SR drive and the evolutionary history of the Y chromosome in *Drosophila simulans*

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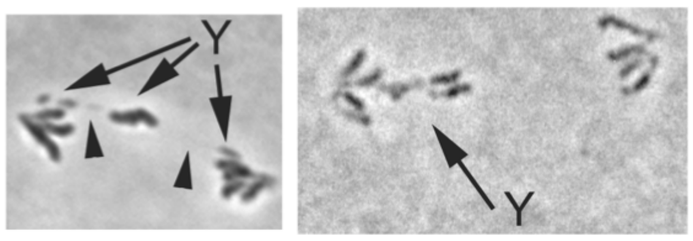
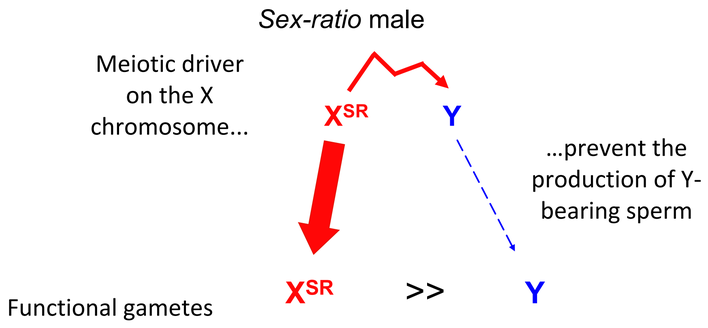
Background



Anaphase II of male carrying the distorter element.
Cazemajor et al., 2000

Sex chromosome meiotic drive is a **non-mendelian transmission of sex chromosomes**, caused by selfish elements called **segregation distorters or meiotic drivers**.

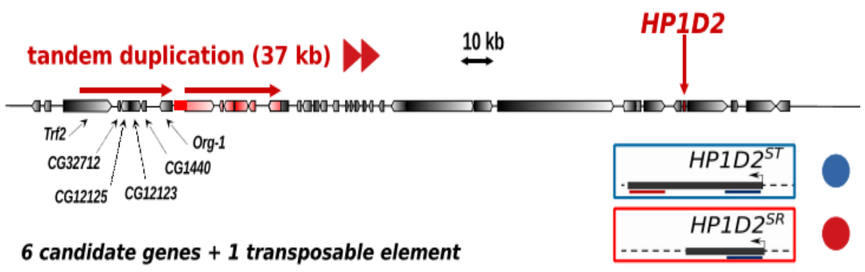
In the **Paris *sex-ratio* system, the drive is caused by two** X-linked elements that together prevent the production of Y-bearing sperm, which results in **strongly female-biased progeny.**



1. Two elements are required for Paris *sex-ratio* (SR) drive:

- **Tandem duplication** (DP^{SR}) comprising 6 genes and a transposable element.

- Dysfunctional ***HP1D2*** *(Helleu et al., PNAS, 2016).*

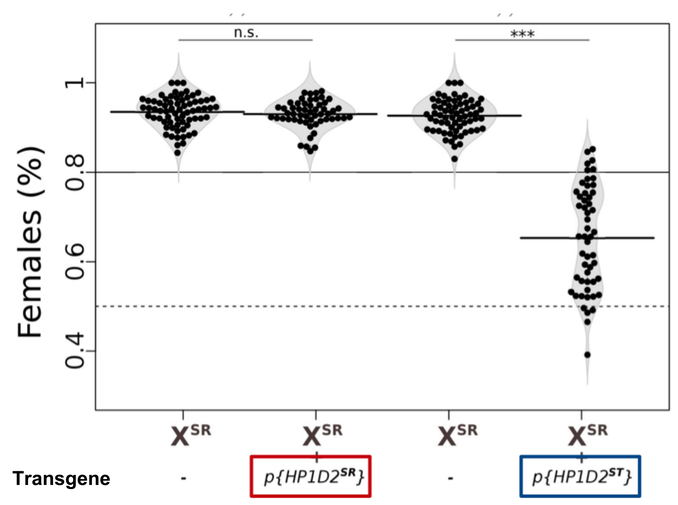


6 candidate genes + 1 transposable element

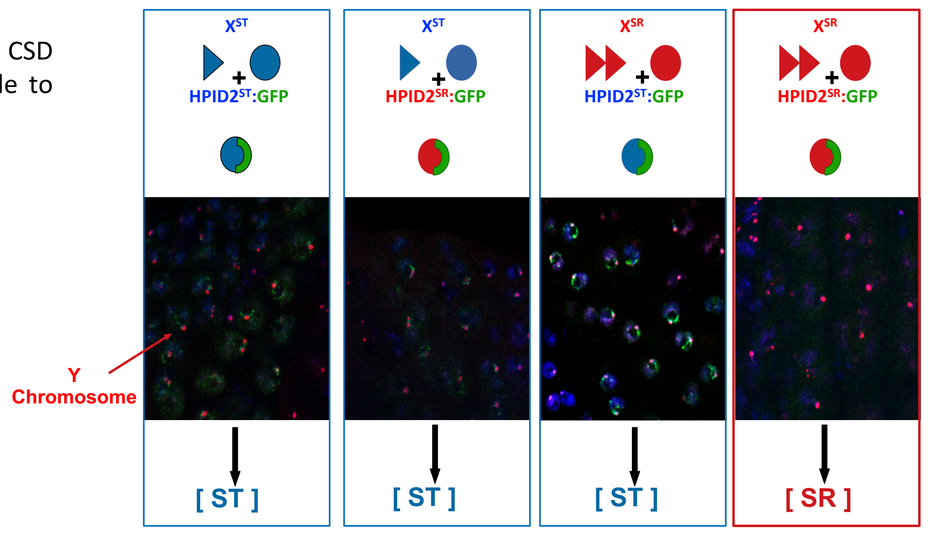
HP1D2 is a member of the HP1 gene family, involved in heterochromatin formation and regulation. Typical HP1 genes encode a Chromo domain (**CD**) interacting with histones, and a Chromoshadow domain (**CSD**) interacting with other proteins.

2. Loss of function of HP1D2 and Paris SR drive.

SR drive is associated with a natural variant of *HP1D2* lacking CSD ($HP1D2^{SR}$). Addition of a functional copy (***$HP1D2^{ST}$***) is able to restore a balanced sex-ratio.



3. HP1D2 accumulates on the heterochromatic Y chromosome.



$HP1D2^{ST}$ is expressed in premeiotic cell (spermatogonia) and binds the heterochromatic Y chromosome.
The drive is associated with the misslocalization of the driver allele, $HP1D2^{SR}$

Y chromosome resistance in natural population

1. Sex-ratio meiotic drive shapes the evolution of the Y chromosome in D. simulans:

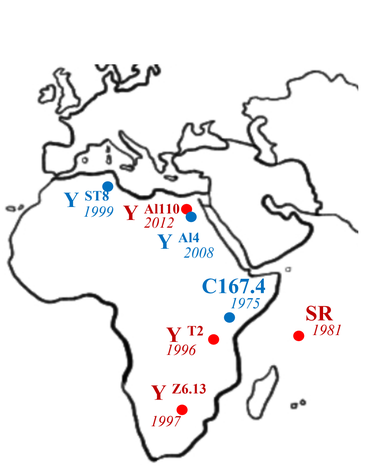
We tested 351 Y chromosomes from 29 population samples (1996-2018).
In each populations we measured the frequency of X^{SR} and the resistance ability of the Y chromosome.
Sequence variation was surveyed among the Y chromosomes by sequencing 13 kb of genes fragments.

Results:
Large variation in SR resistance among Y chromosome.
But **low gene variation** : only 3 polymorphic sites defining 3 haplotypes (TTT, TTA and CAA), **CAA** is associated with SR resistance.

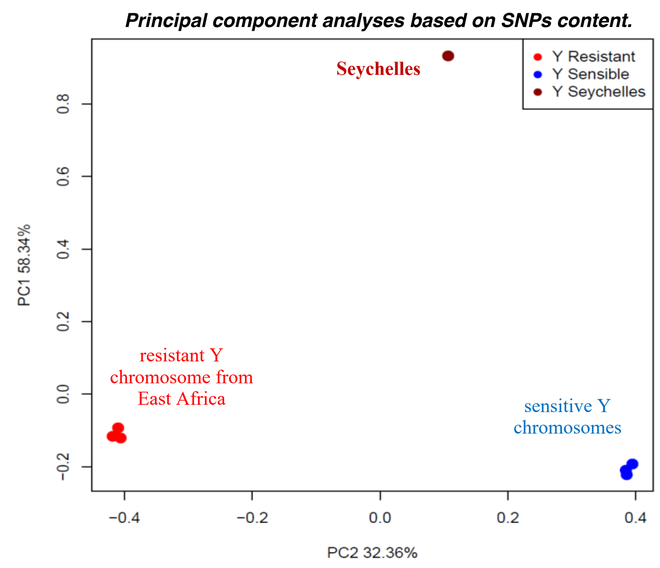
The Paris system is **highly dynamic:** North Africa ongoing invasion of X^{SR} where the resistant CAA Y's replace sensistive TTT Y's . On the opposite, the CAA haplotype is already fixed in Sub-saharan Africa.

2. Molecular polymorphism of the Y chromosome reflect their resistant ability:

We sequenced 7 iso-Y lines, their Y chromosomes came from different locations in Africa, looking for SNPs content between resistants and sensitives Y chromosomes.



Principal component analyses based on SNPs content.



Results:

- We identified **4056** polymorphic sites located on the Y chromosome. This confirm the very low nucleotide diversity (pi=0.000112) among Y chromosomes in this species. While we identified an haplotype composed by **886 SNPs**, with fixed differences between the 3 sensitives and the 4 resistant Y chromosomes.
- The molecular polymorphism allows us to distinguish three distinct groups: the 3 sensitives Y chromosomes (93.7% of identity), the 3 resistant Y chromosome from East Africa (94.45% of identity) and the resistant Y chromosome from Seychelles.
- Surprisingly, the resistant chromosome from **Seychelles** appears highly divergent from all the chromosome collect in Africa.

3. Resistance is the ancestral phenotype :

We also confirm the ancestry of the resistant lineage by examining Y-linked sequences in the sister species of *D. simulans*. Among the 886 SNPs we identified 686 homologous sites for both *D. sechellia* and *D. mauritiana,* **89,35 %** and **90,09%** of them carried the allele associated with the resistant lineage

Conclusion

- Deficient allele of the ***HP1D2*** gene cause sex-chromosome meiotic drive in *D. simulans* due to the misslocalisation of the protein.

→ The drive could occur *via* the **disruption of heterochromatin regulation** of the Y chromosome.

- The Paris SR system is highly dynamic in natural population. In two locations we observed a swift replacement of the Y chromosome along with the rise of the Paris driver.
- The very low nucleotide diversity among Y chromosomes in this species could be considered as a signature of recurrent genetic conflicts. The similarity between the resistant Y chromosomes from African population suggest that they have a recent common ancestor, idem for the 3 sensitives Y chromosome. However the resistant Y chromosome from the Seychelles Island, seems to have a different evolutionary history from the resistant Y chromosomes from the African continent. In addition D. *sechellia* and D. *mauritiana* carries the resistant haplotype improving the hypothesis of a unique and ancestral origin of resistance.

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