



The complete sequence of human Robertsonian chromosomes

Andrea Guaracino
Postdoctoral Scholar

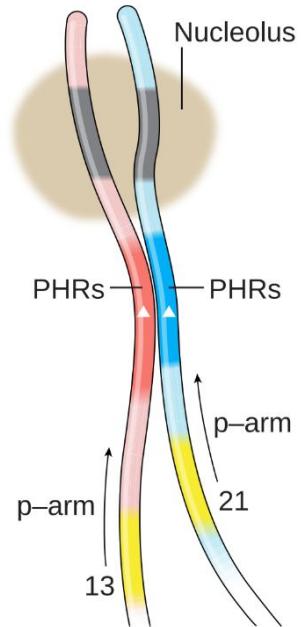


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Outline

- Heterologous recombination in the human pangenome
- A pathological outcome of heterologous recombination
- Robertsonian pangenome
- SST1-mediated interchromosomal exchange
- Epigenetic adaptation in centromere activity



Heterologous recombination in the human pangenome



Article

Recombination between heterologous human acrocentric chromosomes

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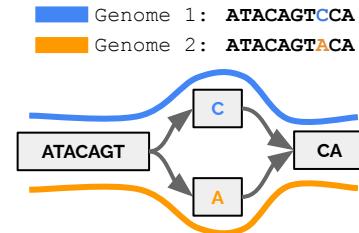
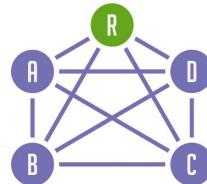
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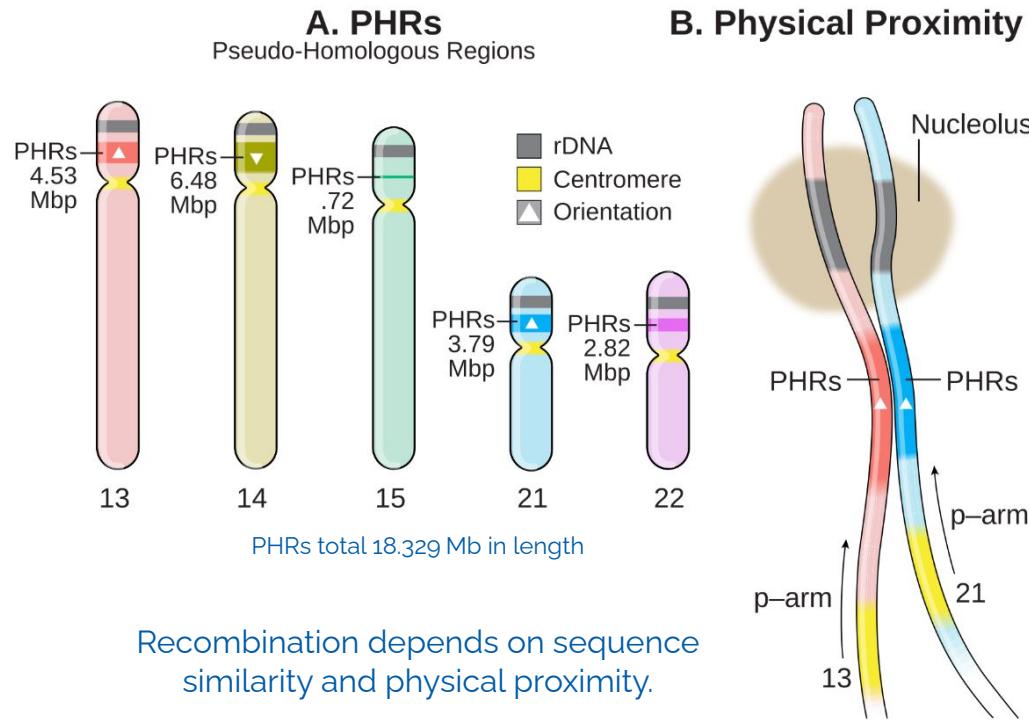
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Andrea Guerracino^{1,2}, Silvia Buonaiuto³, Leonardo Gomes de Lima⁴, Tamara Potapova⁴, Arang Rhee⁵, Sergey Koren⁵, Boris Rubinsteiⁿn⁴, Christian Fischer¹, Human Pangenome Reference Consortium*, Jennifer L. Gerton⁴, Adam M. Phillippy⁵, Vincenza Colonna^{1,3} & Erik Garrison^{1,2}

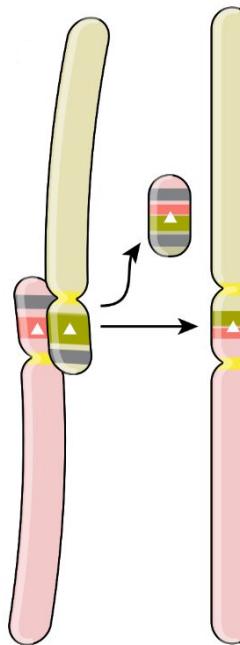


Pseudo-Homologous Regions of human acrocentric chromosomes

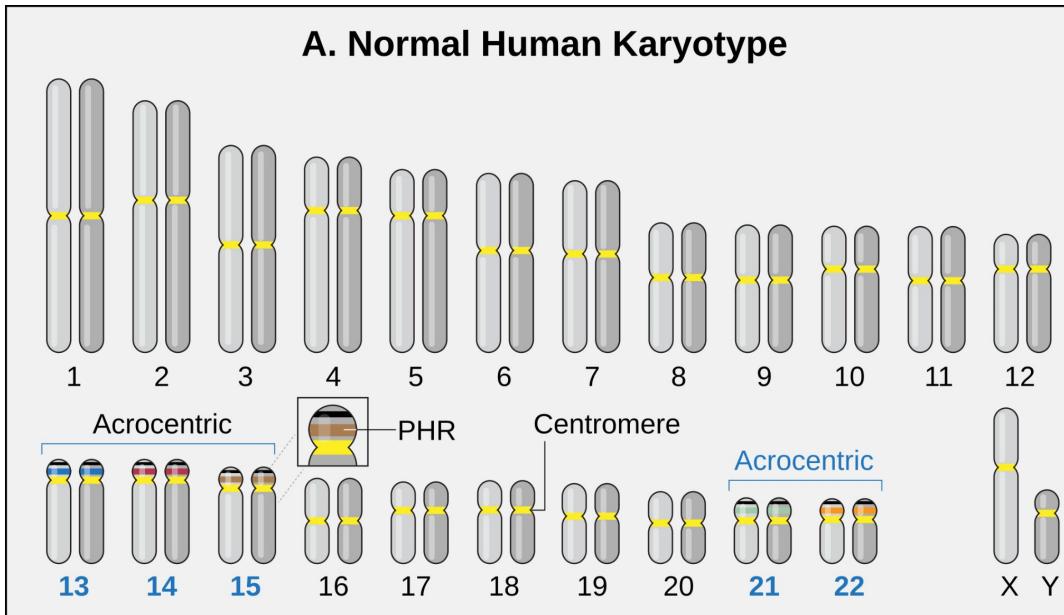


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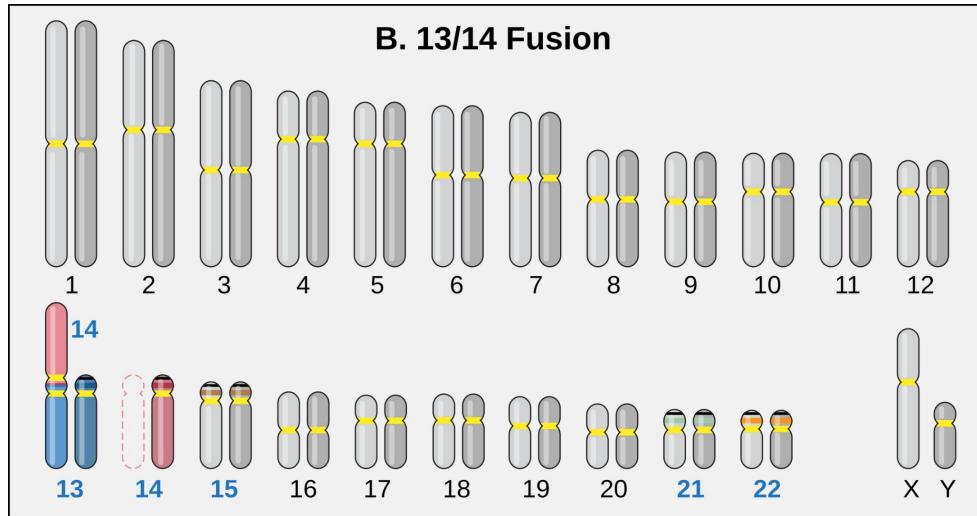
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Robertsonian translocations

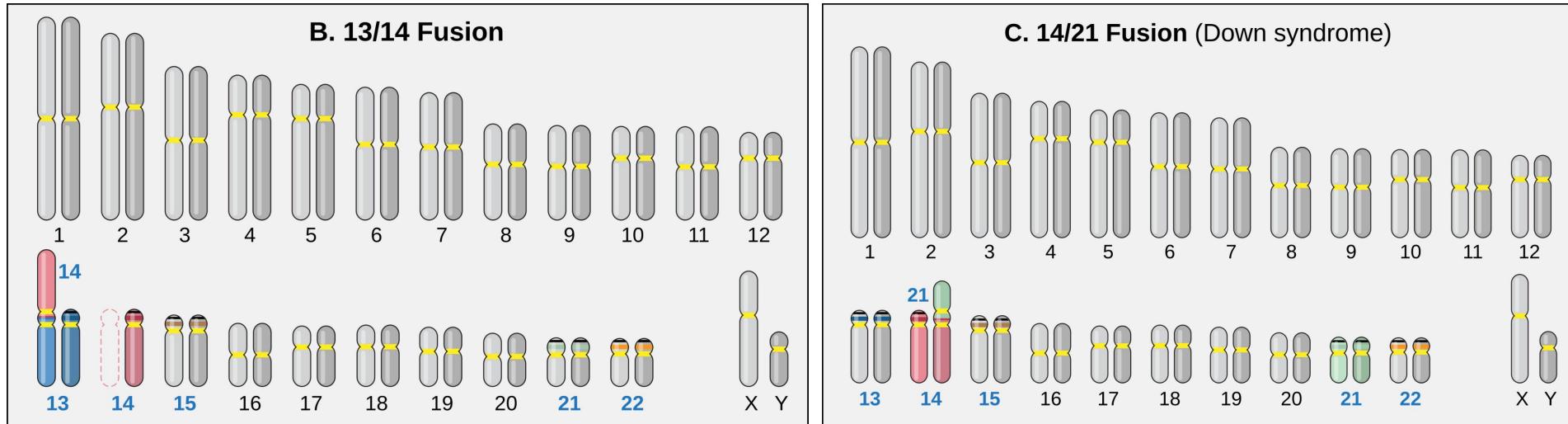


Robertsonian translocations



75% of the cases

Robertsonian translocations

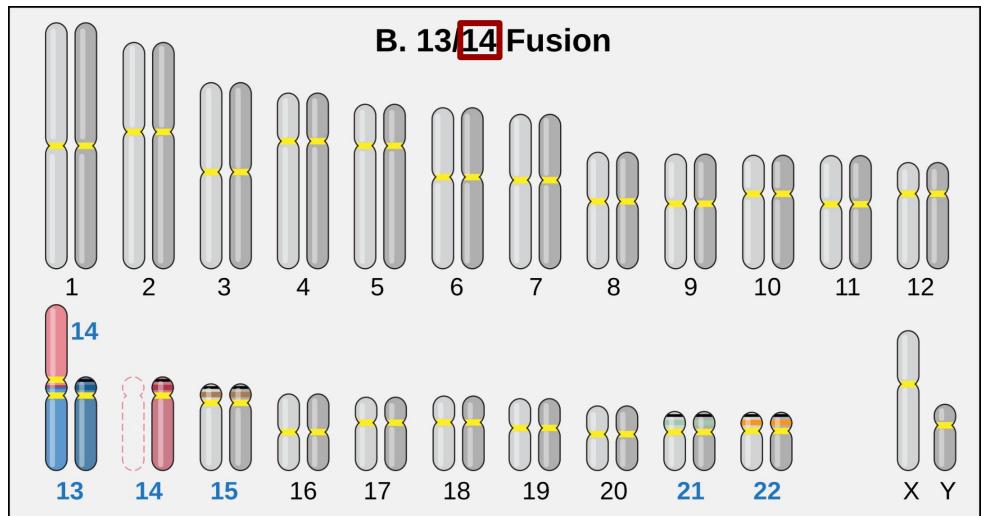


75% of the cases

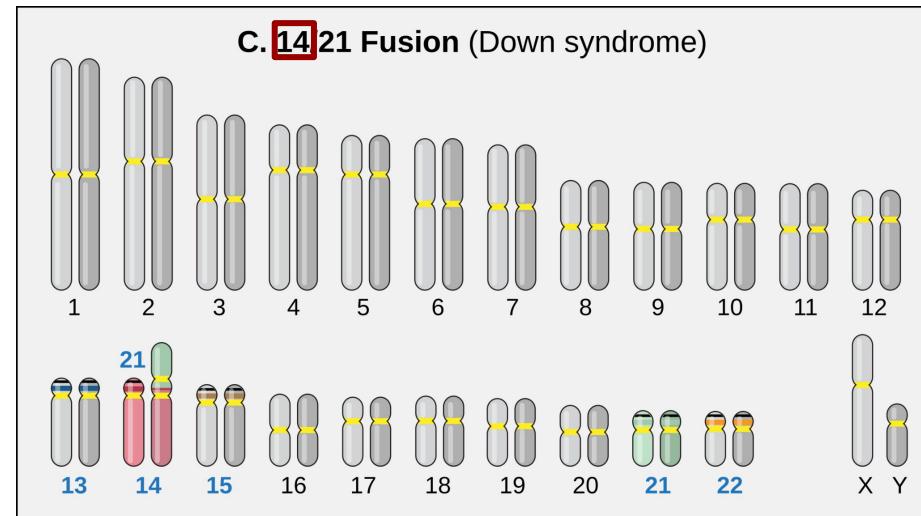
10% of the cases

Robertsonian translocations

chr14 is involved in the majority of the robertsonian translocations

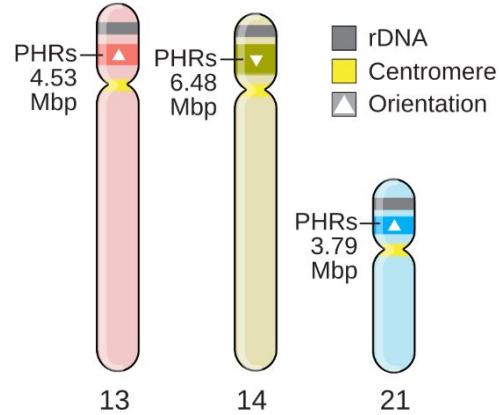


75% of the cases

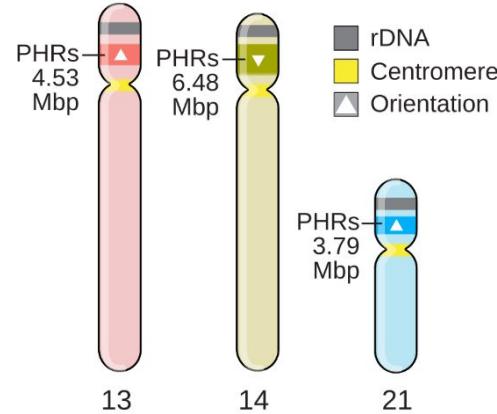


10% of the cases

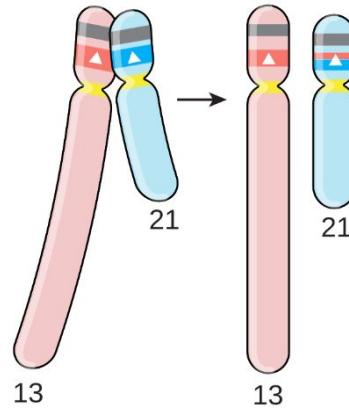
Recombination outcomes



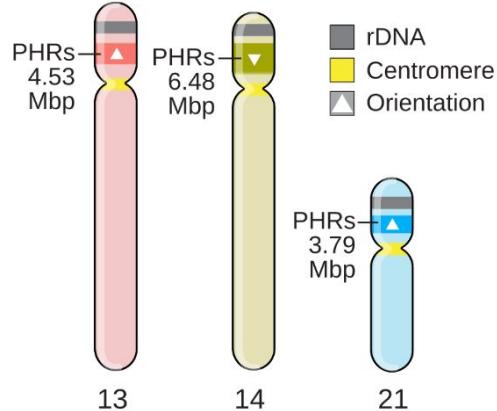
Recombination outcomes



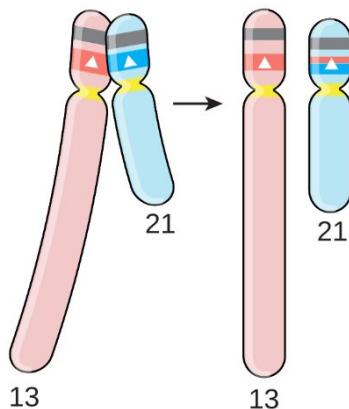
C. Recombination



Recombination outcomes

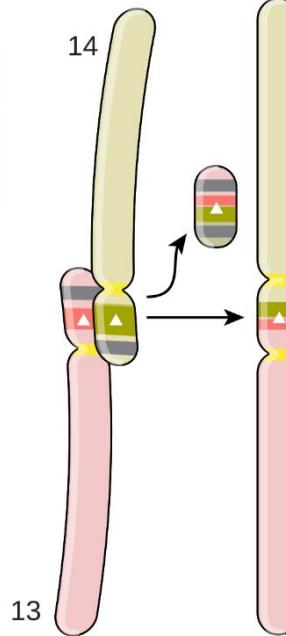


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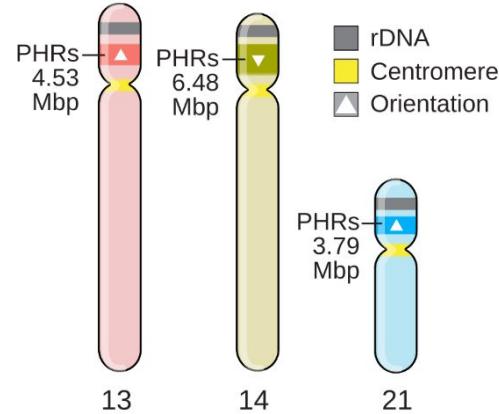


D. ROBs

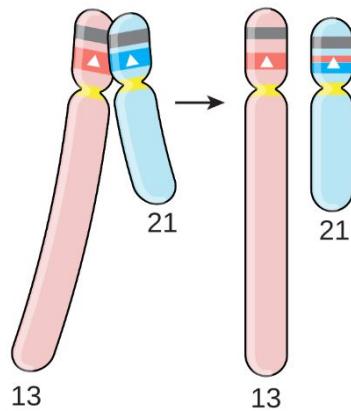
Robertsonian Translocations



Recombination outcomes

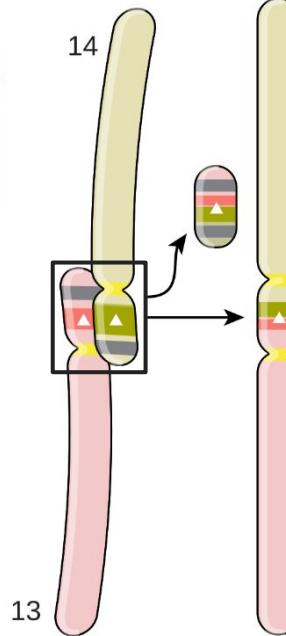


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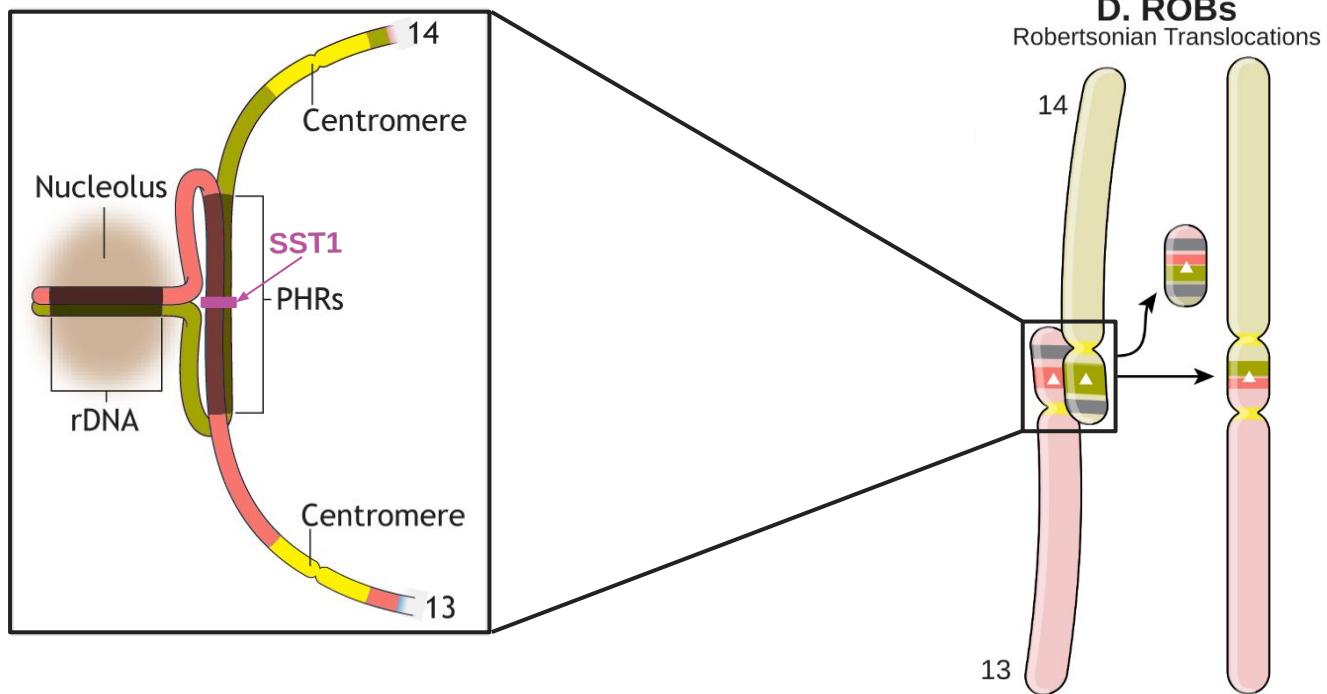


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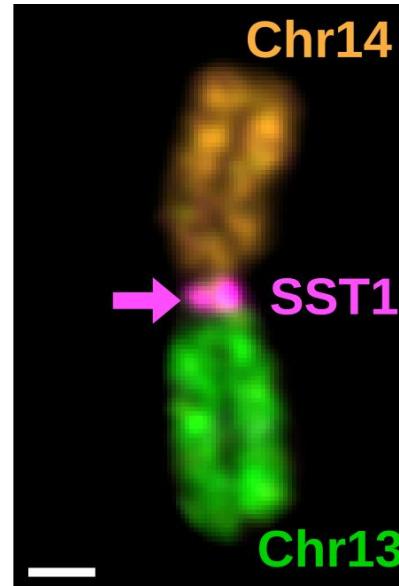


A model for common Robertsonian translocations

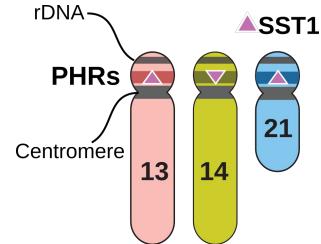


Outline

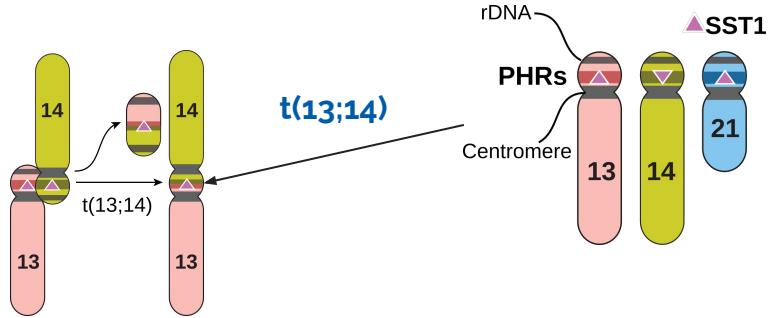
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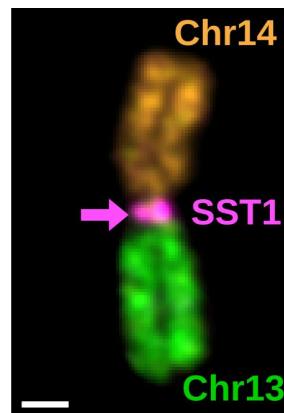
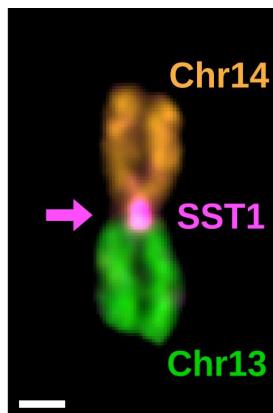
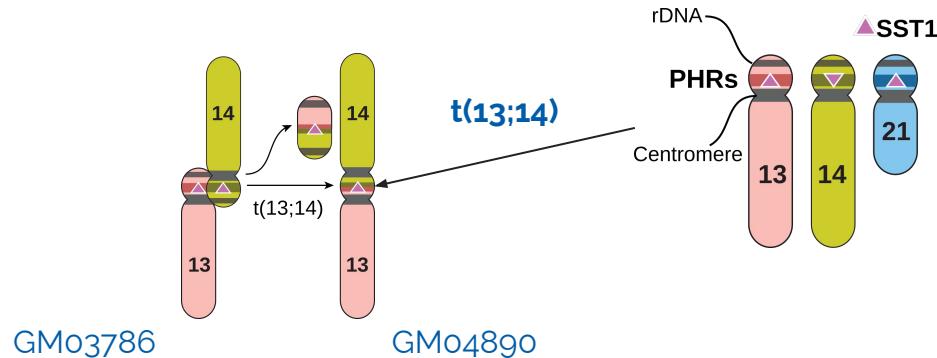
Robertsonian pangenome



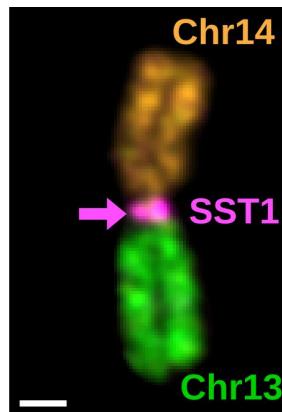
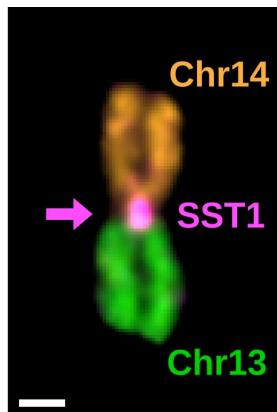
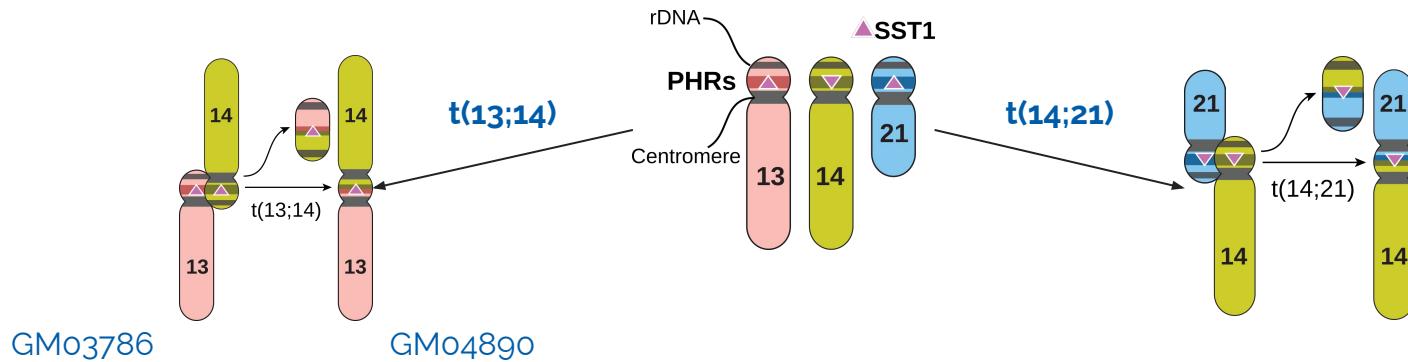
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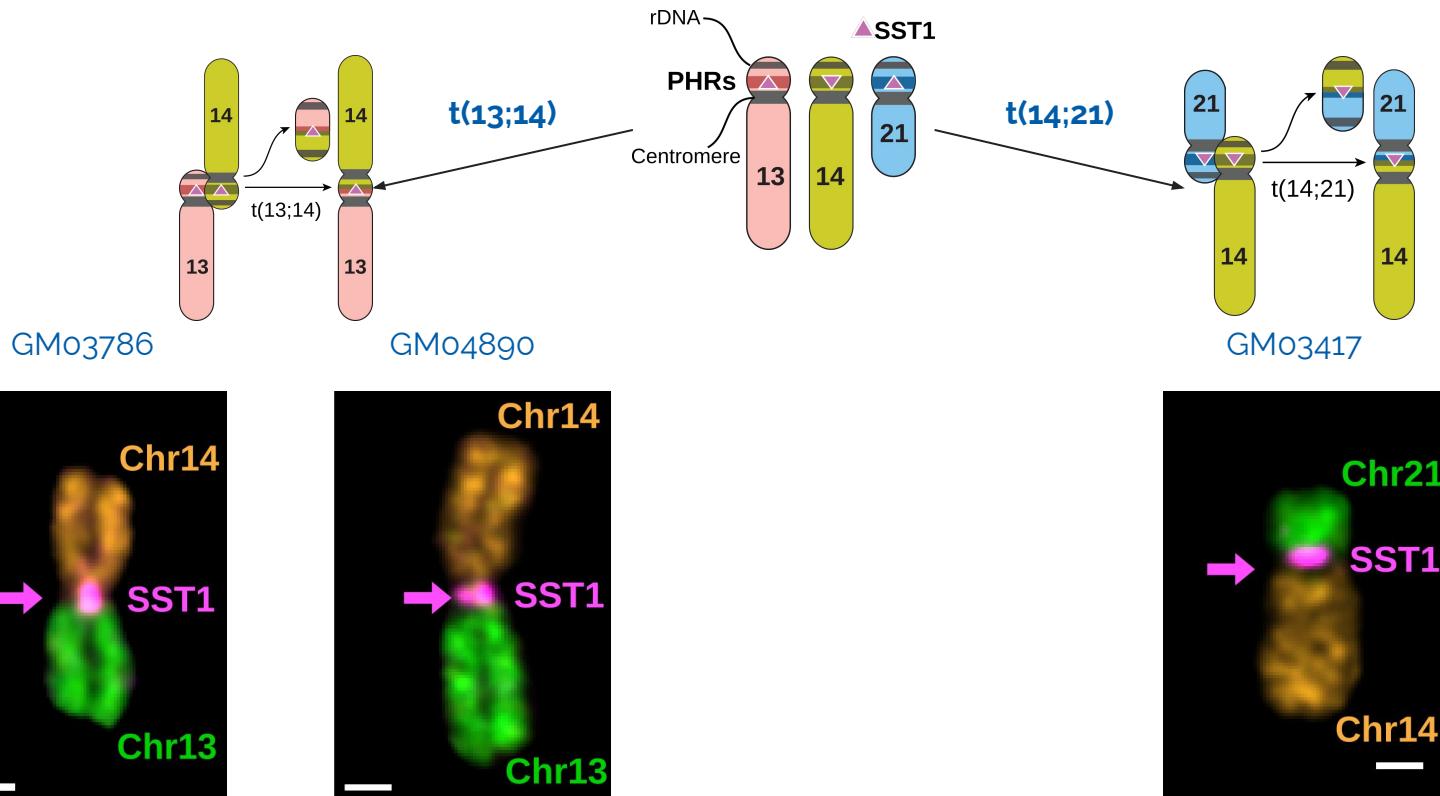
Robertsonian pangenome



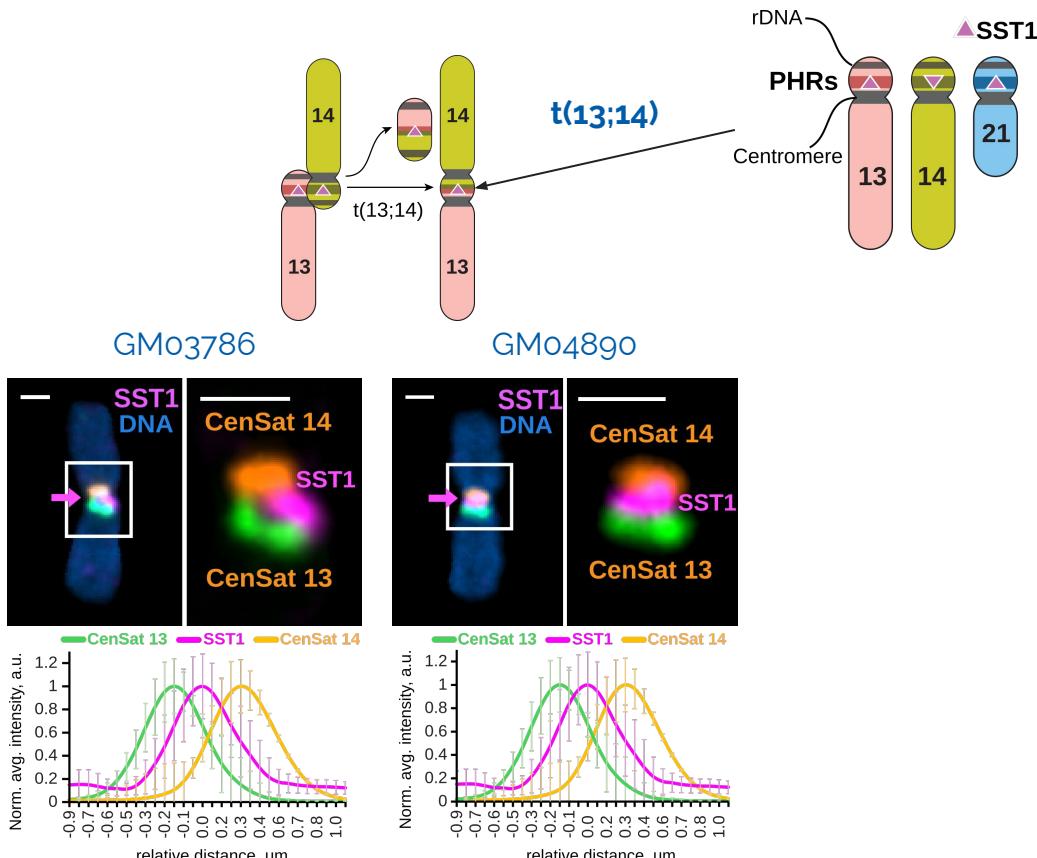
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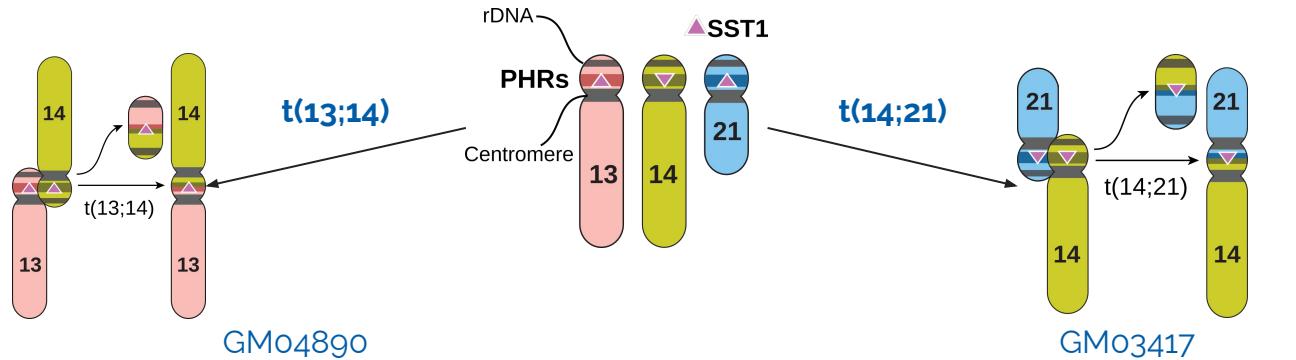
Robertsonian pangenome



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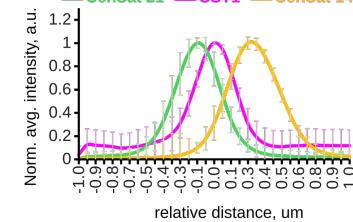
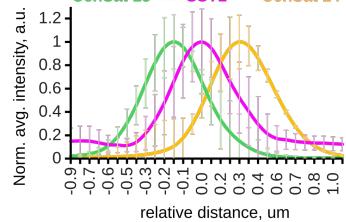
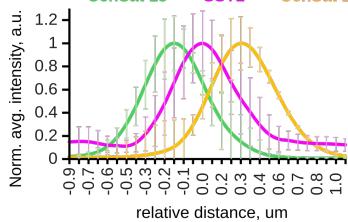
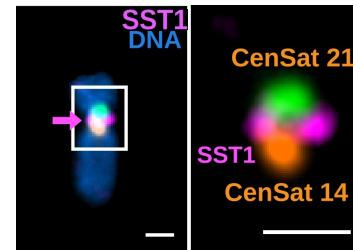
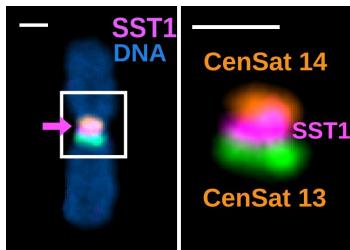
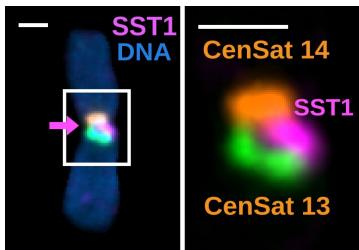
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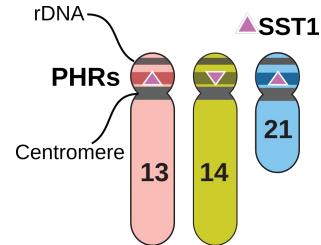
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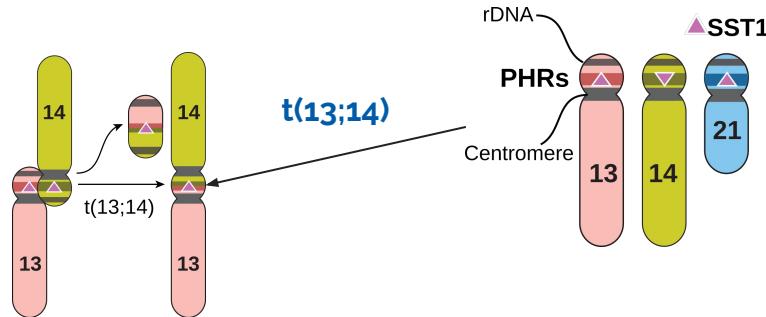
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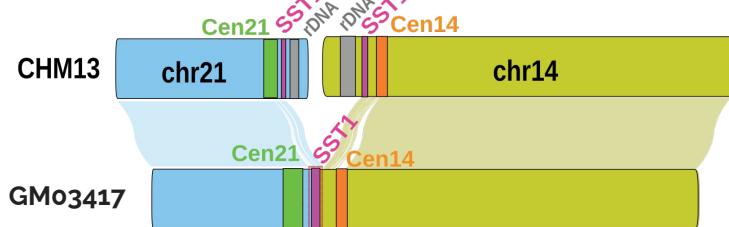
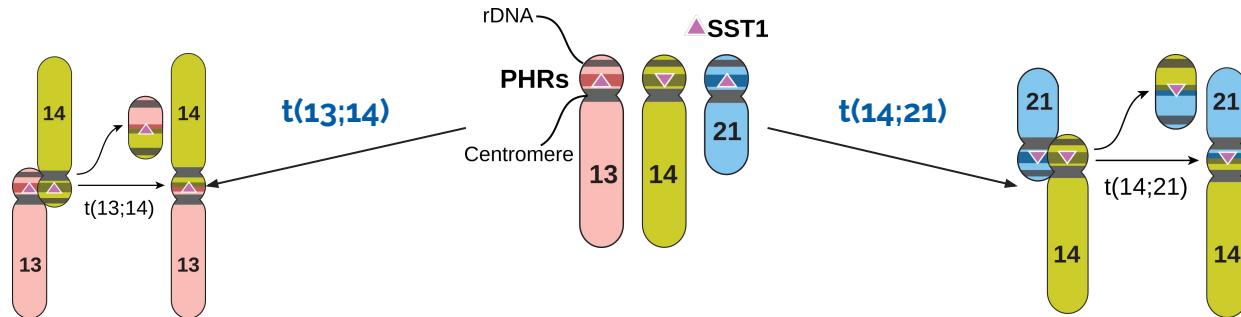
Complete sequence of Robertsonian chromosomes



Complete sequence of Robertsonian chromosomes

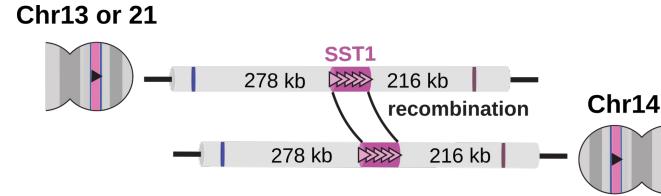


Complete sequence of Robertsonian chromosomes

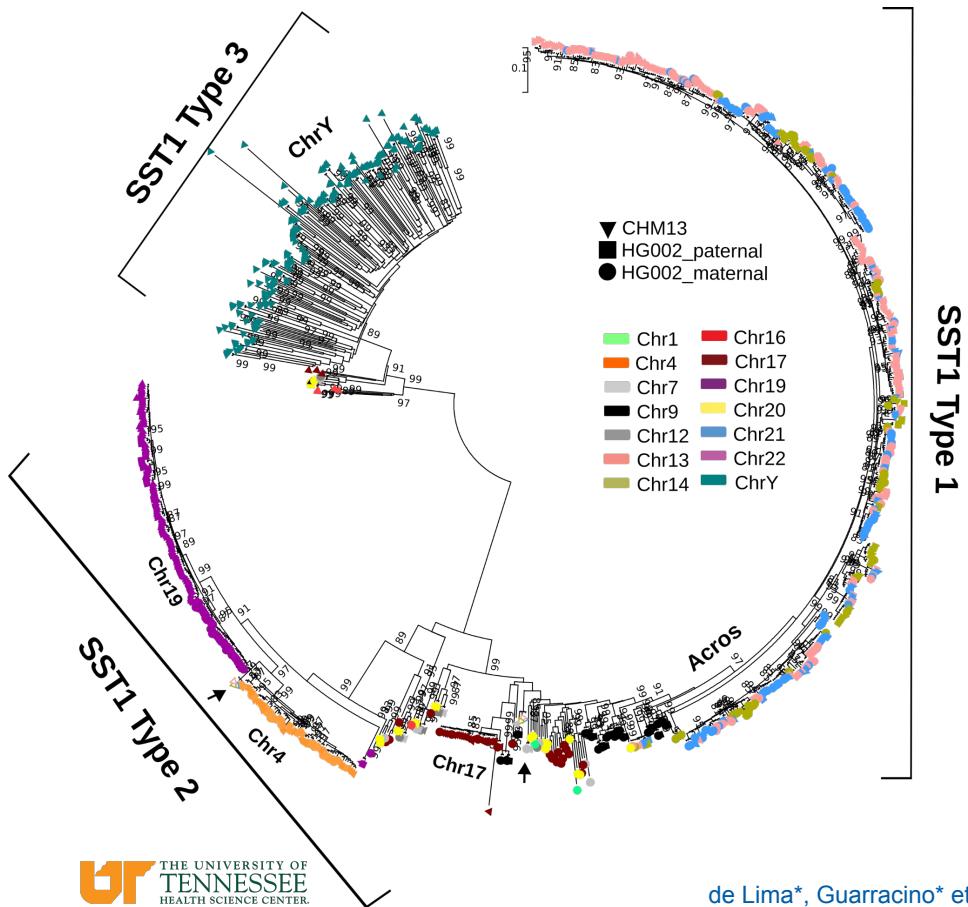


Outline

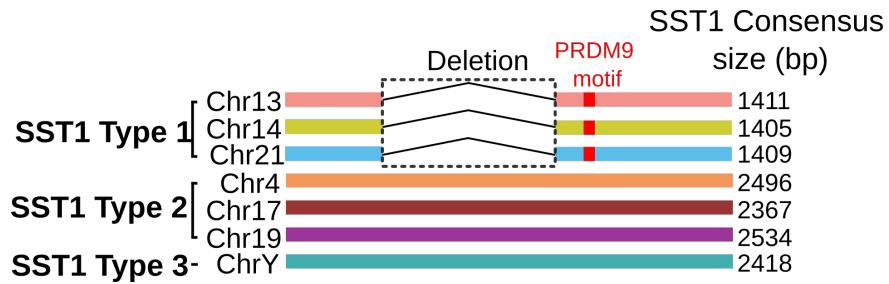
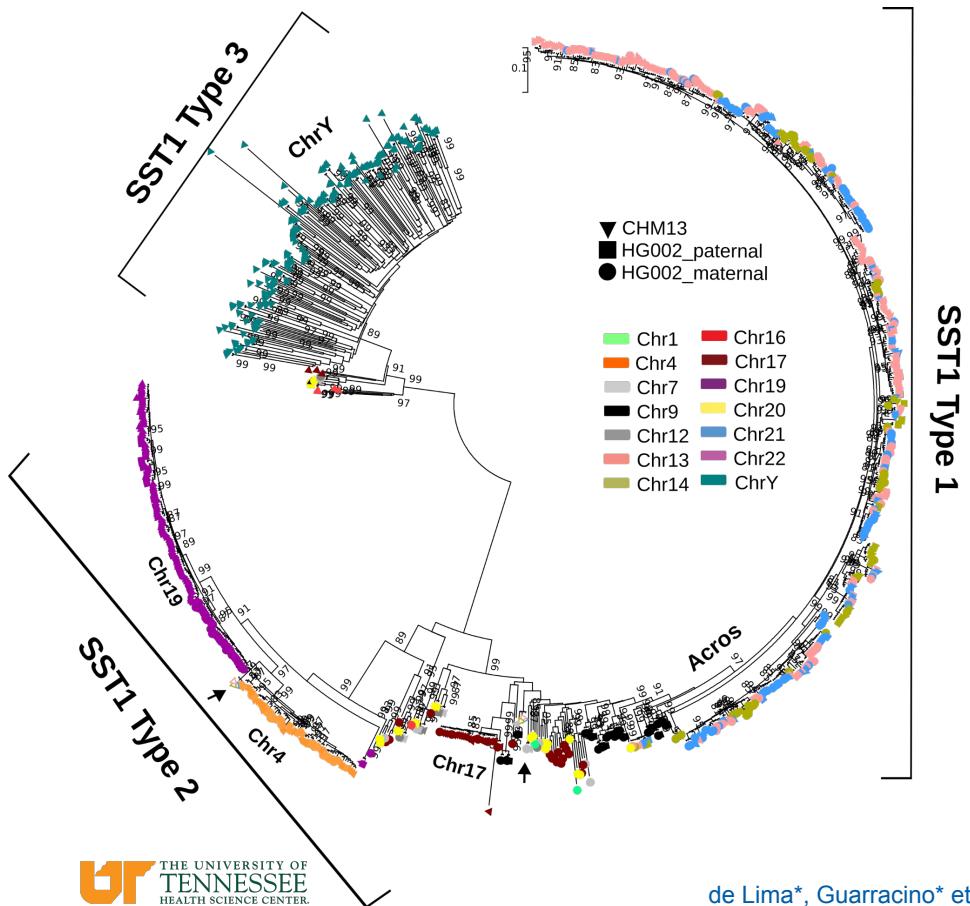
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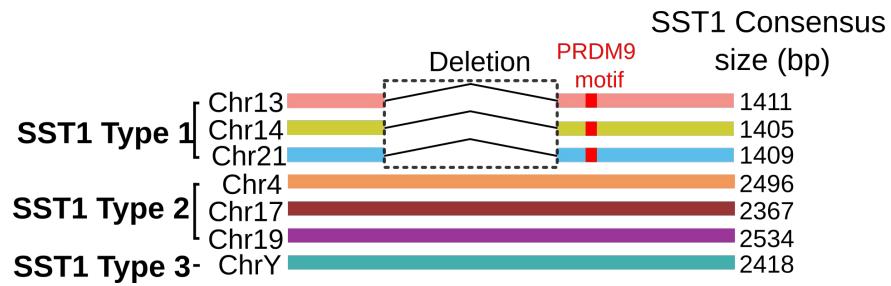
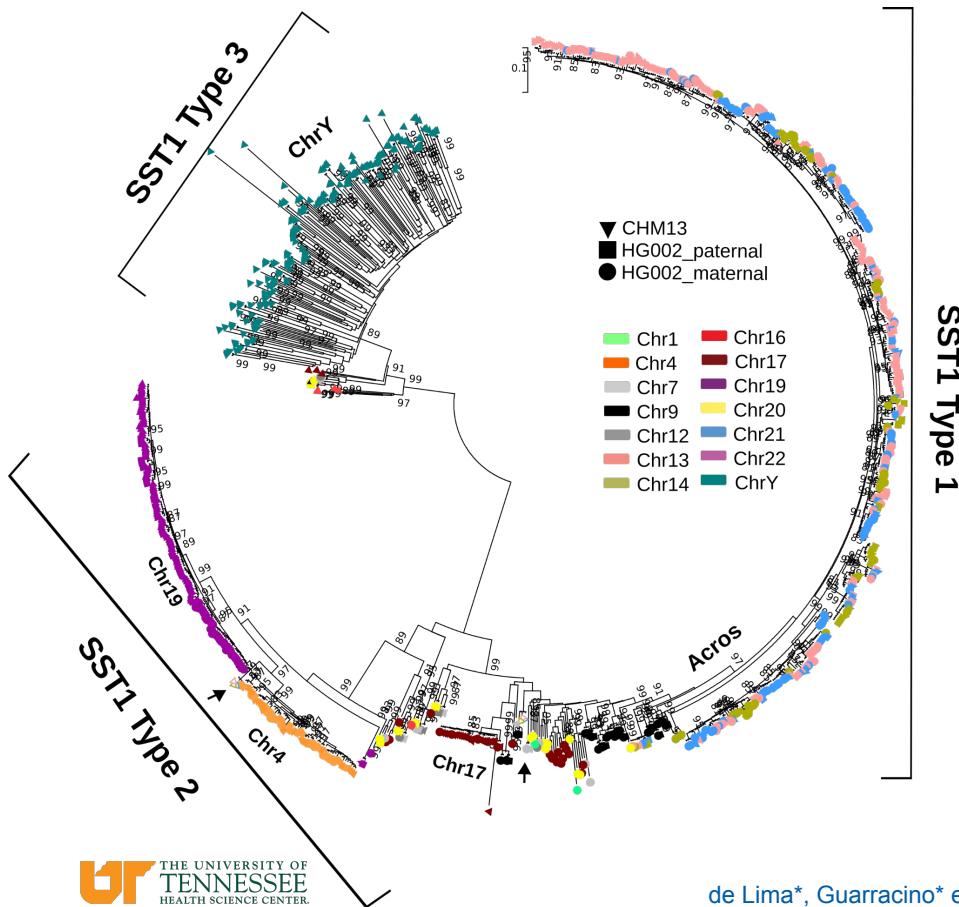
Phylogenetic analysis of SST1 monomers from CHM13 and HG002



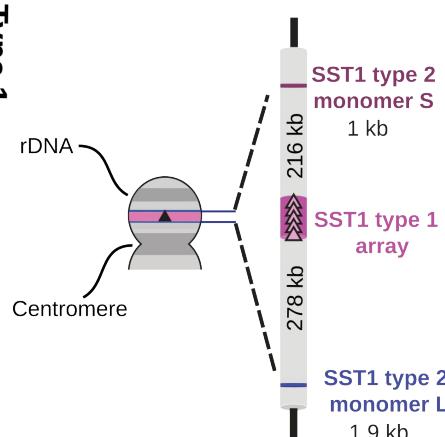
Phylogenetic analysis of SST1 monomers from CHM13 and HG002



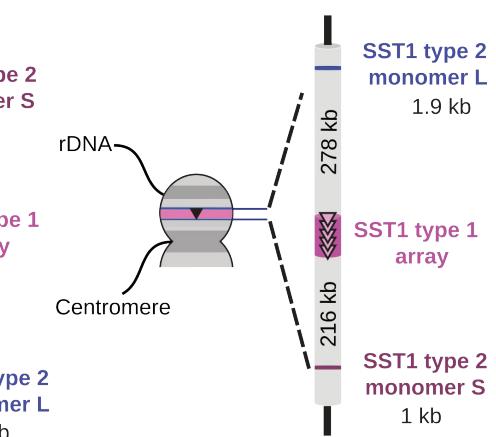
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Chr13 or 21

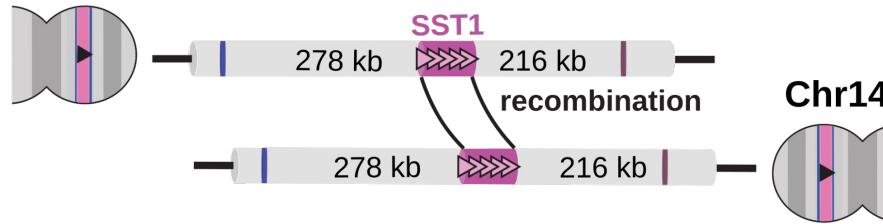


Chr14



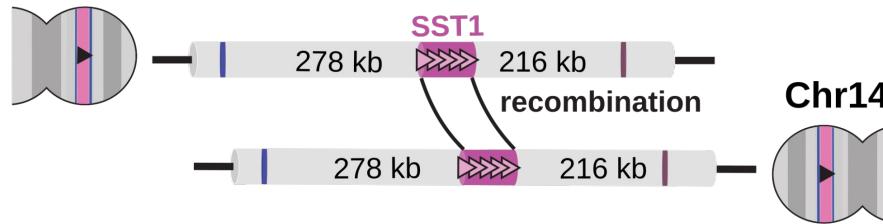
SST1-mediated interchromosomal exchange

Chr13 or 21

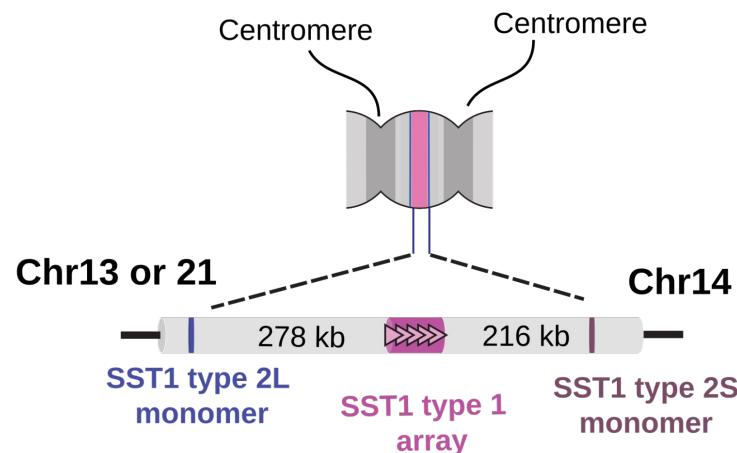


SST1-mediated interchromosomal exchange

Chr13 or 21

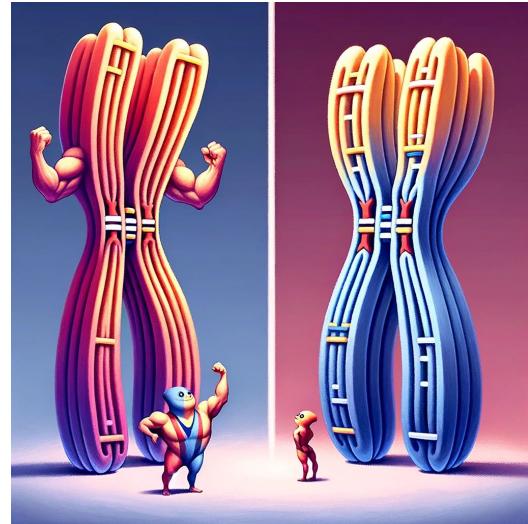


ROB Chromosomes



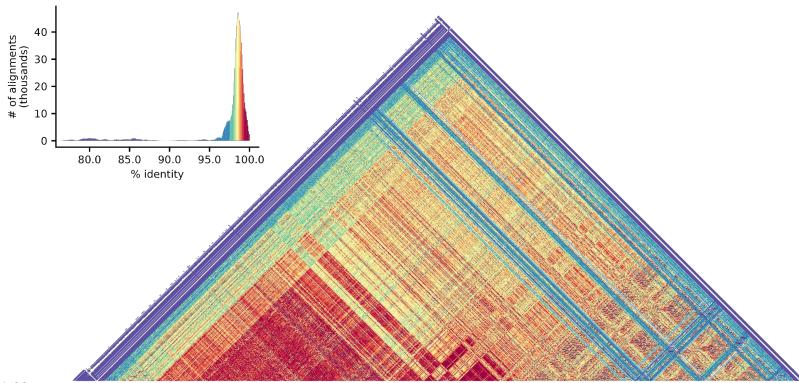
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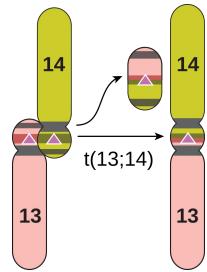
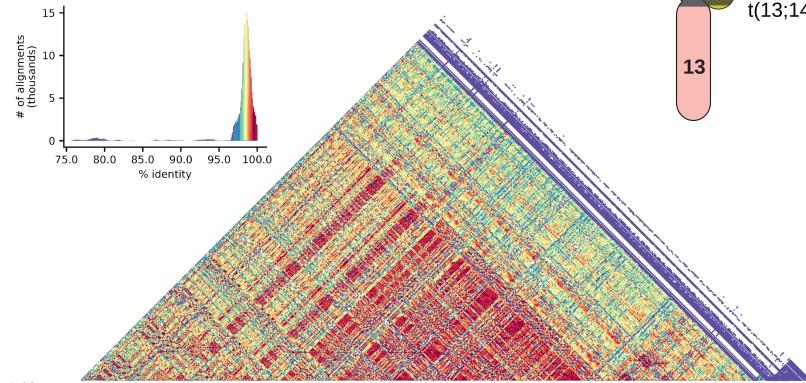


Cen14 is the active centromere in t(13;14)

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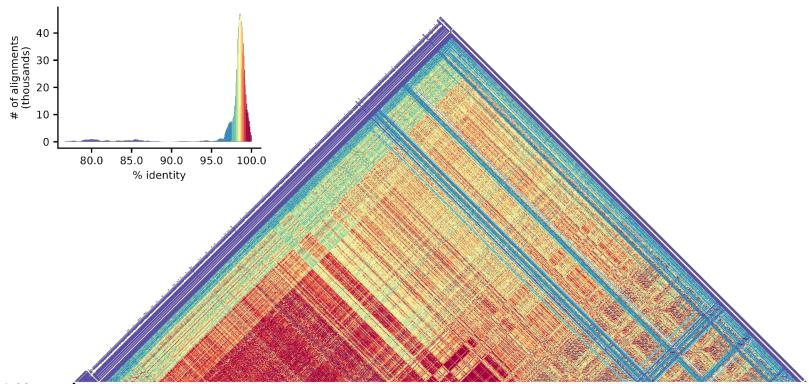


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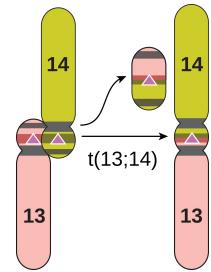
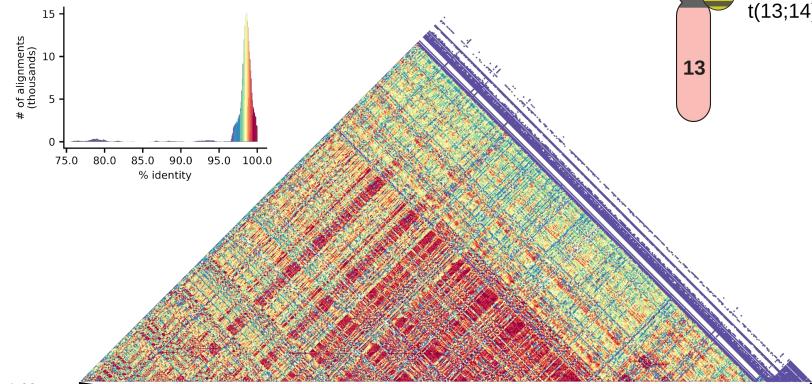


Cen14 is the active centromere in t(13;14)

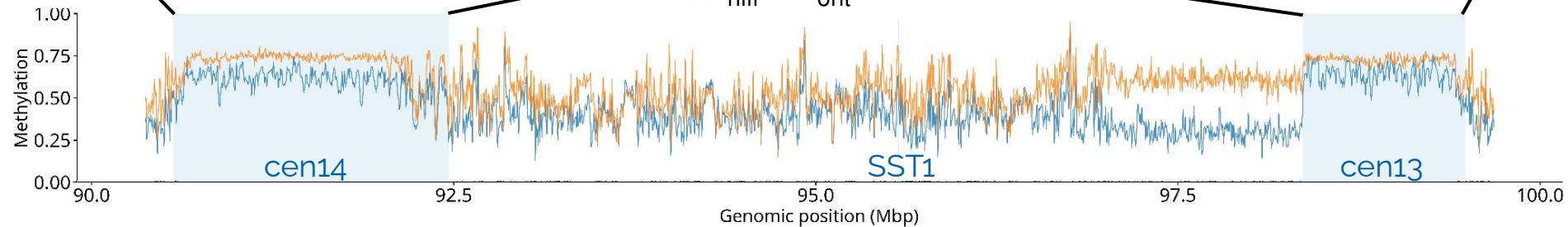
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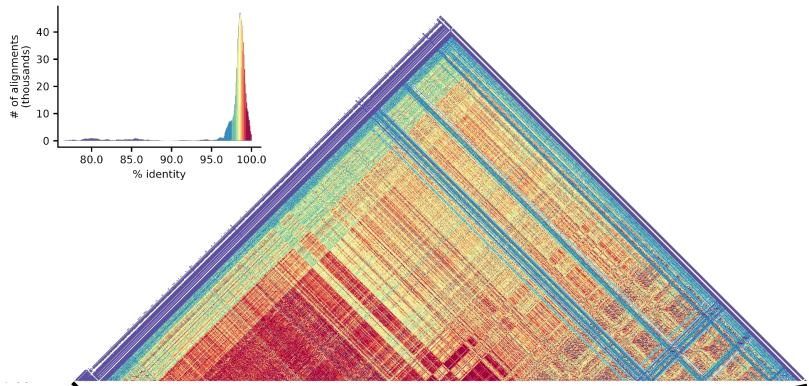


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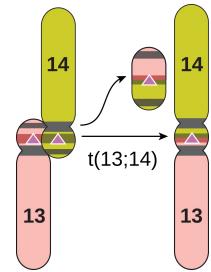
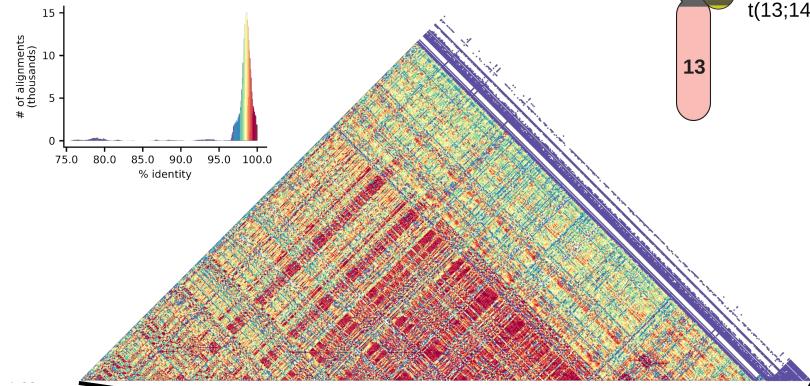


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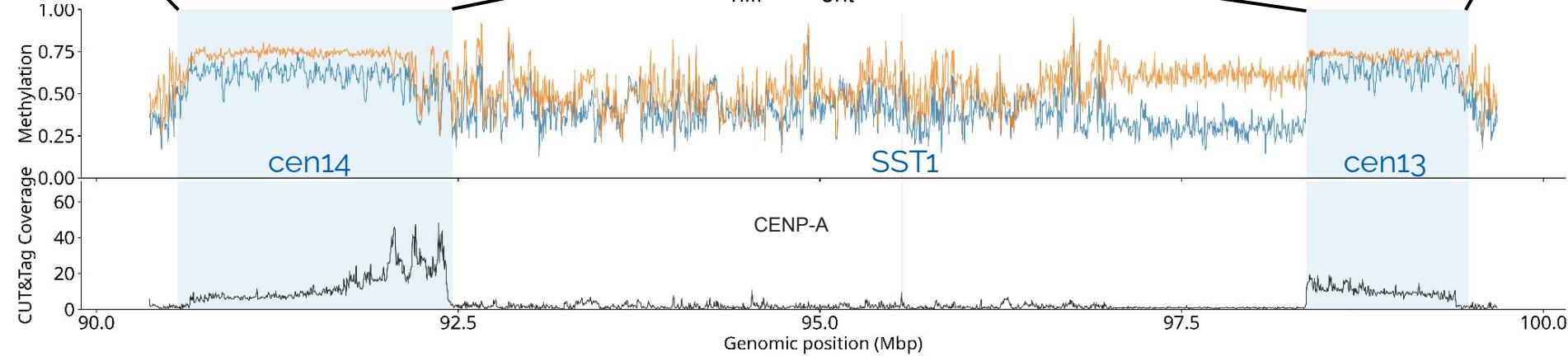
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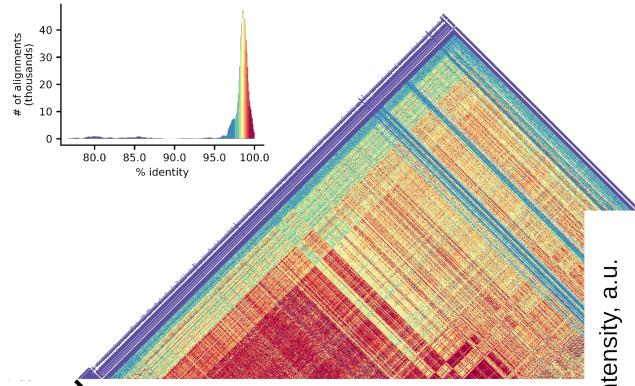


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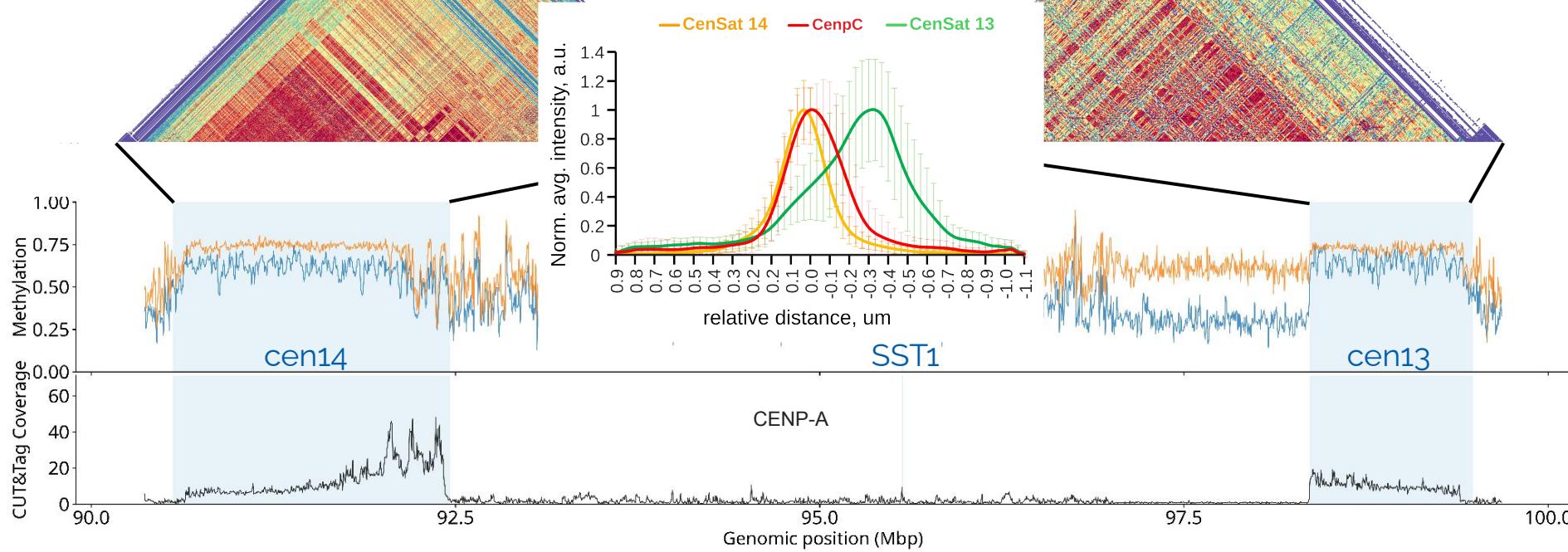
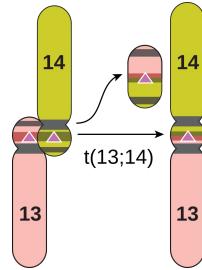
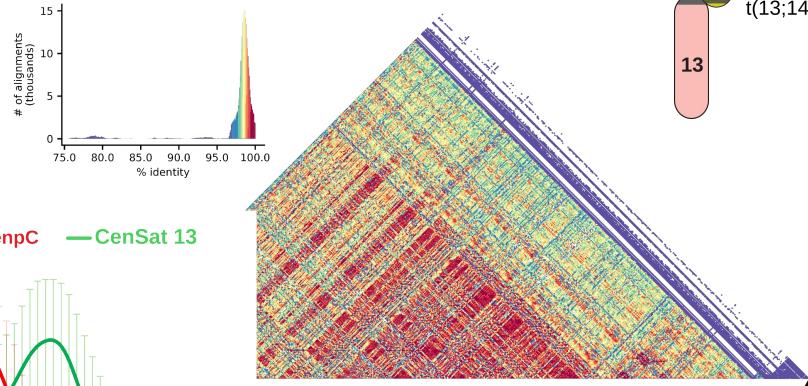


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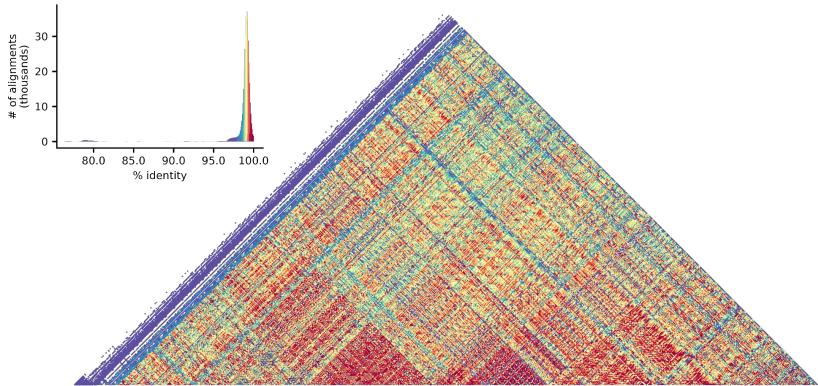


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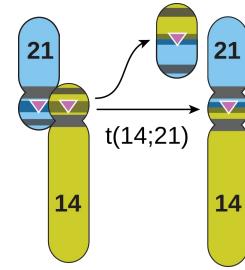
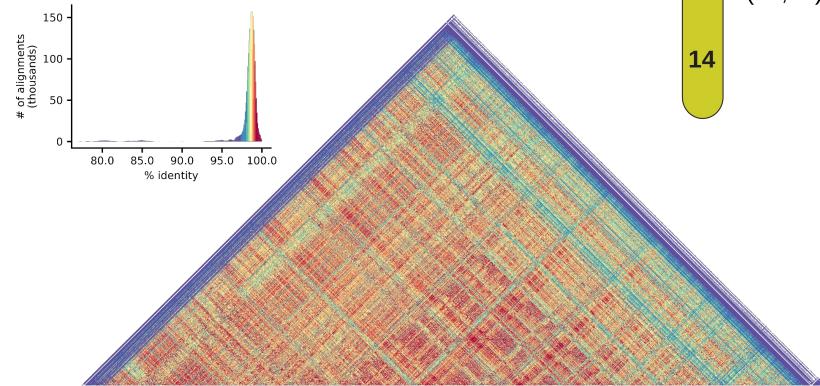


Both cen14 and cen21 may remain active in t(14;21)

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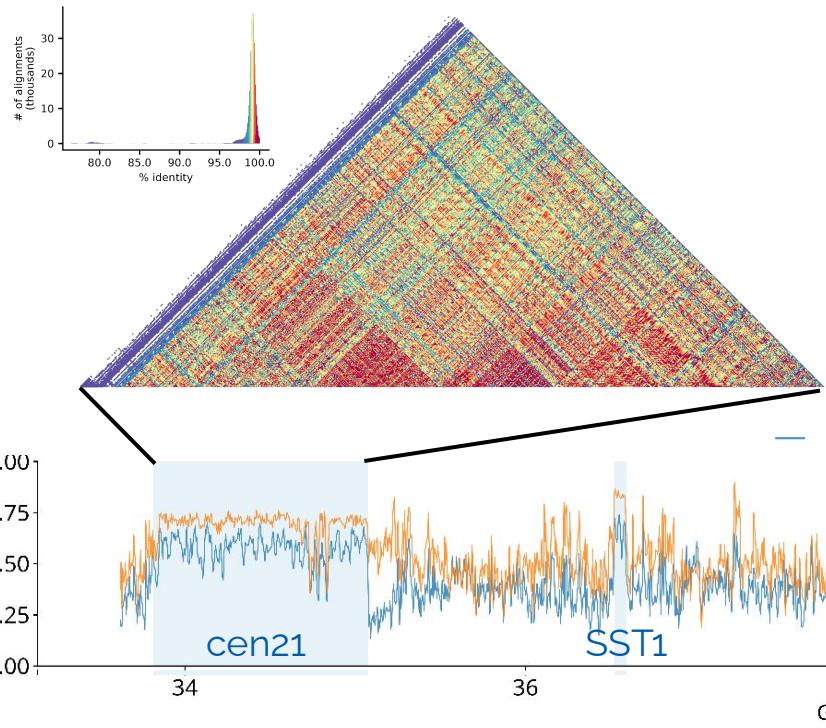


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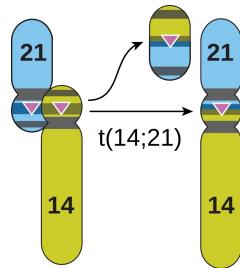
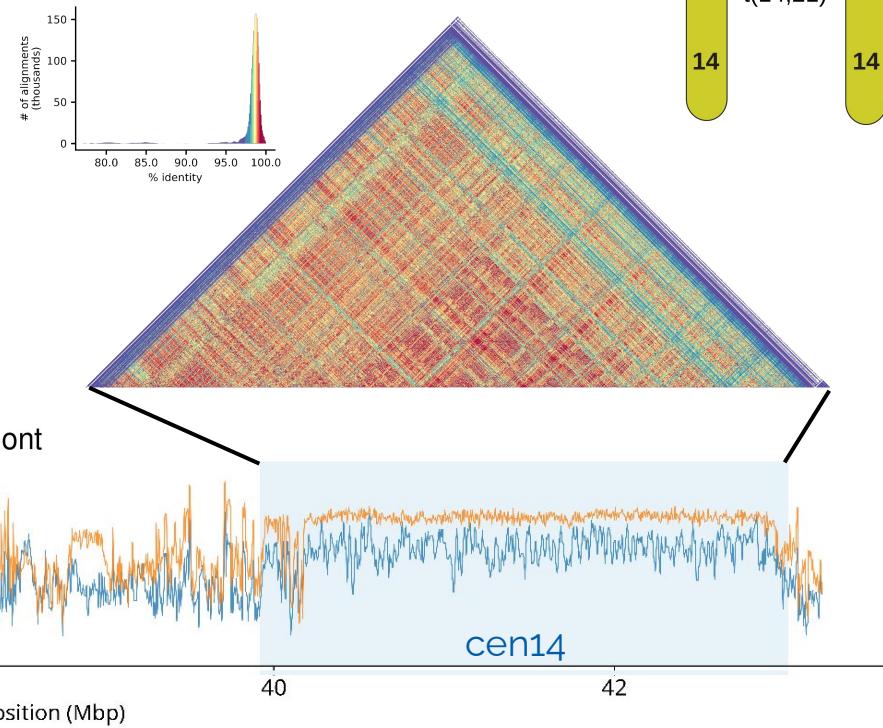


Both cen14 and cen21 may remain active in t(14;21)

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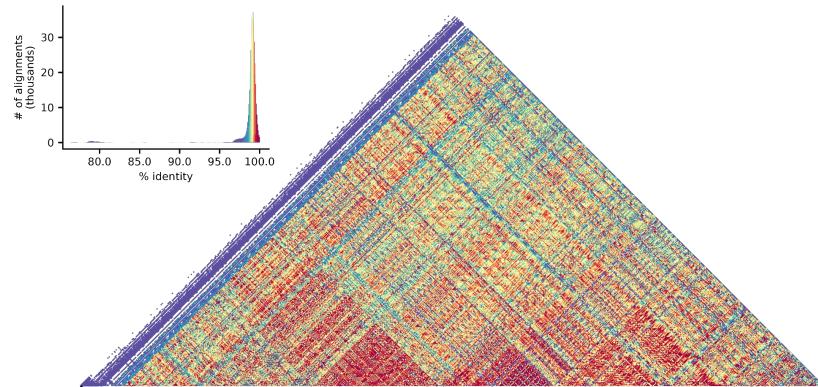


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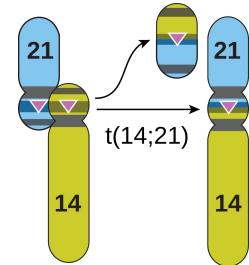
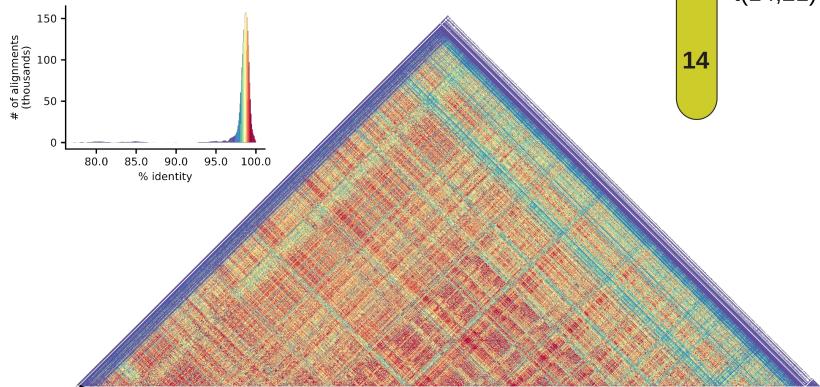


Both cen14 and cen21 may remain active in t(14;21)

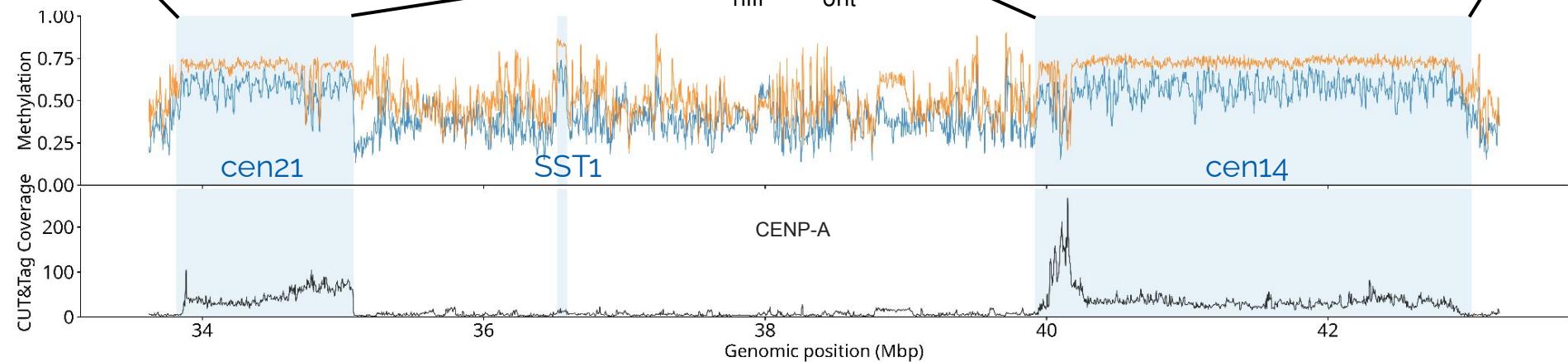
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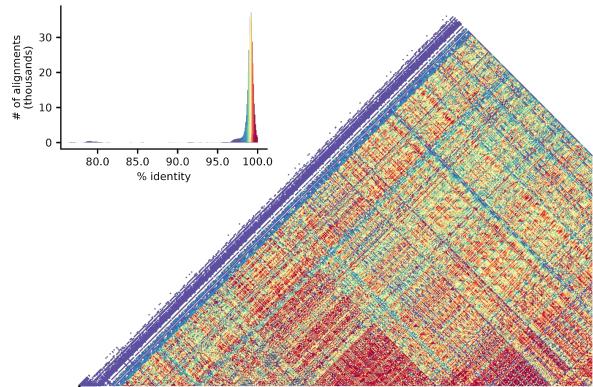


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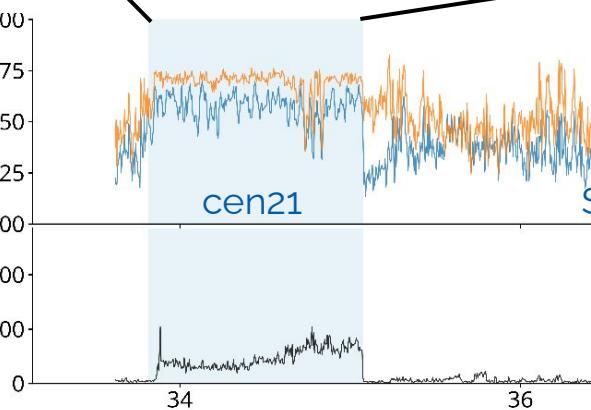


Both cen14 and cen21 may remain active in t(14;21)

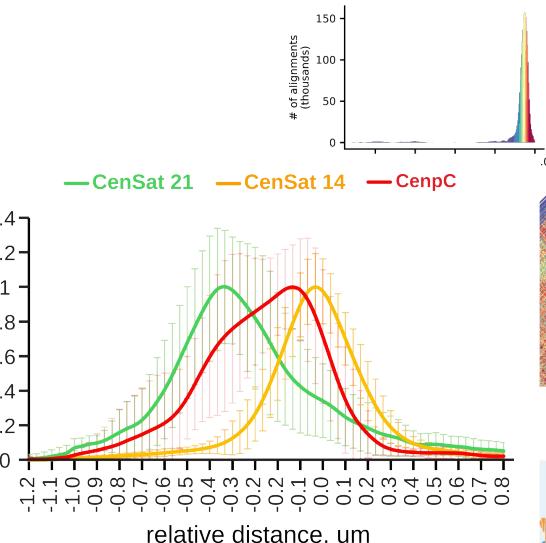
GM03417#chr21#haplotype1-0000006



Methylation

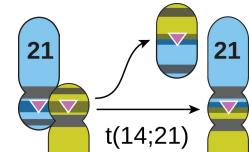
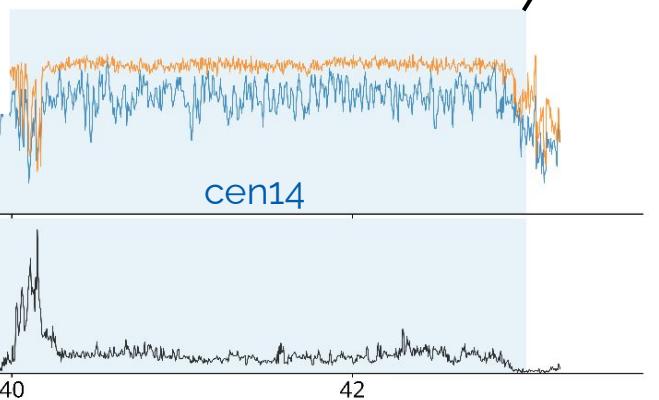


GM03417#chr14#haplotype1-0000006



CENP-A

Genomic position (Mbp)



Take-home messages

- Heterologous acrocentric chromosomes recombine
- Pseudo-Homologous Regions explain common Robertsonian translocations
- Interchromosomal exchanges are mediated by the SST1 array
- Dicentric chromosomes show epigenetic adaptation to support stable mitotic transmission



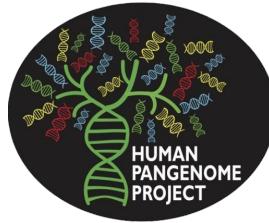
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