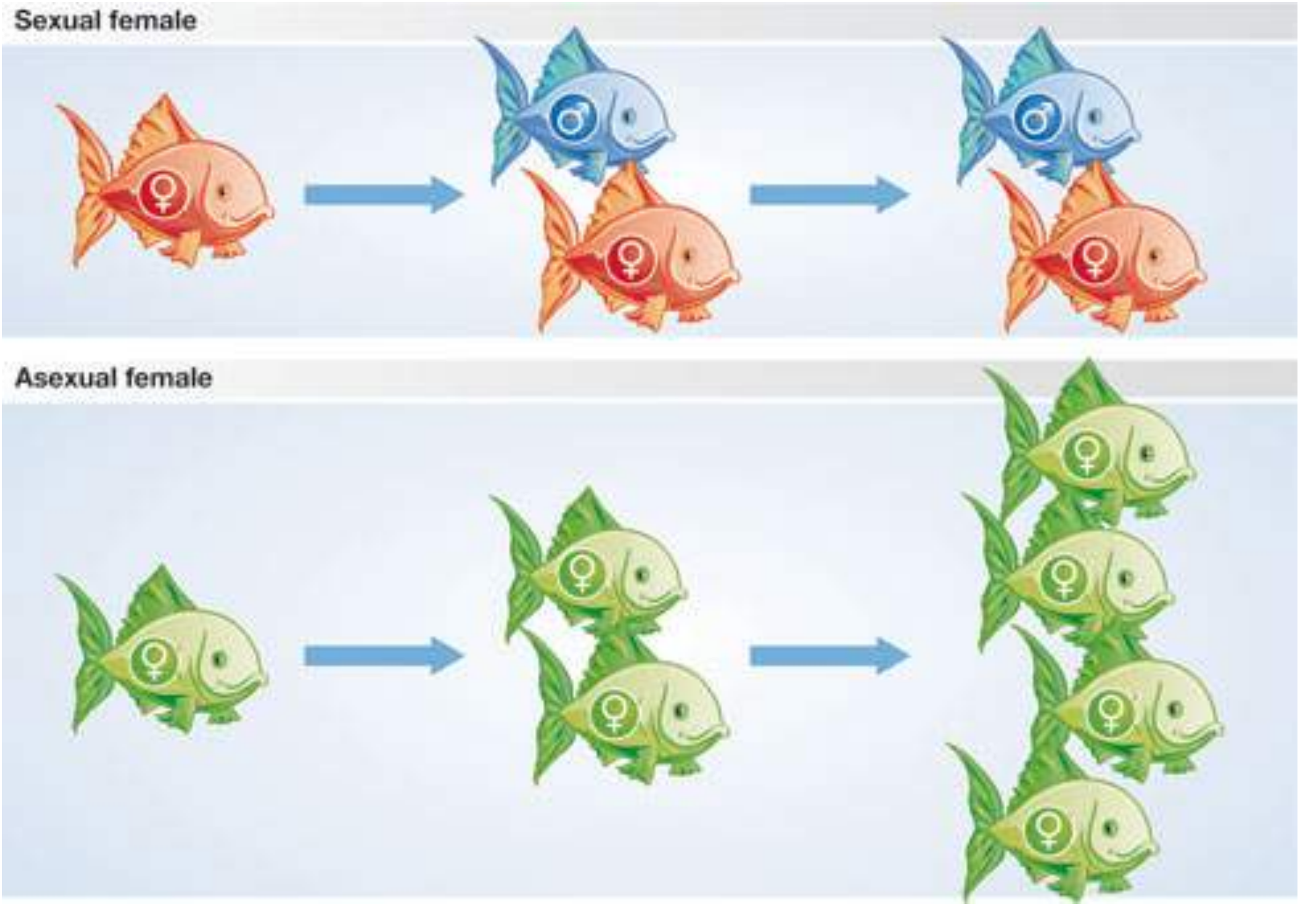
Sex chromosomes and sex determination

Máté Varga (mvarga@ttk.elte.hu)

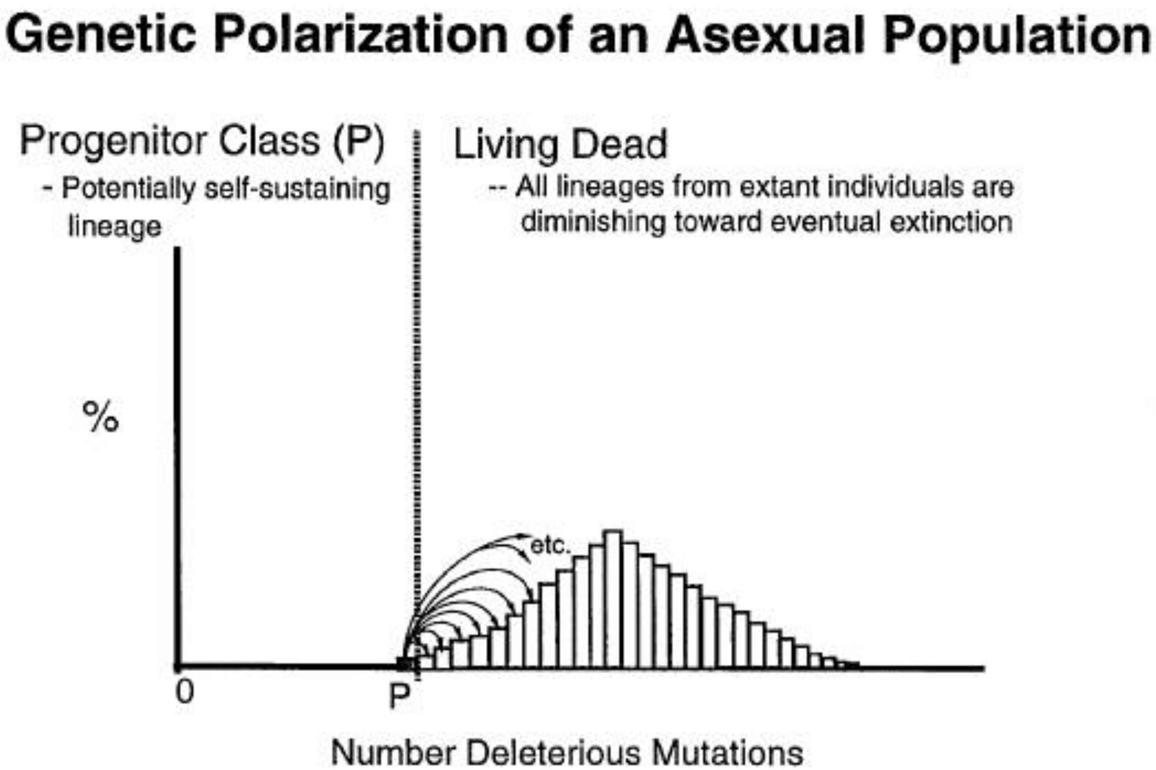
Why bother having sex?



Sex is evolutionarily expensive, so the question is, why did it evolve and how could it be maintained?

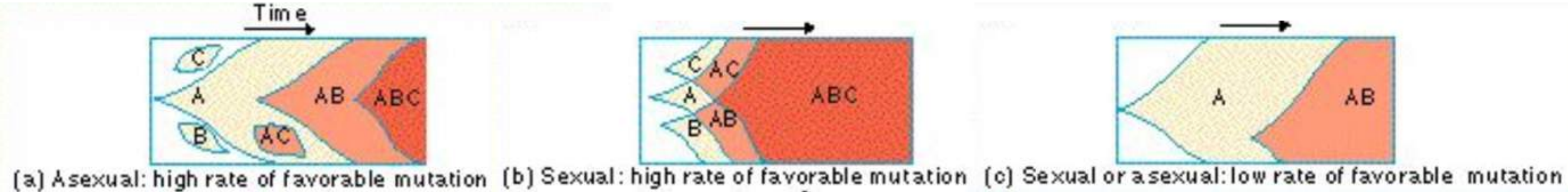
(Colegrave (2012) *EMBO Reports*)

The advantage of sex (and the disadvantage of asexuality)

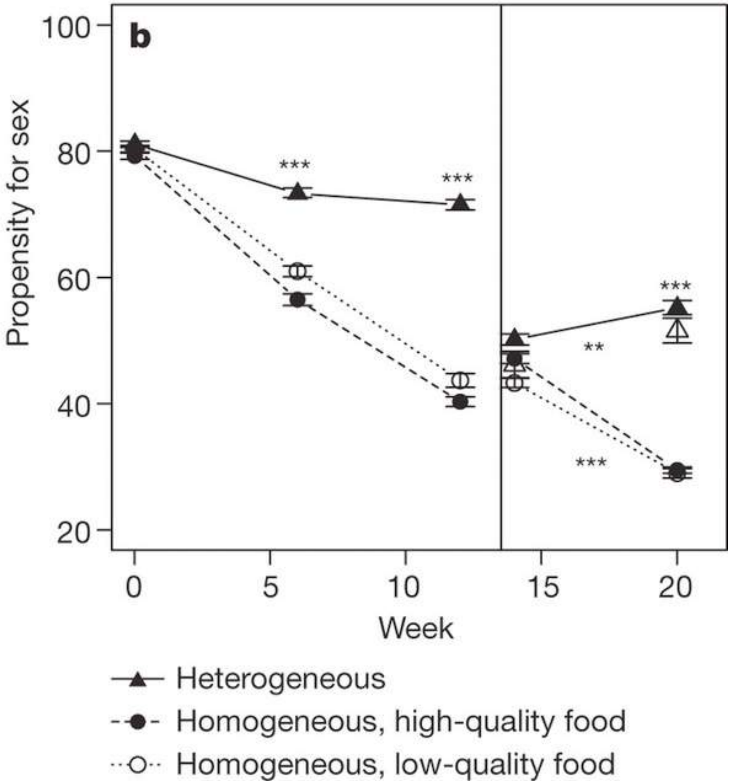


In asexual population, the ratio of harmful mutations increases, and these can not be fixed easily.

The advantage of sex



Advantageous mutations can spread easily in a sexually reproducing population, which could be advantageous for adaptation.

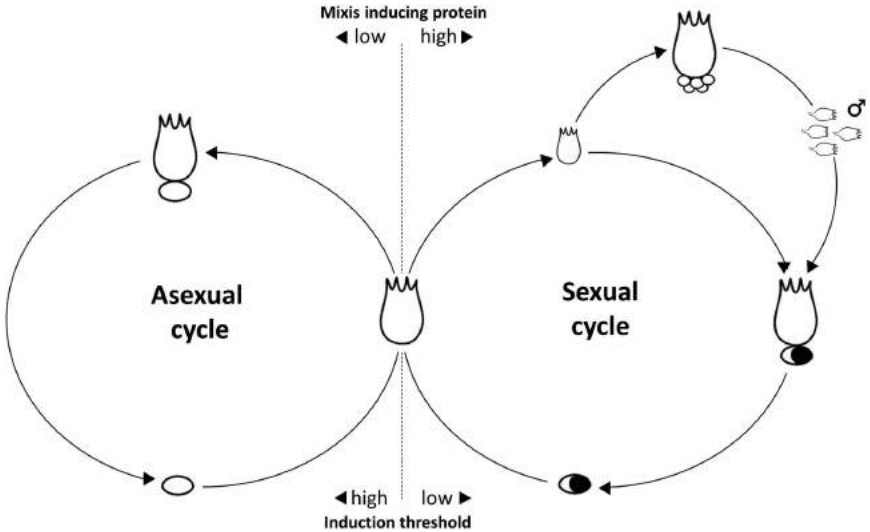


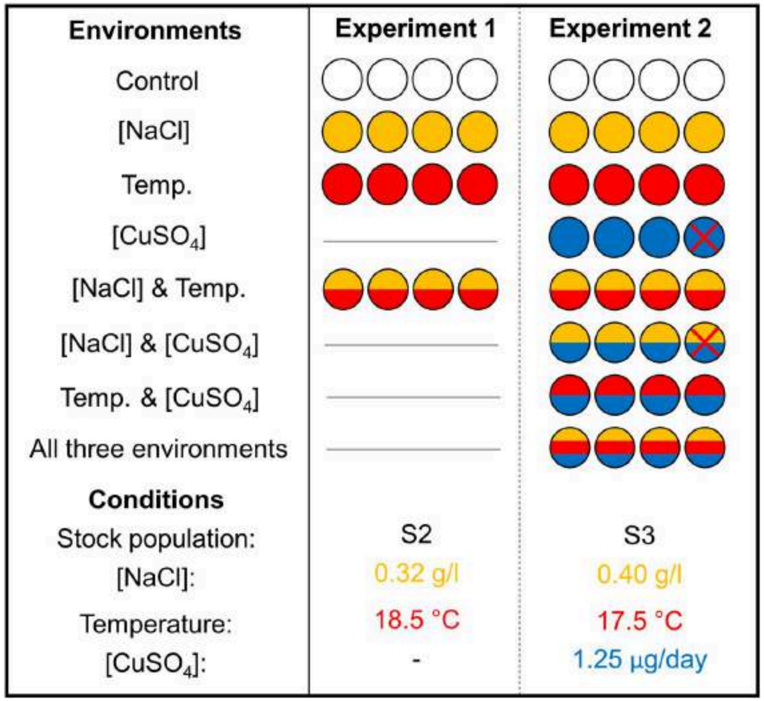
- the females of the *Brachionus calyciflorus* rotatoria species can reproduce both sexually and asexually

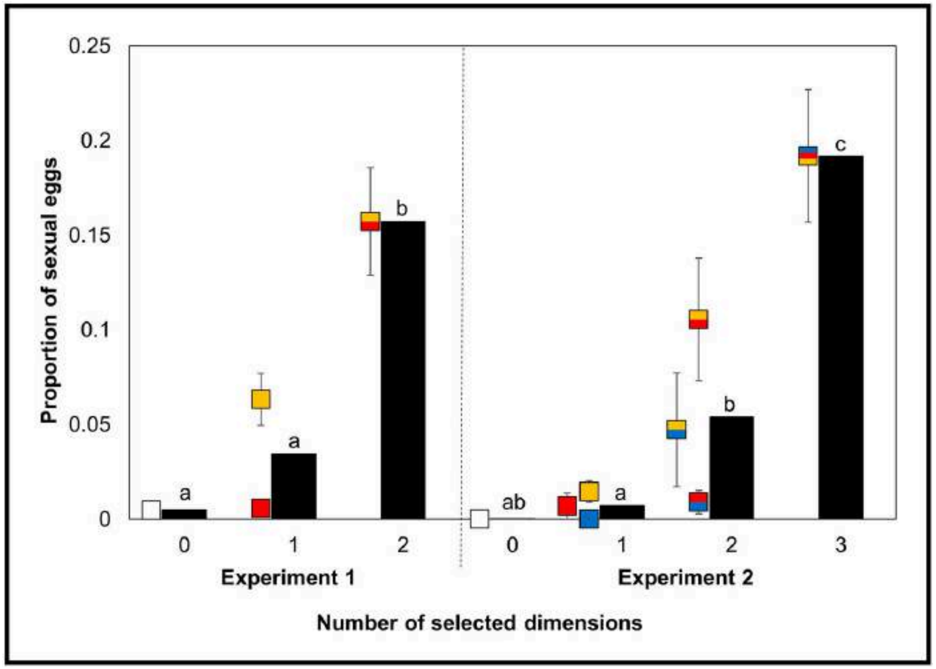
- they use the former when the environment is rapidly changing and the latter when the environment is more homogenous

(Beck és Agrawal (2010) *Nature*)

The advantage of sex (and the disadvantage of asexuality)



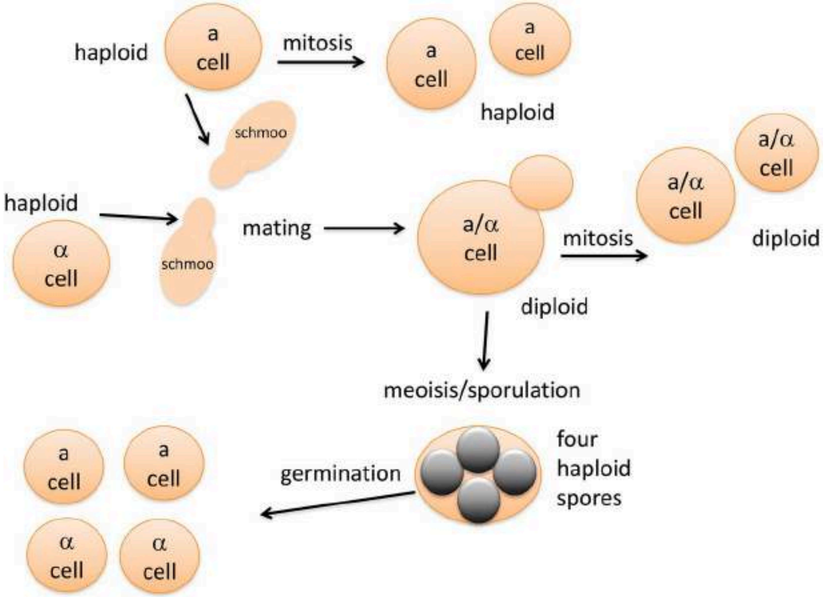




- When more environmental parameters become variable, the number of sexually produced zygotes increases.

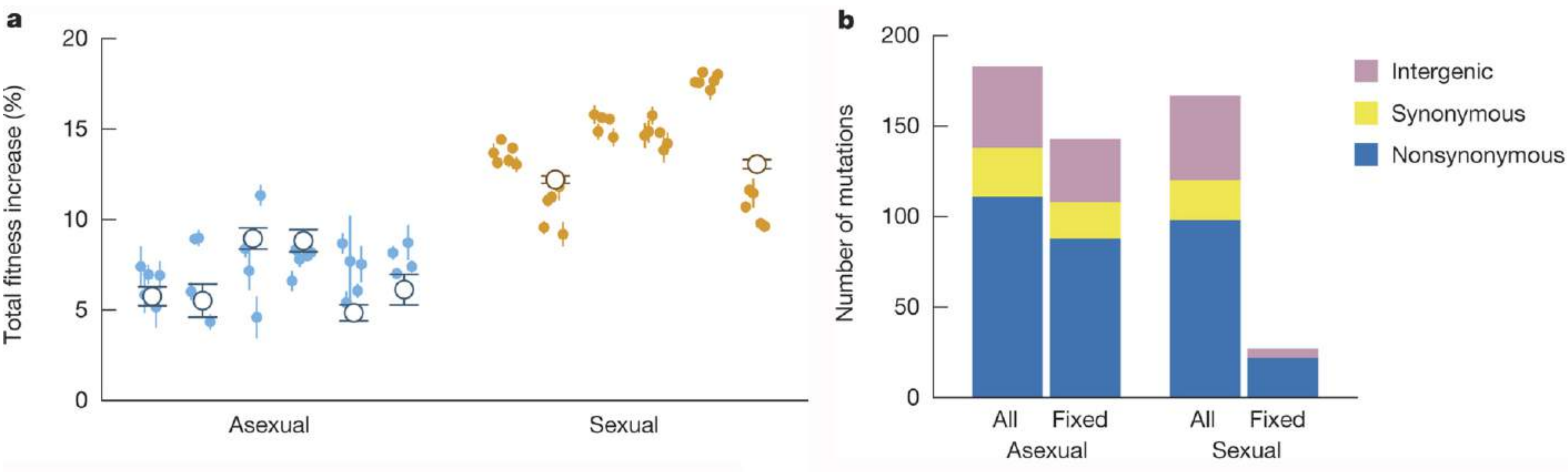
(Lujckx et al. 2017 *PNAS*)

The advantage of sex (and the disadvantage of asexuality)



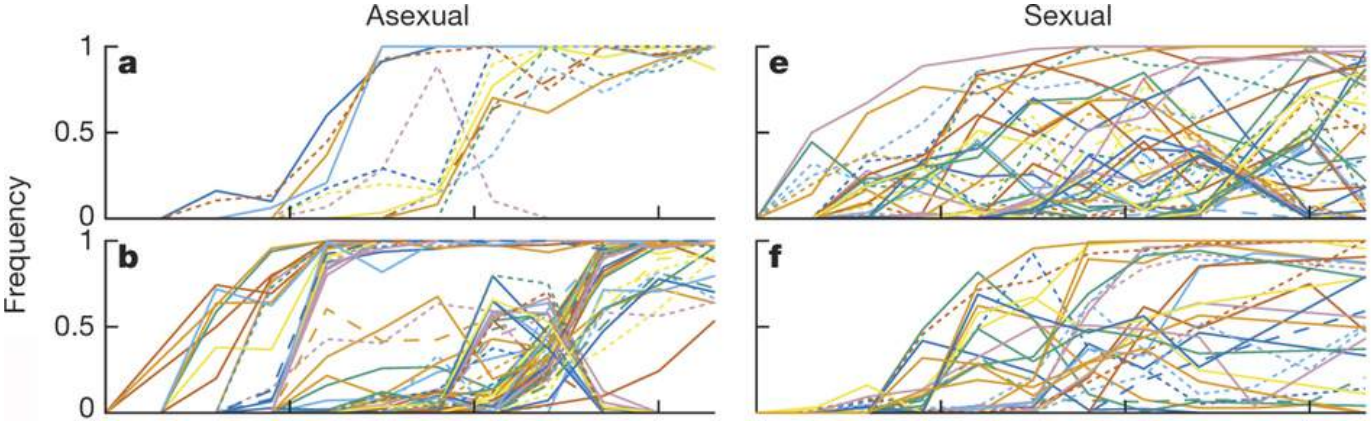
- Sexually reproducing yeast populations have higher fitness than asexually reproducing ones.

- Different mutations appear at the same rate in asexual and sexual populations, but the rate of fixation is very different: in clonal species the ratio of fixed mutation types is more or less the same as they appear, whereas in the case of sexual reproduction mainly non-synonym mutations get fixed.

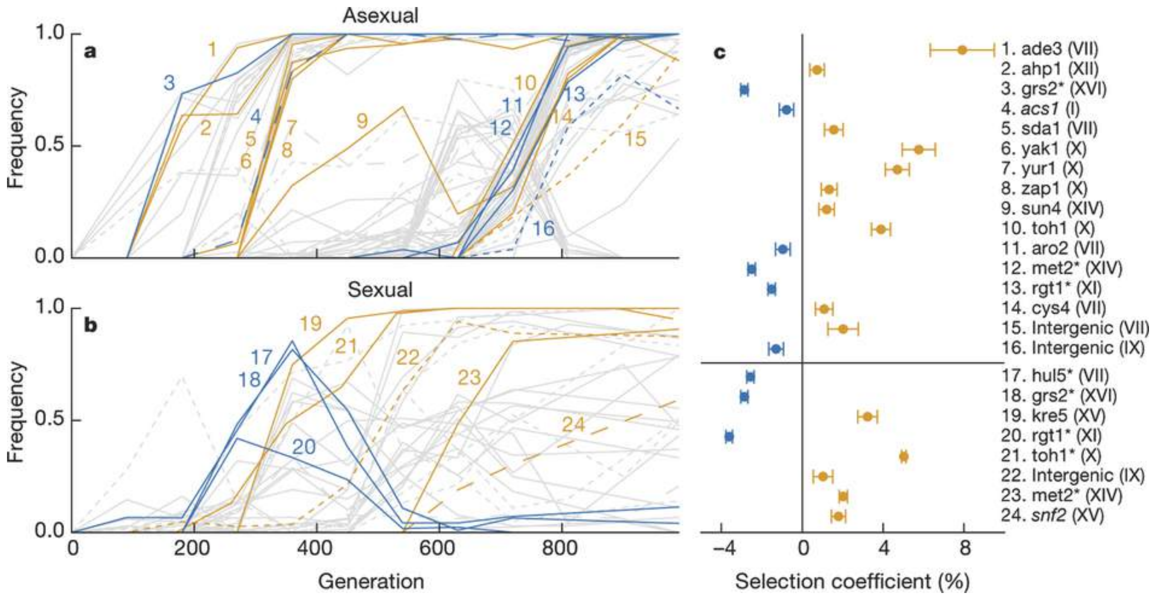


(McDonald et al. 2016 *Nature*)

The advantage of sex (and the disadvantage of asexuality)



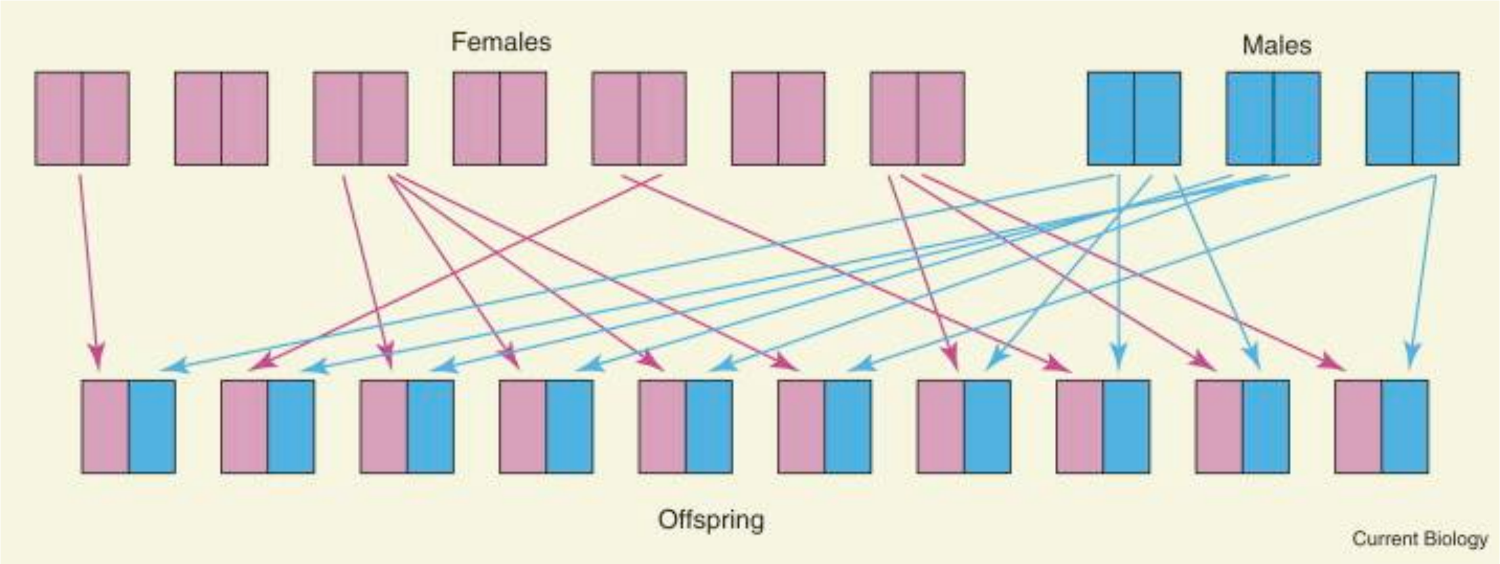
- In asexual populations many mutations are linked: they spread and disappear together.



- Therefore in clonal reproduction harmful mutations can get fixed, when they segregate together with advantageous ones, decreasing overall fitness.

(McDonald et al. 2016 *Nature*)

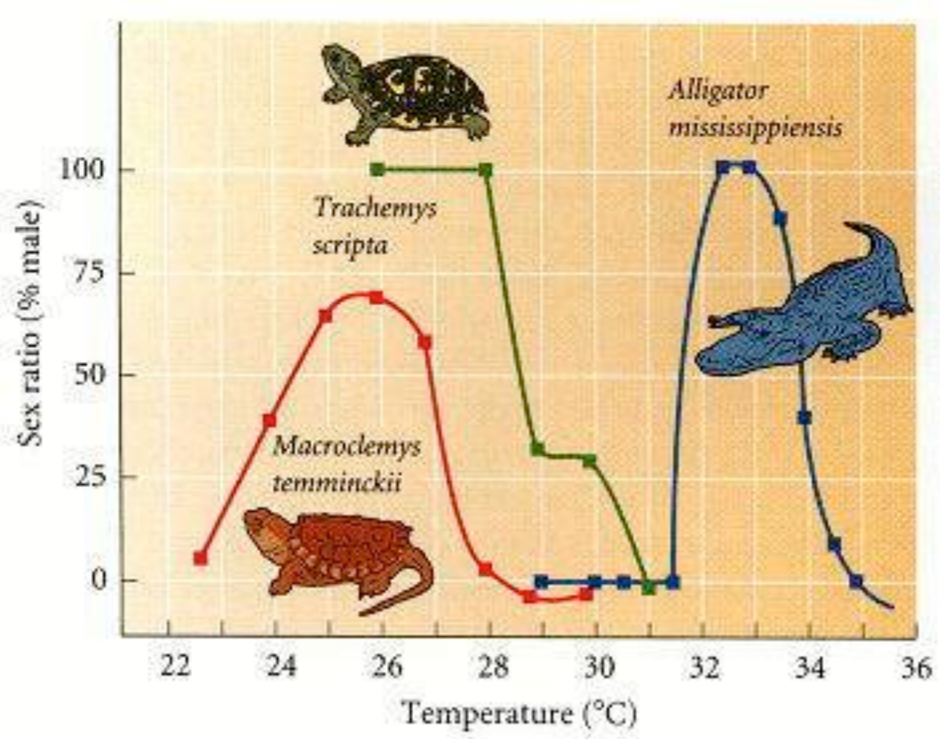
The logic behind 1:1 sex-ratio - the Düsing-Fisher model

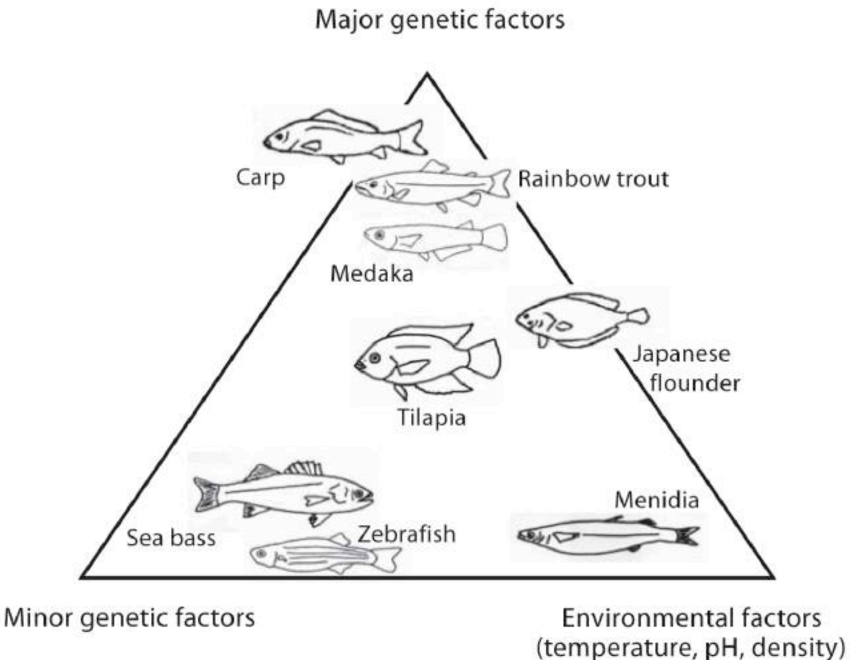


If there are more females than males in a population, the average female will be less successful, therefore the mothers who have more boys will have an advantage in the terms of selection (and vice versa).

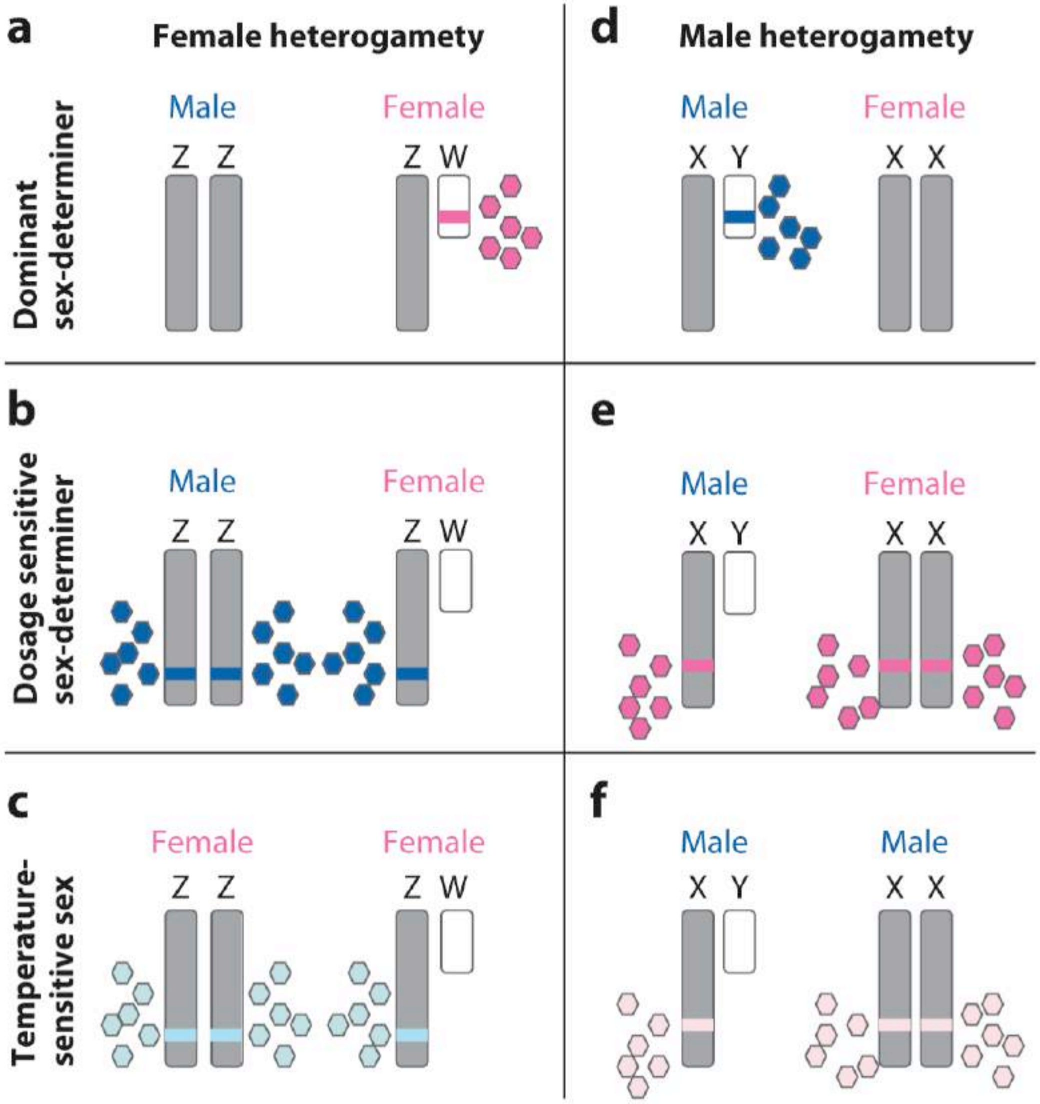
As the total contribution for reproduction of the two sexes is equal, the sex with less individuals will be more sought after, and therefore successful – thus the alleles that promoted the formation of the given sex will spread more widely. This creates an equilibrium.

Environmental sex-determination



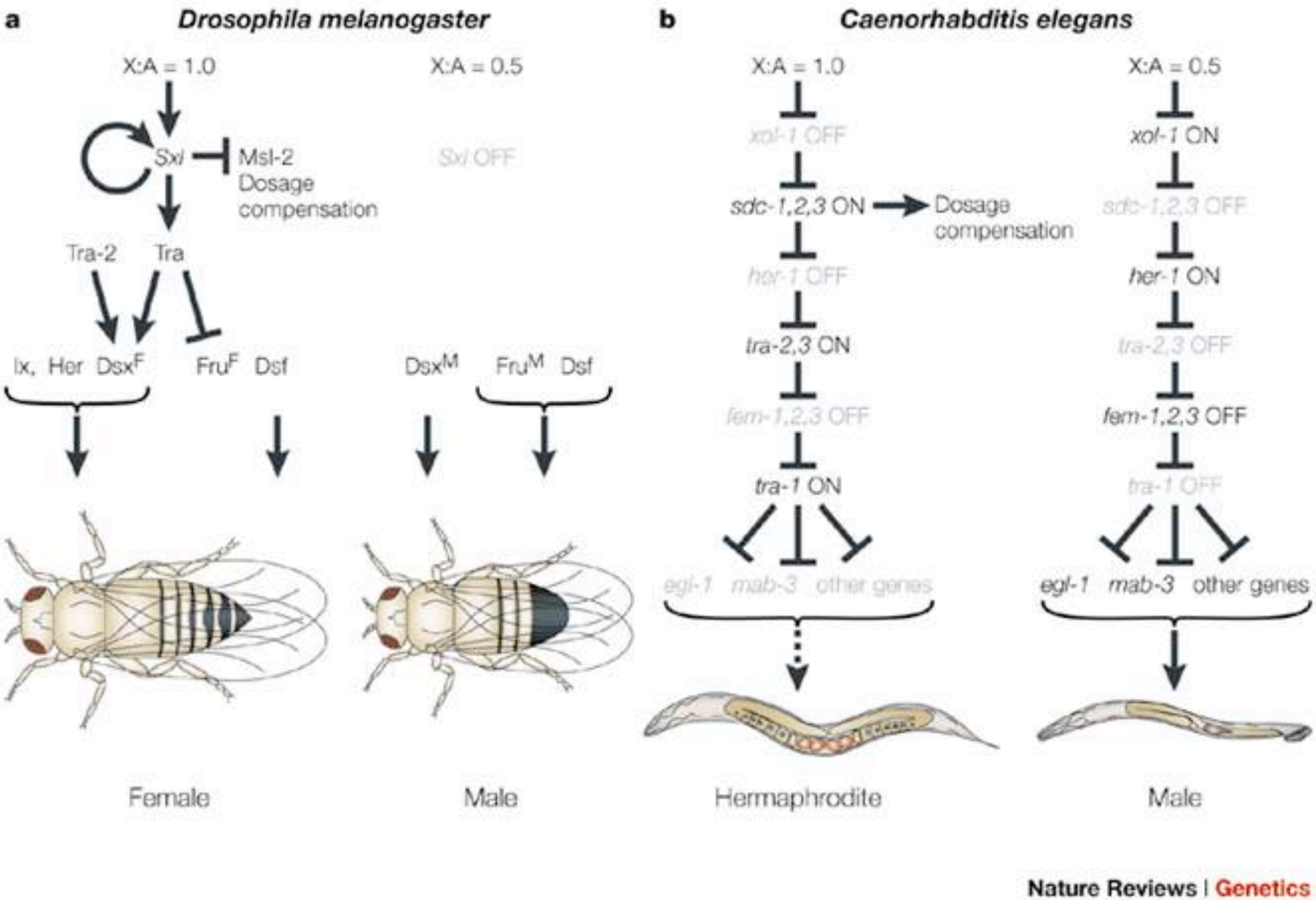


Genetic sex-determination systems (GSD)



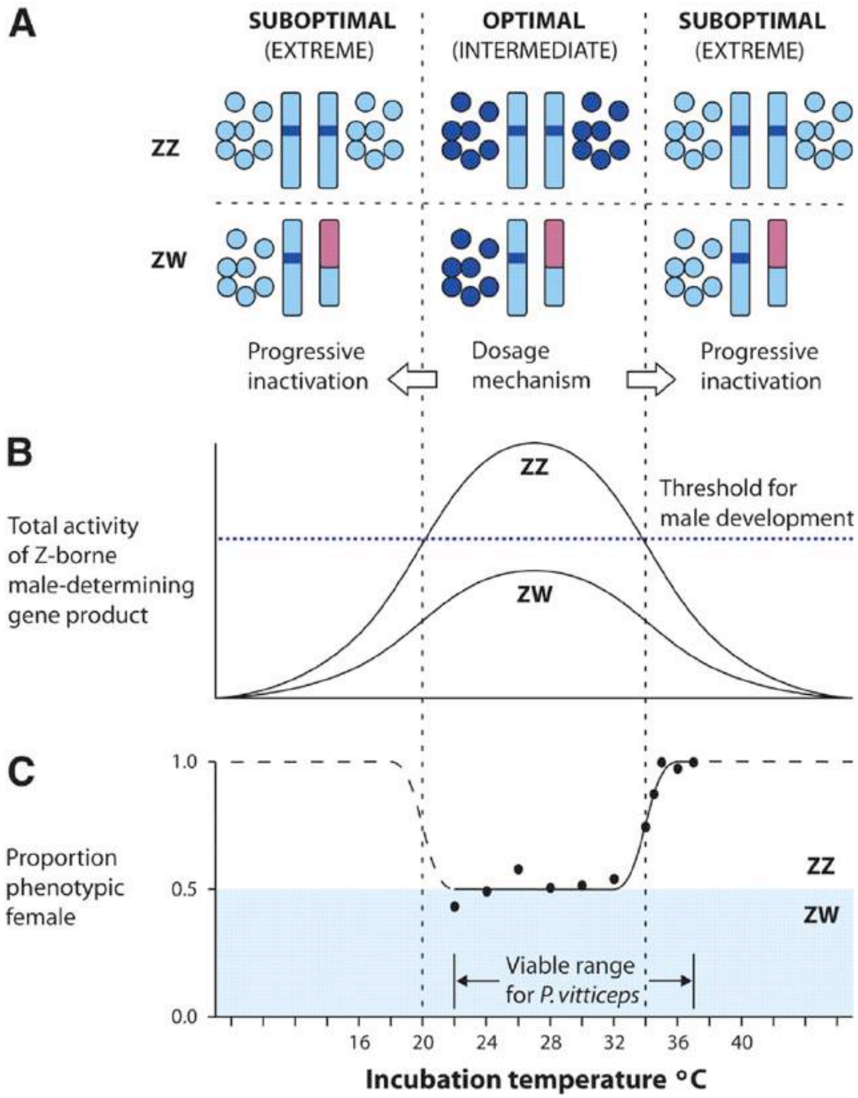
(Graves (2008) *Annu Rev Genet*)

Dose-dependent sex determination



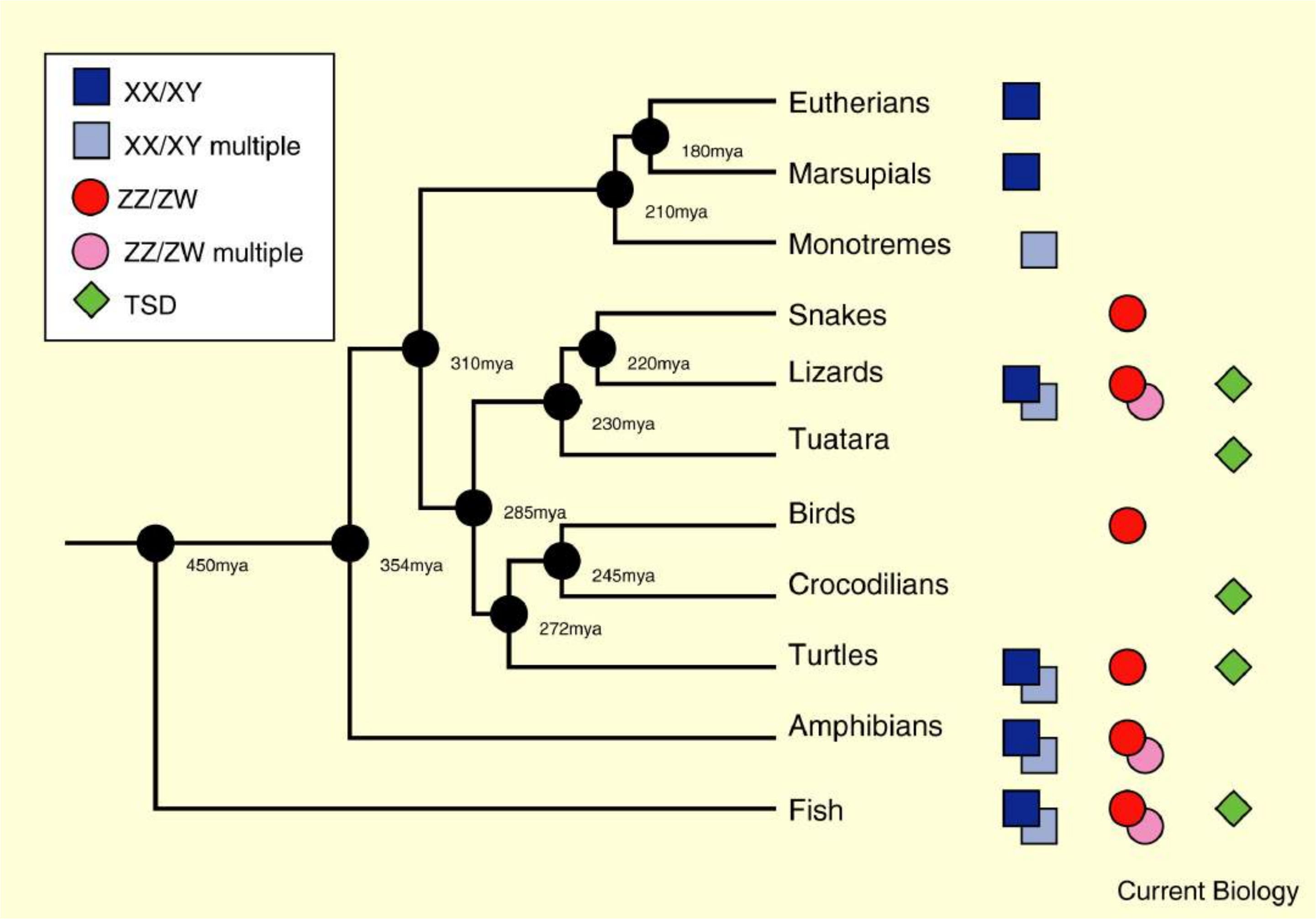
(Zarkower (2001) *Nat Rev Gen*)

Sex determinations in bearded agamas

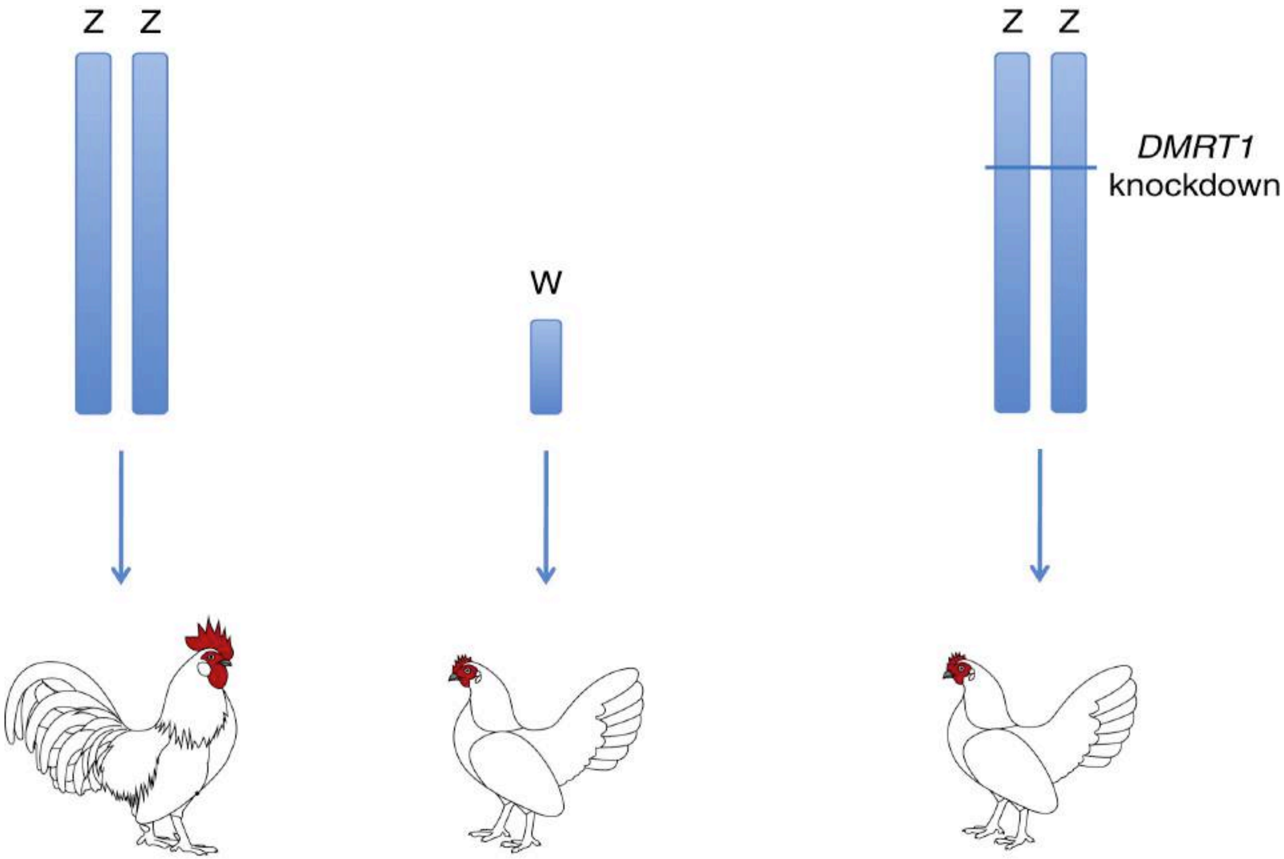


(Quinn et al. (2007) *Science*)

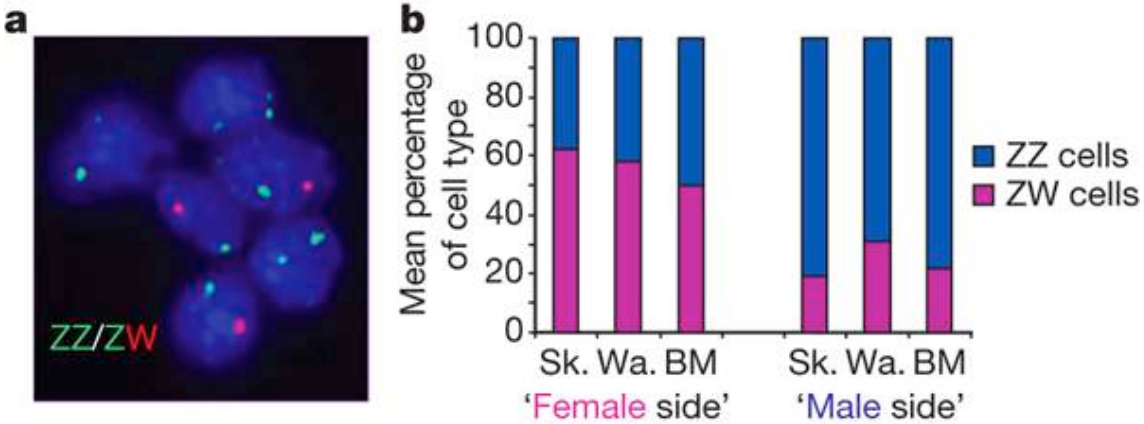
Vertebrate sex determination systems



The ZW sex-determination of birds: an example for dose dependency?

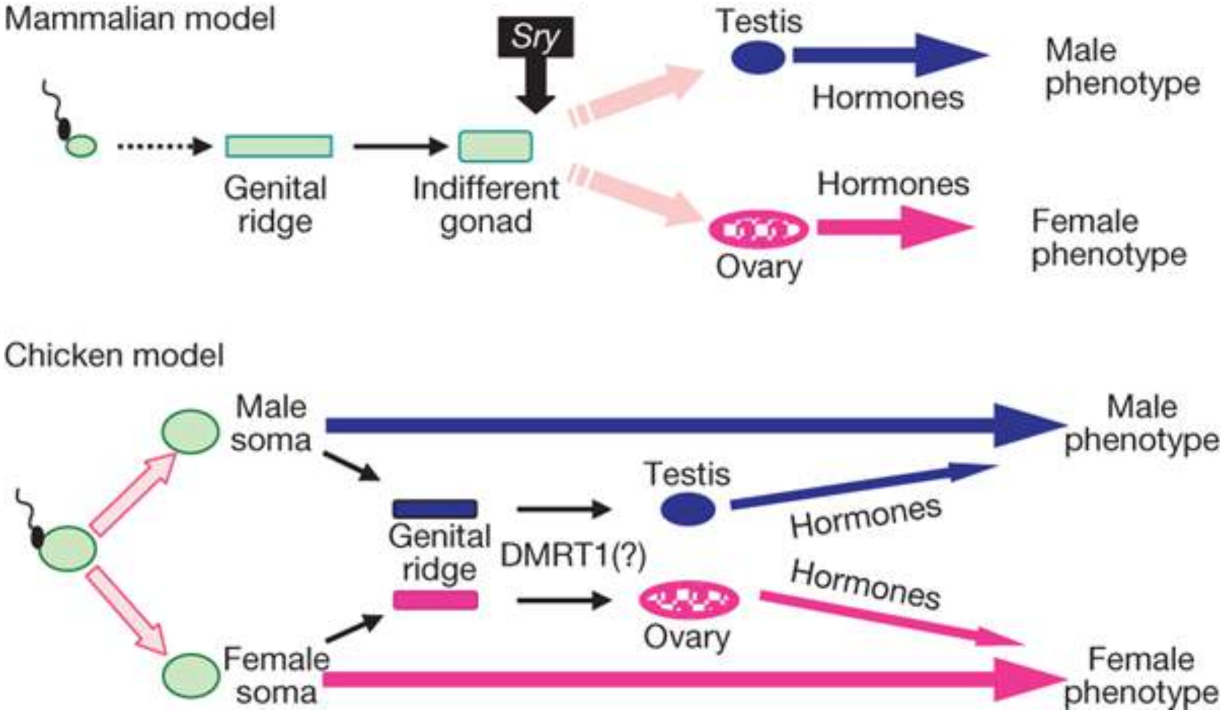


Other bird curiosities: gynandomorphs



(Zhao et al. (2010) *Nature*)

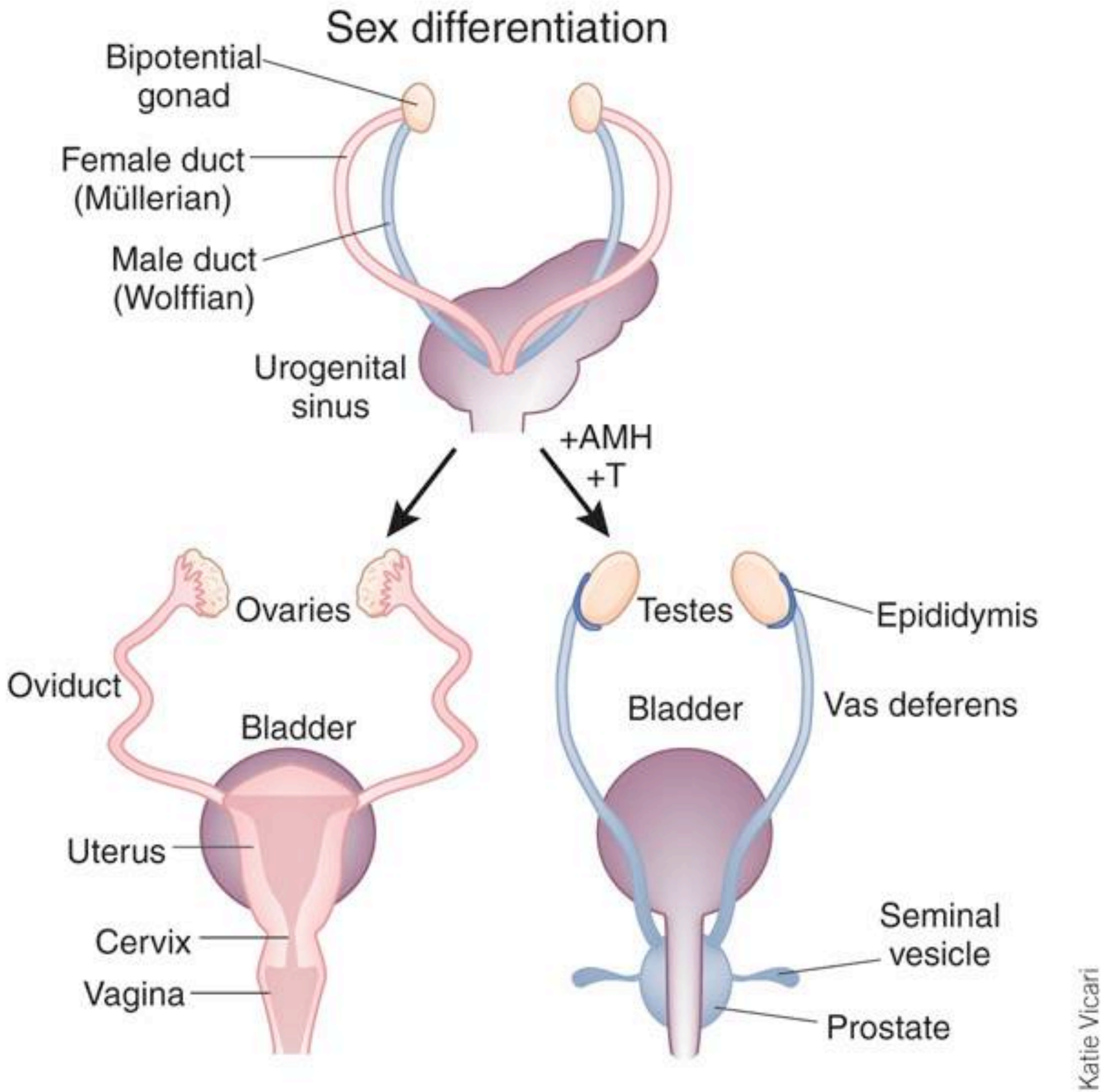
Other bird curiosities: gynandromorphs



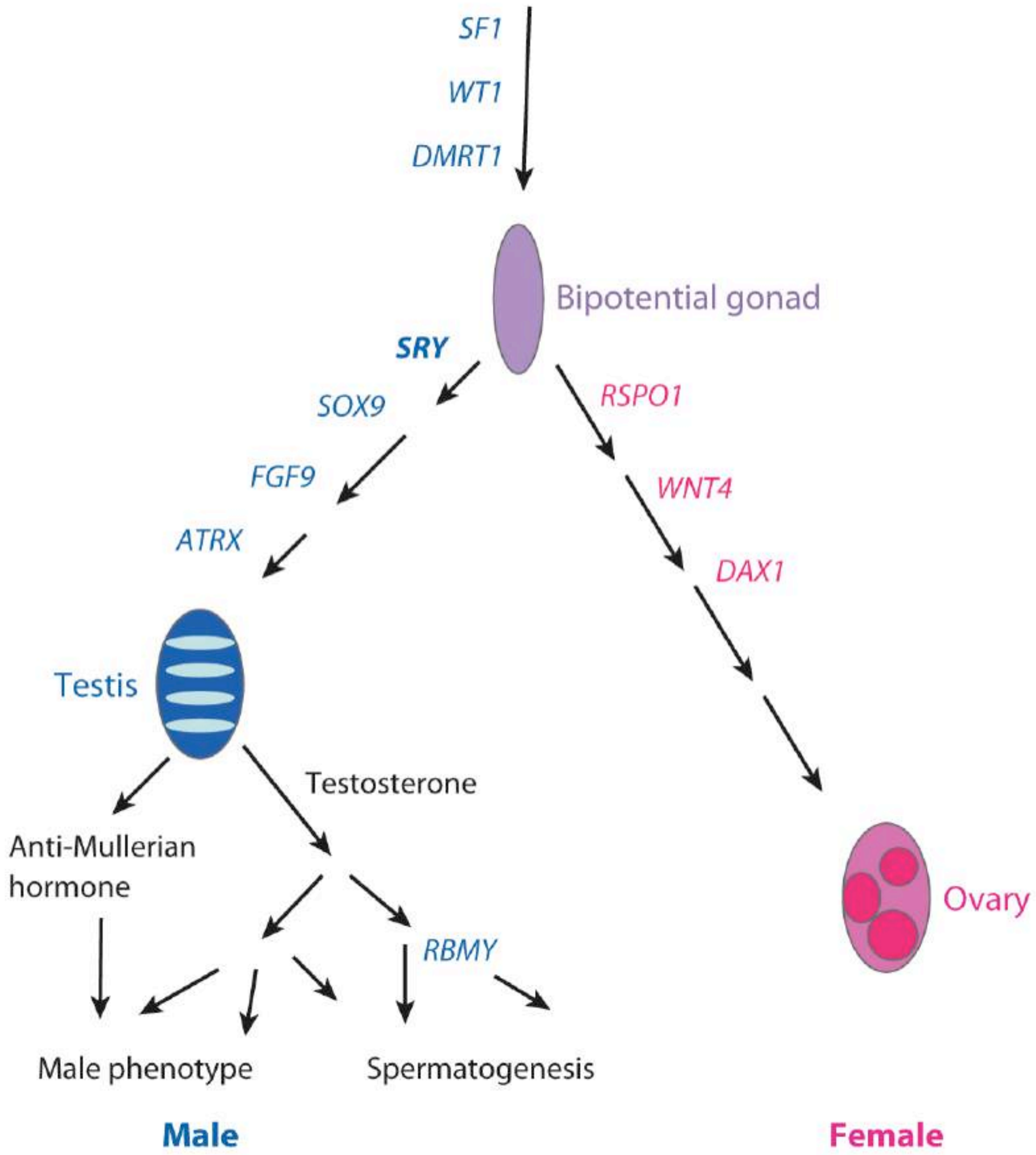
- The identity of somatic cells is independent of the gonads.

(Zhao et al. (2010) *Nature*)

Sex differentiation in mammals

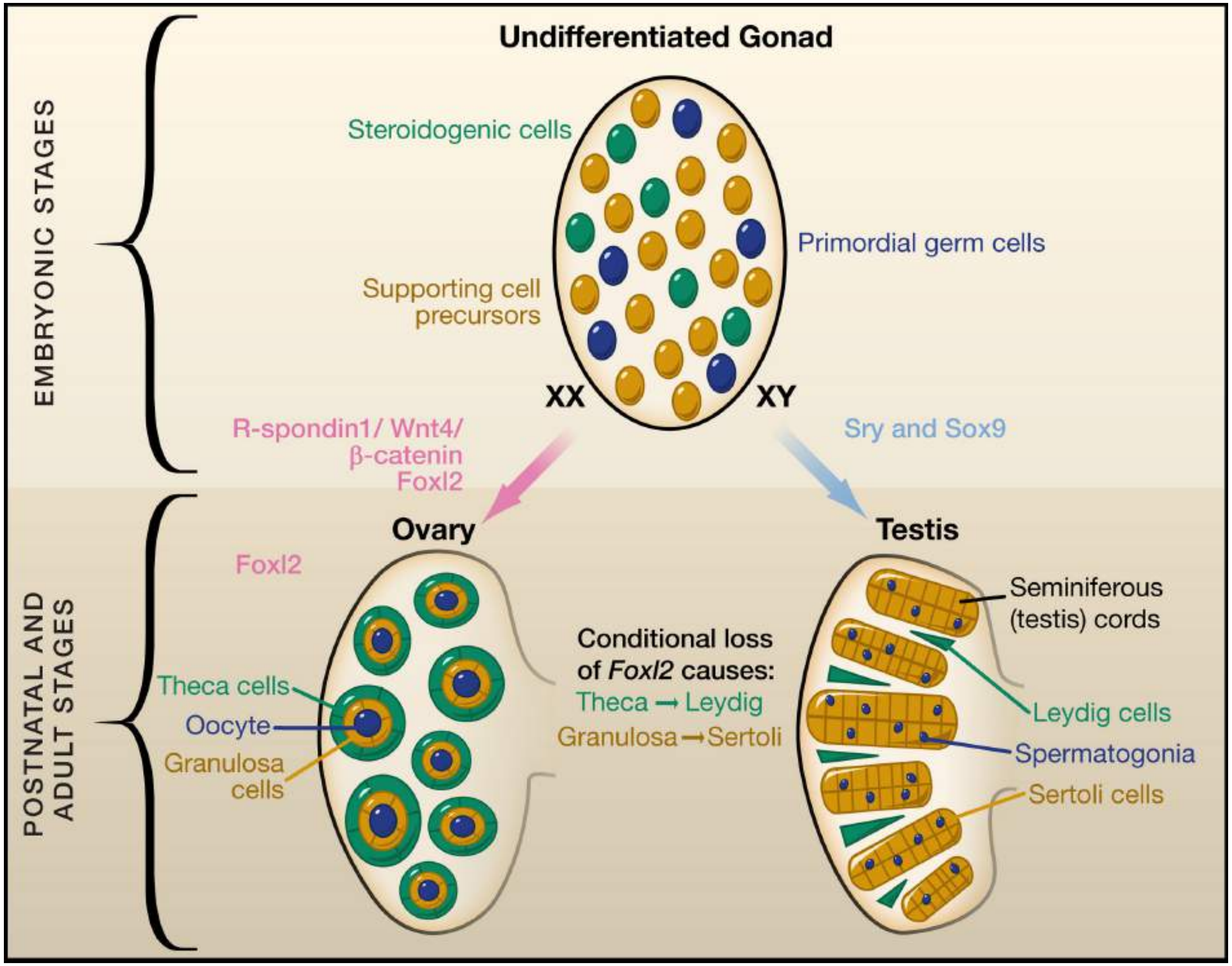


The genetic control of gonad-differentiation in mammals



(Graves (2008) *Annu Rev Genet*)

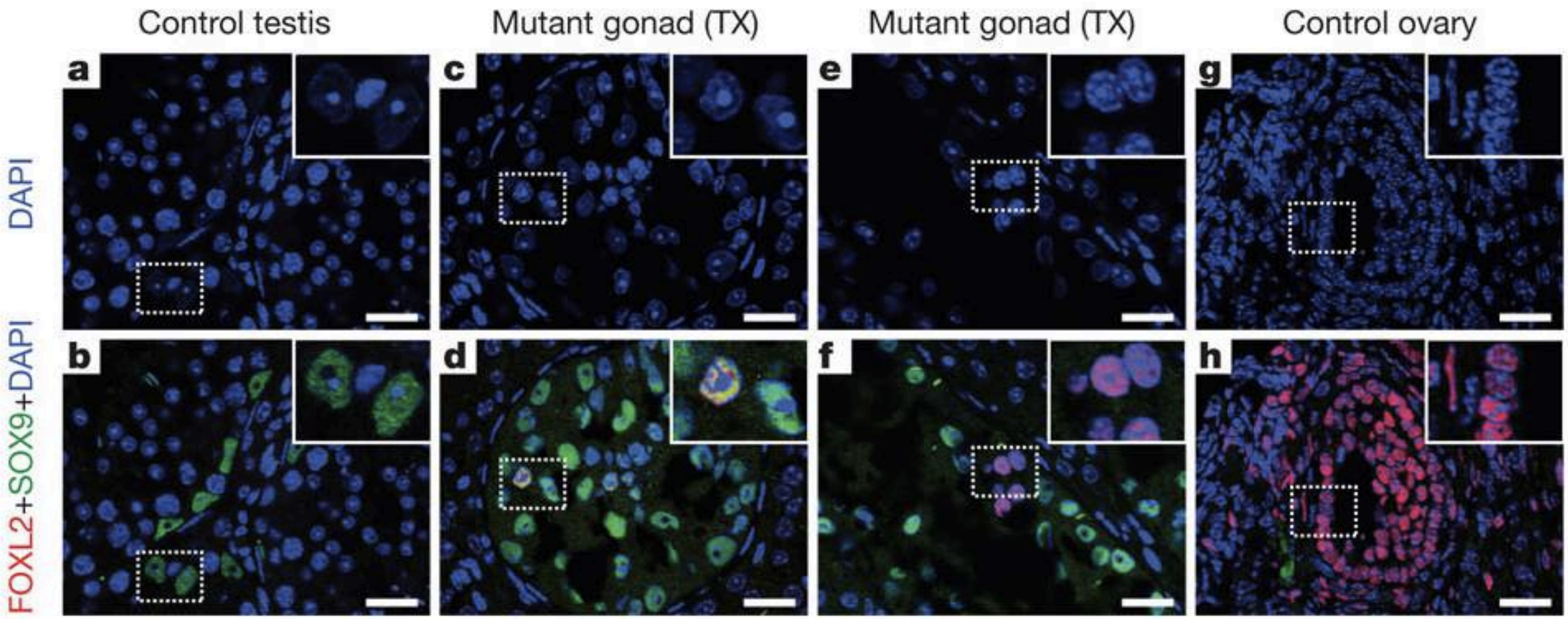
The genetic control of gonad-differentiation in adult mammals



(Sinclair és Smith (2009) *Cell*)

The genetic control of gonad-differentiation in adult mammals

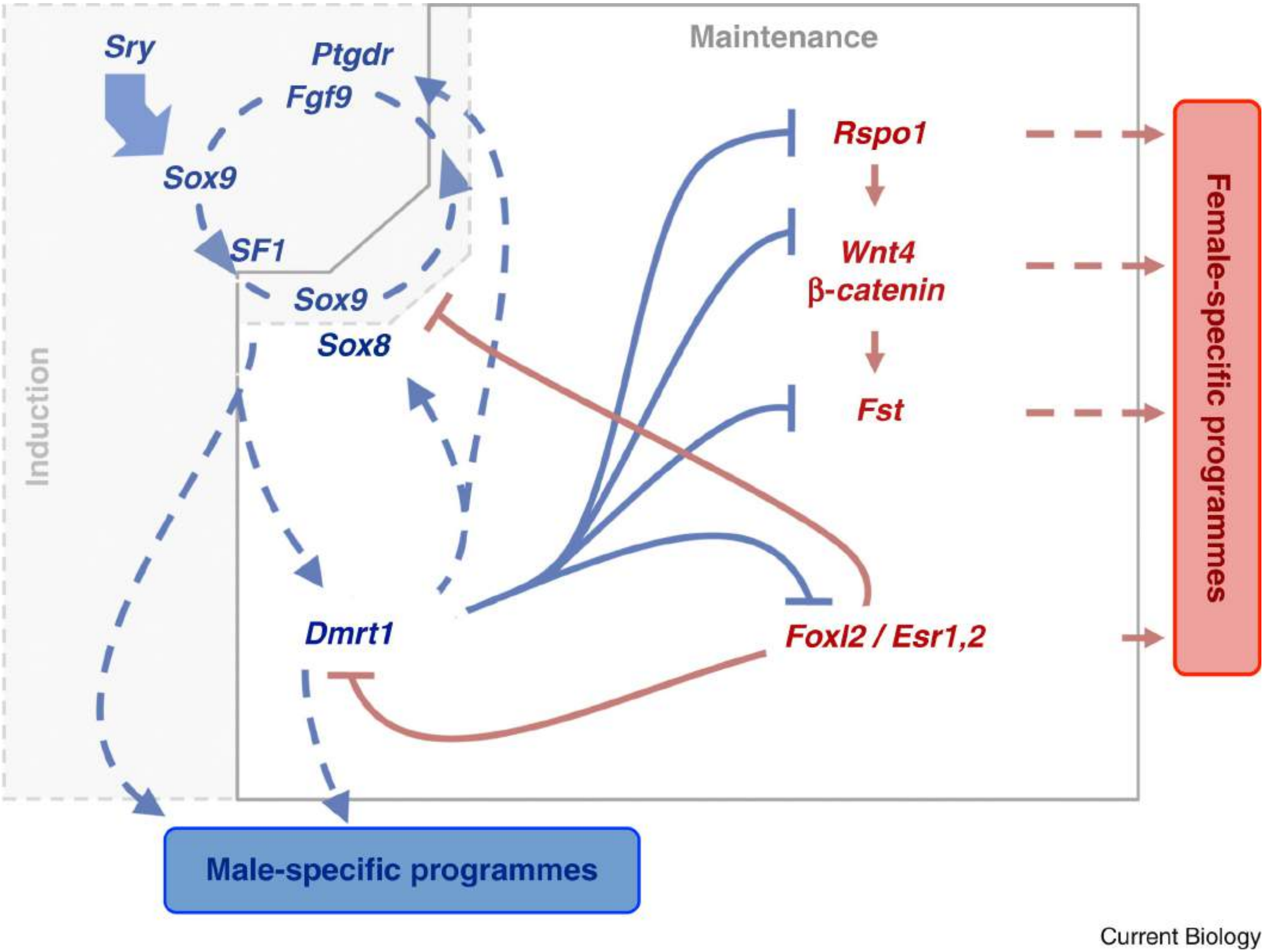
UBC-cre/ERT2; Dmrt1$^{flox/flox}$



- Loss of Dmrt1-function induces Sertoli -> granulosa transdifferentiation in the adult testis.

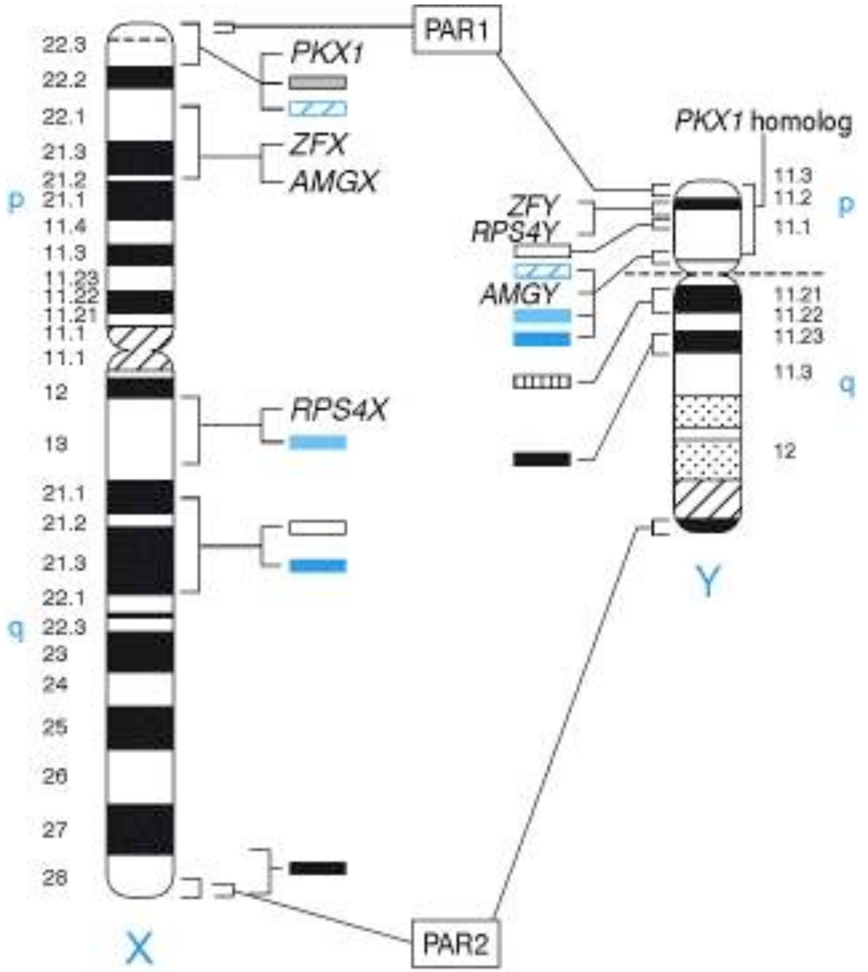
(Matson et al. (2011) *Nature*)

The genetic control of gonad-differentiation and gonad-identity

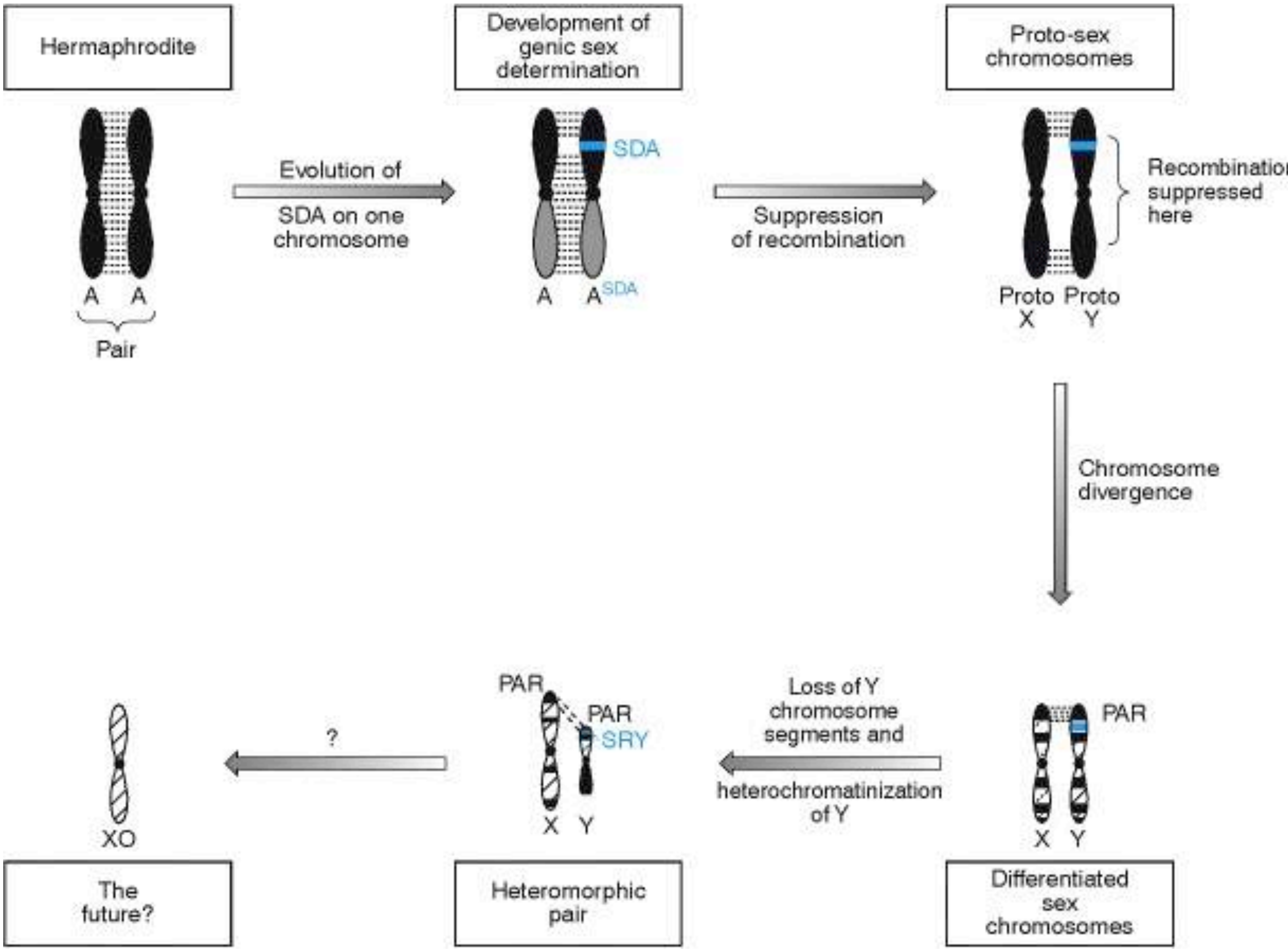


(Herpin & Schart (2011) *Curr Bio*)

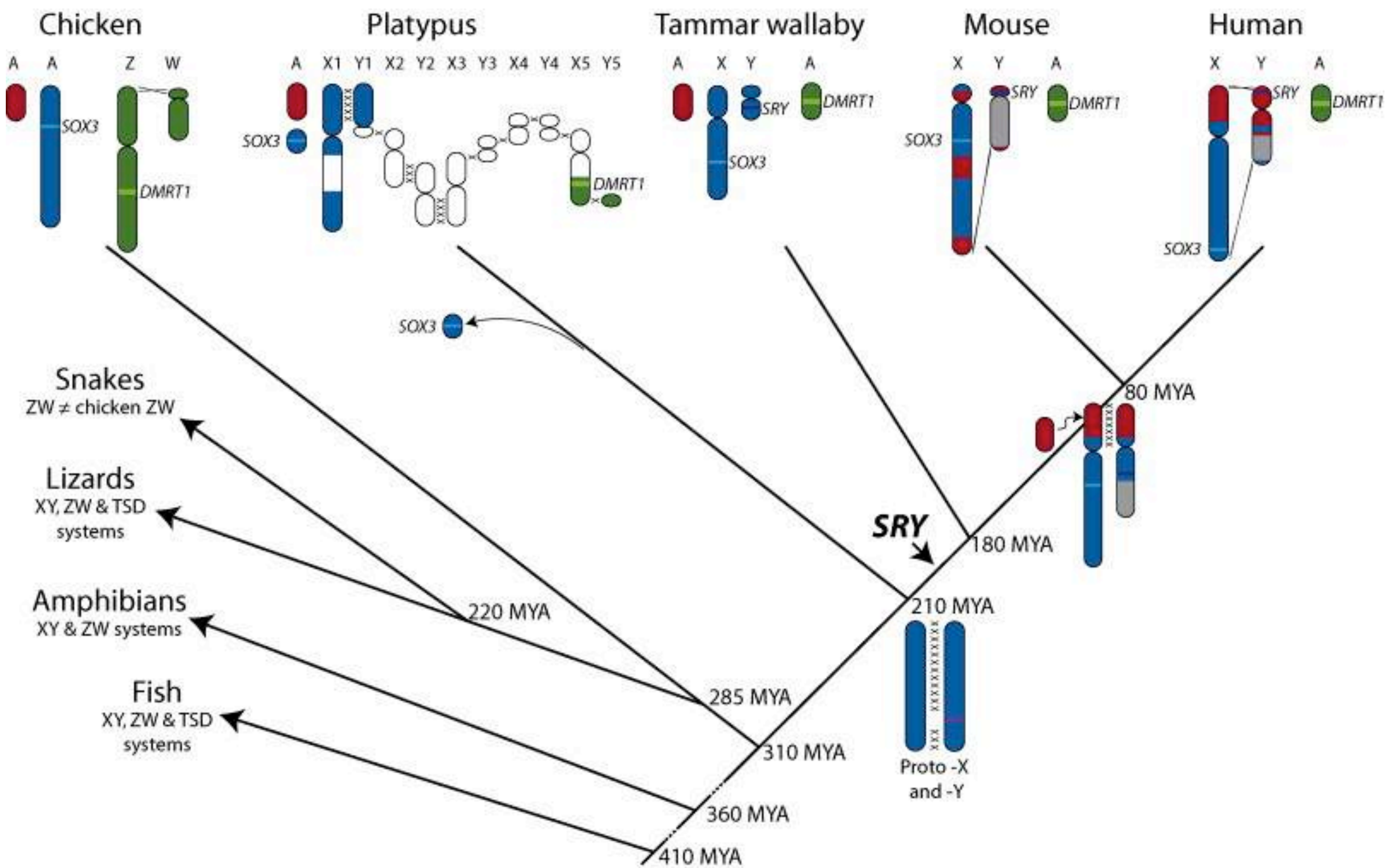
Human sex chromosomes



Steps in sex chromosome evolution

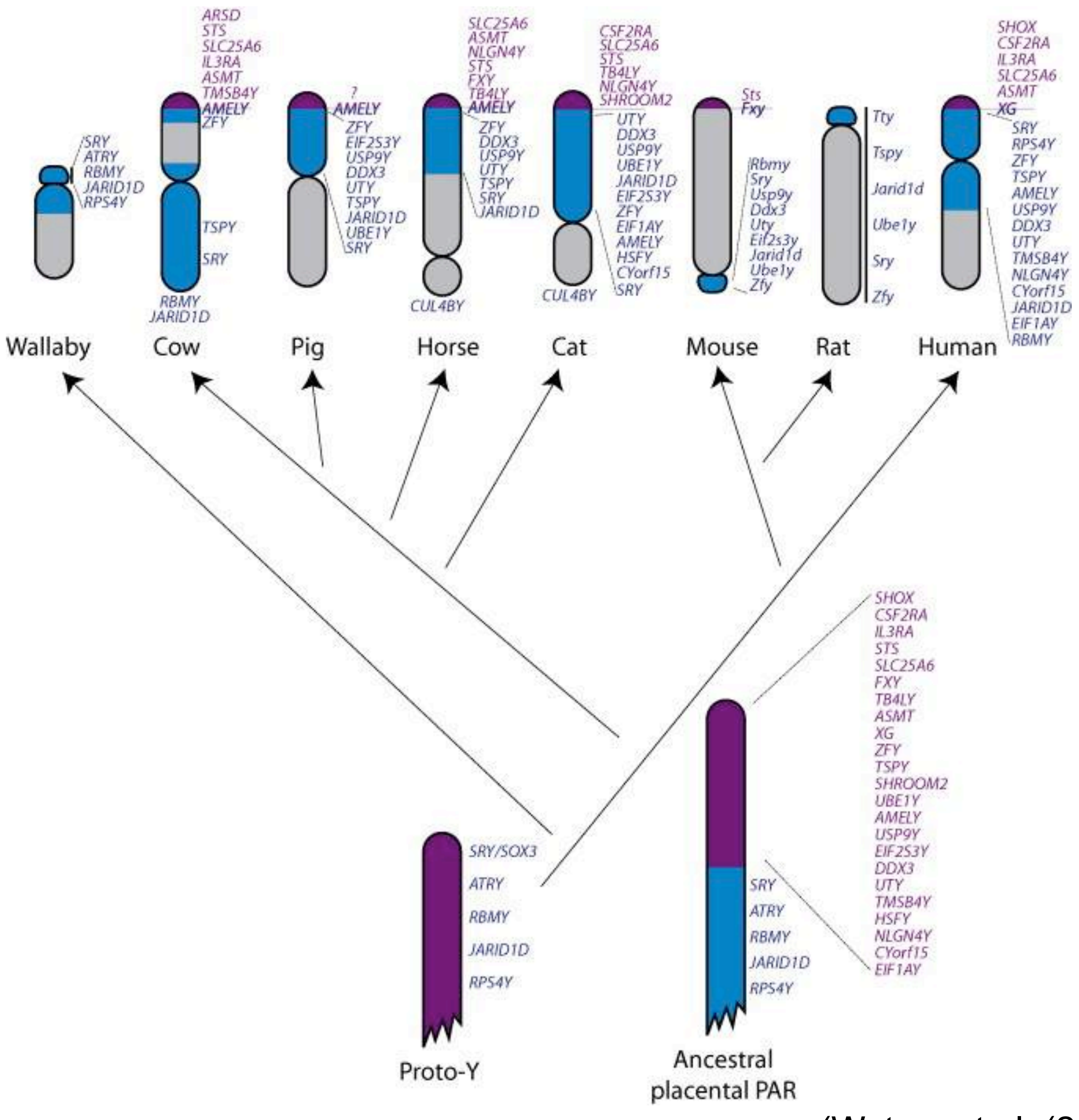


Sex chromosome evolution in mammals



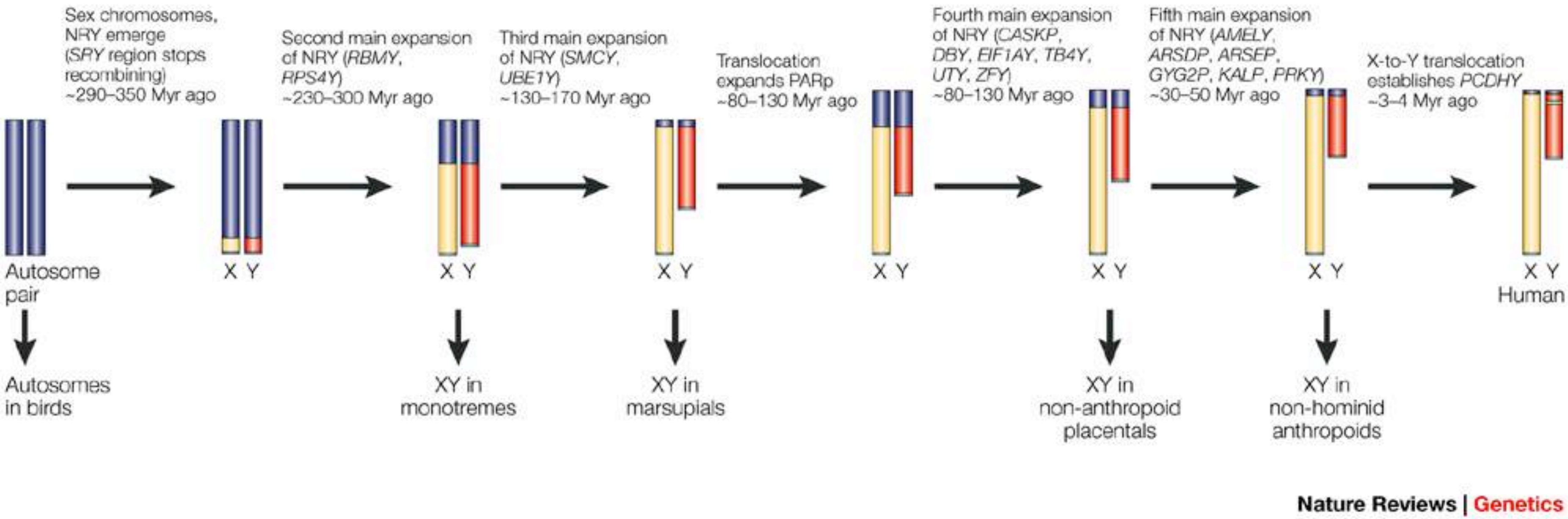
(Waters et al. (2007) *Sem in Cell & Dev Bio*)

Sex chromosomes of extant mammals

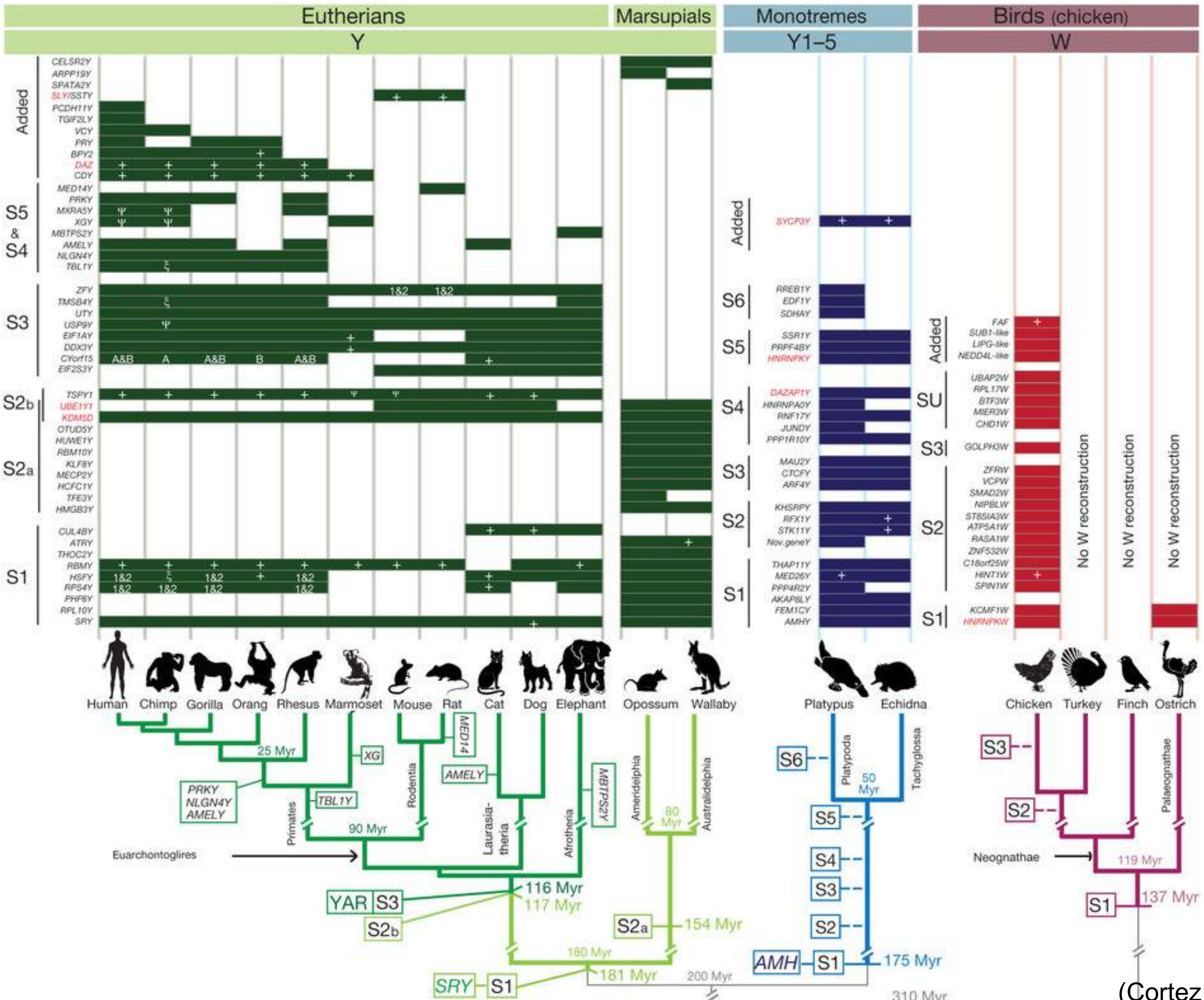


(Waters et al. (2007) *Sem in Cell & Dev Bio*)

Human Y chromosome evolution



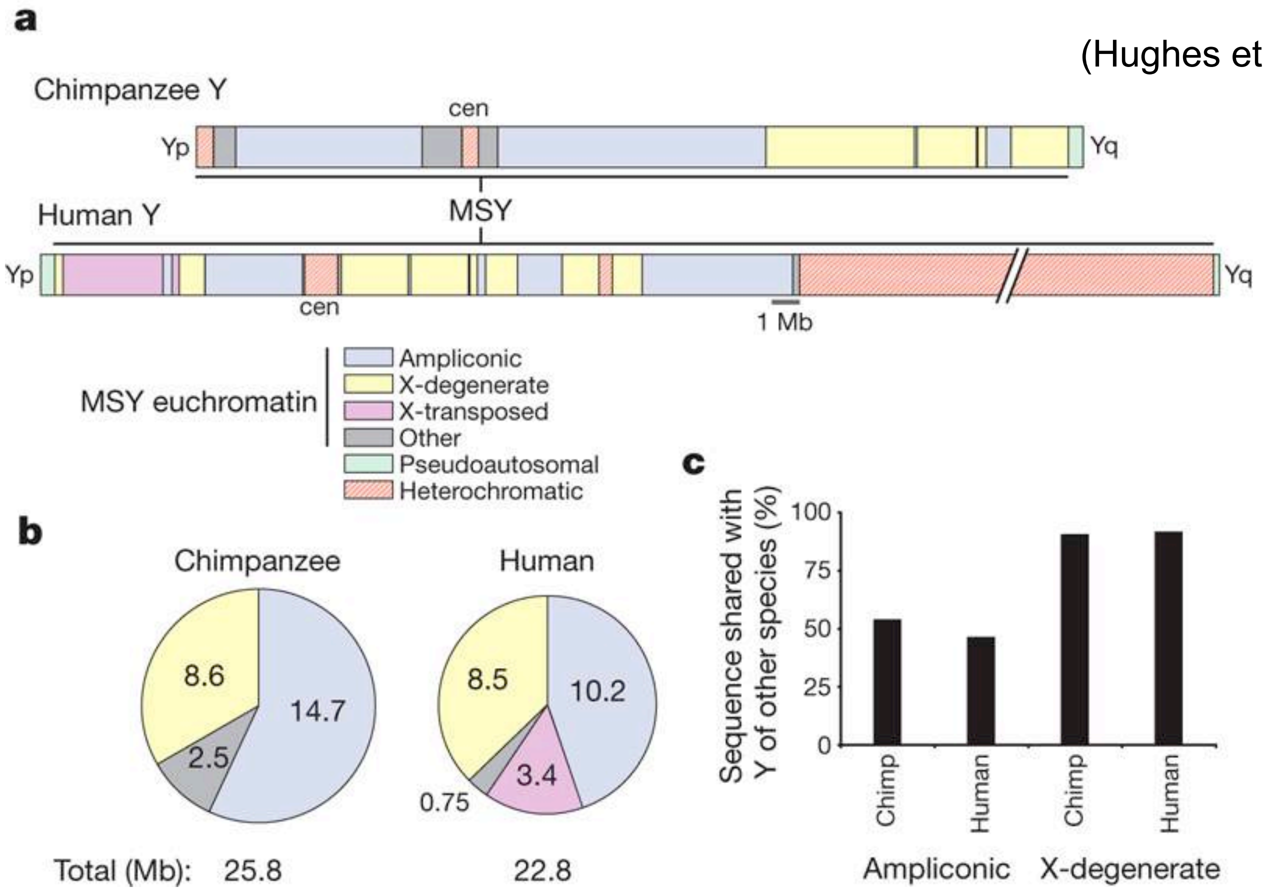
Mammalian Y chromosome evolution



(Cortez et al., 2014 *Nature*)

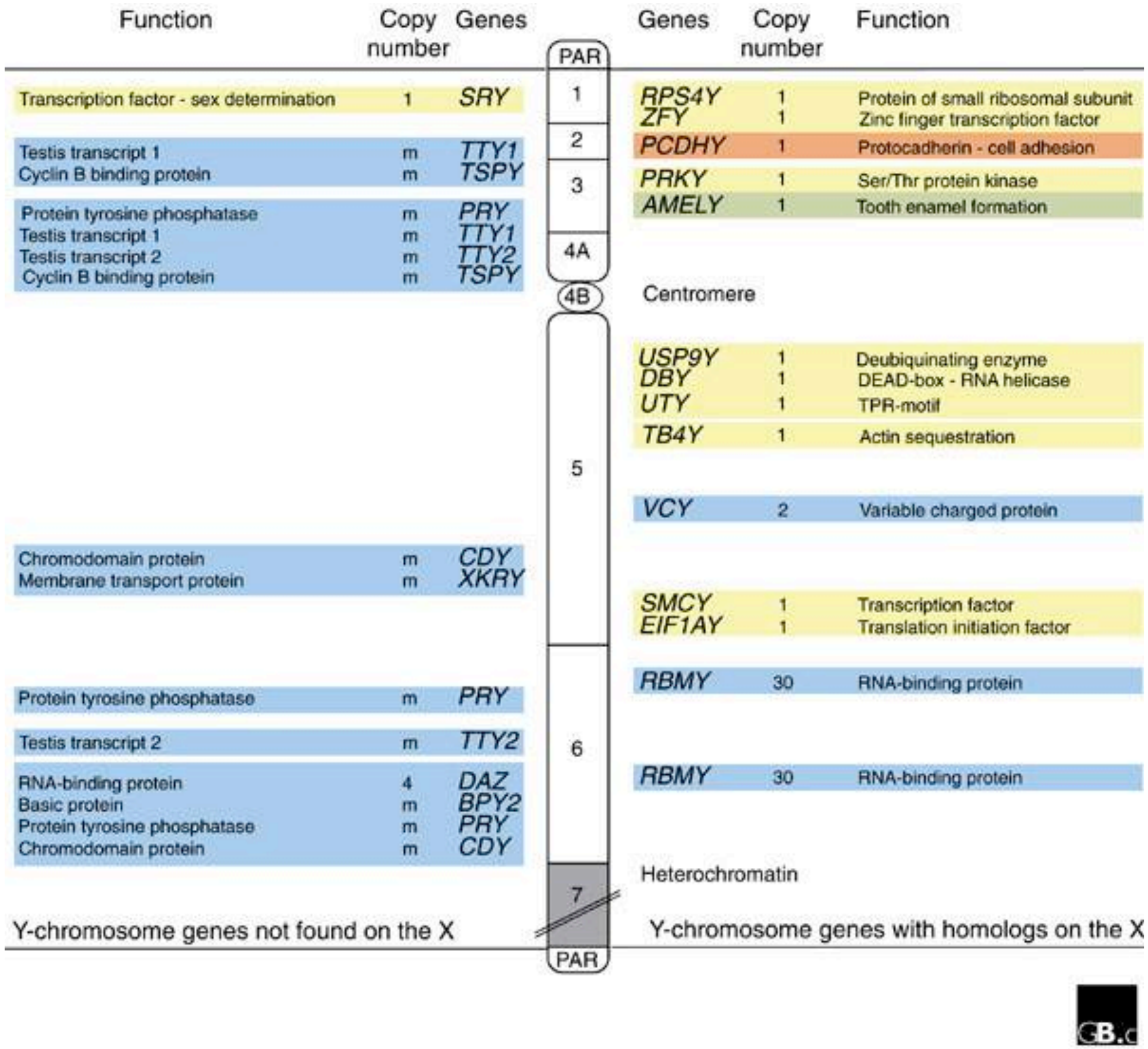
Human and chimp Y chromosomes are very different

(Hughes et al. (2010) *Nature*)

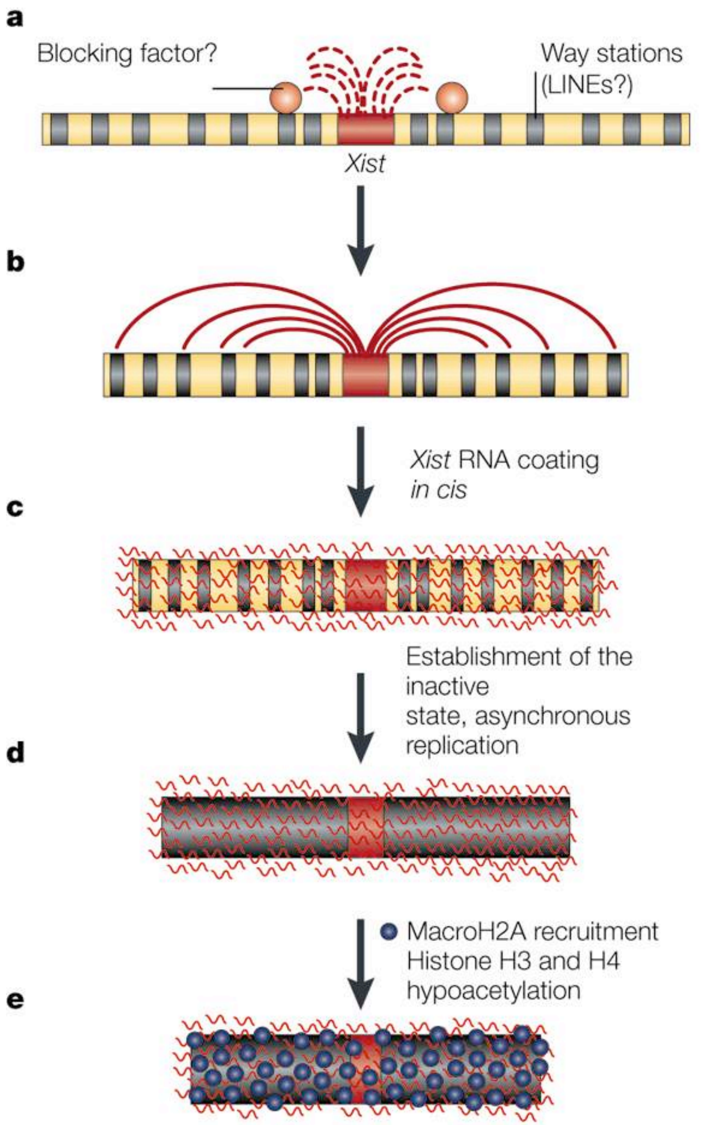


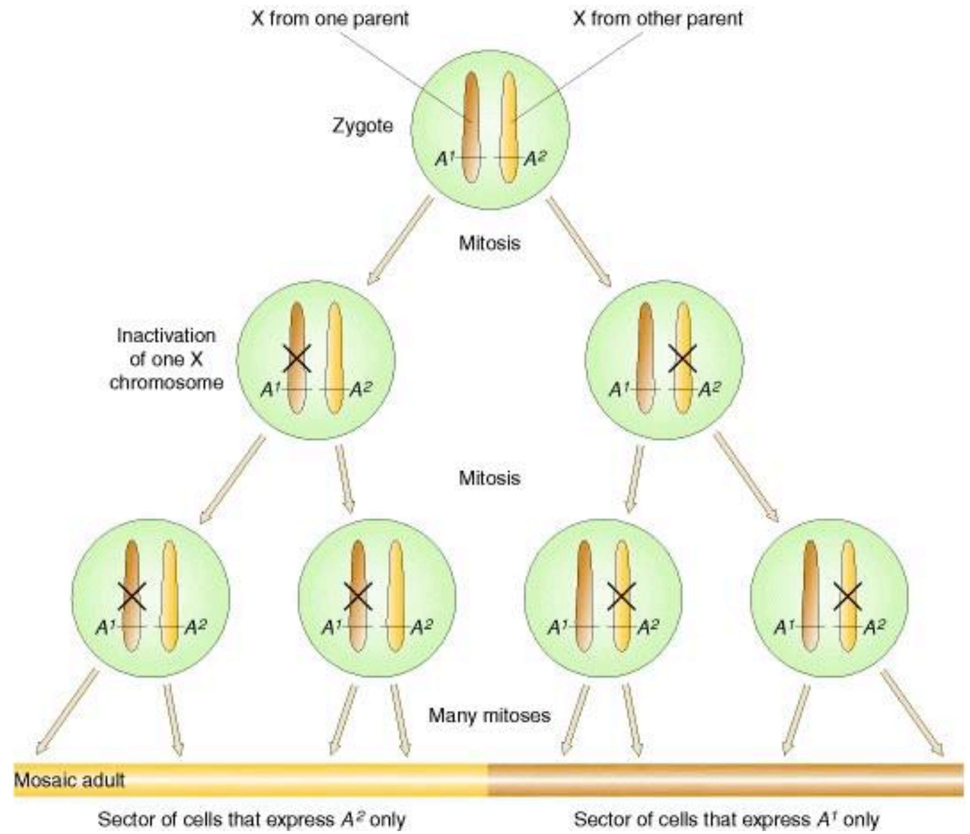
- the chimp Y chromosome has only 2/3 as many genes and gene families as its human counterpart, and only 47% of protein coding elements
- 30% of the chimp chromosome can not be aligned to the human Y (whereas for the whole genome this value is ~2%)

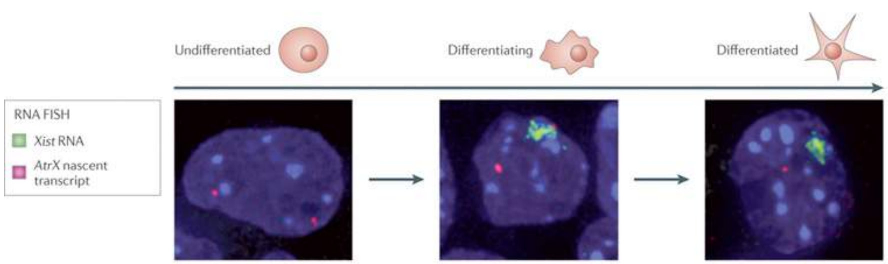
The genetic map of the non-recombining Y chromosome regions



Dose compensation based on random X chromosome inactivation (XCI)





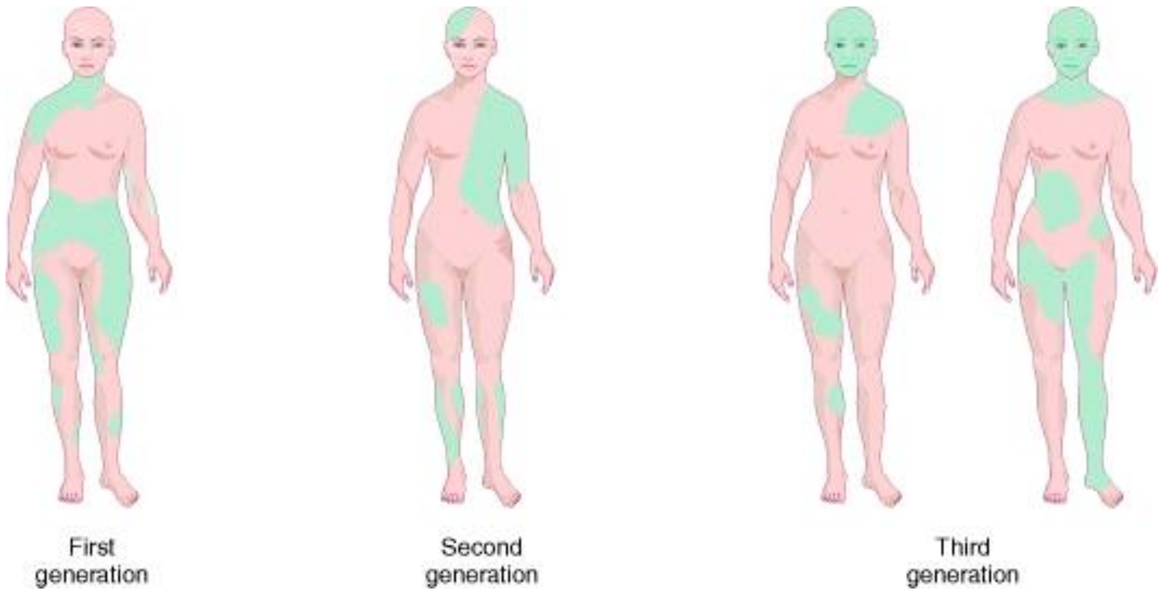


Nature Reviews | Genetics

The phenotypic result of XCI

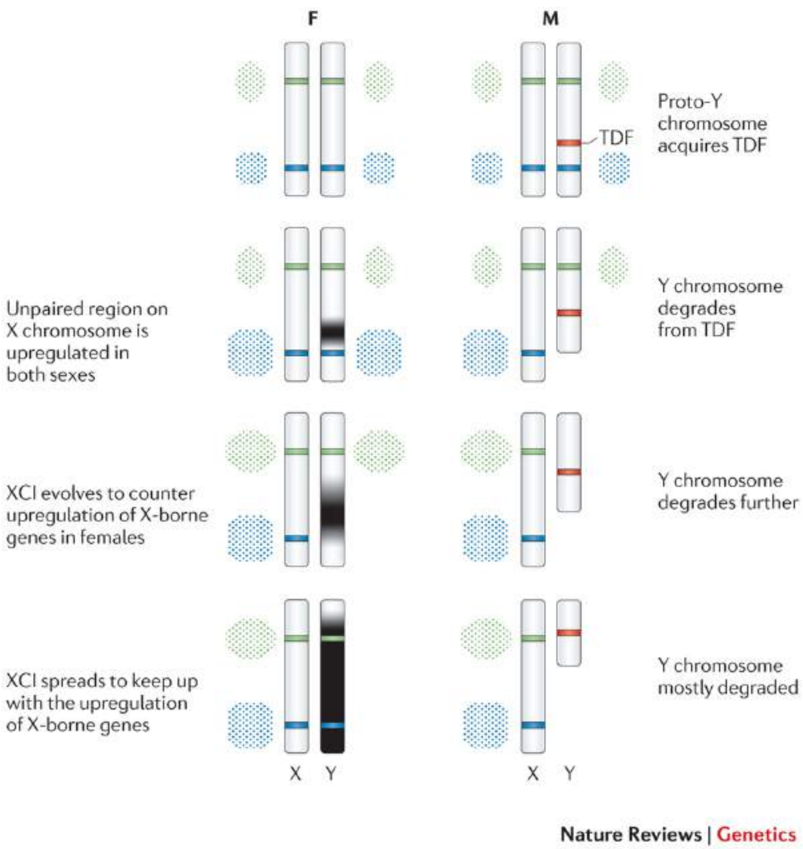
- X-linked traits will be mosaic

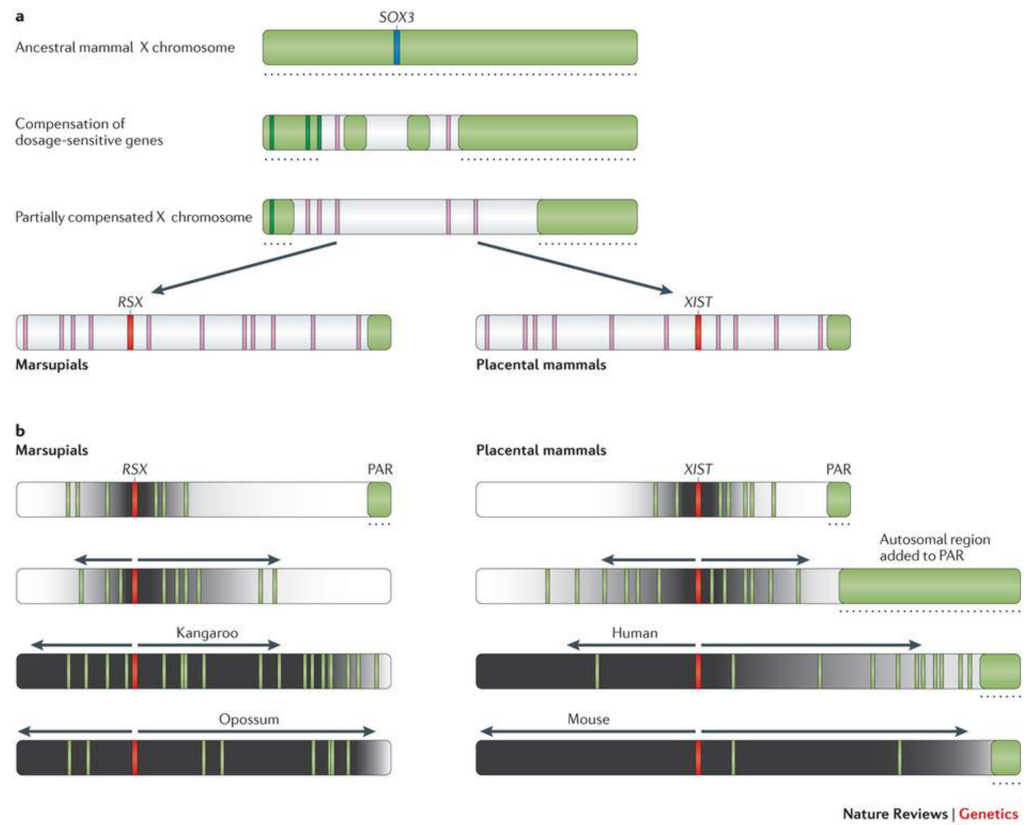
- calico cats:



- Heterozgyote women with anhydroticus ectodermalis dysplasia (absence of sweat glands).

XCI evolution in mammals



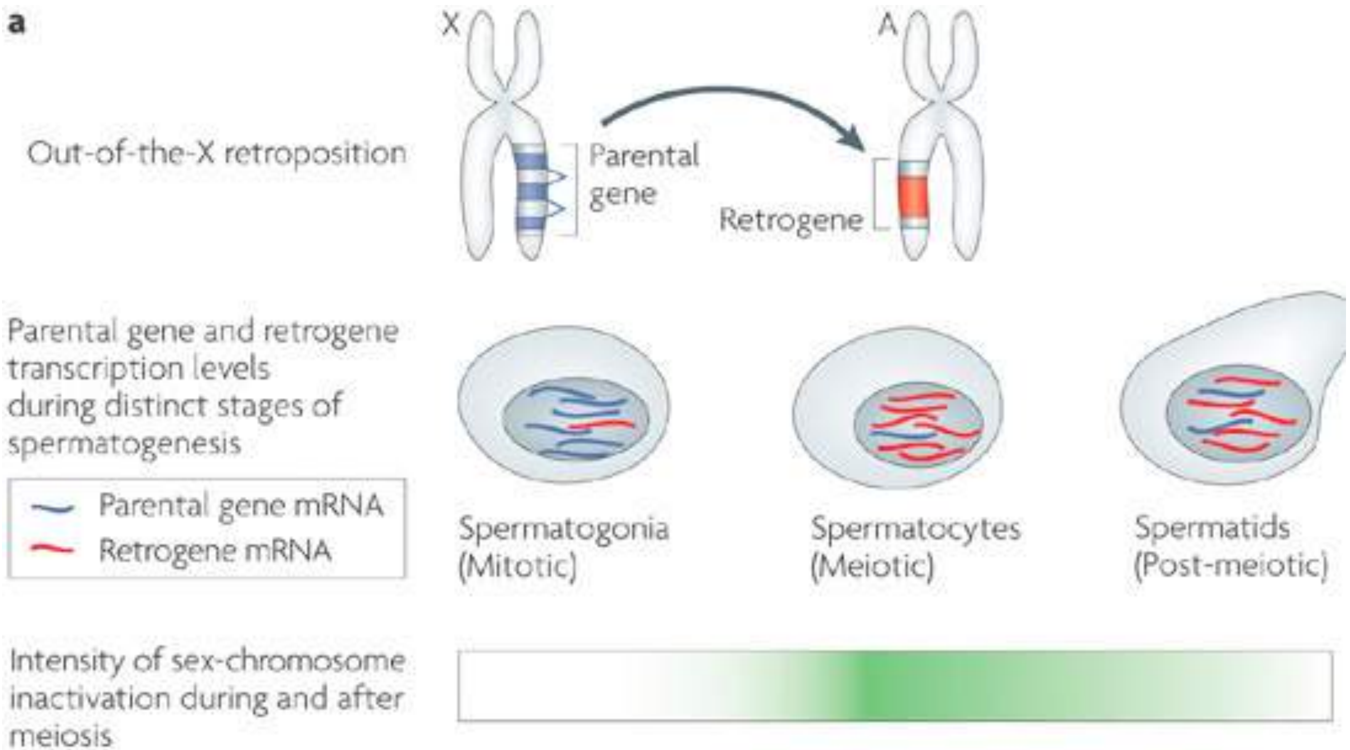


In parallel with the degradation of the proto-Y chromosome, the expression of Y-derived genes on X chromosome gets stronger and finally is counterbalanced by XCI.

- In placental mammals *XIST*, while in marsupials *RSX* (*RNA on the silent X*) is involved in XCI.
- The level of XCI is different in different species – green bars denote escaper genes. (In humans 15% of genes gets transcribed, in mouse only 3%.)

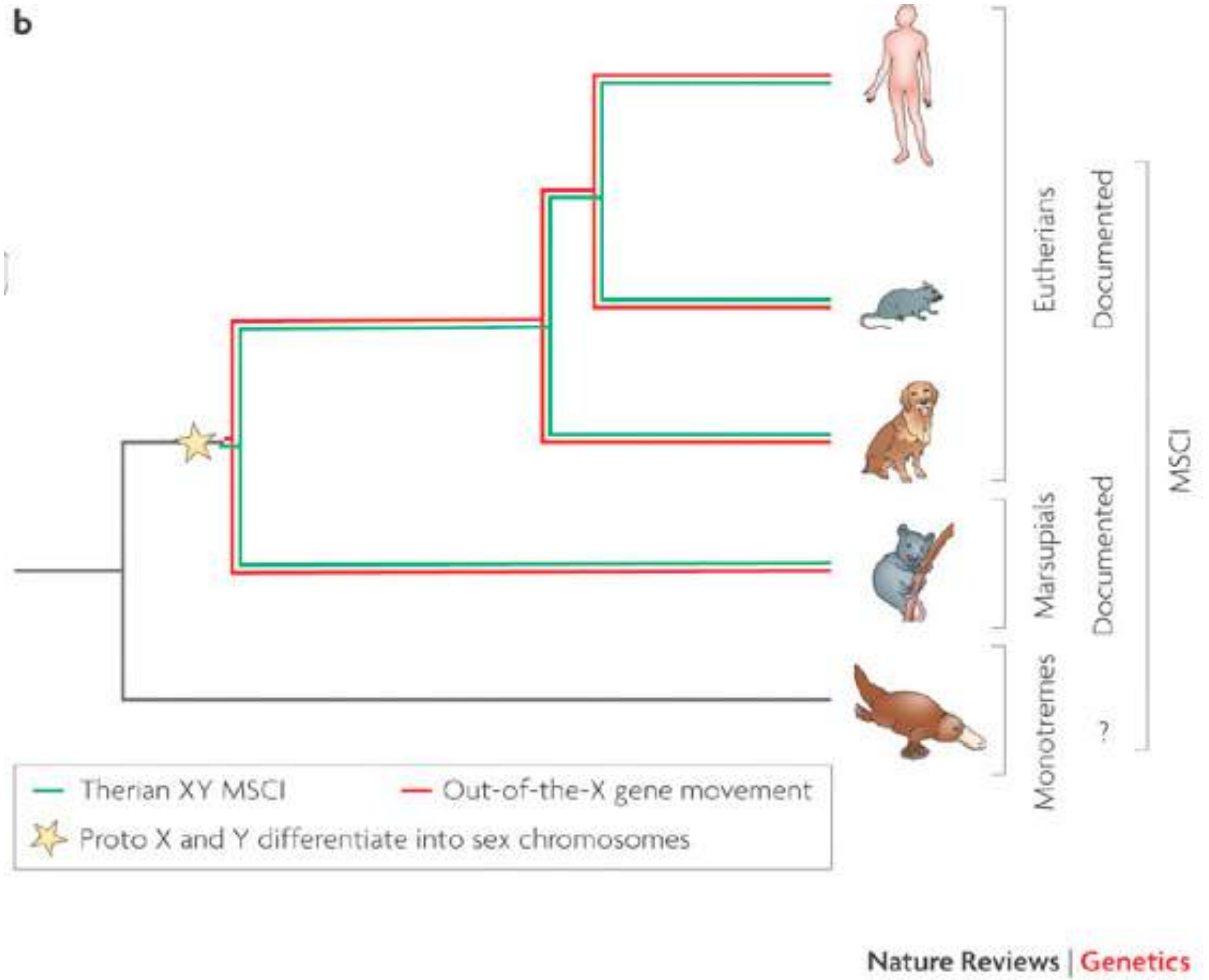
(Graves 2016 *Nat Rev Gen*)

Meiotic sex chromosome inactivation results in the transposition of some genes



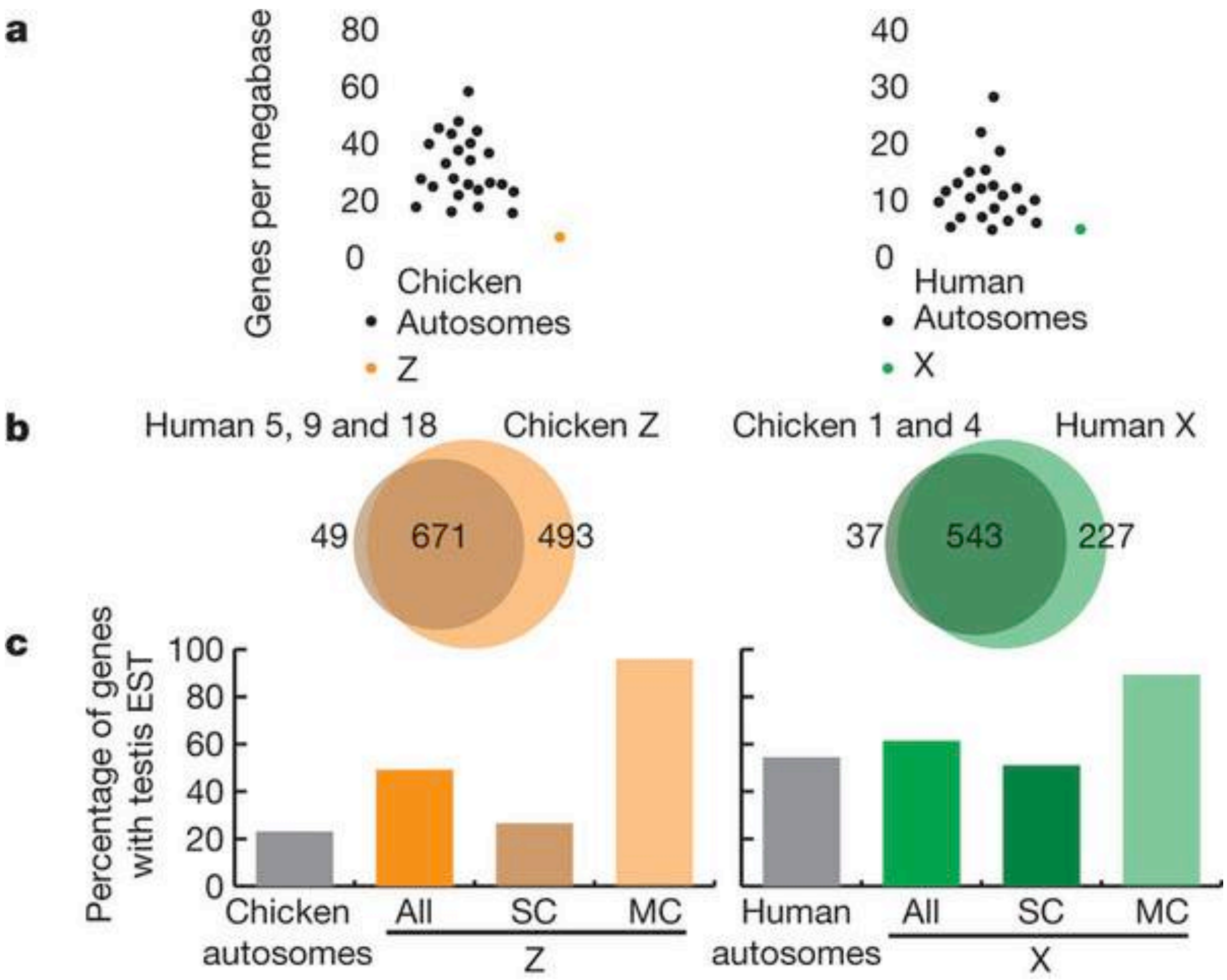
MSCI = meiotic sex chromosome inactivation (the transcriptional shut down of X and Y chromosomes during spermatogenesis (meiosis)

Meiotic sex chromosome inactivation results in the transposition of some genes



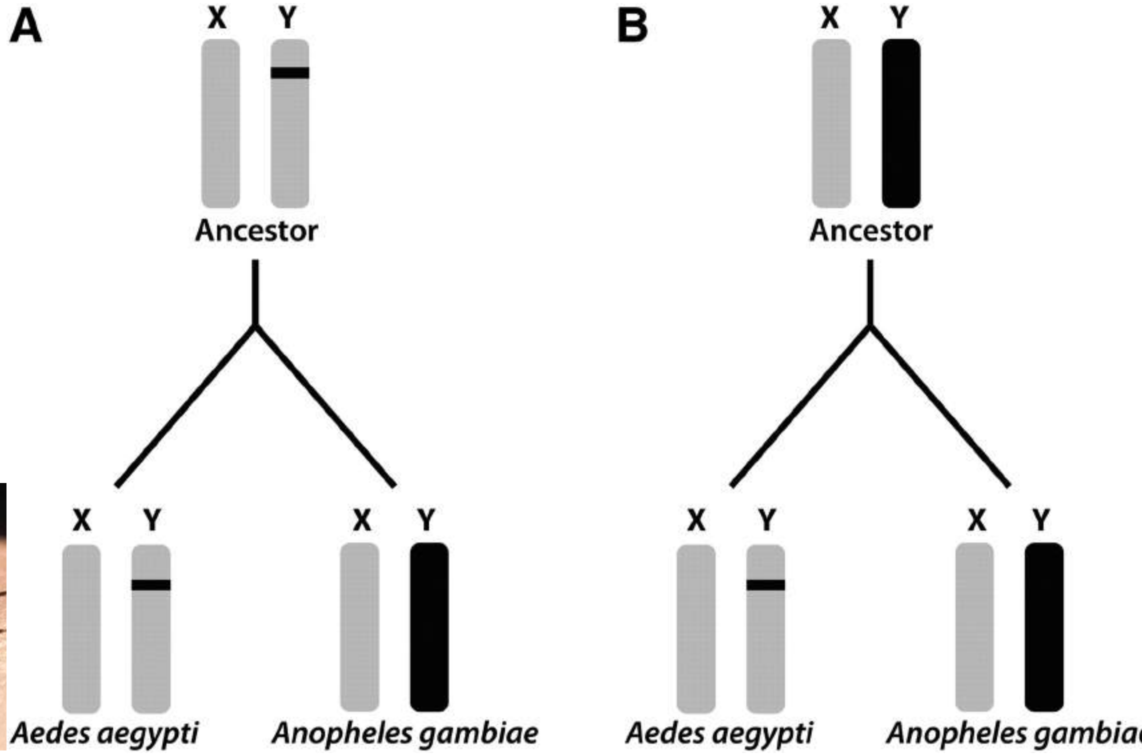
Retrogenes from X chromosome get expressed more often in testes than other, testis-specific retrogenes. Therefore it is likely that there was strong selection to preserve them to compensate for MSCI.

Meiotic sex chromosome inactivation can also result in gene duplication



(Bellott et al. (2010) *Nature*)

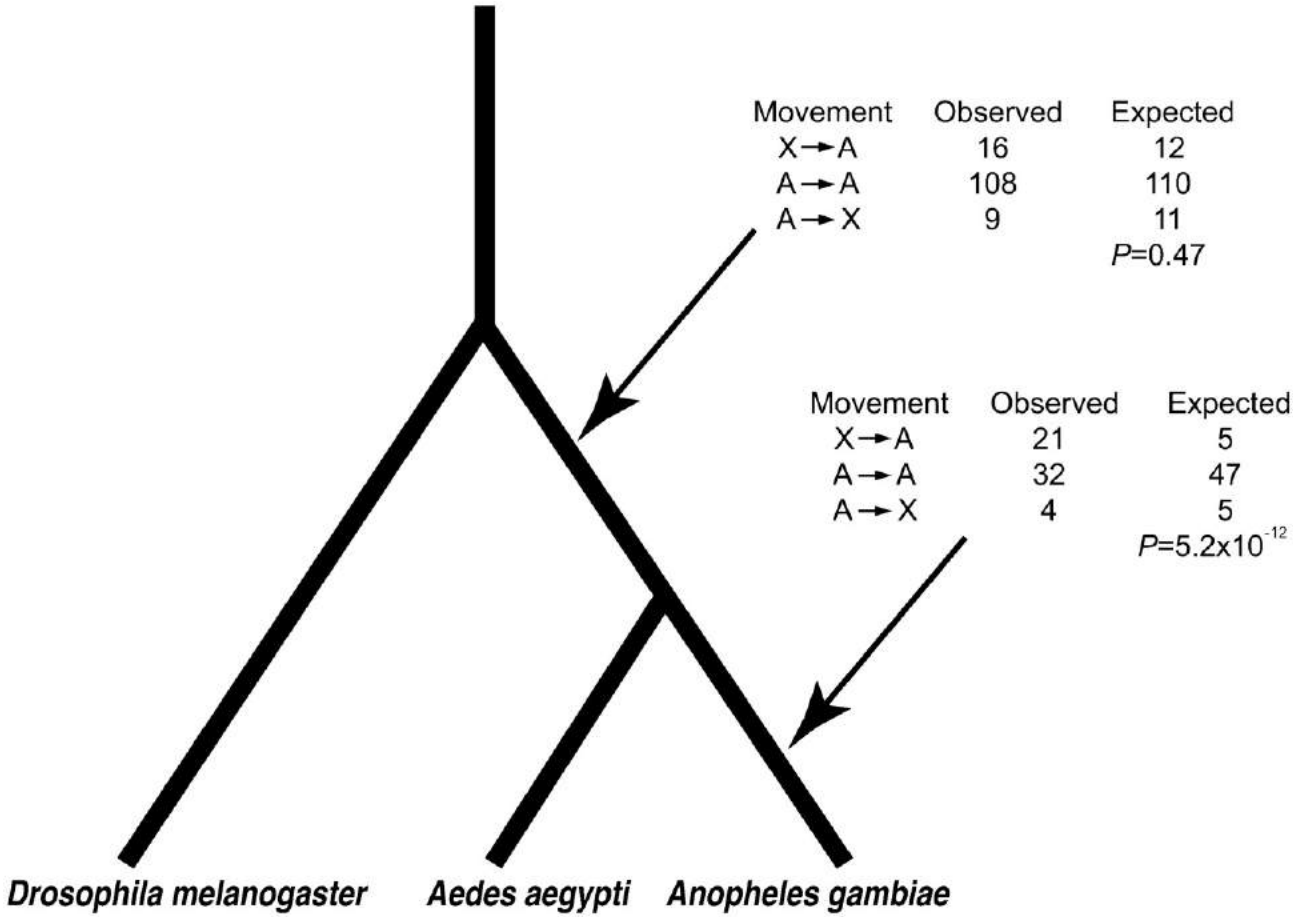
Sex chromosome evolution in mosquitoes



If the common ancestor of *Ae. aegypti* and *An. gambiae* had homomorphic sex chromosomes (Figure 1A), there should be an excess of retrogene movement off the X chromosome in An. gambiae only after the divergence of the two lineages (i.e., since An. gambiae evolved a differentiated X chromosome). In contrast, if the common ancestor had fully heteromorphic chromosomes (Figure 1B), then our prediction is that there will be an excess of gene movement off the An. gambiae X on both the shared ancestral branch and the Anopheles-specific branch after the split with Aedes.

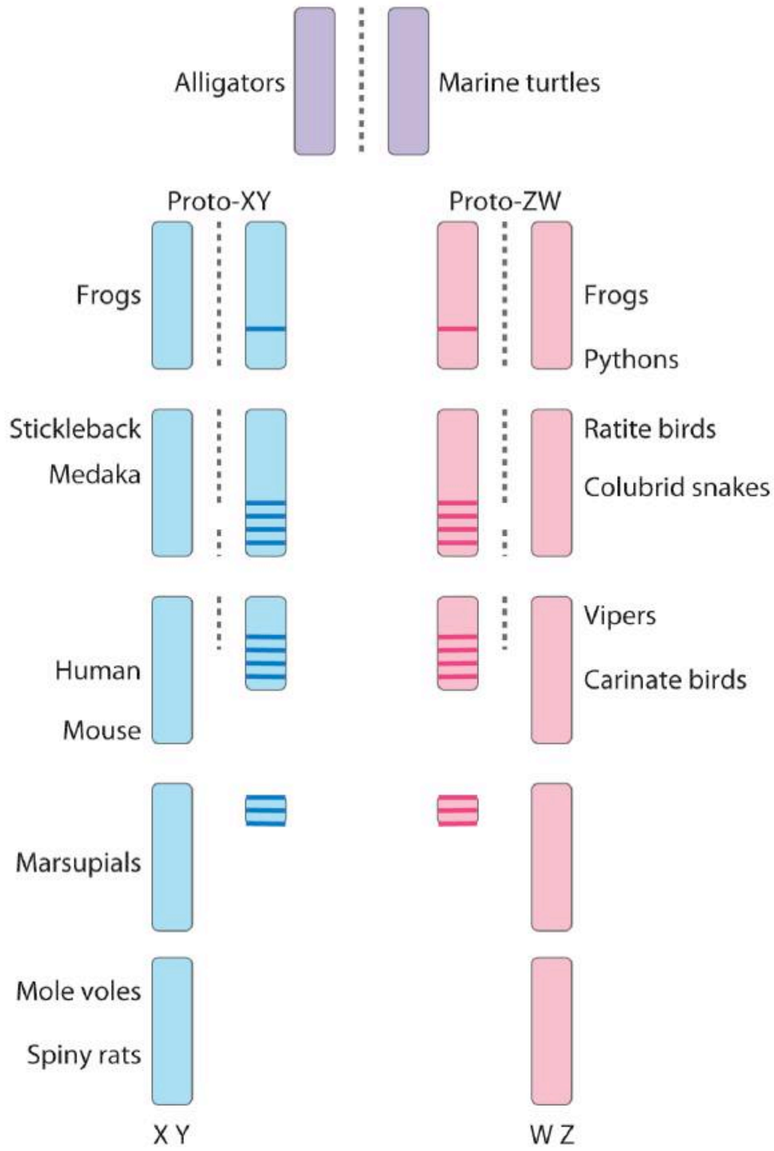
(Toups and Hahn (2010) *Genetics*)

Sex chromosome evolution in mosquitoes



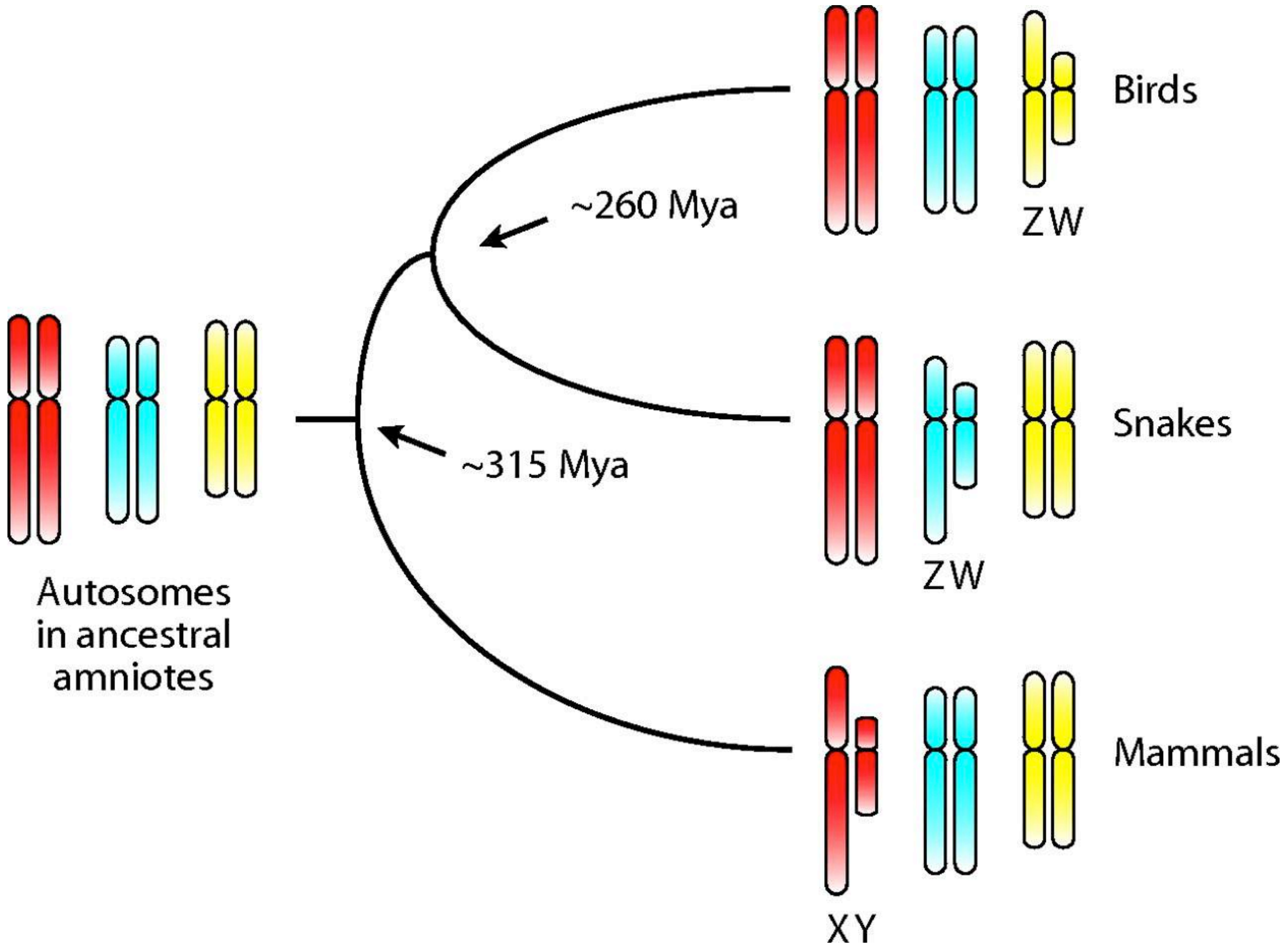
(Toups és Hahn (2010) *Genetics*)

Sex-specific element evolution from autosomes



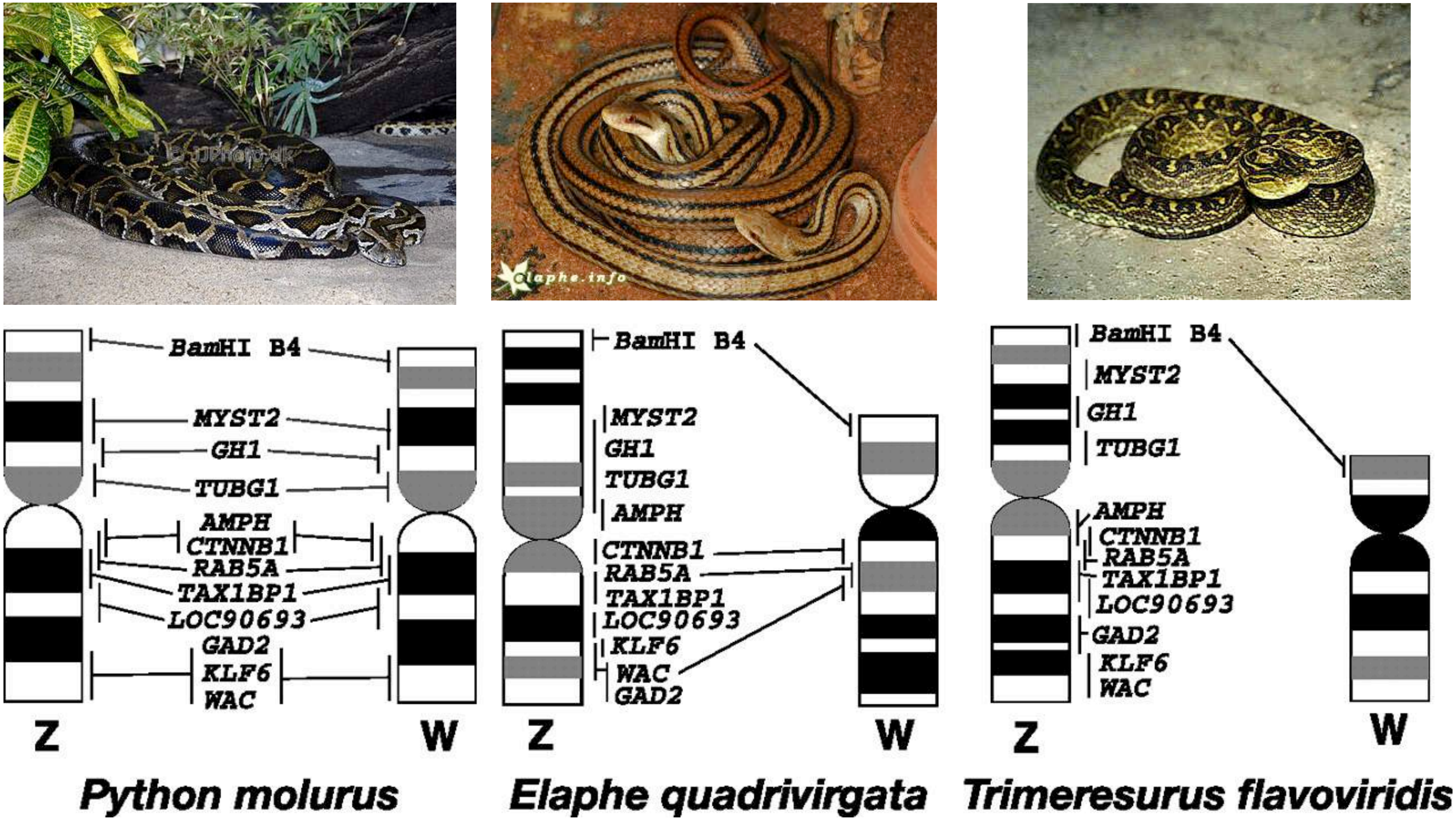
(Graves (2008) *Annu Rev Genet*)

The independent origin of amniote sex-chromosomes



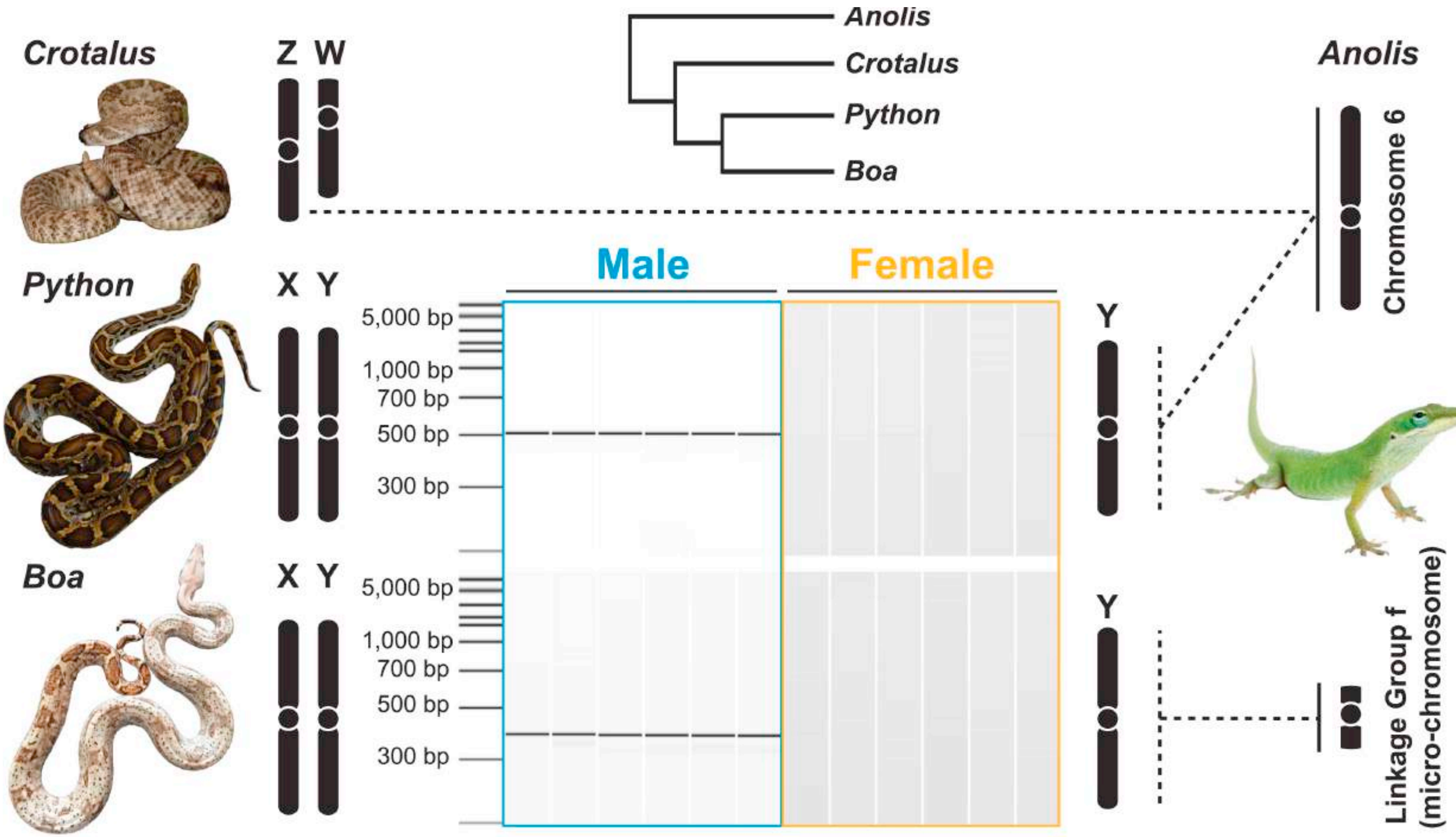
(Vallender and Lahn (2006) *PNAS*)

The cytogenetic map of snake sex chromosomes



(Matusbara et al. (2006) *PNAS*)

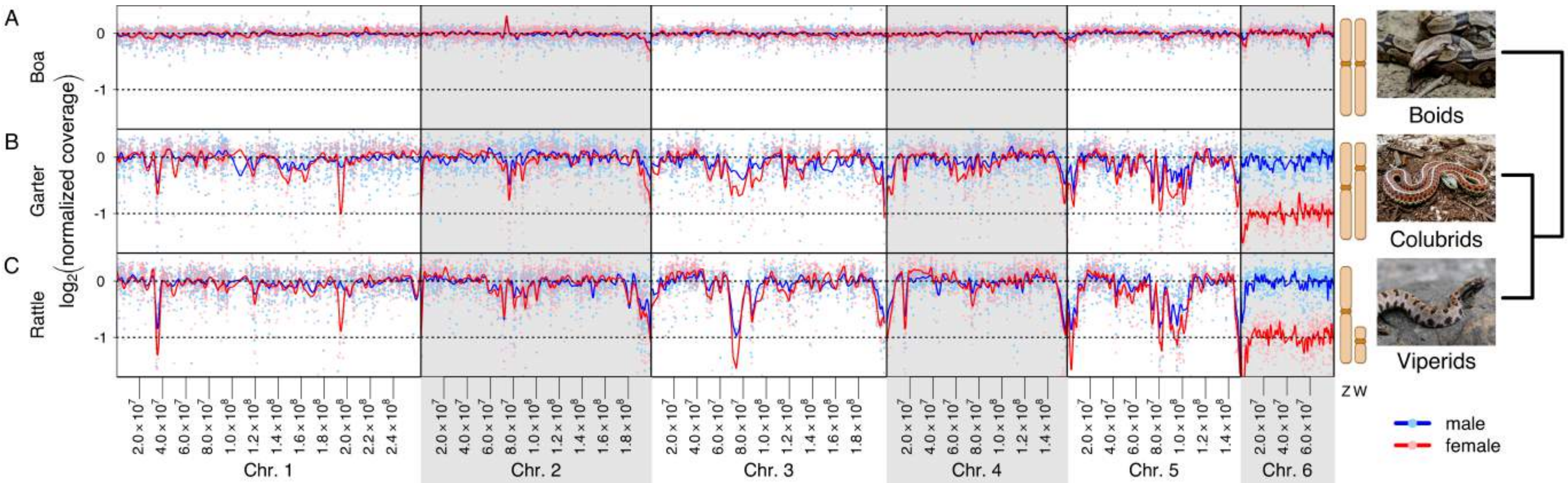
BUT: boas and pythons do not have a ZW system!

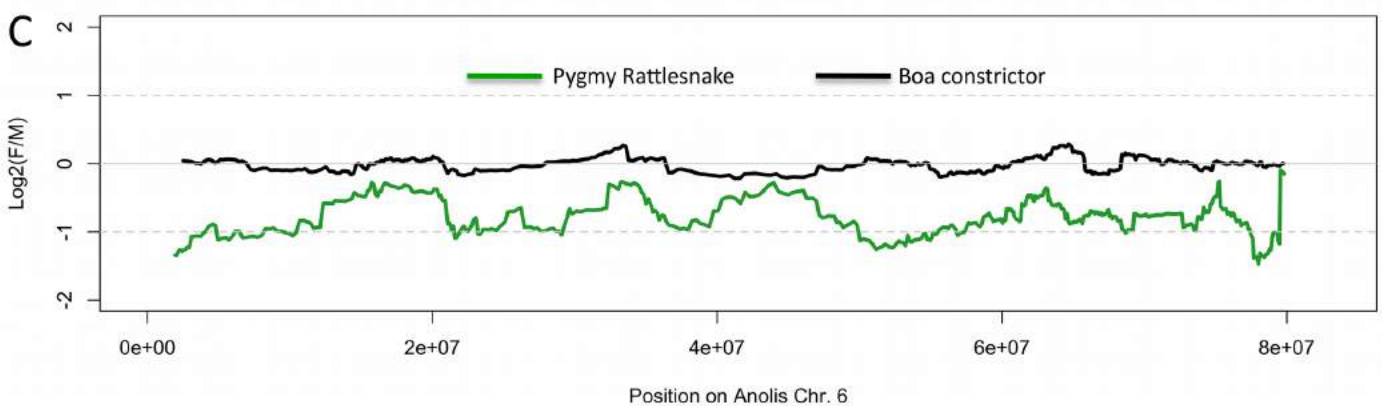


- Furthermore: in other species with a ZW system the animals born from parthenogenesis are ZZ males, whereas in boids they are females.
- Mating parthenogenetic females with wild-type males, the offspring sex ratio is 1:1 (this suggests an XY system).

(Gamble et al. 2017 *Curr Bio*)

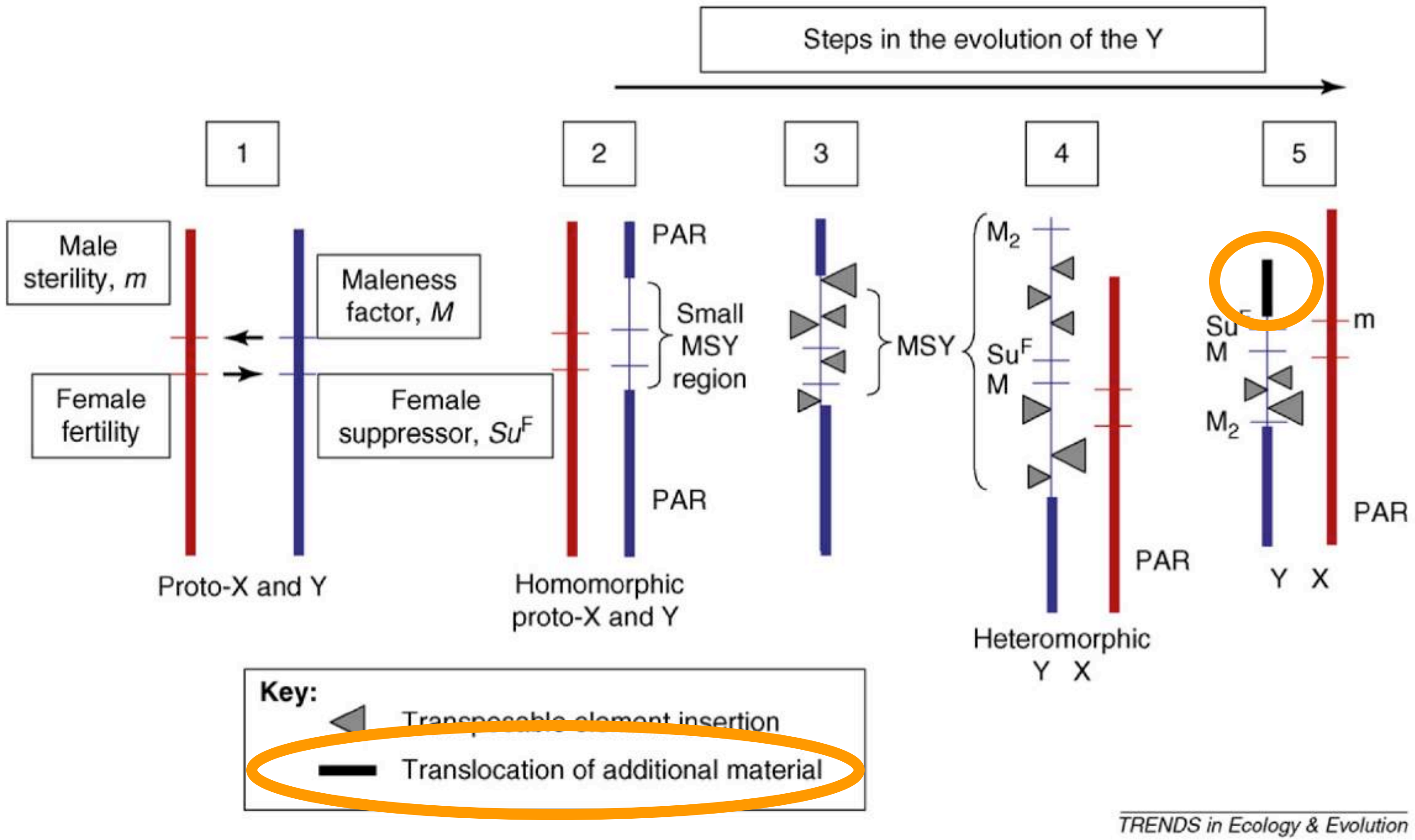
No sign for dose-compensation in snakes





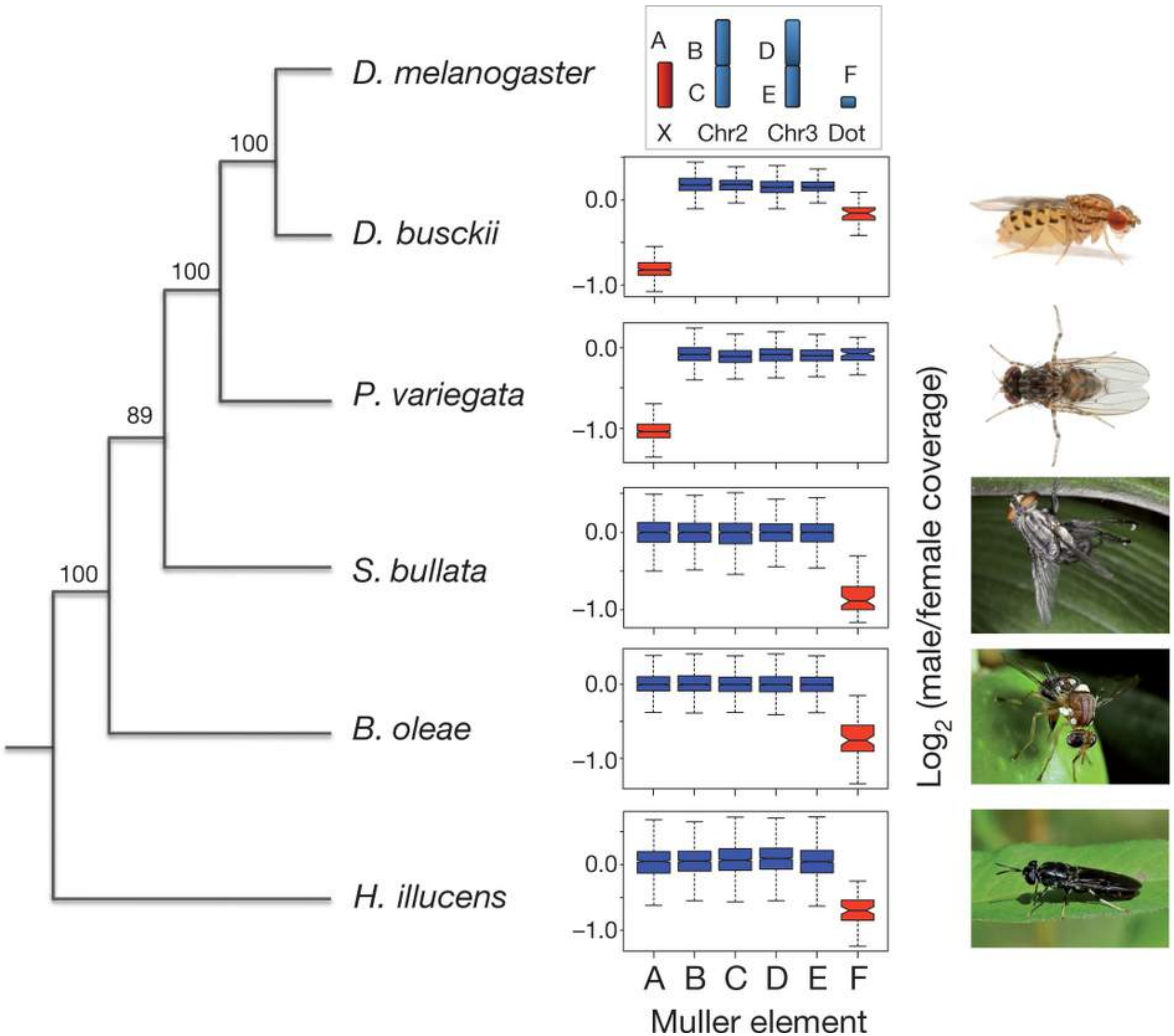
(Vicoso et al. (2013) *PLOS Bio*)

Sex chromosome evolution – II.



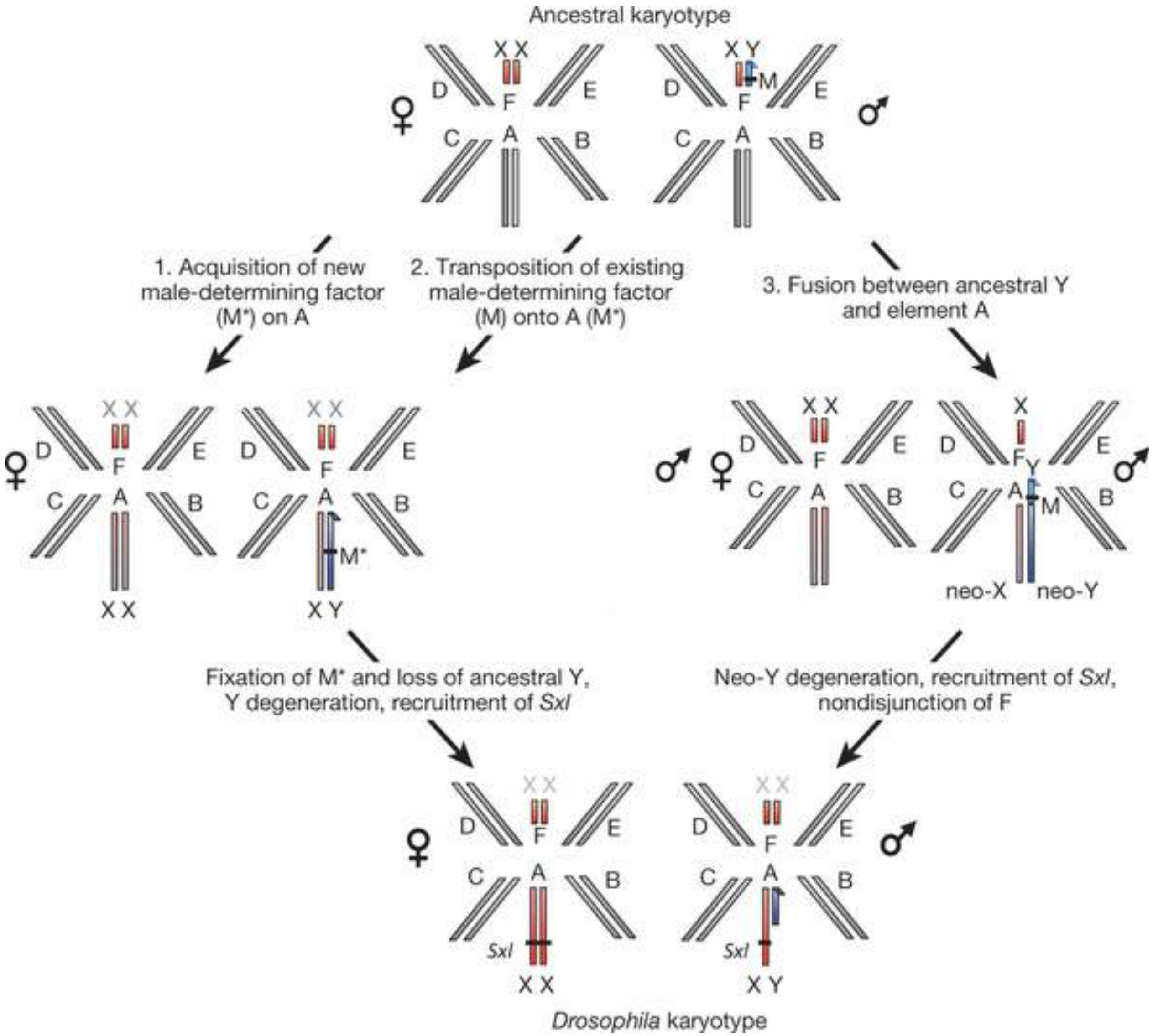
(Bergereo and Charlesworth (2009) *Trends in Ecol and Evol*)

Sex chromosome evolution in Diptera



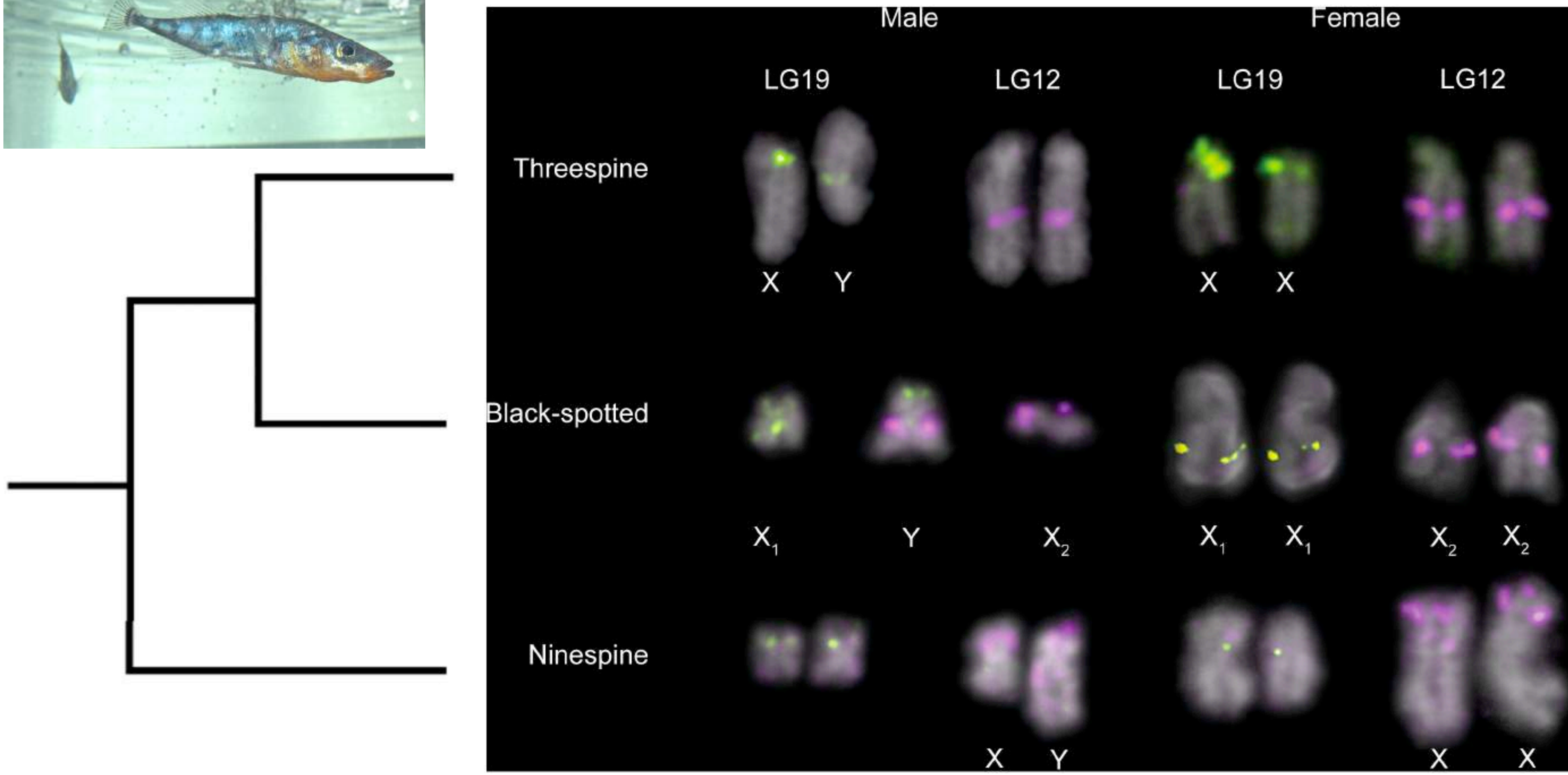
(Vicoso and Bachtrog (2013) *Nature*)

Sex chromosome evolution in Diptera



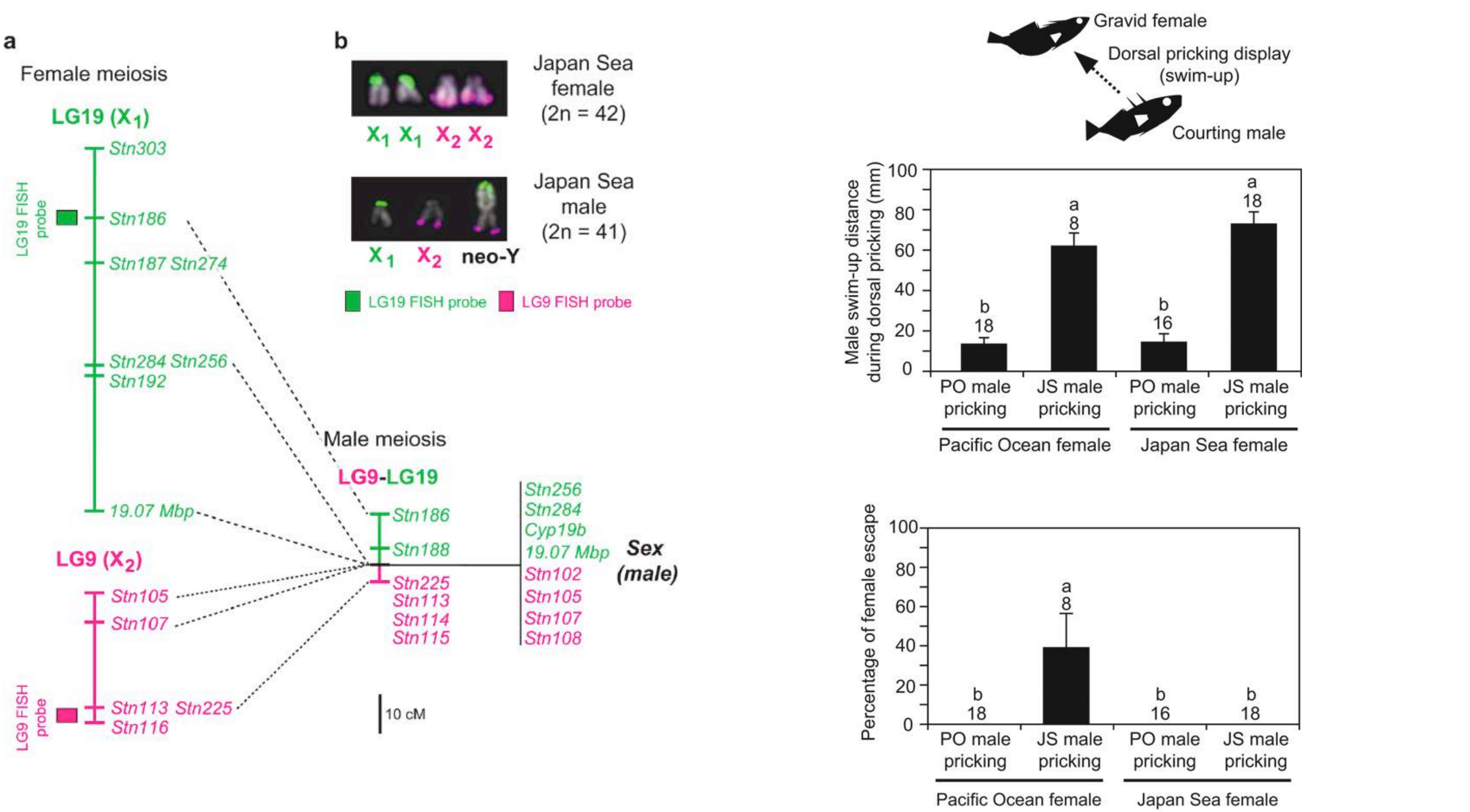
(Vicoso and Bachtrog (2013) *Nature*)

Sex chromosome evolution in sticklebacks



(Ross et al. (2009) *PLoS Genetics*)

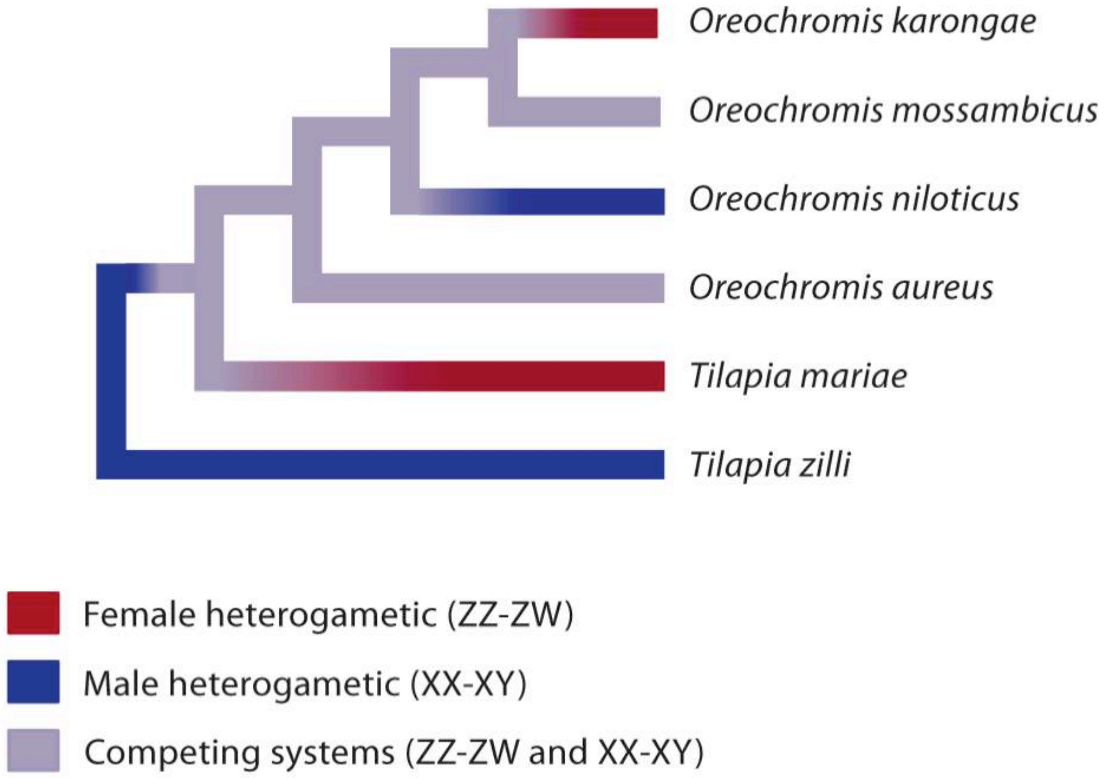
The evolution of a neo-sex chromosome can form the base of reproductive isolation



The length of the dorsal spine and the aggressive courting behaviour are both encoded on LG9.

(Kitano et al., 2009 *Nature*)

The fast evolution of sex-determination systems in cichlids



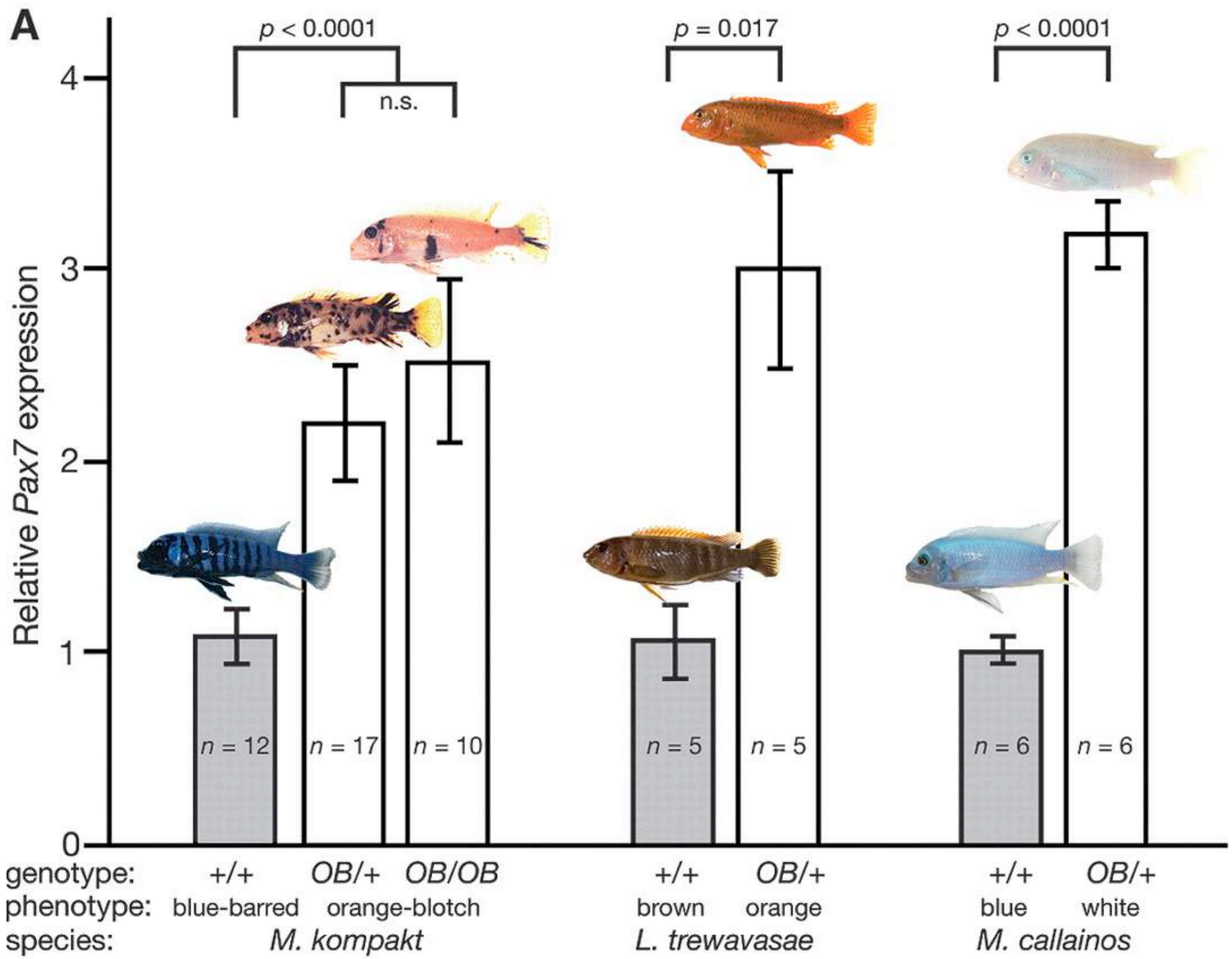
(Mankd and Avise (2009) *Sex Dev*)

The OB phenotype: how can sex chromosome evolution resolve a sexual conflict

- The “orange blotch” phenotype is advantageous for females, increases their survival, but is disadvantageous for males as it destroys their trademark nuptial colors.

(Roberts et al. (2009) *Science*)

The OB phenotype is the result of a regulatory mutation in the *pax7* gene



(Roberts et al. (2009) *Science*)

The OB allele and the gene responsible for sex determination are inherited together

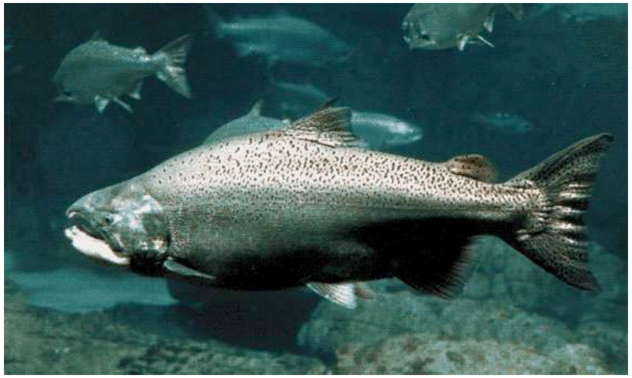
- Theory suggests that the genetic conflict arising from antagonistic seection can be resolved by the sex-linked inheritance of the allele.

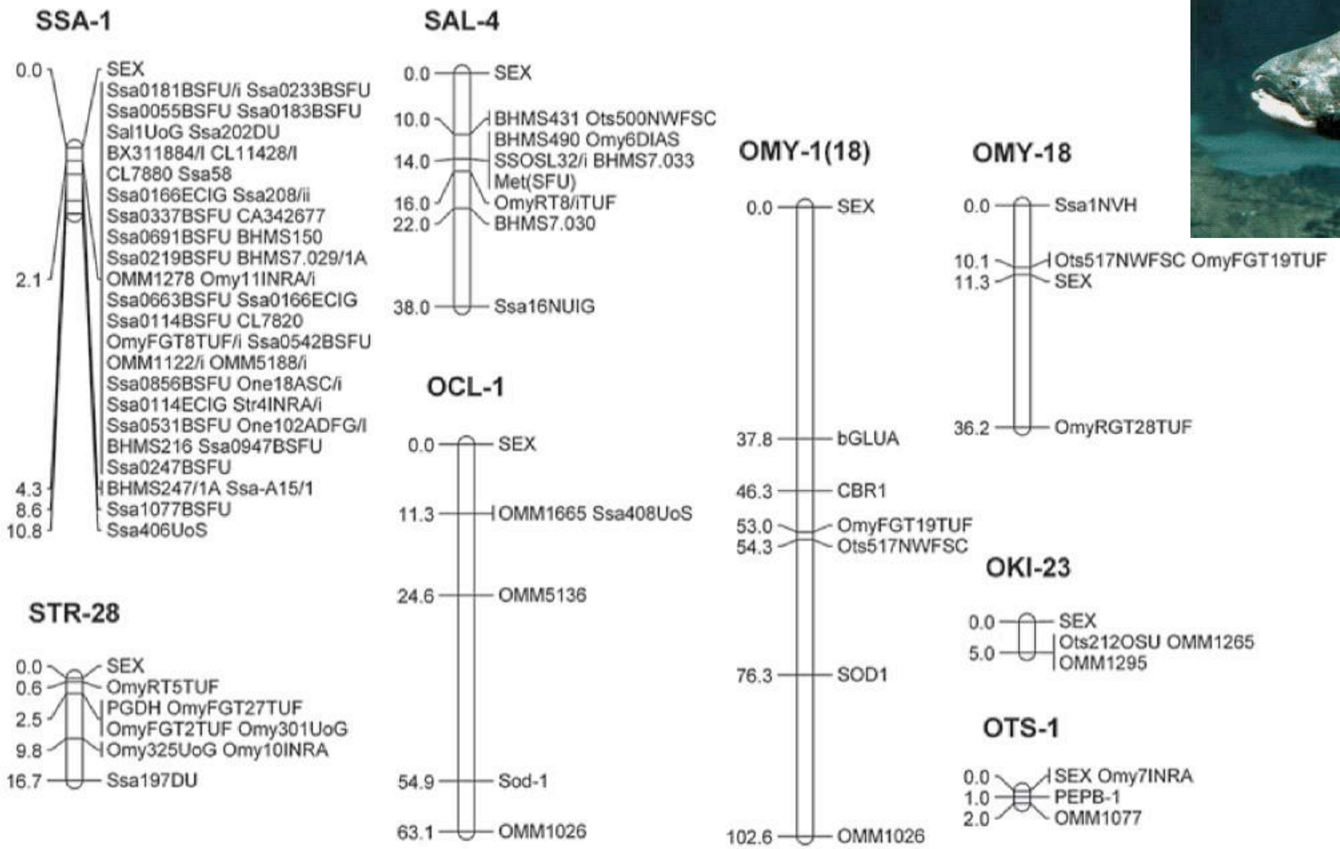
This is what is happening:

- The OB allele is linked with the sex-determination factor (W) and both of them are in LG5
- There are very few OB males: in fact these are genetically females (they do have the W factor), just due to environmental stimuli they develop as males.

(Roberts et al. (2009) *Science*)

Salmonids represent an extreme case in the evolution of the sex-determination systems.

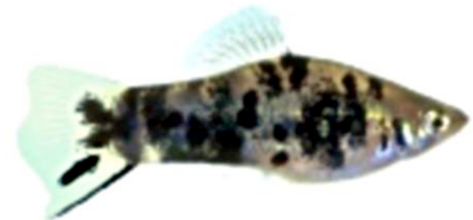


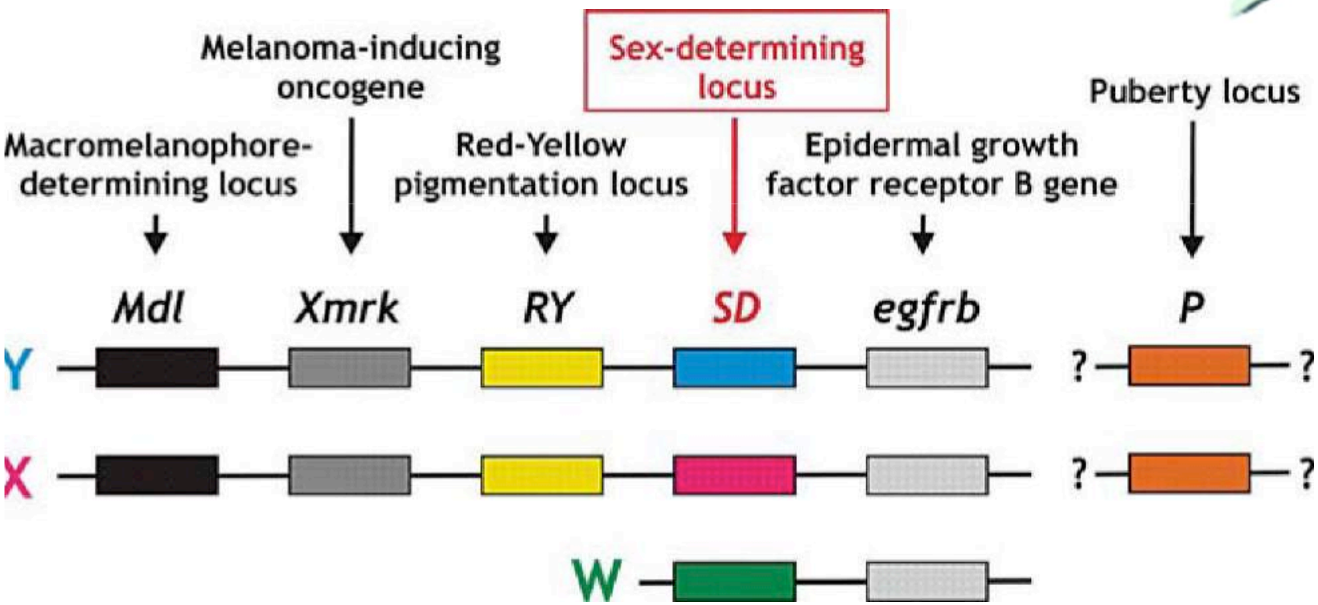


- Genetic markers close to the *SEX* locus are similar in different species => most likely there is a small genomic region associated with sex-determination which can translocate to other chromosomes.

The curious case of the Xiphos (*Xiphophorus maculatus*): XYW system!

Female genotypes: XX, XW, YW
Male genotypes: XY, YY



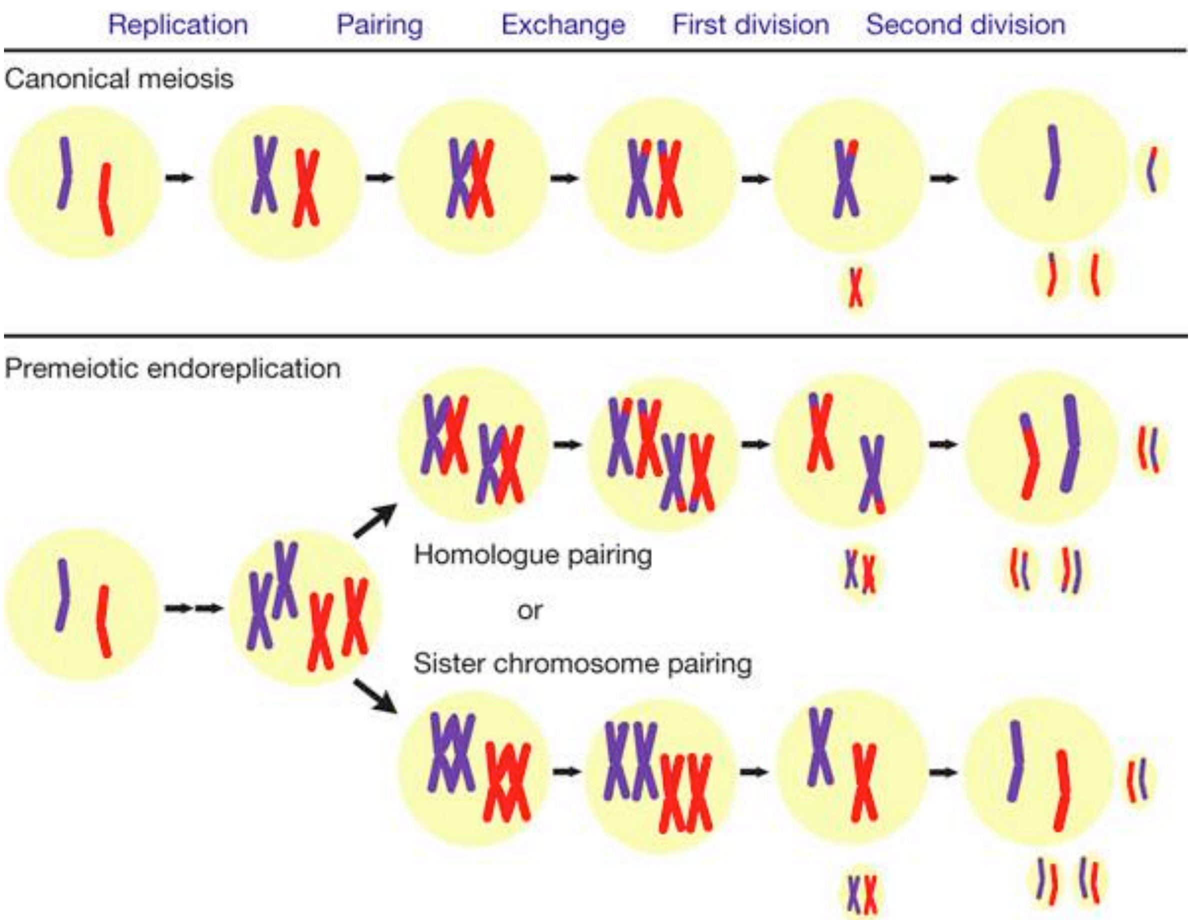


Possible explanations:

1. SD = male sex-determination factor, with only the Y allele being active. X is inactive and W is a specific supressor of SD^{Y}.
2. Dosage effect: Y chromosome has two copies of the gene, X has one and W has none.

A hybrid tegu species and how heterozygosity can be maintained in a parthenogenetic species

Generally, in parthenogenetic species the amount of heterozygosity decreases over time.



The tegu's example shows that this can be avoided, with the special segregation of sister chromosomes.

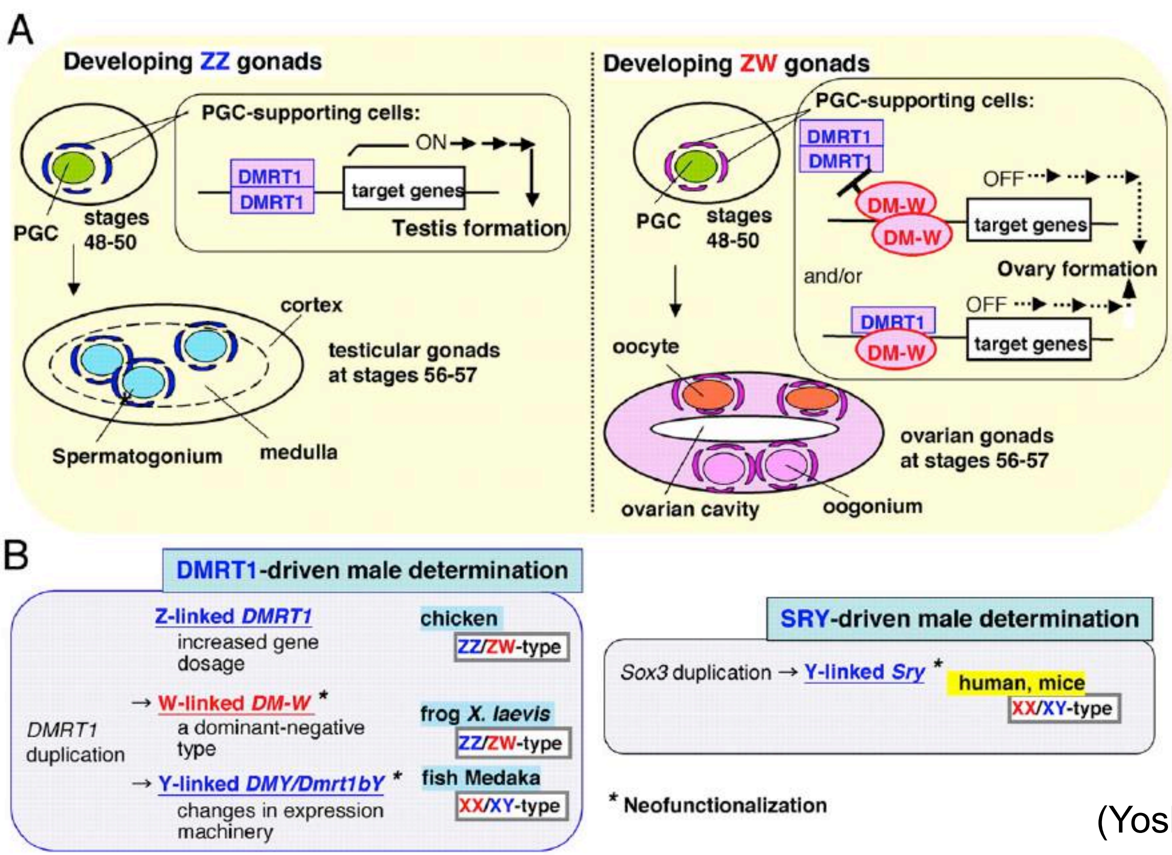
(Lutes et al. (2010) *Nature*)

Further literature

Matt Ridley: The Advantage of Sex
http://www.pbs.org/wgbh/evolution/sex/advantage/
Current Biology - Biology of Sex Special Issue
http://www.cell.com/current-biology/issue?pii=S0960-9822%2806%29X0354-8
Nature Scitable - Chromosomes and Cytogenetics
http://www.nature.com/scitable/topic/chromosomes-and-cytogenetics-7
Strachan and Read: Human Molecular Genetics 2
http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hmg&part=A1680
Gilbert: Developmental Biology (9th Edition) - Chapter 14: Sex Determination
http://9e.devbio.com/chapter.php?ch=14

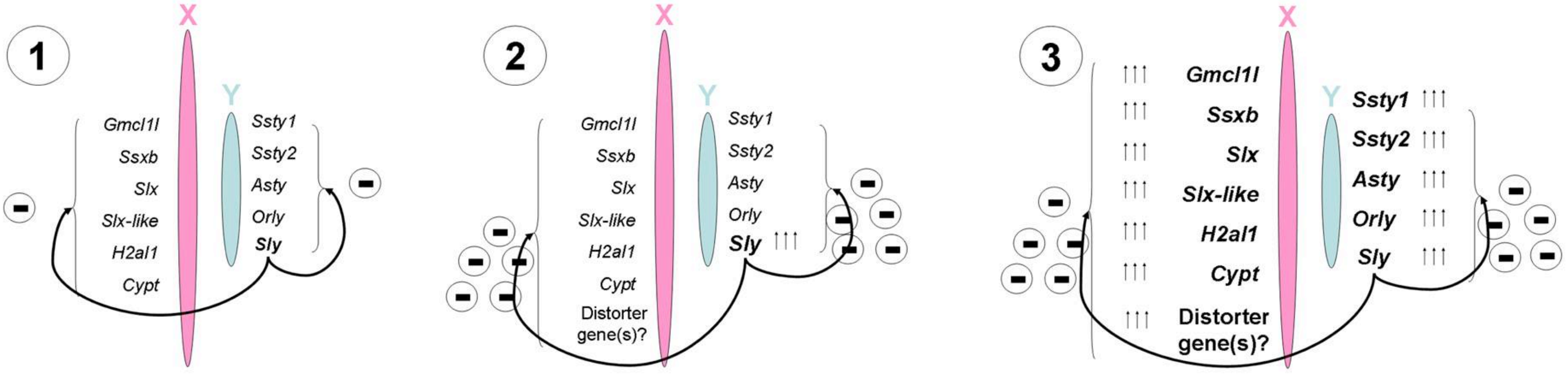
A *Xenopus laevis* ZW rendszere

- nem dózis függő
- a W-n található, *DM-W* szex-determinációs gén határozza meg a nemet
- a *DM-W* a *DMRT1* domináns negatív formájaként működik



(Yoshimoto et al. (2010) *Development*)

Sly alapú meiotikus szex kromoszóma inaktiváció és ezt kompenzáló gén duplikáció egérben



- az Y kromoszómán kódolt Sly fehérje a szex kromoszómákhoz kötődik és ez szerepet játszik az inkativációjukban

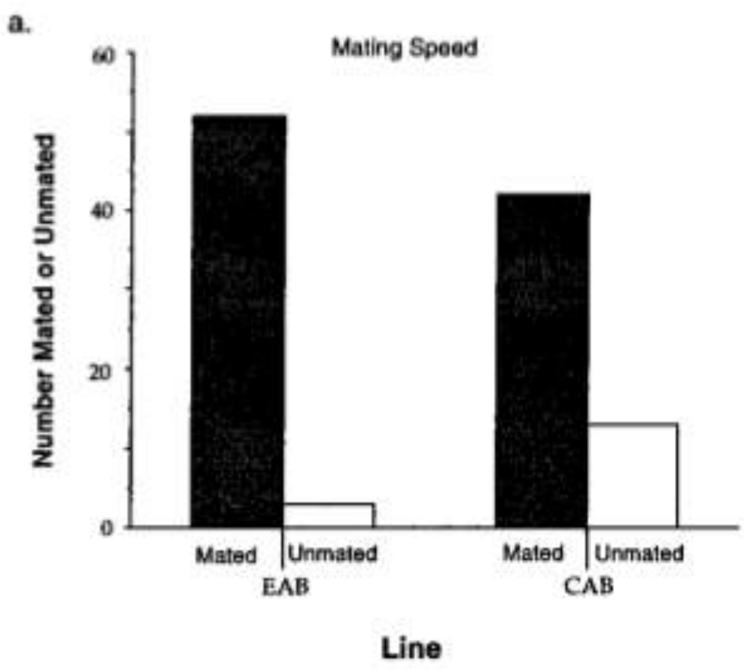
- a here specifikus gének ezért duplikáción mentek át, hogy meg tudják tartani (össz)expressziós szintjüket

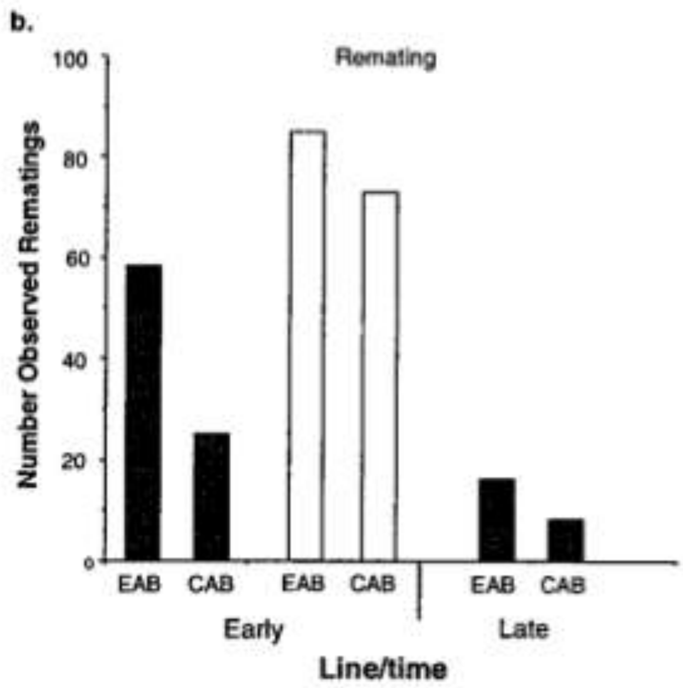
(Cocquet et al. (2010) *PLoS Bio*)

A nemek közti evolúciós verseny is magyarázza a kromoszómák összetételét

-William Rice kísérlete (1996, 1998): *Drosophilá*ban olyan rekombináció mentes rendszert hozott létre, ahol a teljes genetikai állomány Y kromoszómaként működött (egy külső pool-ból biztosította a nőstényeket)

-Kb 35 generáció után jelentős fitness előny alakult ki ezekben a hímekben a kontroll hímekhez képest

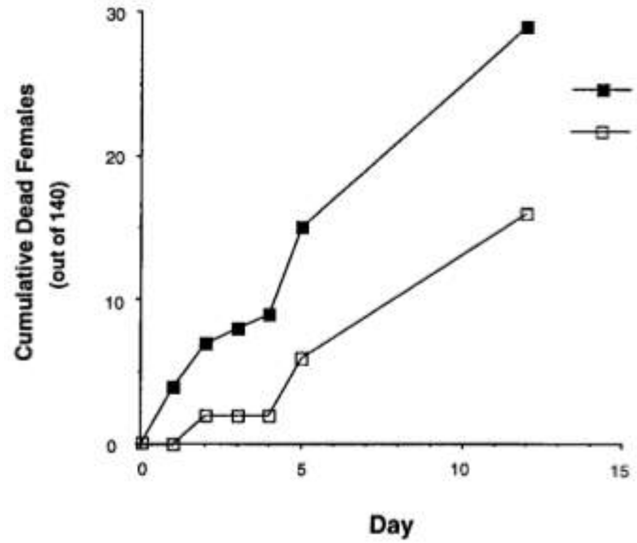


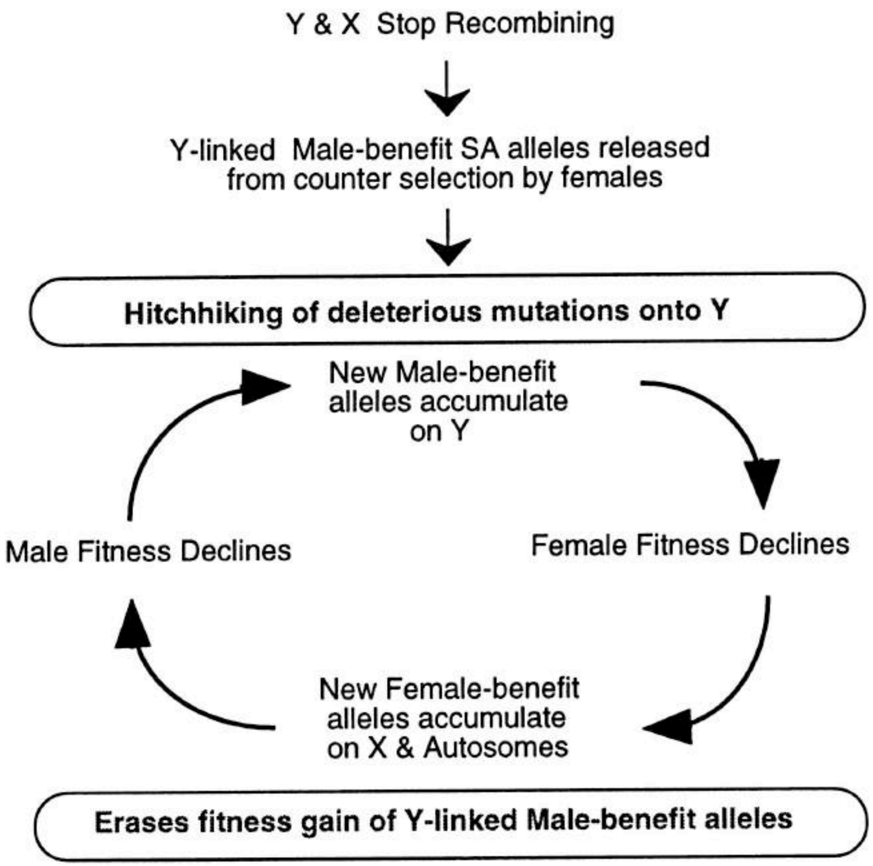


(Rice (1998) *PNAS*)

A nemek közti evolúciós verseny is magyarázza a kromoszómák összetételét

-ennek az ára azonban a nőstény fitness csökkenése volt





(Rice (1998) *PNAS*)