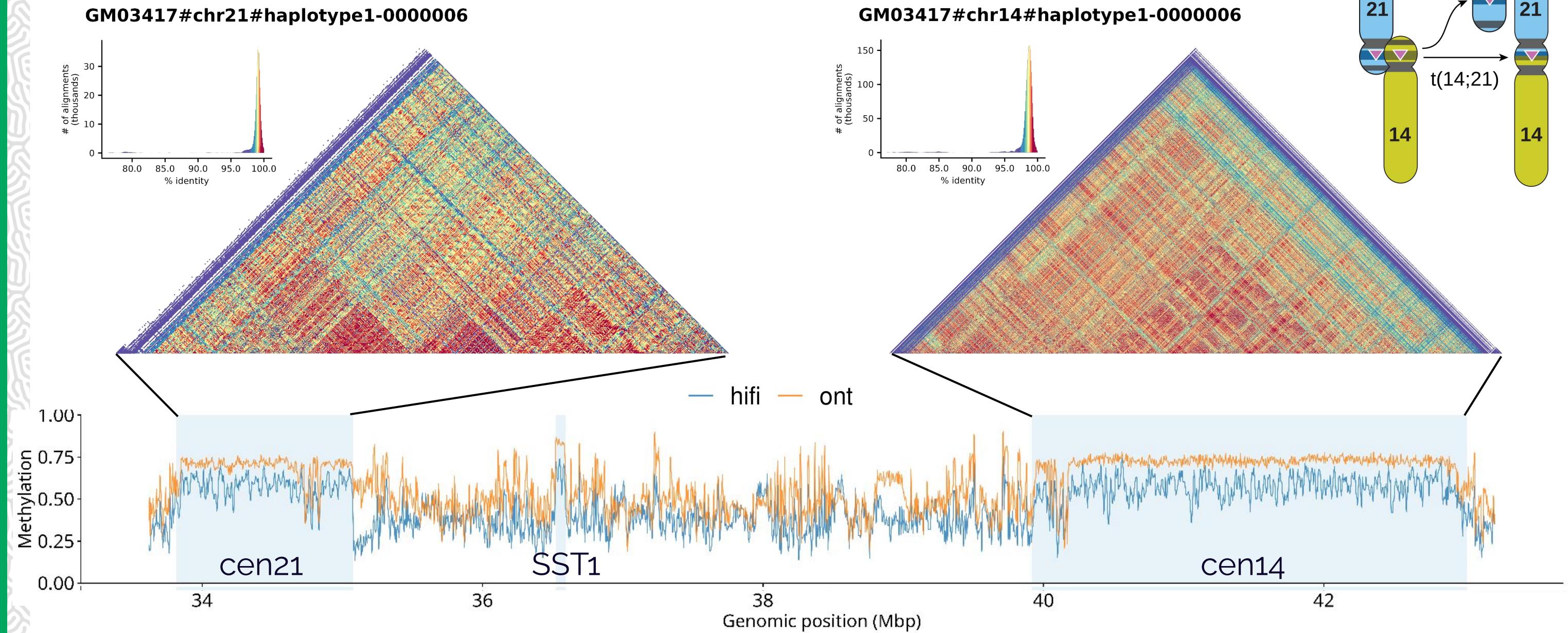


Gerton, Phillippy, Garrison, in prep

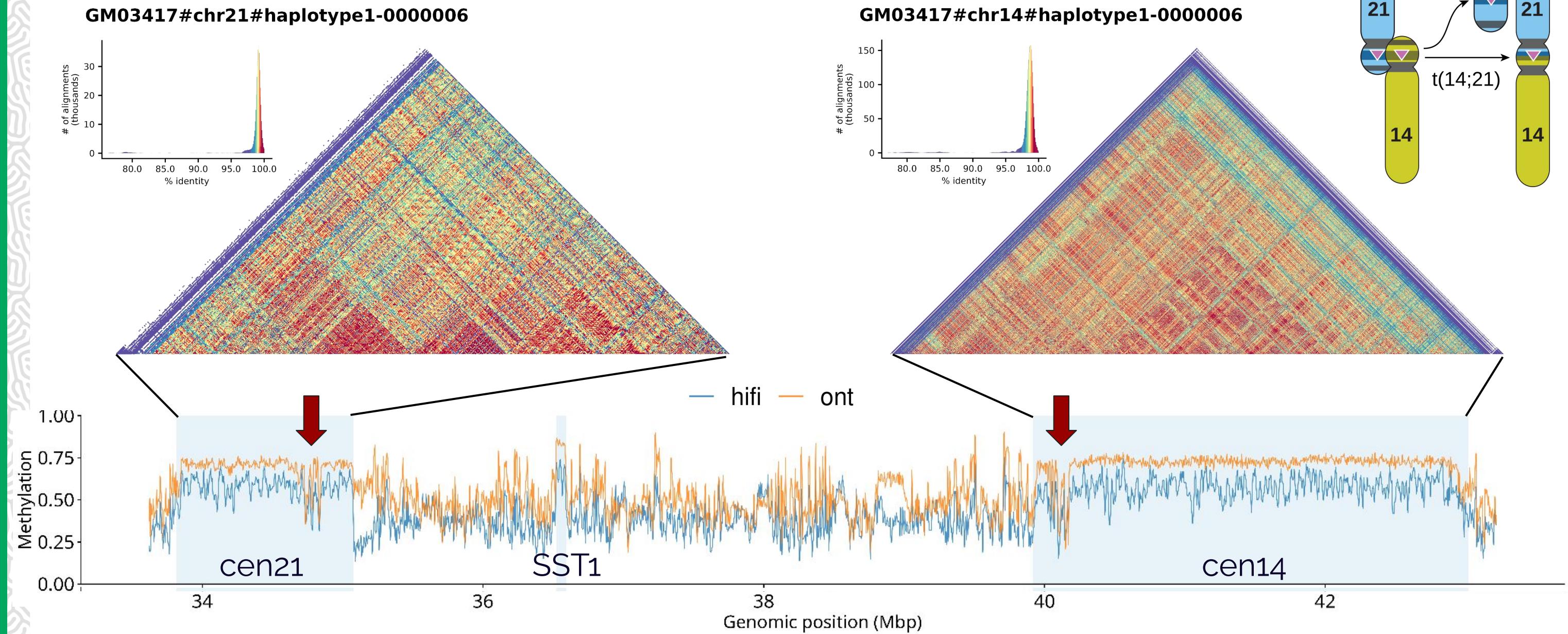
Both cen14 and cen21 may remain active in t(14;21)



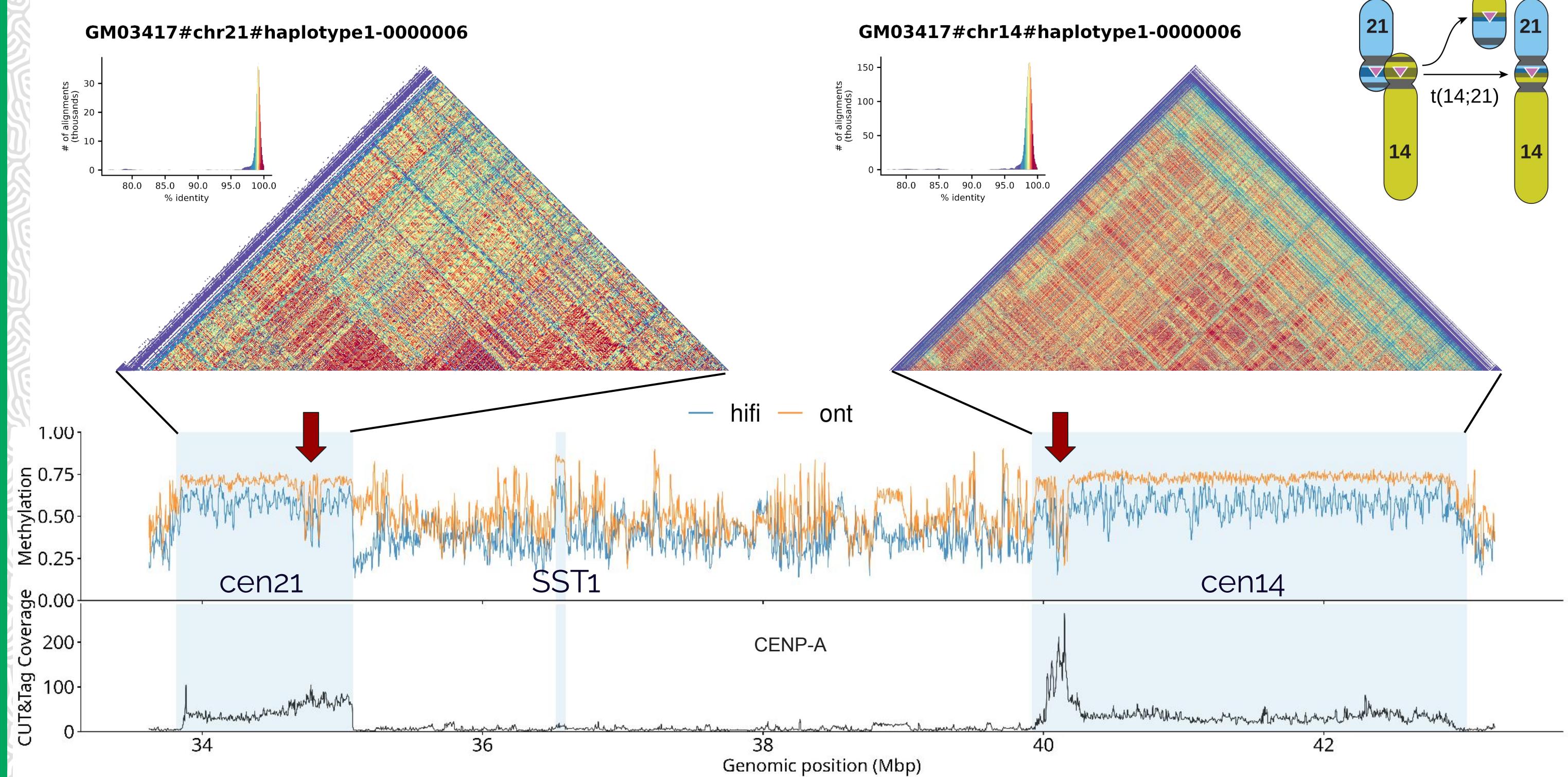
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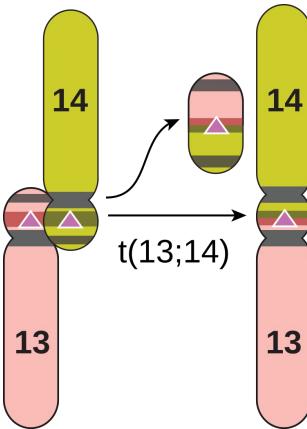
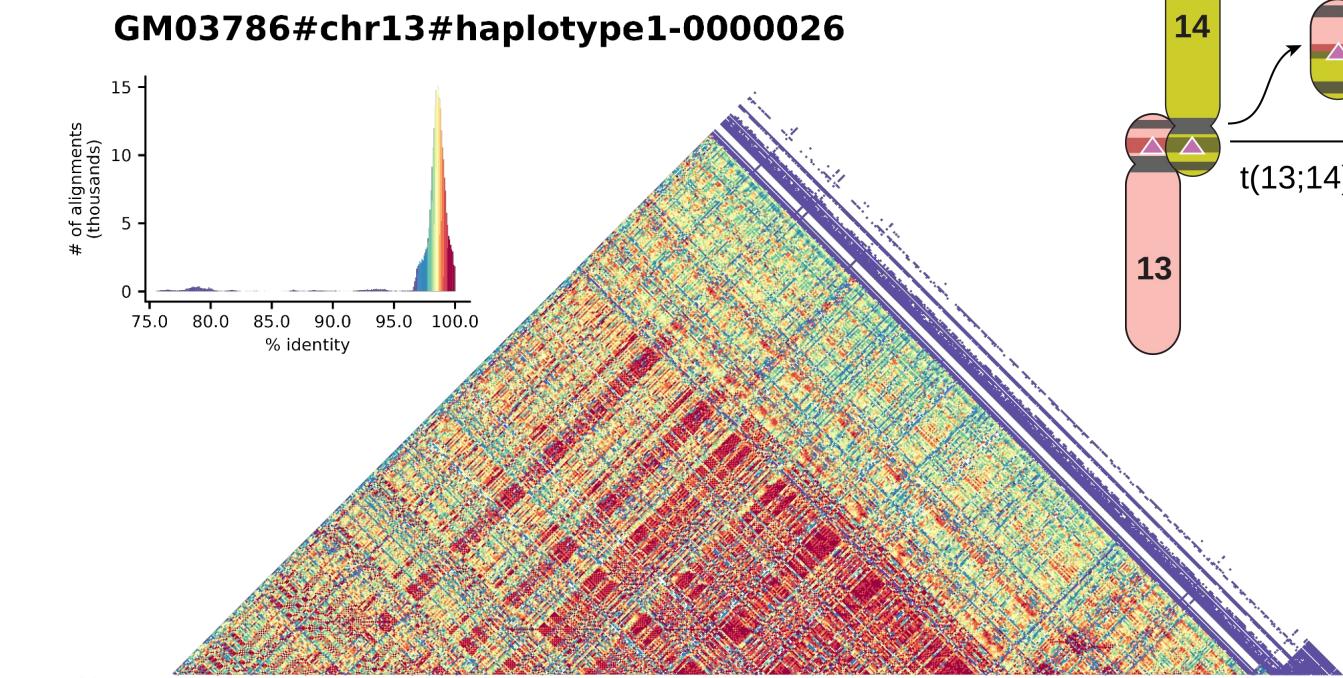
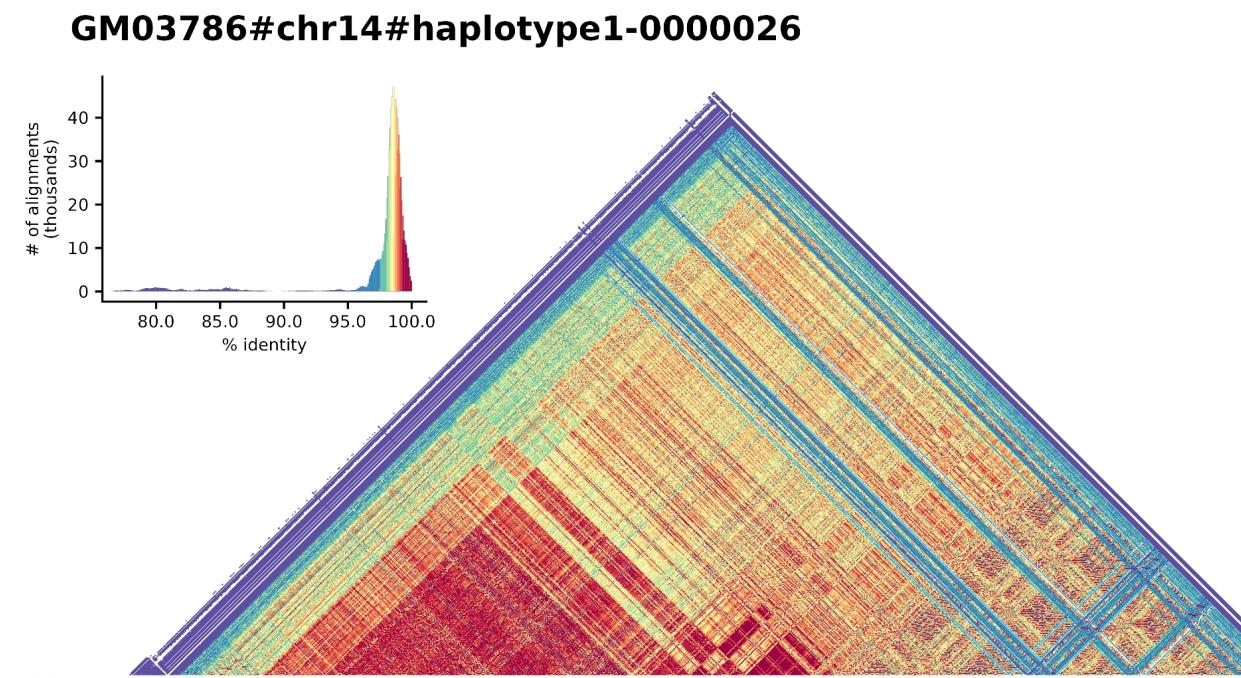
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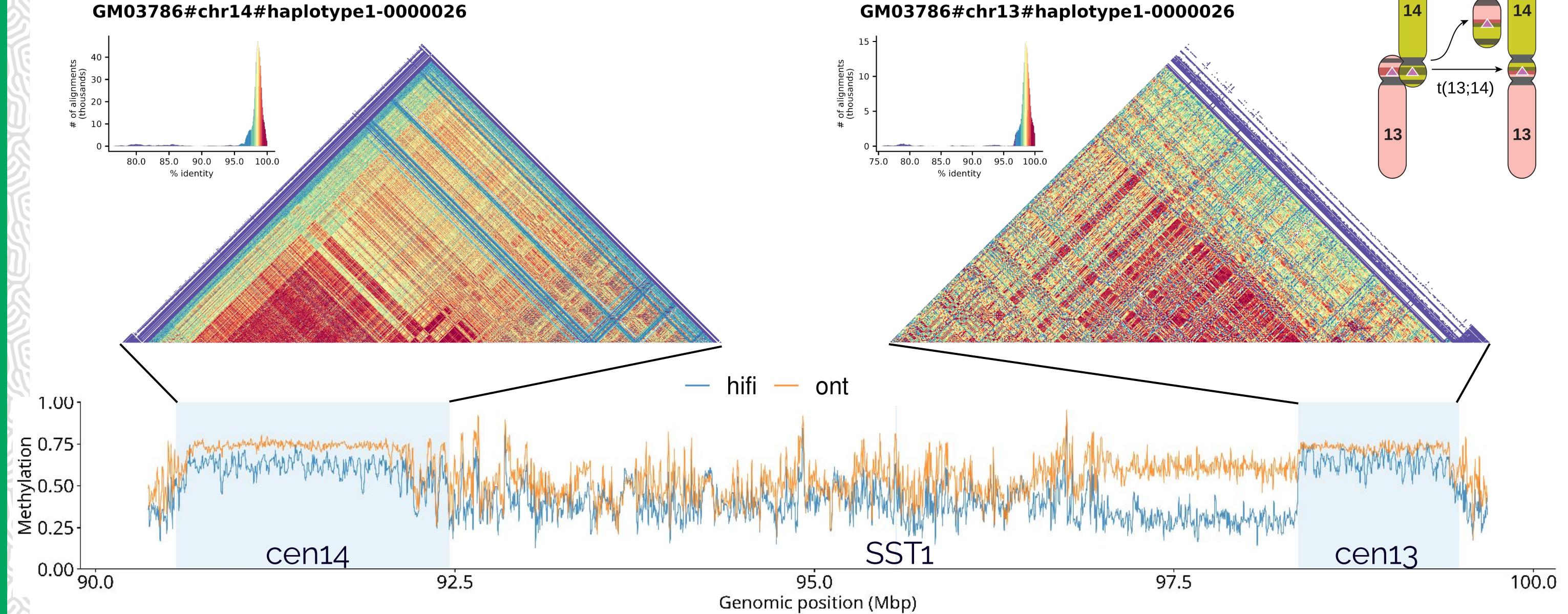
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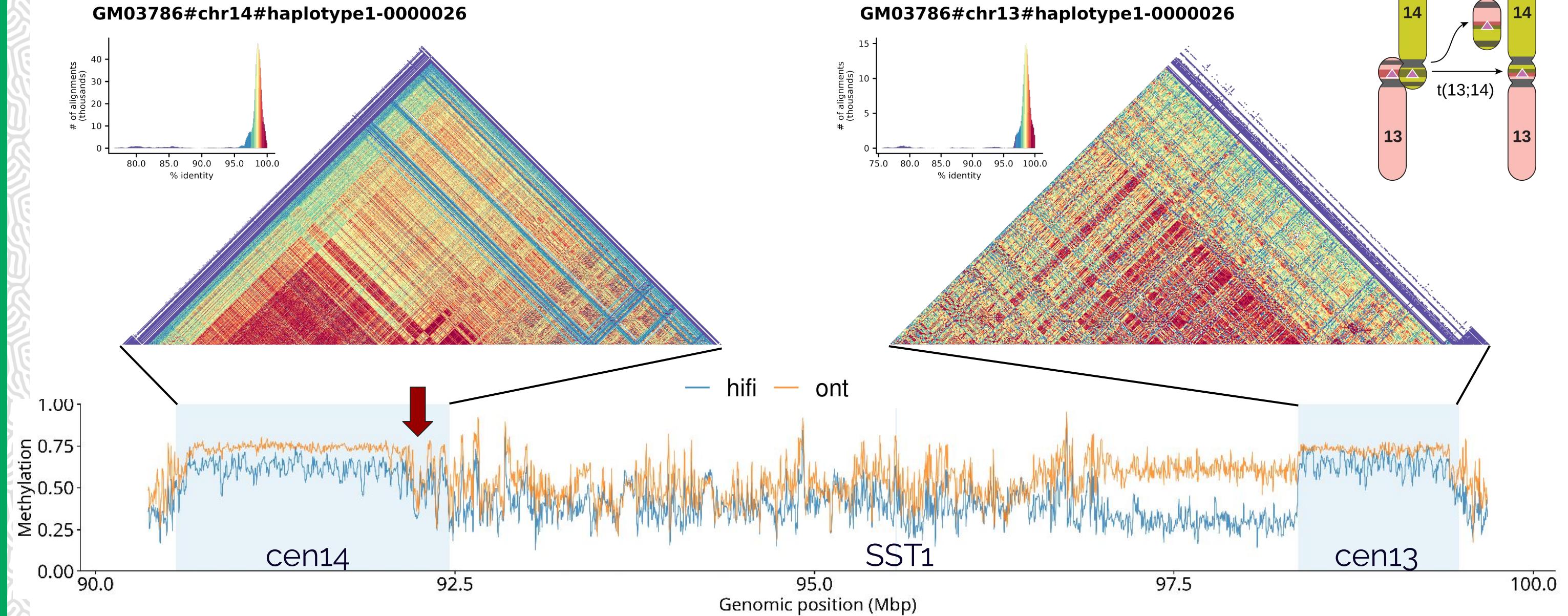
Cen14 is active, cen13 is inactive in t(13;14)



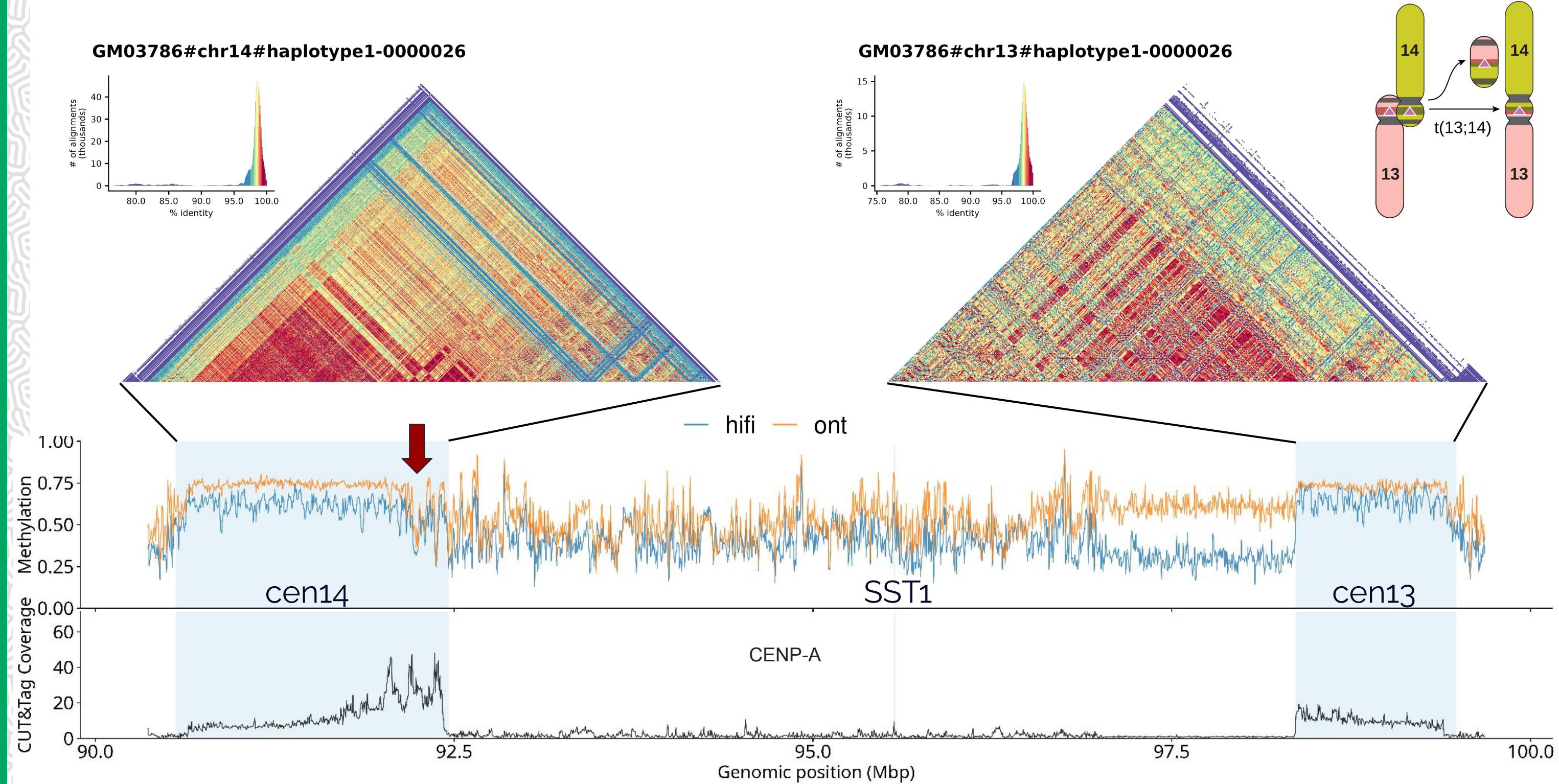
Cen14 is active, cen13 is inactive in t(13;14)



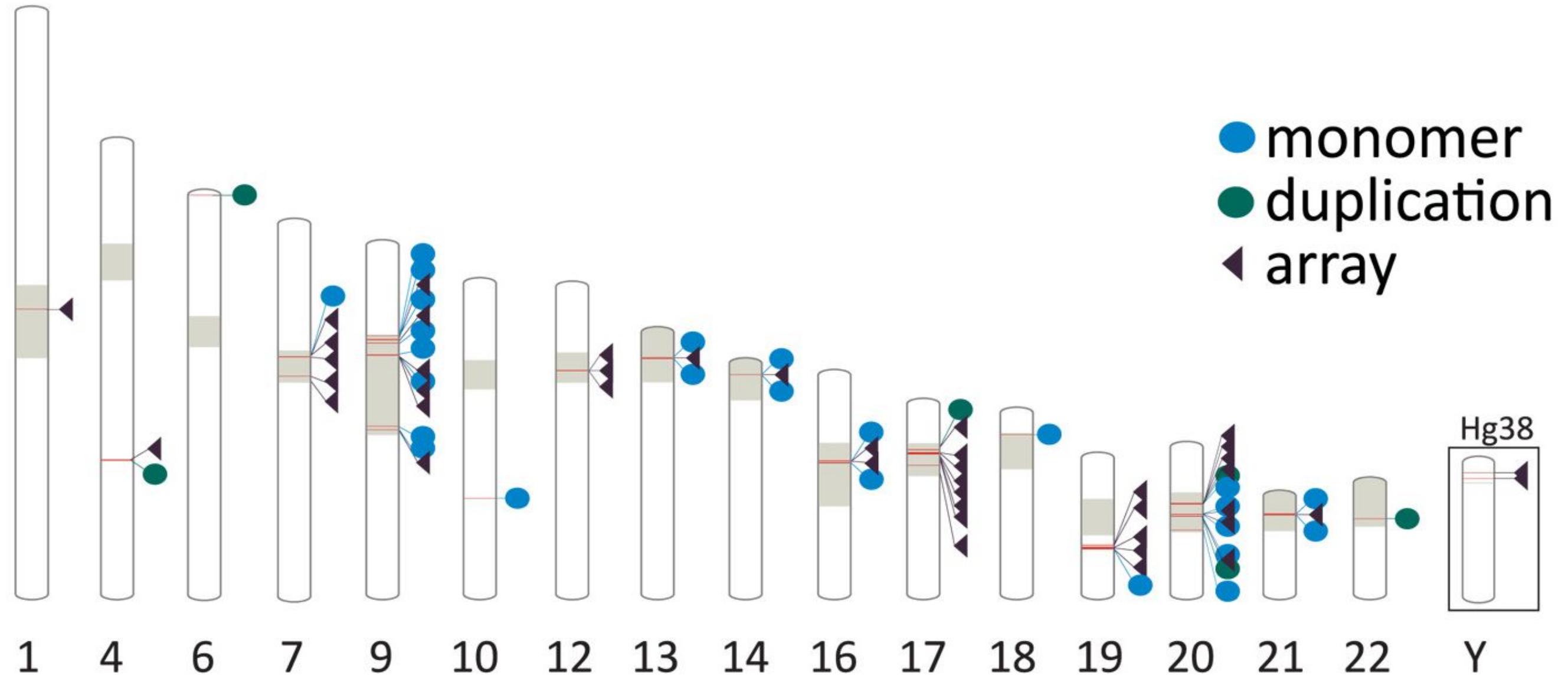
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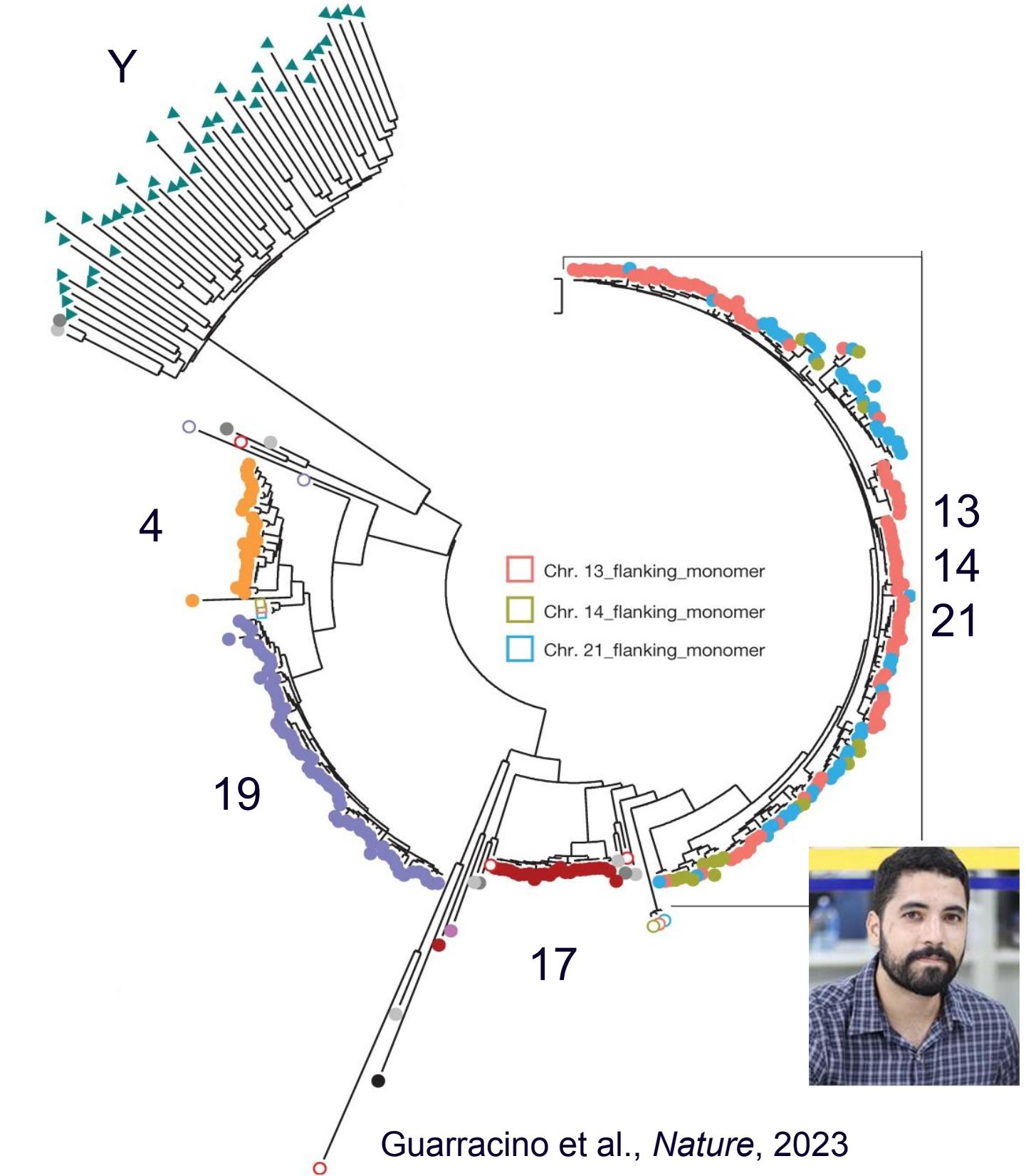
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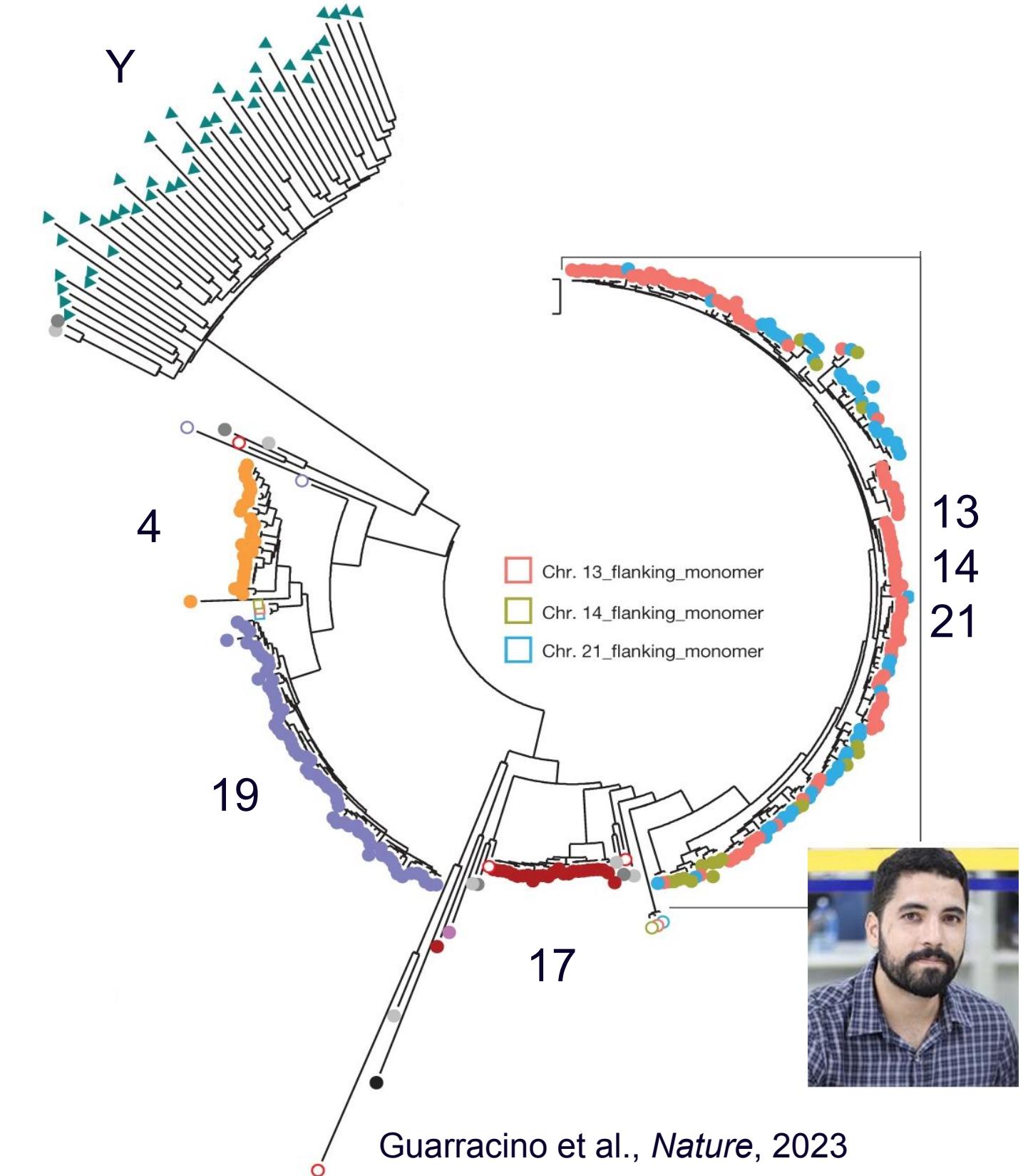
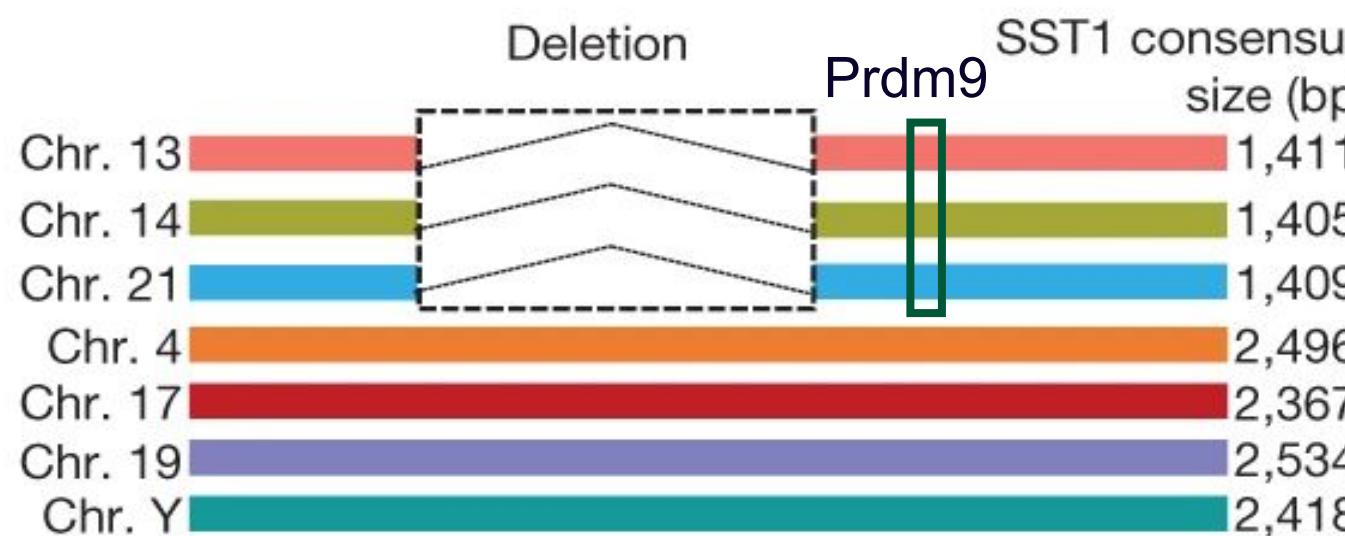
SST1-a key regulator of structural variation



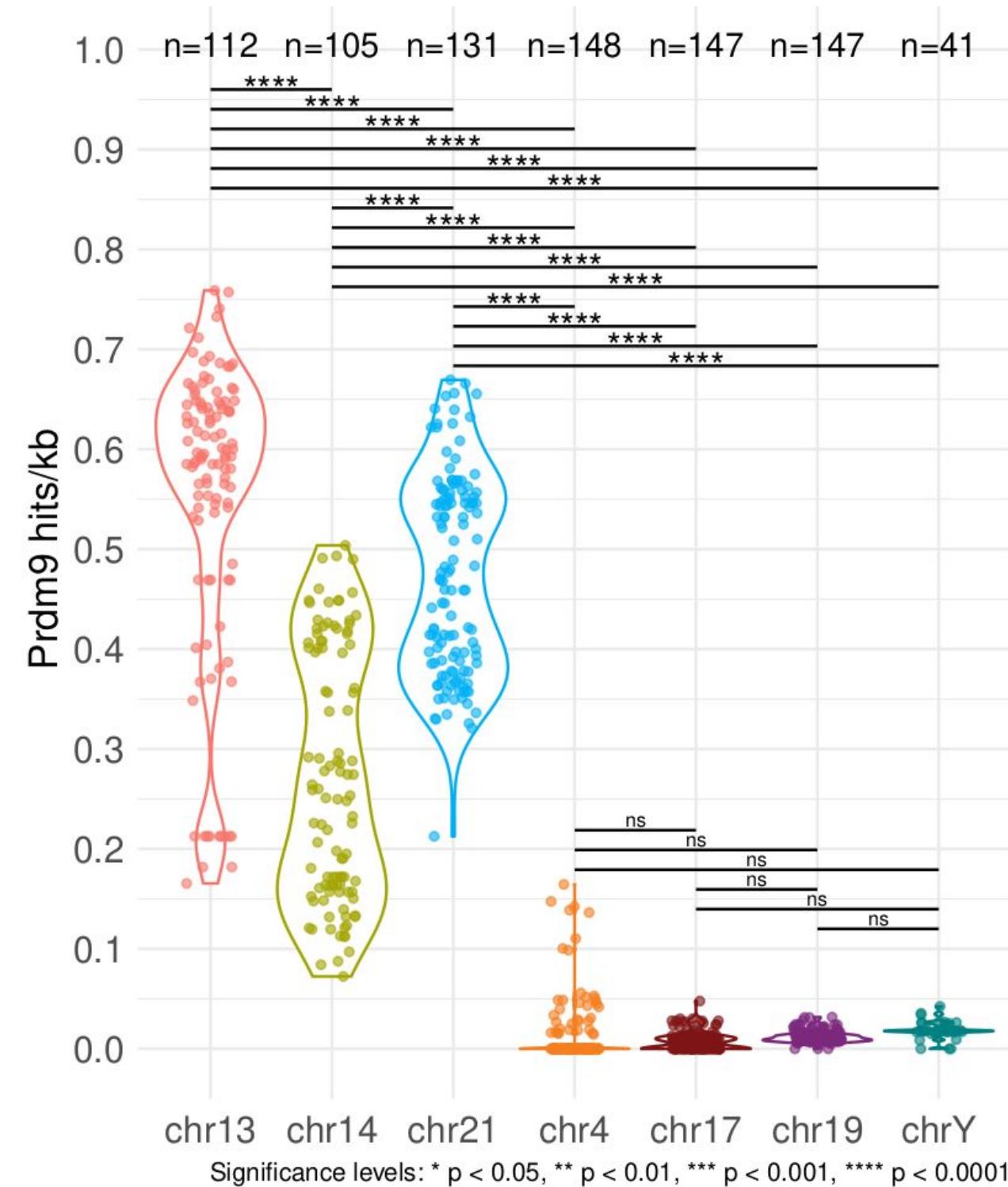
Phylogenetic analysis indicates frequent recombination between SST1 repeats on acrocentric chromosomes



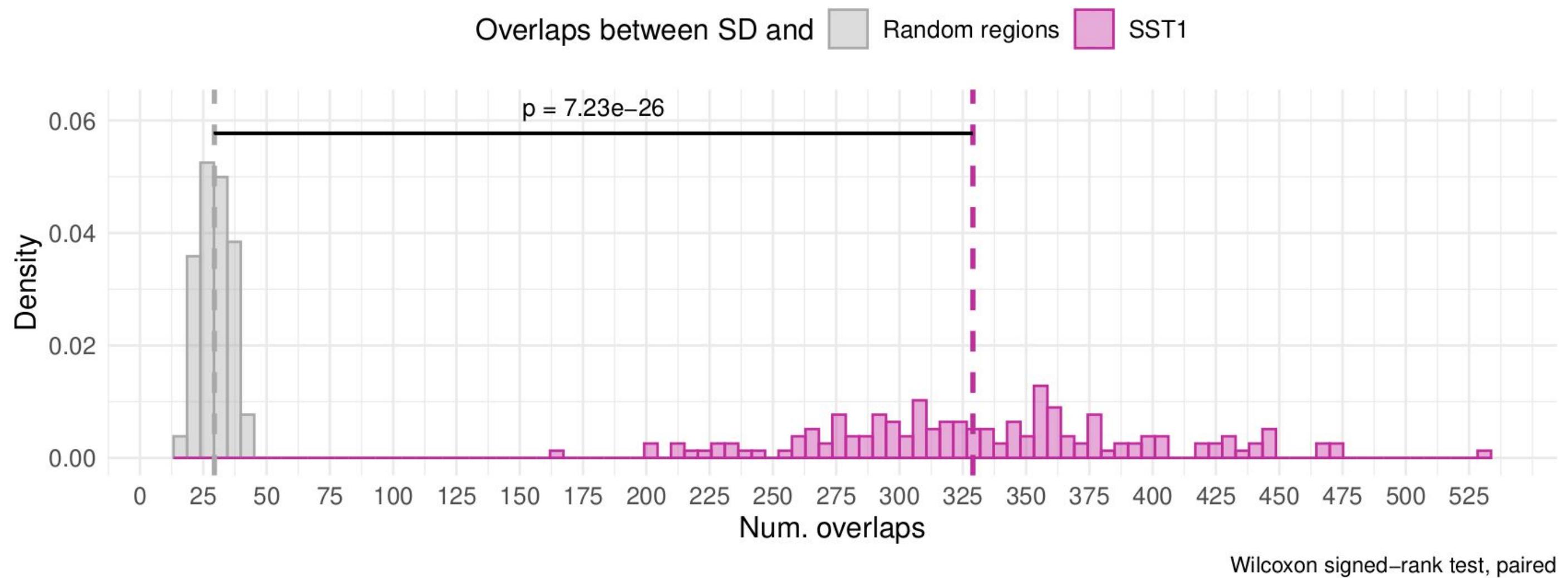
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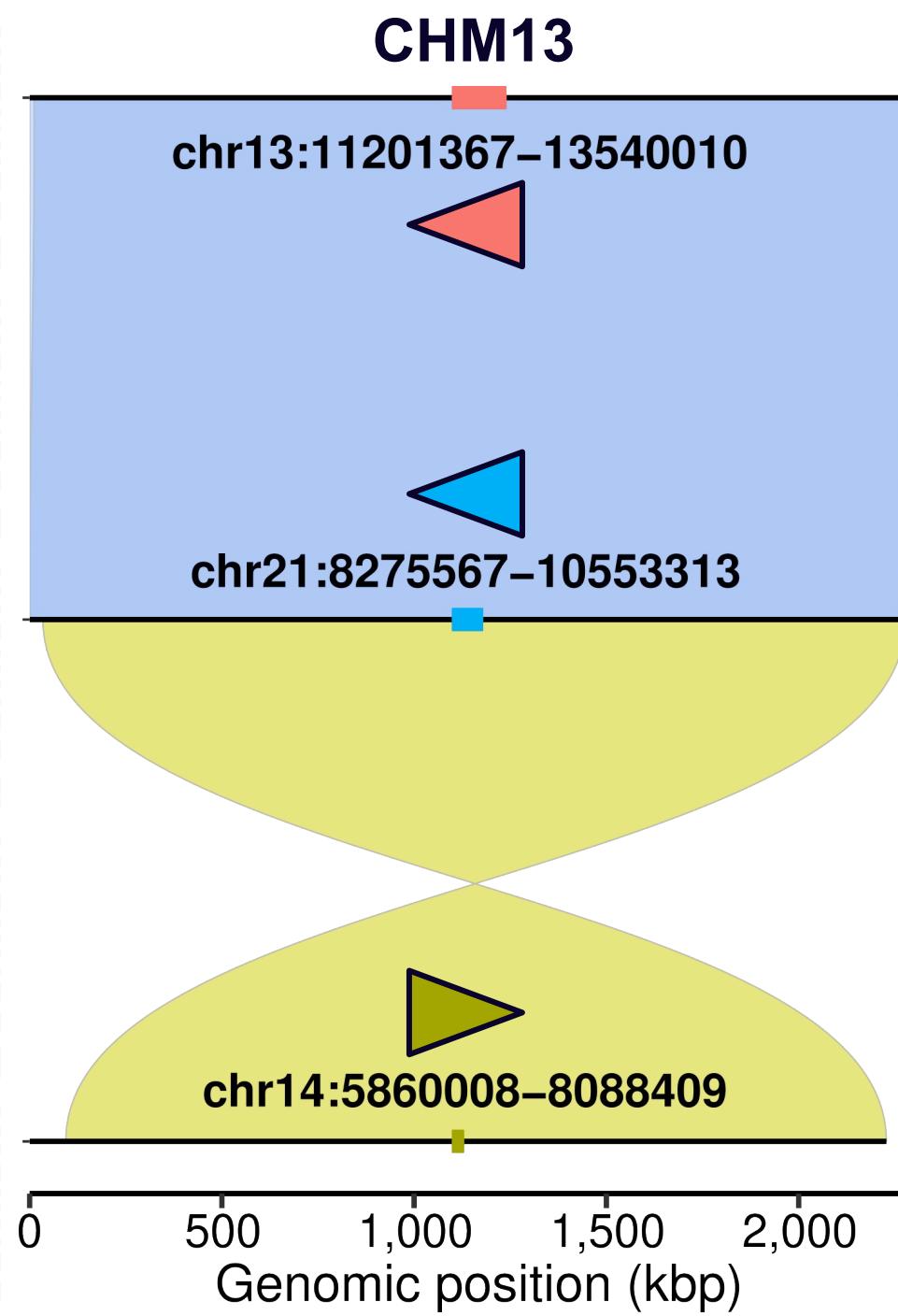
Density of Prdm9 sites in SST1 in the pangenome



Association between SST1 and segdups



PHR polymorphisms



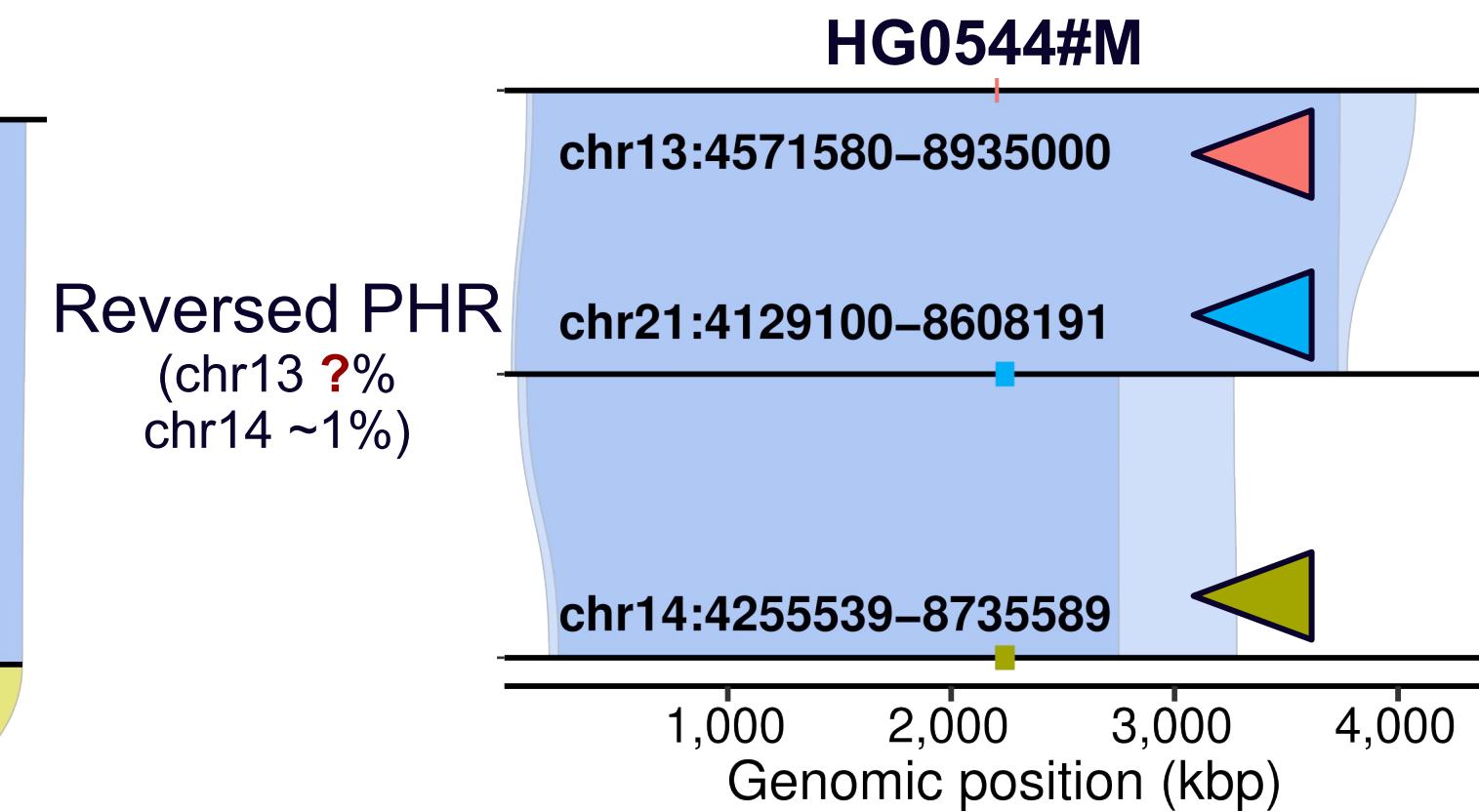
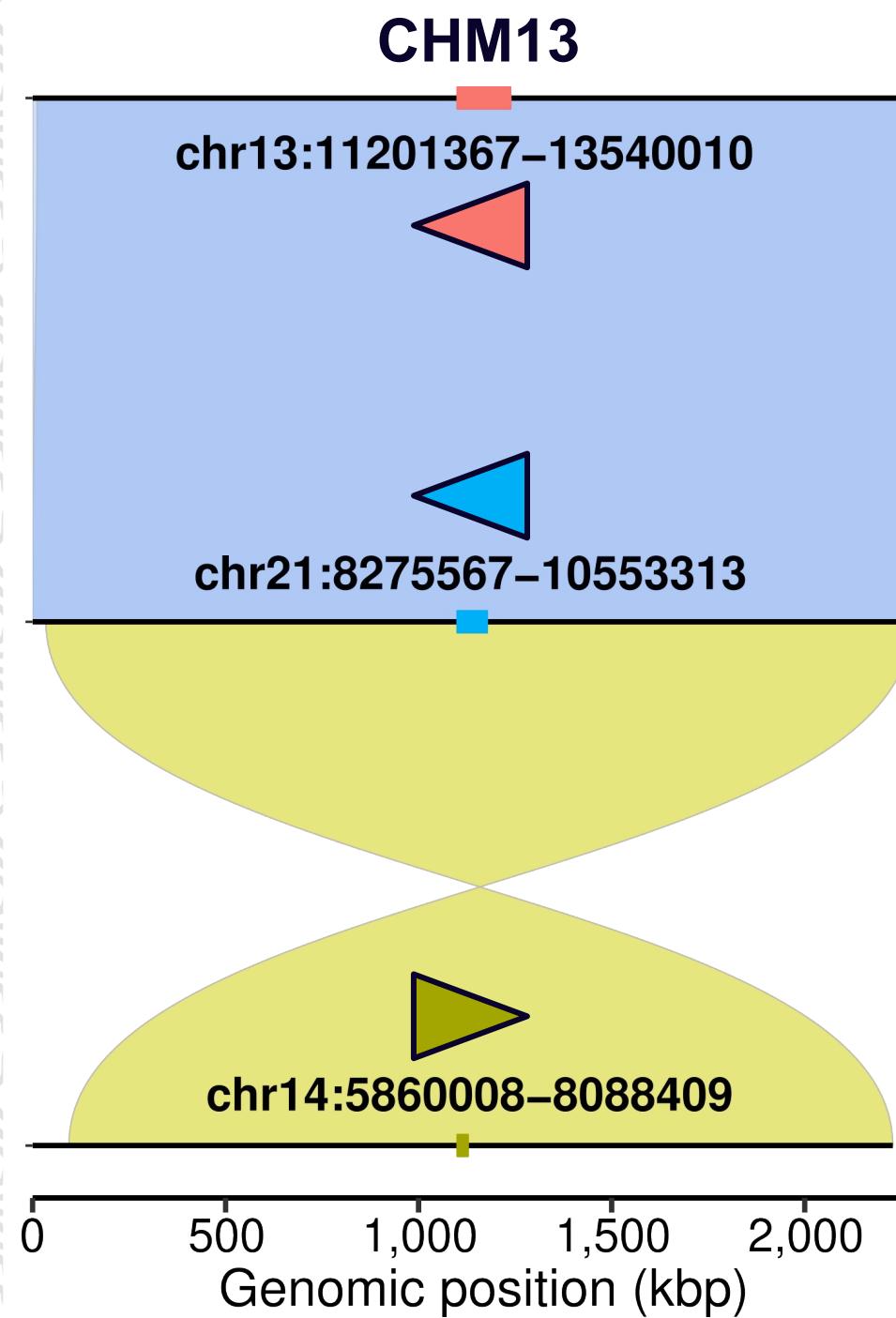
Annotation

- SST1_chr13
- SST1_chr14
- SST1_chr21

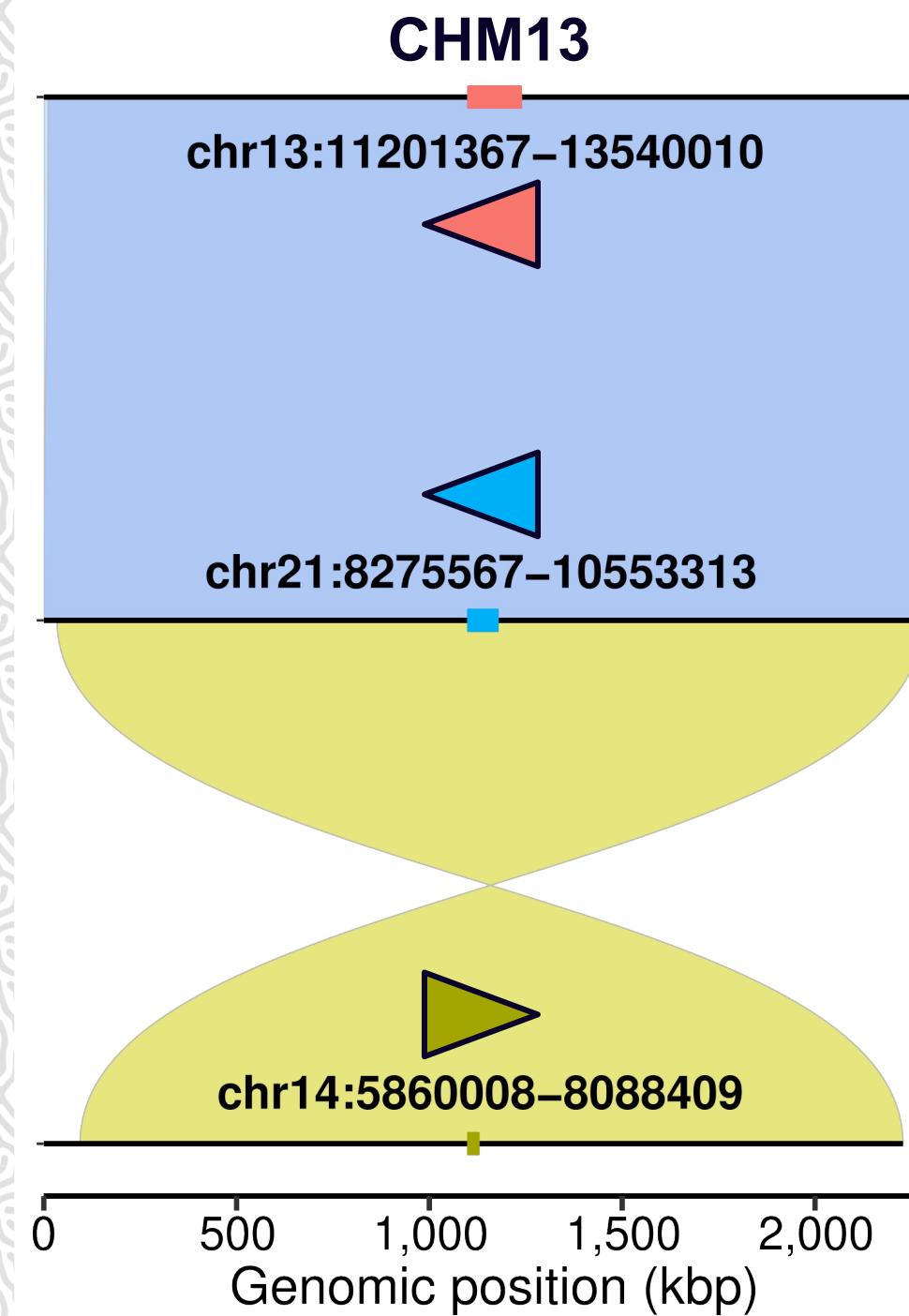
Alignment direction

-
- +

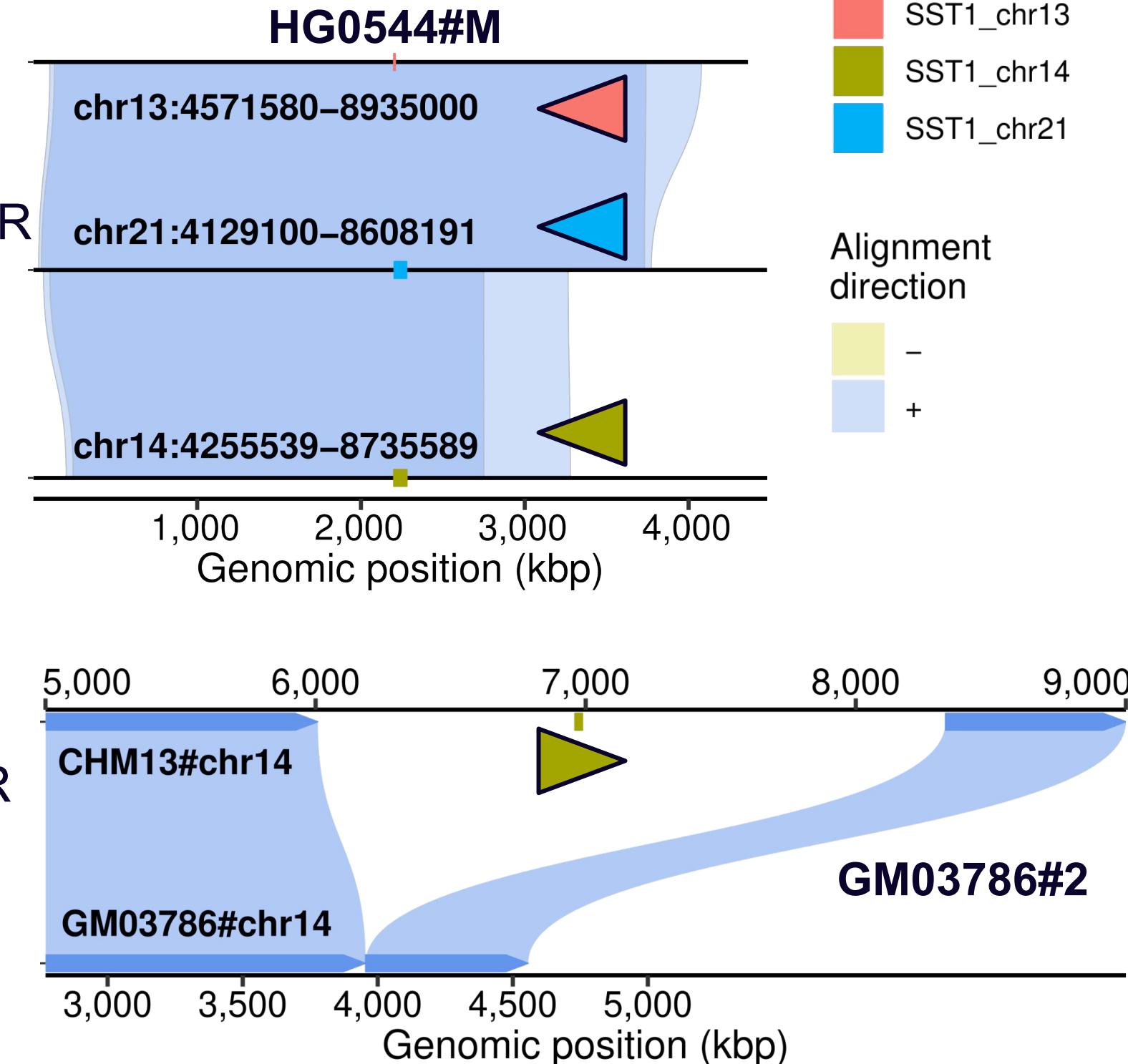
PHR polymorphisms



PHR polymorphisms



Reversed PHR
(chr13 ?%
chr14 ~1%)



Summary

- The formation of Robertsonian chromosomes depends on homology, proximity, and recombination initiation
- Robertsonian chromosomes can propagate as functional monocentrics or dicentrics
- The macrosatellite SST1 may have a broad role in genome variation and chromosome evolution



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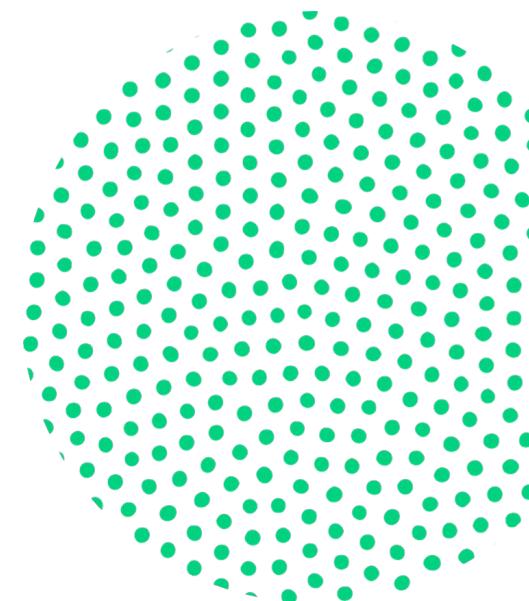


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