Inativação do cromossomo X

Espécies dioicas = apresentam indivíduos de dois sexos (macho e fêmea)

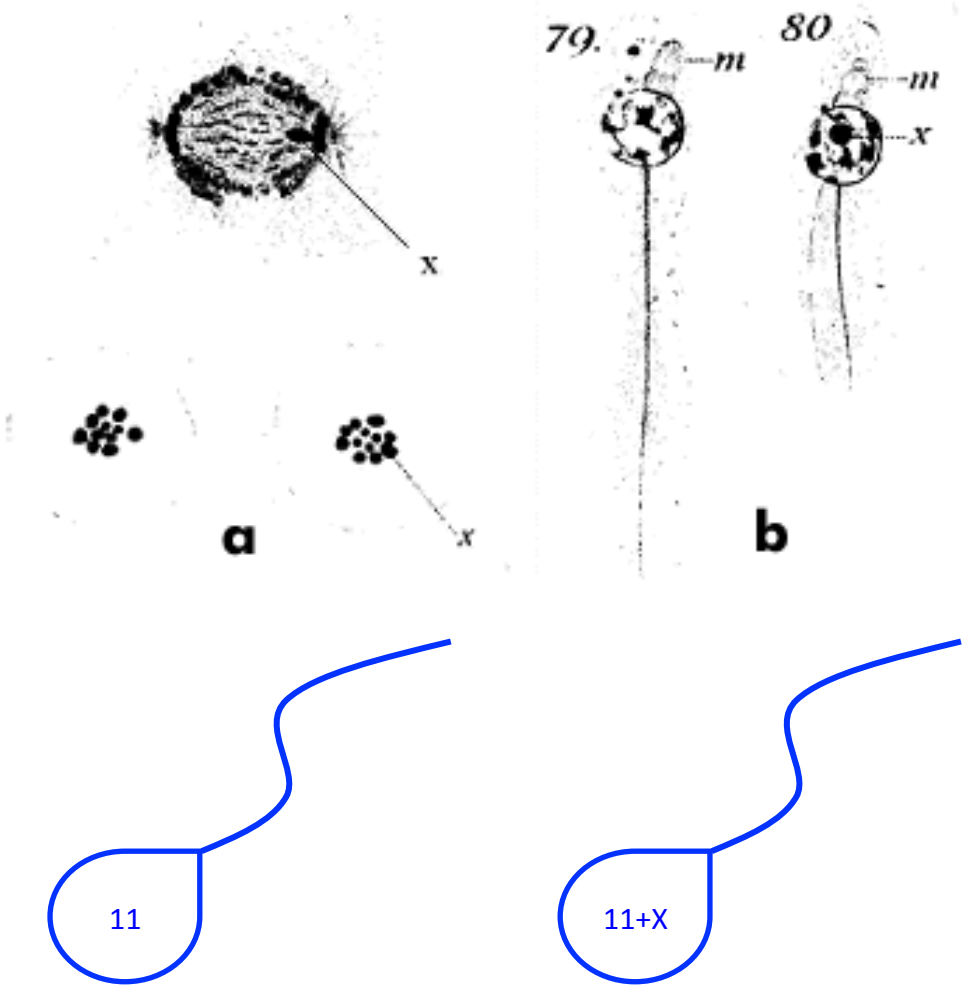
Dimorfismo sexual:

- Morfologia, anatomia, fisiologia

- Comportamento

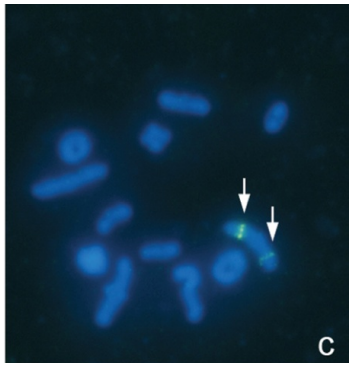
- Genética ???

Henking (1891): The X element



♂

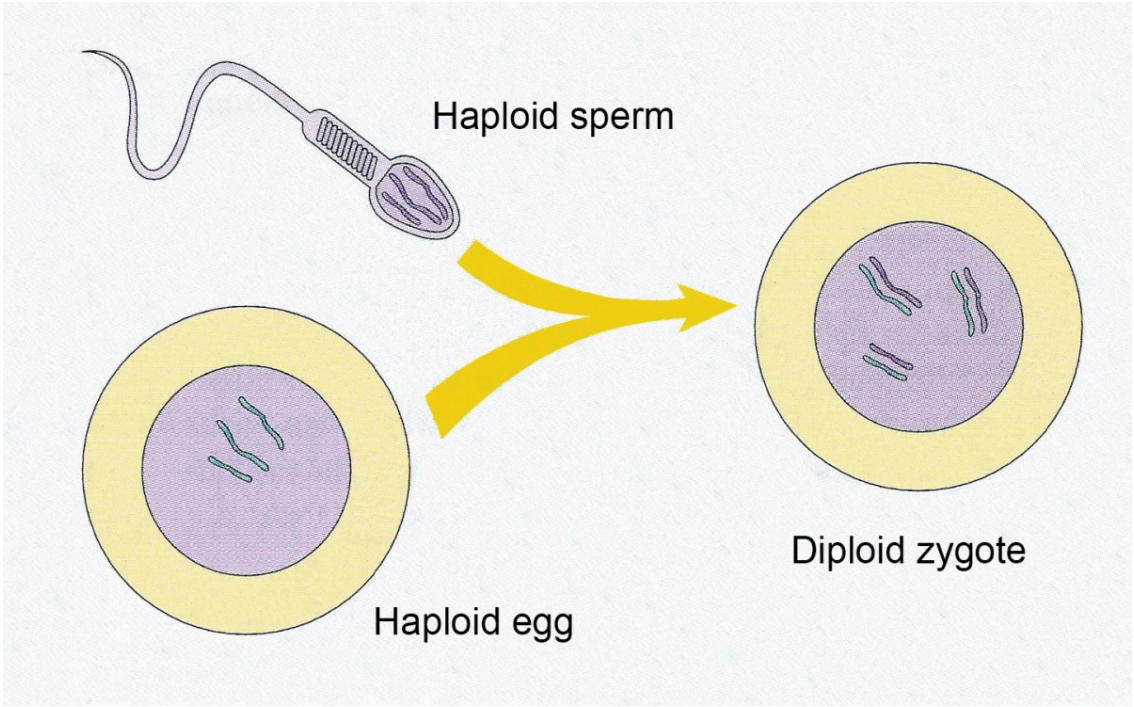
Pyrrhocoris apterus

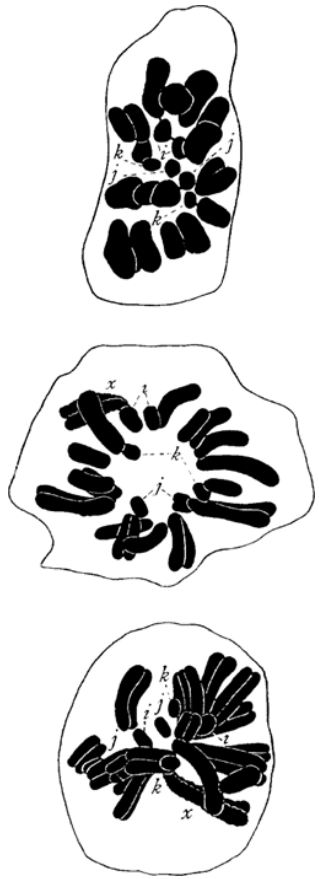


Reproduzido de [1]

"[…] That is, spermatozoa are of two kinds: one with the nucleolus [the X element] and one without."

Sutton (1902)

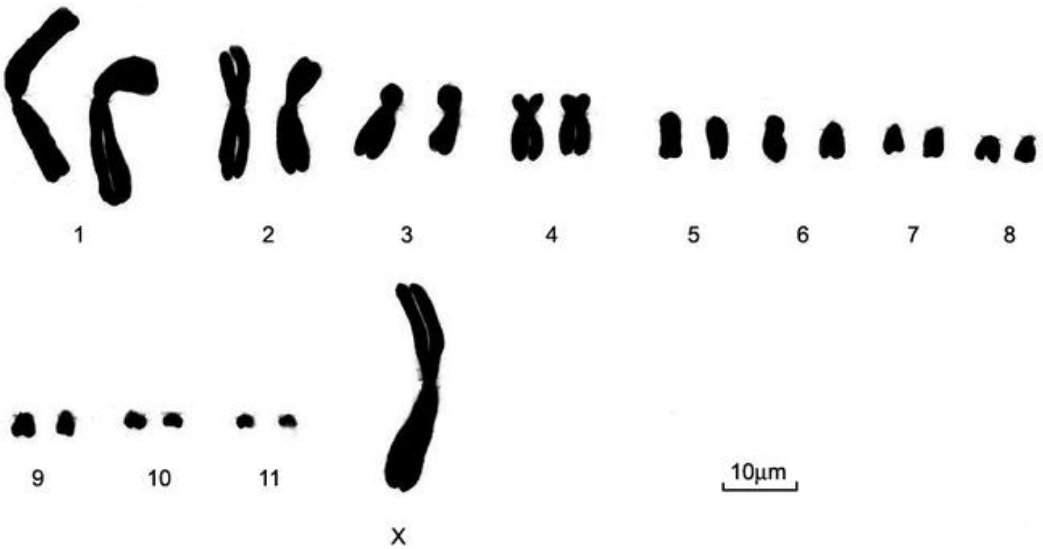




Sistema X0

♀ homogaméticas = produzem dois gametas iguais em relação ao cromossomo sexual = A +X e A+X

♂ heterogaméticos = produzem dois gametas diferentes em relação ao cromossomo sexual = A+X e A+0



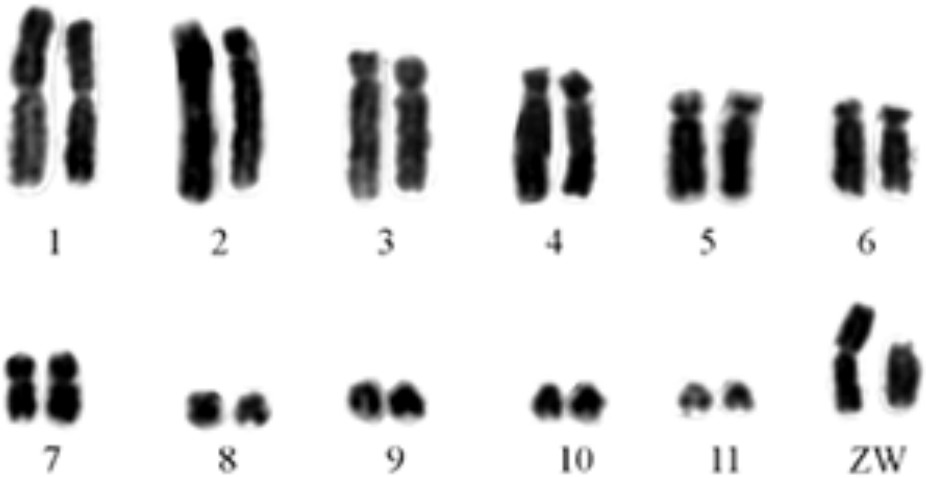
Reproduzido de [2]

Cariótipo do *Callimenus macrogaster*: 22+XX ou 22+X0

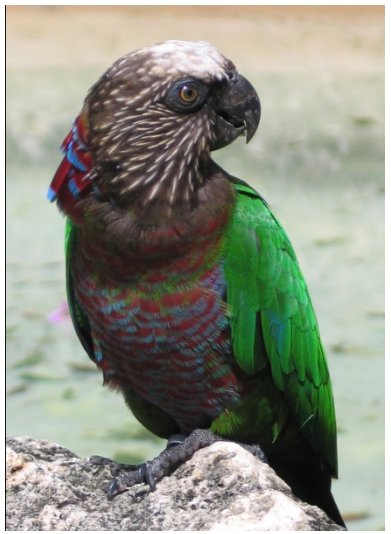
Sistema ZW

♀ heterogaméticas = produzem dois gametas diferentes em relação ao cromossomo sexual = A+Z e A+W

♂ homogaméticos = produzem dois gametas iguais em relação ao cromossomo sexual = A+Z e A+Z



Reproduzido de [3]

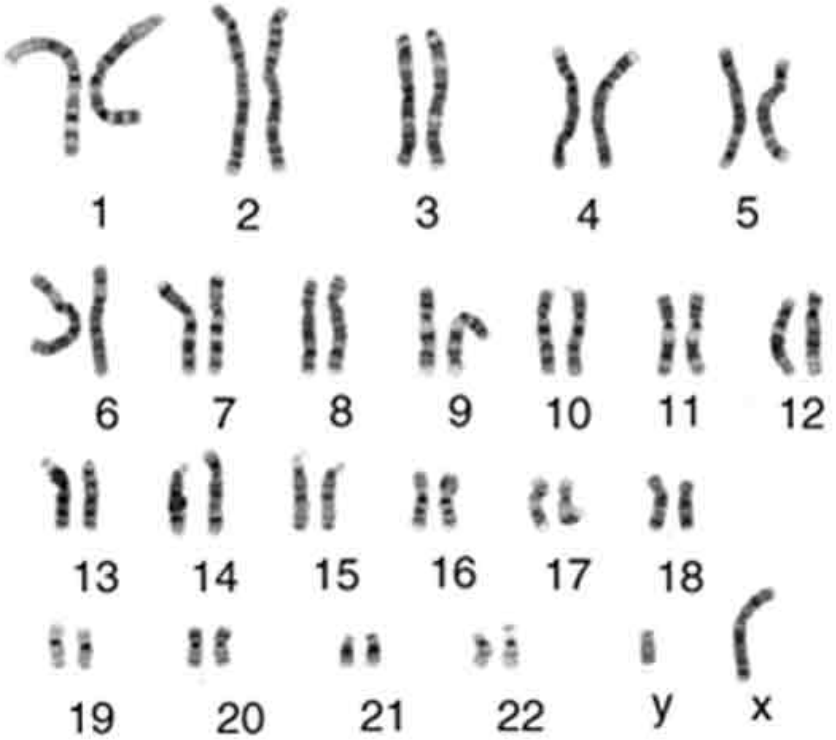


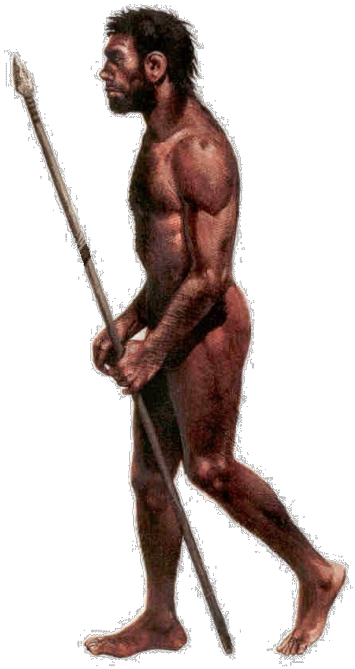
Cariótipo de *Deroptyus accipitrinus*: 22+ZW ou 22+ZZ

Sistema XY

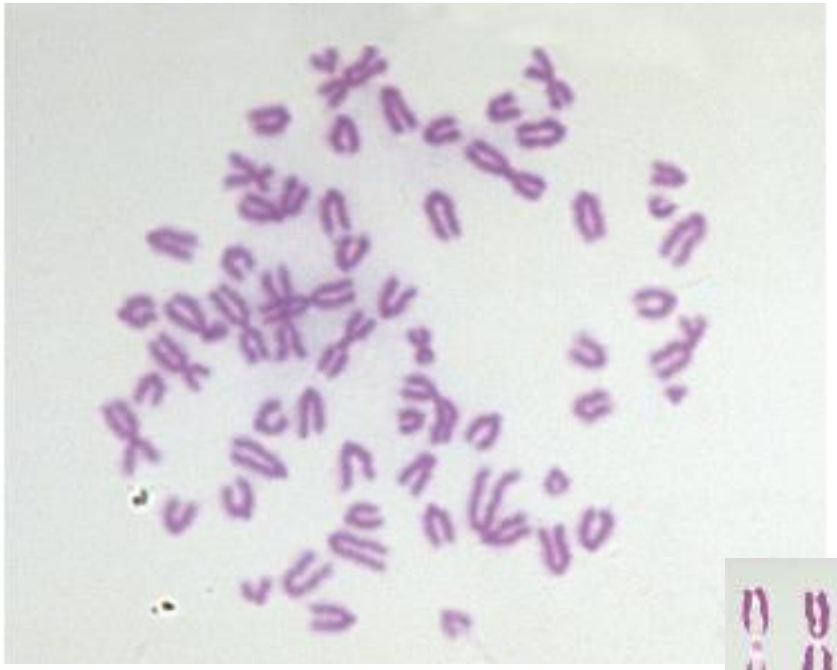
♀ homogaméticas = produzem dois gametas iguais em relação ao cromossomo sexual = A+X e A+X

♂ heterogaméticos = produzem dois gametas diferentes em relação ao cromossomo sexual = A+X e A+Y

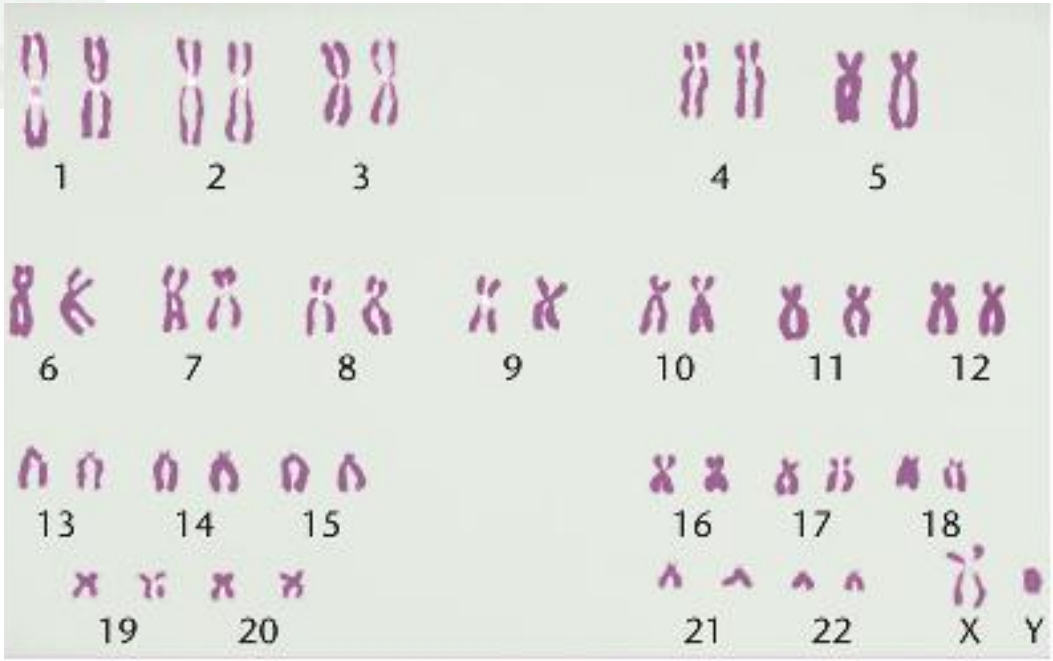




Cariótipo humano (*Homo sapiens*):
44+XX ou 44+XY



Citogenética a partir de células metafásicas



Reproduzido de [4]

E nas células interfásicas?

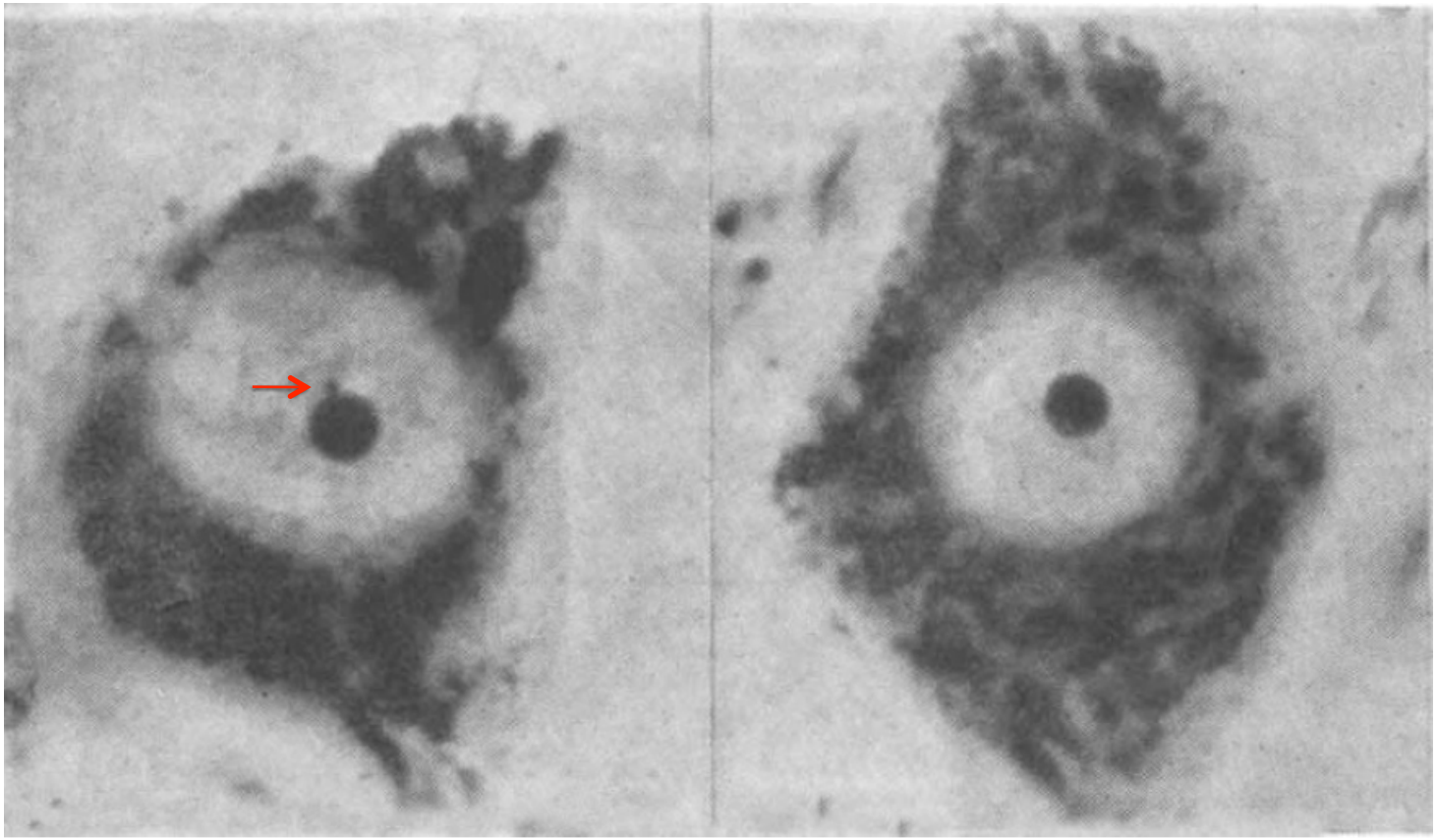


Fig. 1 Fig. 2

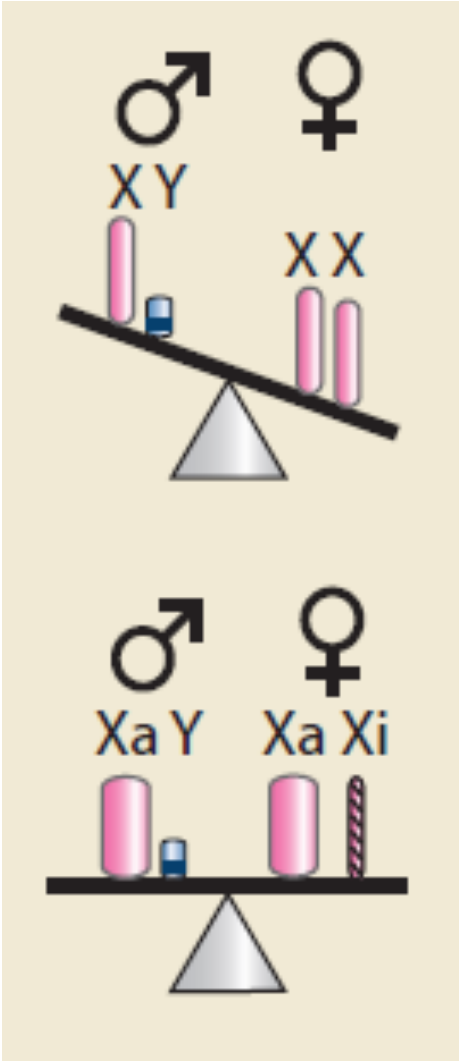
Presença de "satélite nucleolar" no núcleo do neurônio do hipoglosso de uma gata fêmea (Fig. 1) *vs*. ausência desta estrutura nas células do macho (Fig. 2)

Barr e Bertram (1949)

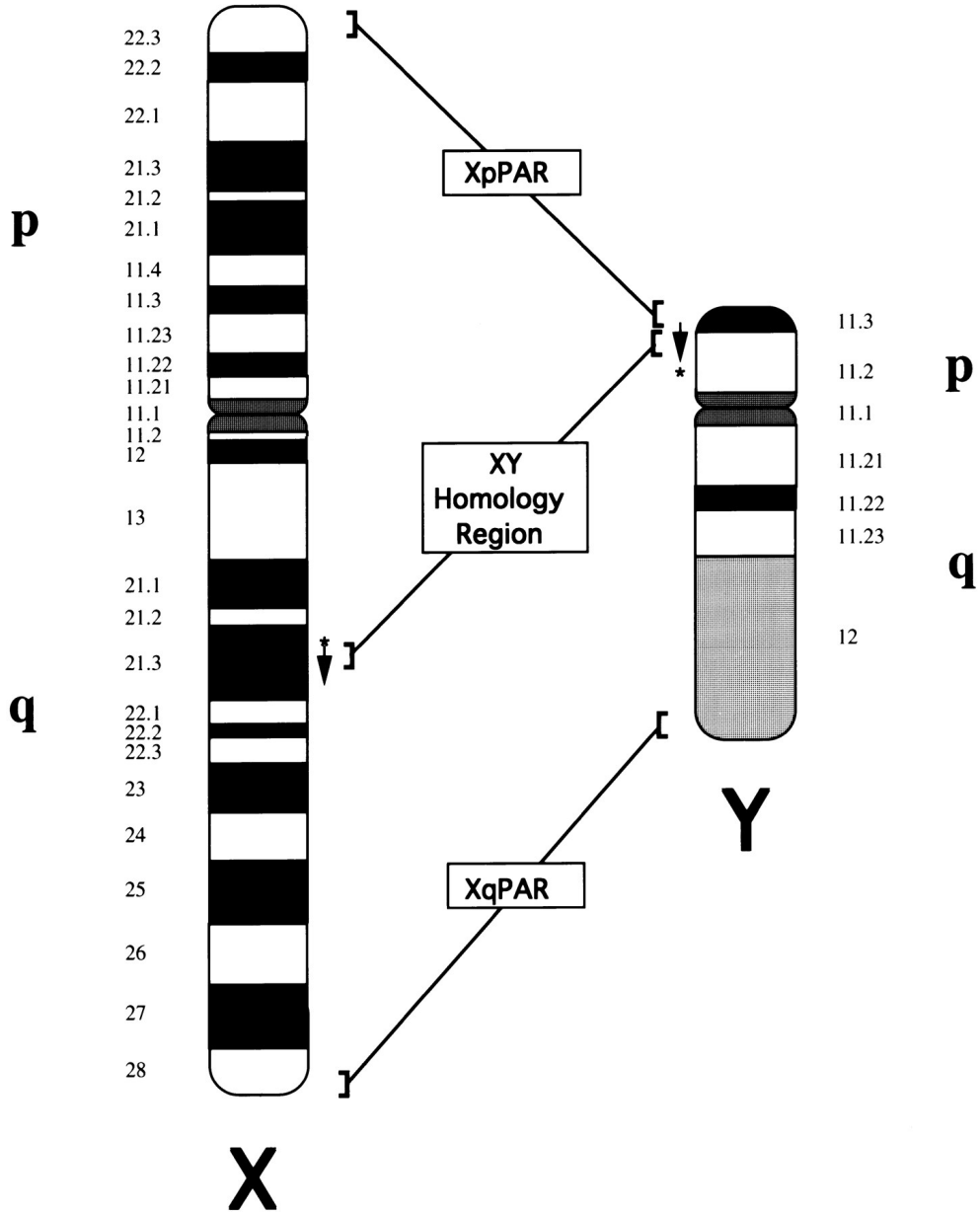
Mas por que um dos cromossomos X das fêmeas é heterocromático, ou seja, transcricionalmente inativo ?

(1961, 1962)

Mecanismo de compensação de dose



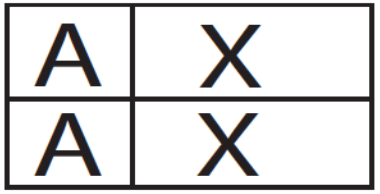
Payer e Lee (2008)



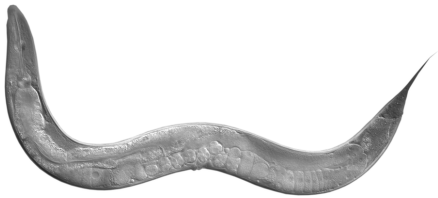
Reproduzido de [6]

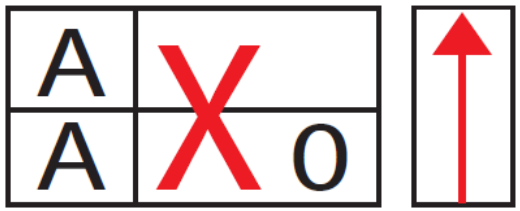
Outros mecanismos de compensação de dose: *Drosophila* e *C. elegans*

macho



fêmea





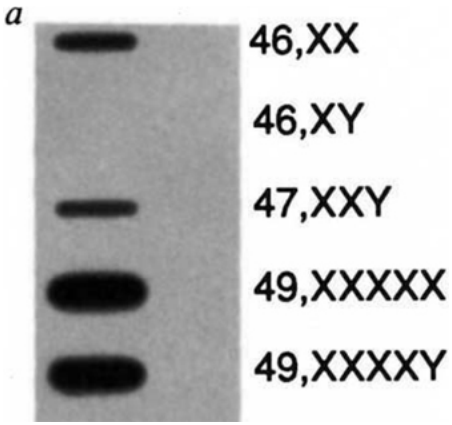
macho

hermafrodita

Prestel *et al*. 2010

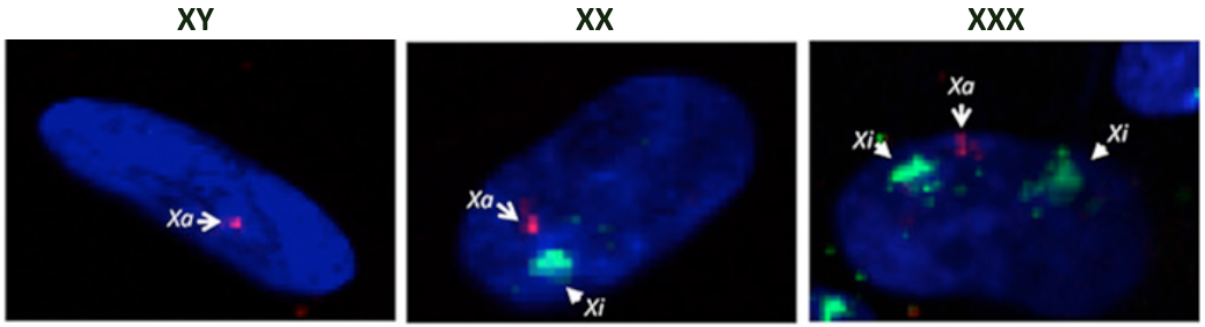
Inativação do cromossomo X em mamíferos

Mecanismos de inativação do cromossomo X: contagem



Brown *et al*. (1991)

nº de X inativos por célula: nº total de X – 1



Modificado de [5]

Mecanismos de inativação do

cromossomo X: escolha

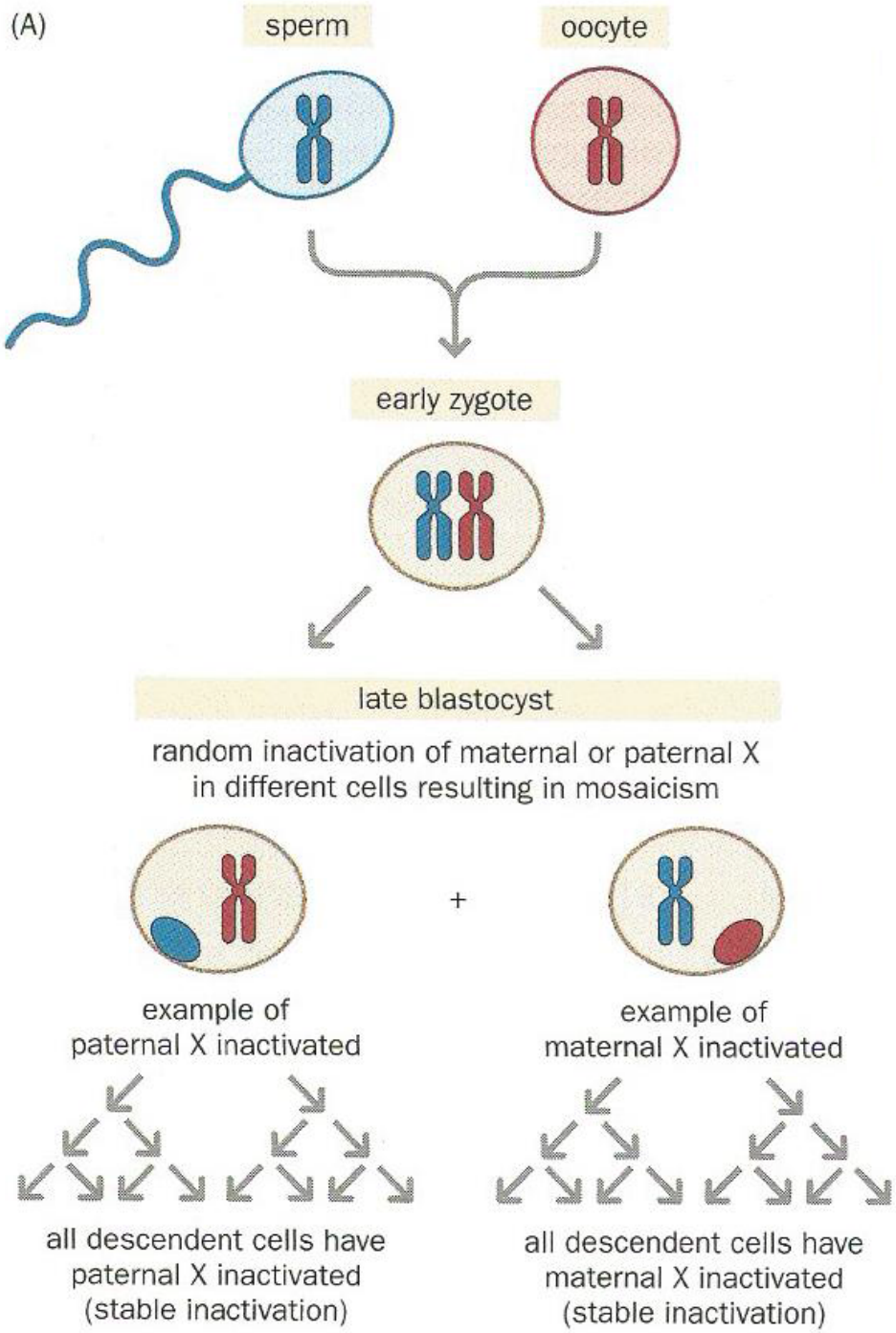
A inativação do X ocorre bem no início

do desenvolvimento embrionário e

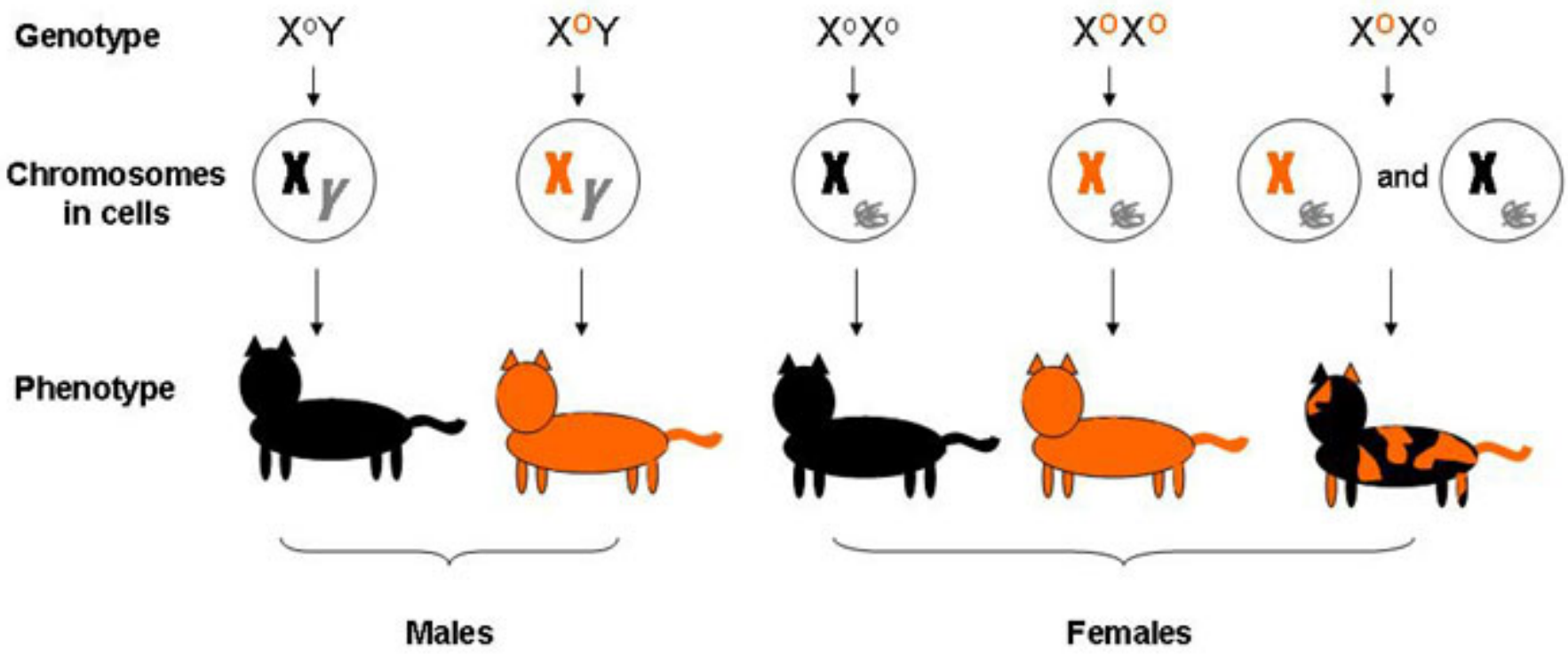
propaga-se de forma clonal: uma vez

determinado o X a ser inativado, as

células filhas seguirão o mesmo padrão



Reproduzido de Strachan e Read (2011)



Gatas com pelagem malhada: **mosaico**

Moisacismo somatico

in a mosaic pregnancy might be found only in extraembryonic tissue and not in the embryo proper (**confined placental mosaicism**; see Chapter 17), might be present in some tissues of the embryo but not in the gametes (pure **somatic mosaicism**), might be restricted to the gamete lineage only and nowhere else (pure **germline mosaicism**), or might be present in both somatic lineages and the germline—all depending on whether the mutation occurred before or after the separation of the inner cell mass, the germline cells, and the somatic cells during embryogenesis (see Chapter 17). Because there are approximately 30 mitotic divisions in the cells of the germline before meiosis in the female and several hundred in the male (see Chapter 2), there is ample opportunity for mutations to occur in germline cells

tal NF1 could be at risk for having an affected child, whose phenotype would be typical for NF1, that is, *not* segmental. Whether the patient is at risk for transmitting the defect will depend on whether the mutation occurred before separation of germline cells from the somatic cell line that carries the mutation.

Germline Mosaicism

In pedigrees with germline mosaicism, unaffected individuals with no evidence of a disease-causing mutation in their genome (as evidenced by the failure to find the mutation in DNA extracted from their peripheral white blood cells) may still be at risk for having more than one child who inherited the mutation from them

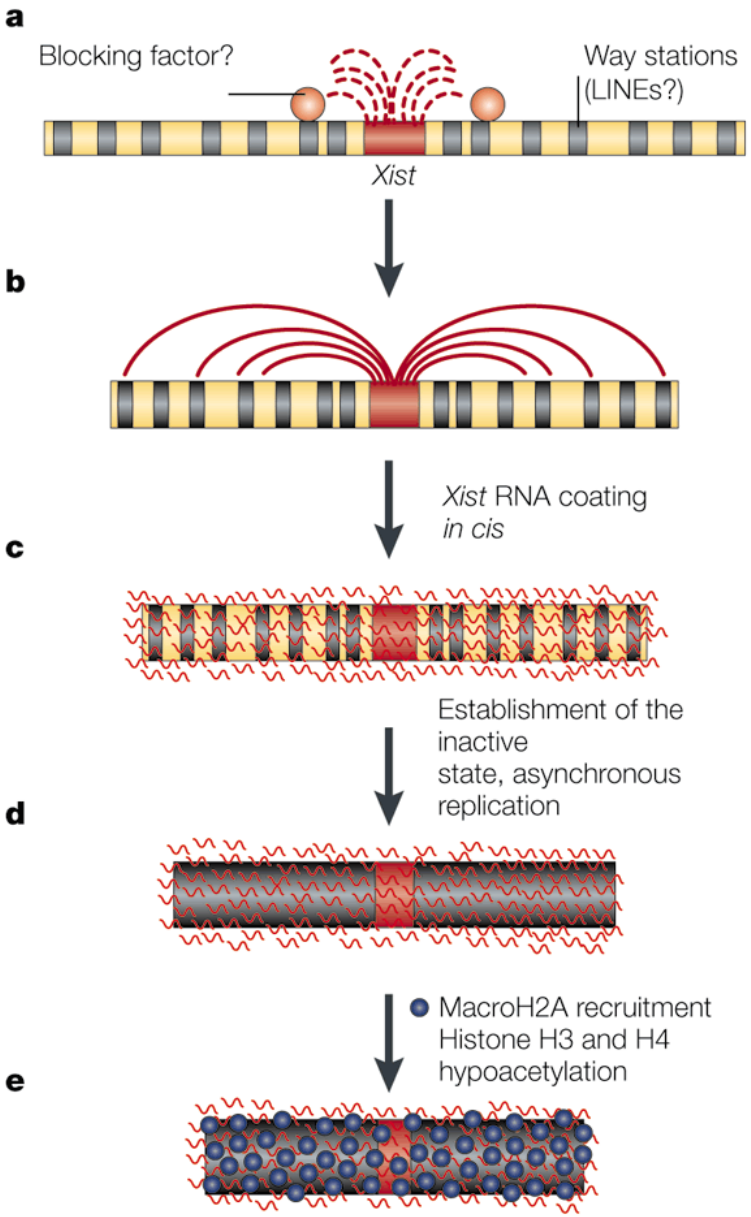
Moisacismo germinativo

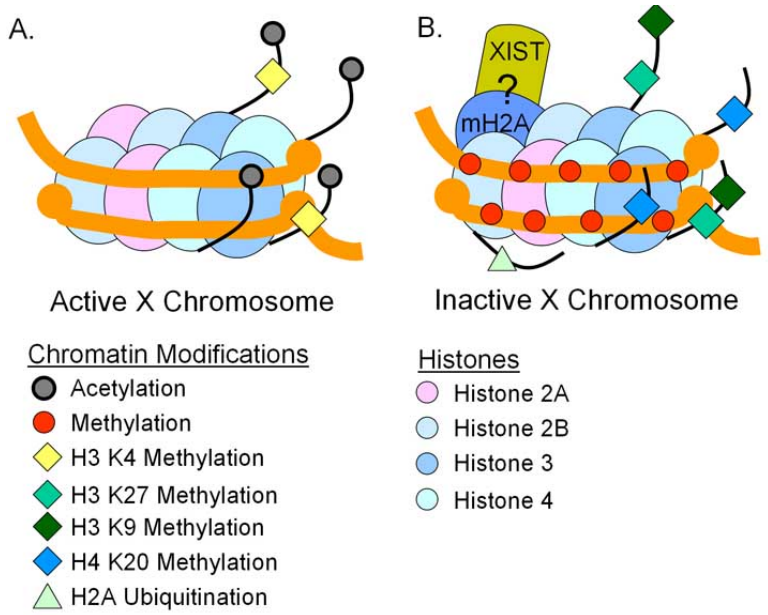
abnormality determines whether there is expression of the disorder in a child. This is very different from sex-limited inheritance (described earlier in this chapter), in which expression of the disease depends on the sex of the child who *inherits* the abnormality.

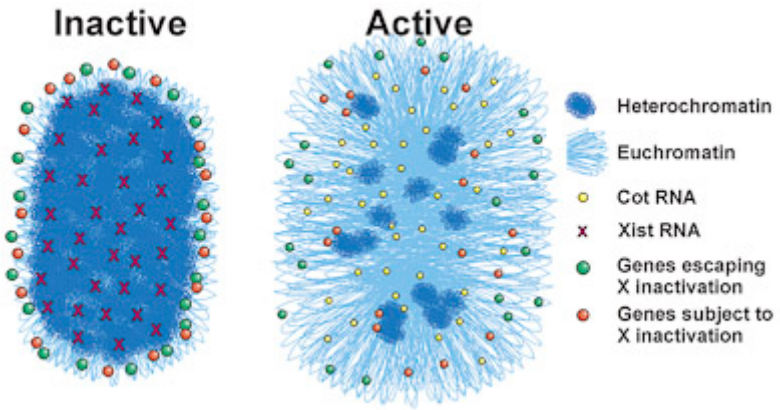
Imprinting can cause unusual inheritance patterns in pedigrees, in that a disorder can appear to be inherited in a dominant manner when transmitted from one parent, but not the other. For example, the **hereditary paragangliomas** (PGLs) are a group of autosomal dominant disorders in which multiple tumors develop in sympathetic and parasympathetic ganglia of the

nucleotides, such as CAG
therefore be CAGCAGC
CCG. In general, genes a
all have wild-type alleles t
there is a variable number
population, as we saw in
passed from generation
number of repeats can incr
far beyond the normal pc
abnormalities in gene expr
covery of this unusual grou
the orthodox notions of ge

Mecanismo(s) de inativação do cromossomo X

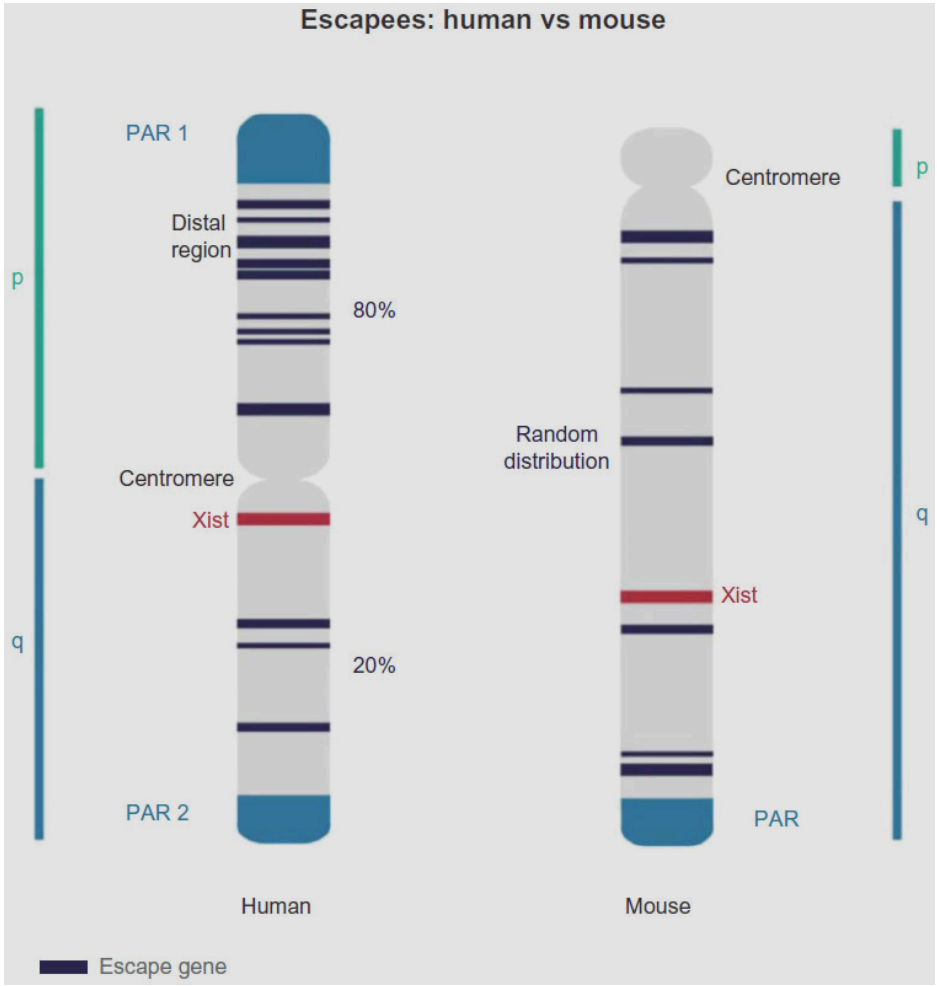






Genes que escapam à inativação do X

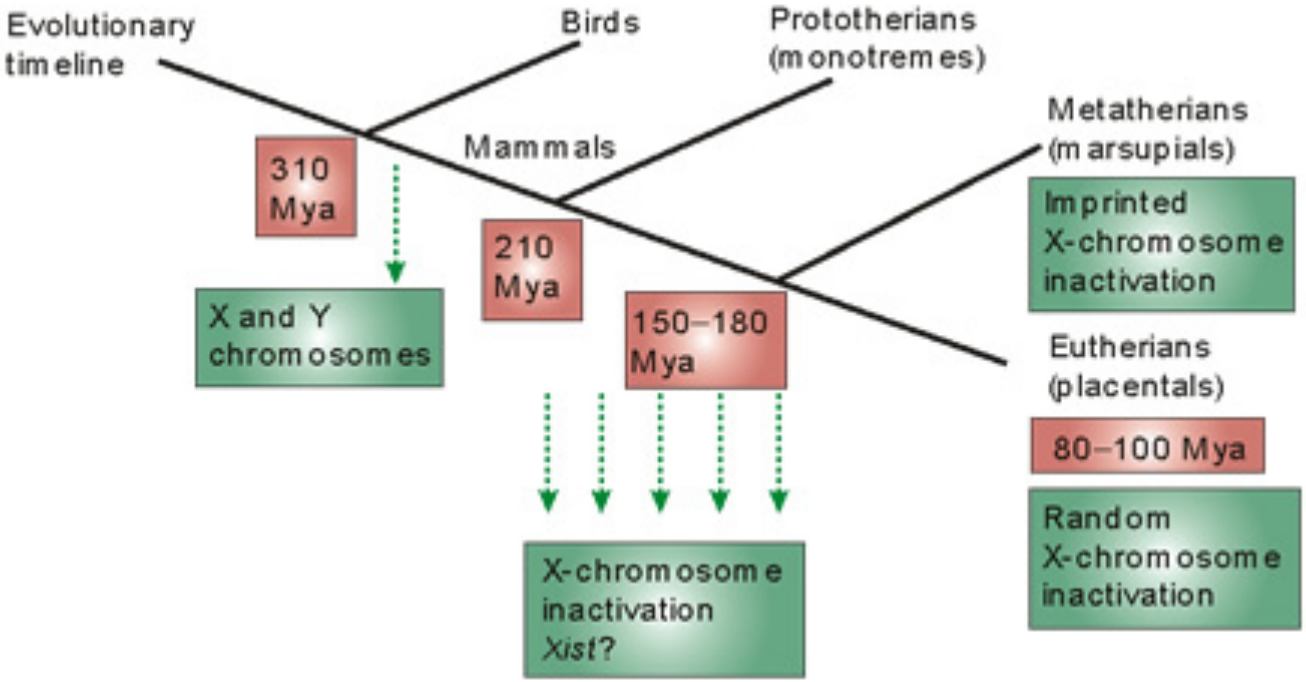
Por que camundongas 39,X são normais enquanto mulheres 45,X apresentam síndrome de Turner?



Cerca de 15% dos genes no cromossomo X escapam à inativação (e outros 10% exibem inativação variável) em humanos, enquanto em camundongos este número é de apenas 3%

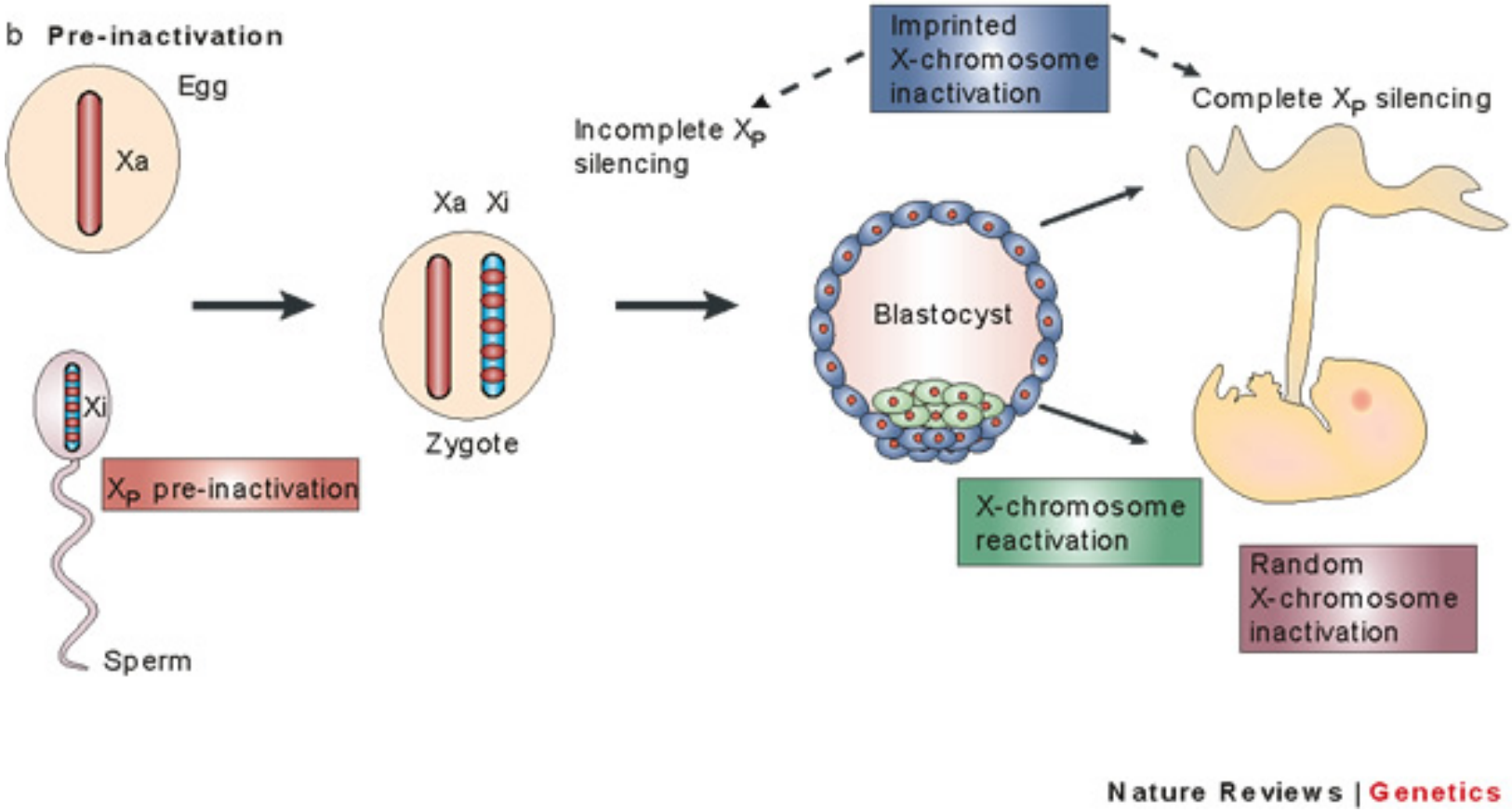
A inativação do cromossomo X ocorre de maneira aleatória?

Os cromossomos X provenientes do pai e da mãe têm igual probabilidade de serem inativados?



Huynh e Lee (2005)

Huynh e Lee (2005)



Inativação "imprintada" do X: marsupiais e tecidos murinos extra-embrionários

Inativação aleatória: vantagem adaptativa