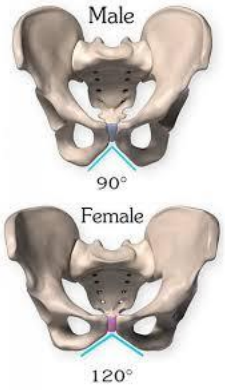
Sex determination

Lecture 6

SLE254 Genetics

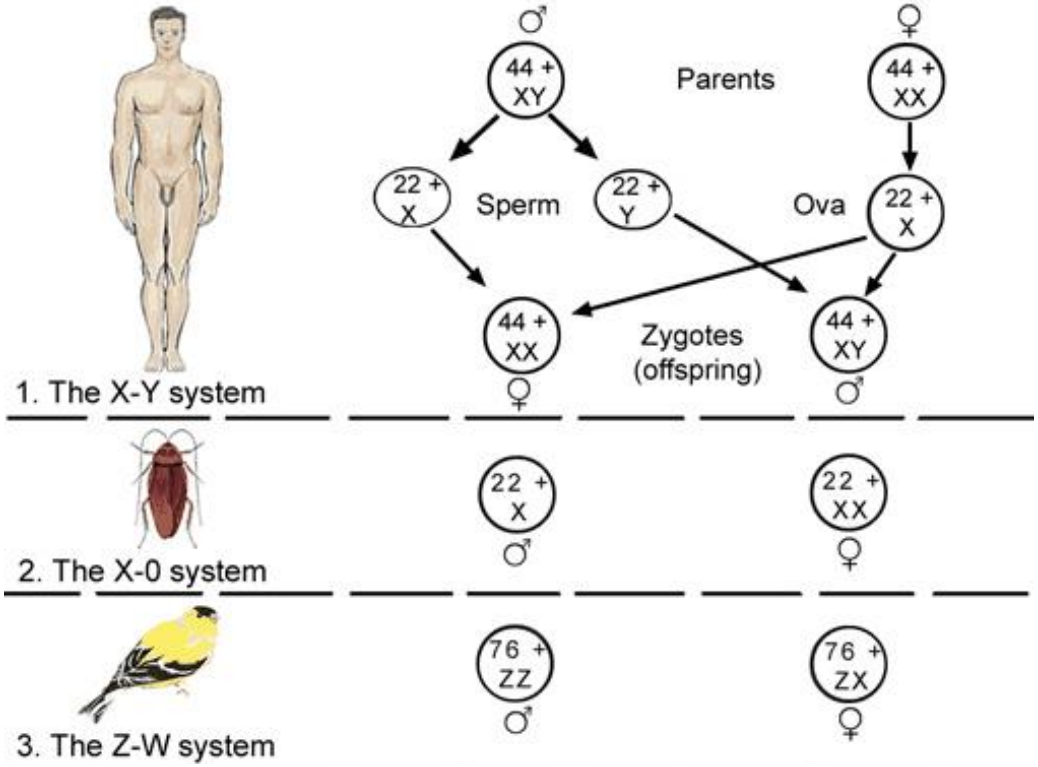
Chapter 5 Concepts of Genetics (12th ed)

Pages 131-150



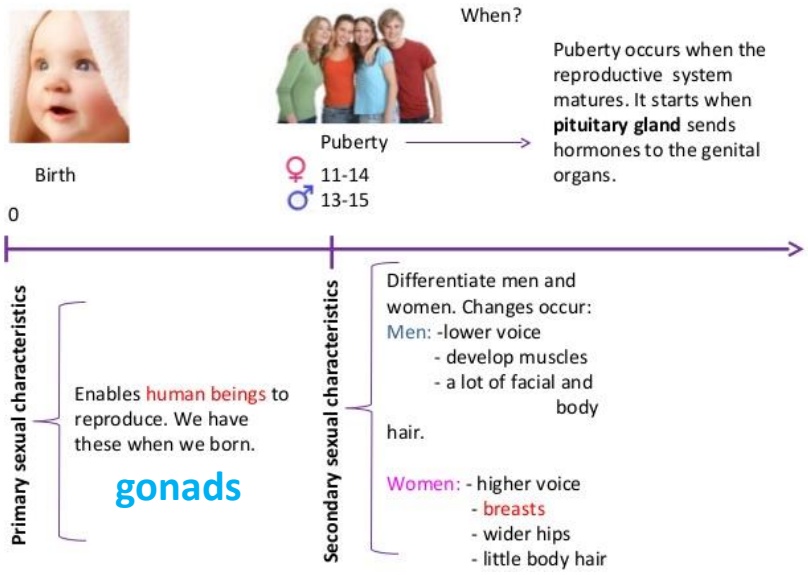
How is sex determined?

- Mechanisms of sex determination vary from species to species



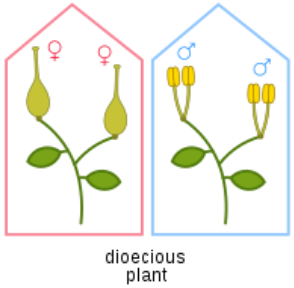
Sexual differentiation

- In animals
  - **Primary** sex differentiation
    - Gonad development, where gametes are produced
  - **Secondary** sex differentiation
    - Overall appearance of organism, including sexual characteristics

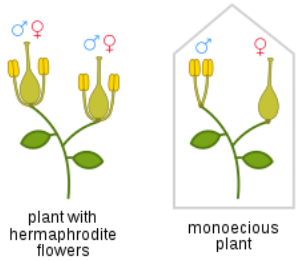


Sexual differentiation

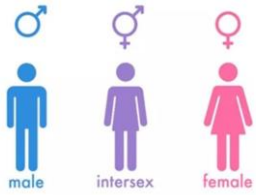
- Unisexual, dioecious and gonochoric
  - Individuals with male **OR** female reproductive organs



- Bisexual, monoecious and hermaphroditic
  - Individuals with male AND female reproductive organs. Produce eggs and sperm.

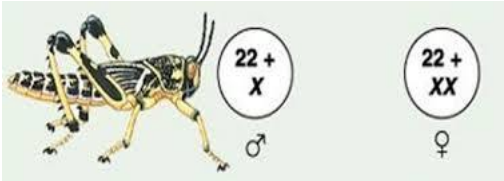


- Intersex (intermediate sexual condition)
  - Sterile



X0 sex-determination

- **There is only one sex chromosome, referred to as X.**
  - Males only have one X chromosome (X0), while females have two (XX)
- Maternal gametes always contain an X chromosome,
  - **So the sex of the offspring is decided by the male**
  - Sperm contains either one X chromosome or no sex chromosomes at all



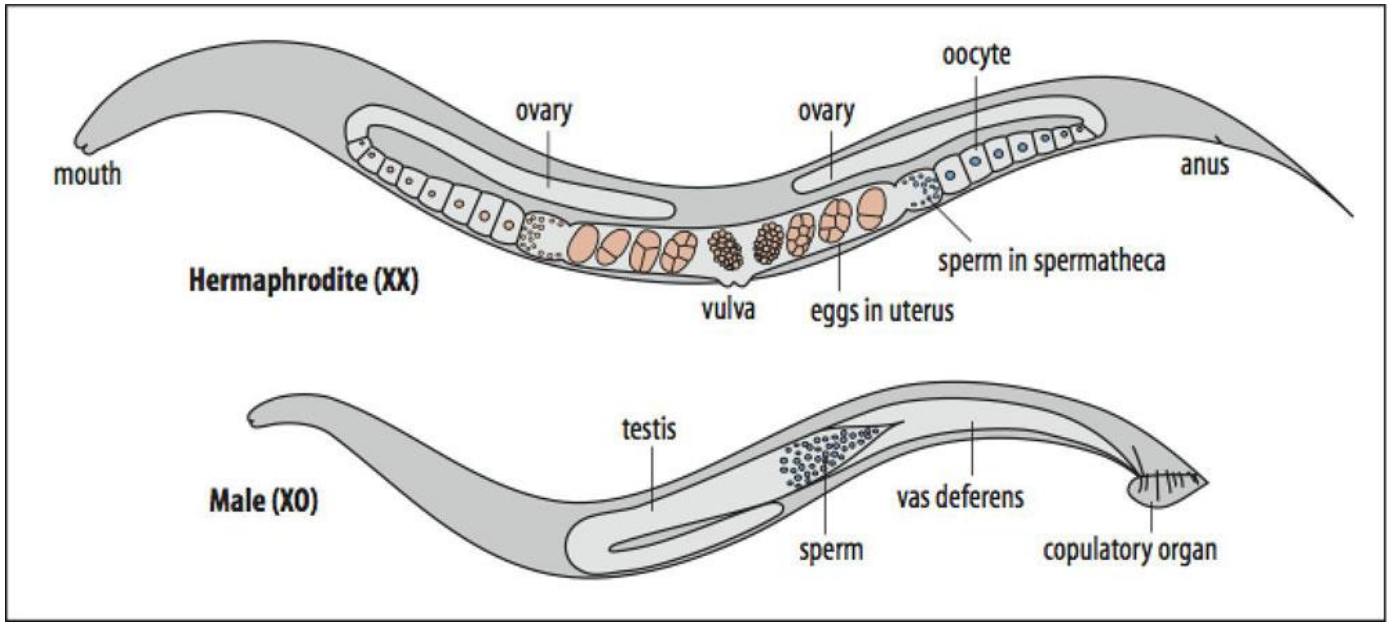
- In a variant of this system, certain animals are hermaphroditic with two sex chromosomes (XX) and male with only one (X0)

XO sex-determination – *Caenorhabditis elegans (see-no-rab-dite-iss)*

- Transparent nematode (roundworm), about 1 mm in length. Lives in soil.
- Has two sexes:
  - **Hermaphrodites** and **males**
  - Individuals are almost all hermaphrodite, with males comprising just 0.05% of the total population
- Hermaphrodite *C. elegans* have a matched pair of sex chromosomes (XX); the **rare males** have only one sex chromosome (X0)

XO sex-determination – *C. elegans*

- Males have only testes-
- Hermaphrodites have testes and ovaries
  - Eggs produced in adult stage are self-fertilised
- When self-inseminated, the worm will lay approximately 300 eggs

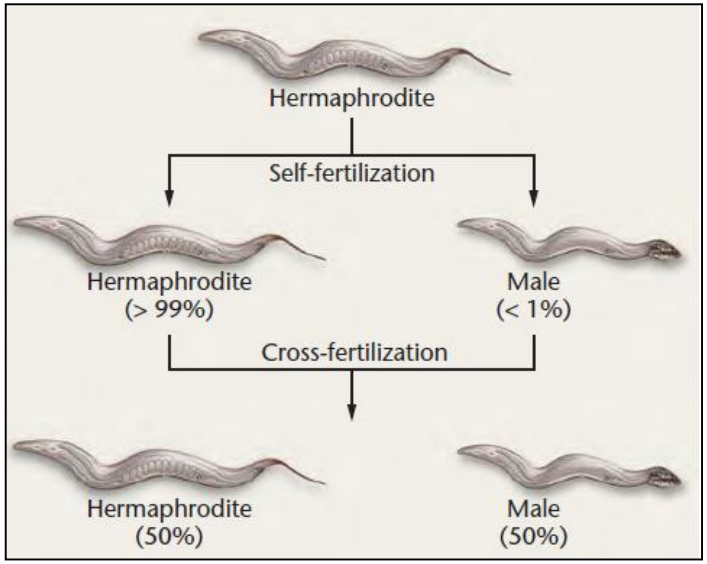


XO sex-determination – *C. elegans*

- Majority of offspring are hermaphrodites
- Less than 1% of offspring are males
- A mating between an adult male and a hermaphrodite produces **half male and half hermaphrodite offspring**
  - When inseminated by a male, the number of offspring can exceed 1,000

It is believed the ratio of X chromsomes to the number of sets of autosomes determines the sex of *C. elegans*

Ratio of 1.0 (2 X and 2 copies of each autosomes) = hermaphrodite (XX)
Ratio 0.5 = male (X0)



ZW sex determination

- In the ZW system it is the **ovum** that determines the sex of the offspring
  - In contrast to the XY system and the X0 system
  - The letters Z and W are used to distinguish this system from the XY system.
- Males are the homogametic sex (ZZ)
- Females are heterogametic (ZW)
- The Z chromosome is larger and has more genes, like the X chromosome in the XY system

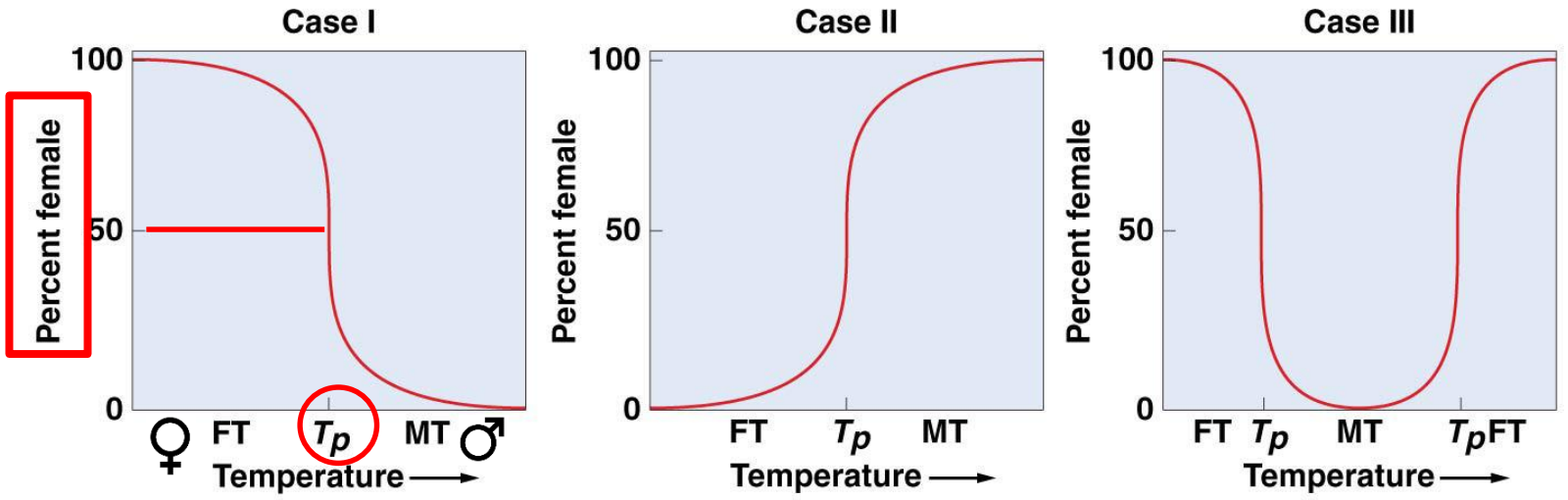
ZW sex determination

- TSD (Temperature dependent Sex Determination)

  Sex determination depends on incubation temperature of eggs during critical period of embryonic development.

  - **Pivotal temperature (Tp)**
  - How does it work? Unclear
  - Metabolic / Physiological parameters

  Androgen → Aromatase → Estrogen



TSD (Temperature dependent Sex Determination) can override chromosomal sex determination

Climate change is causing DRAGONS to change gender: Researchers find Australian reptiles are switching sex

- Australian Central Bearded Dragons affected by temperatures
- Animals that are genetically male hatch as females and give birth
- Happening in one of the fastest warming places in Australia in last 40 years

♀ZW, ♂ZZ

http://www.nature.com/nature/journal/v523/n7558/full/nature14574.html

Current Biology

REPORT

The Discovery of XY Sex Chromosomes in a *Boa* and *Python*

Tony Gamble[6], Todd A. Castoe, Stuart V. Nielsen, Jaison L. Banks, Daren C. Card, Drew R. Schield, Gordon W. Schuett, Warren Booth

[6] Lead Contact

Publication stage: In Press Corrected Proof

DOI: http://dx.doi.org/10.1016/j.cub.2017.06.010

Highlights

- All snakes were thought to possess the same ZW sex chromosome system
- There is no evidence that boas and pythons have ZW sex chromosomes
- Male-specific genetic markers in boa and python indicate XY sex chromosomes
- Comparative genomics reveals boa and python independently evolved XY systems

Comparative genomics shows the Pythons and Boas have evolved independently of ZW

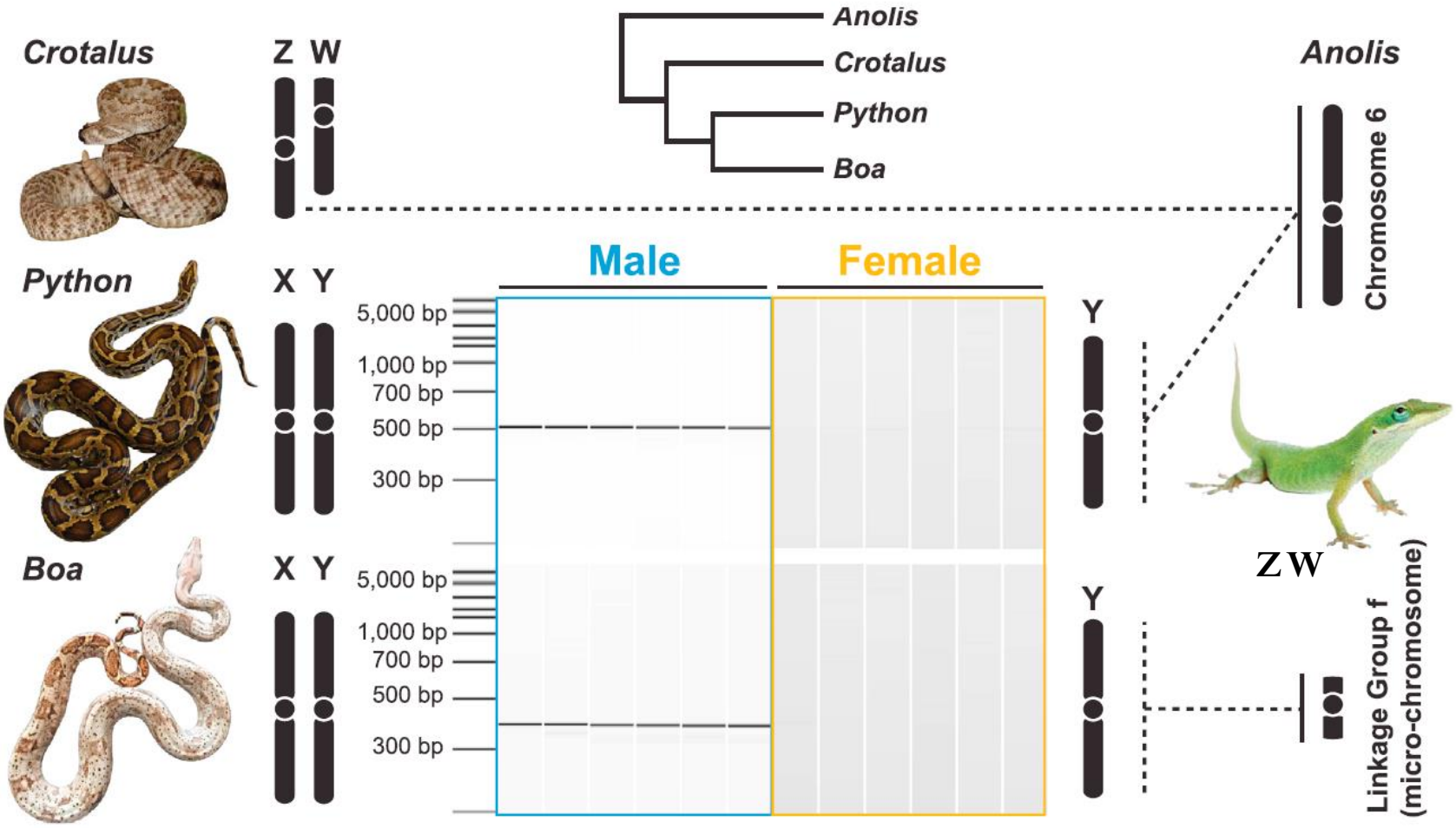
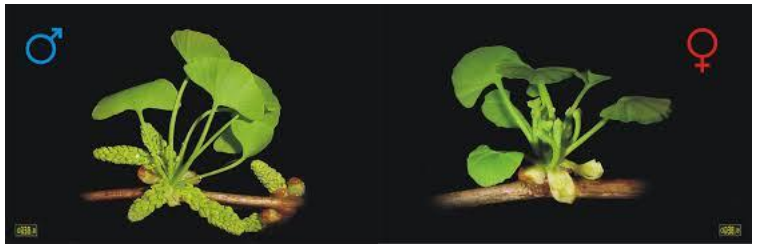
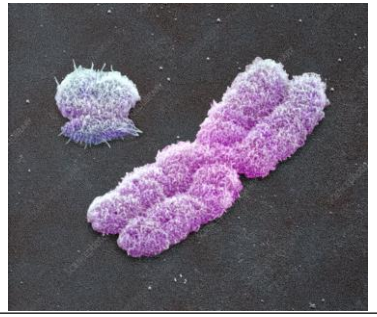


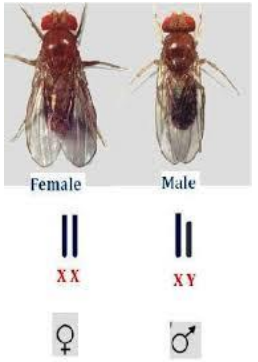
Figure 1. Male-Specific RAD Markers in *Boa* and *Python*

XY sex determination

- Found in humans, most other mammals, some insects (*Drosophila*) and some plants (*Ginkgo*)
- Females have two of the same kind of sex chromosome (XX) – the **homogametic** sex
- Males have two distinct sex chromosomes (XY) – the **heterogametic** sex
  - In humans, the presence of a Y chromosome = male and the absence of a Y chromosome = female
  - Not the case in all XY organisms (Drosophila)



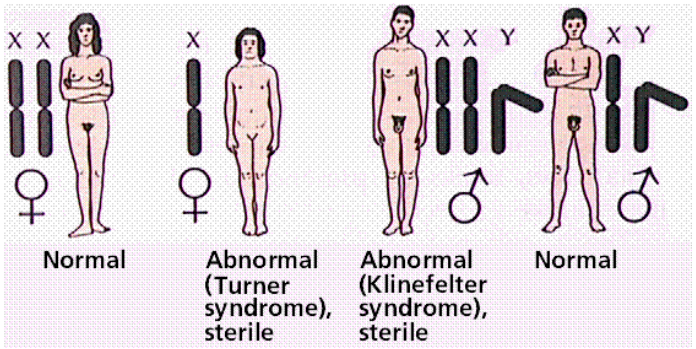




XY sex determination – Humans

- Sex of an individual is defined at three levels
  - 1) Chromosomal sex
  - 2) Gonadal sex
  - 3) Phenotypic sex

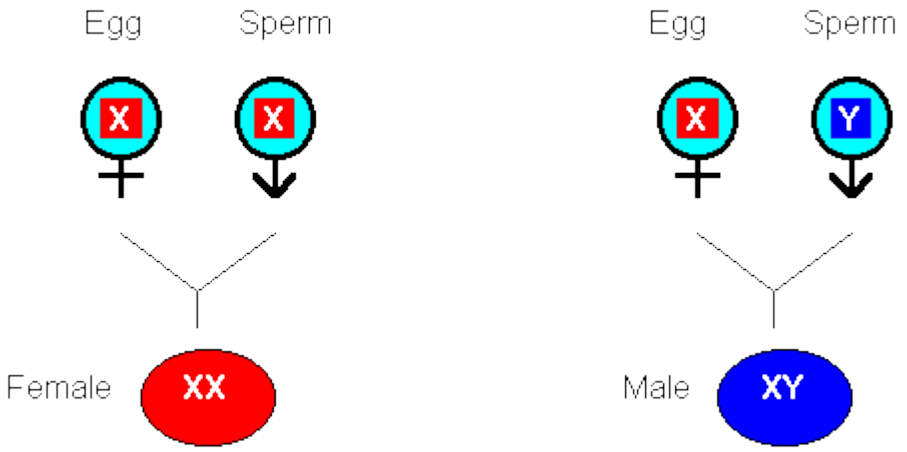
- The chromosomal sex of an individual (XX or XY) can differ from the phenotypic sex



http://biologyhumanbody.blogspot.com/2011/01/human-chromosomal-abnormalities.html

XY sex determination – Humans

1. Chromosomal sex is established at fertilisation



- Other aspects of sex depend on the interaction of genes and environmental factors, especially hormones

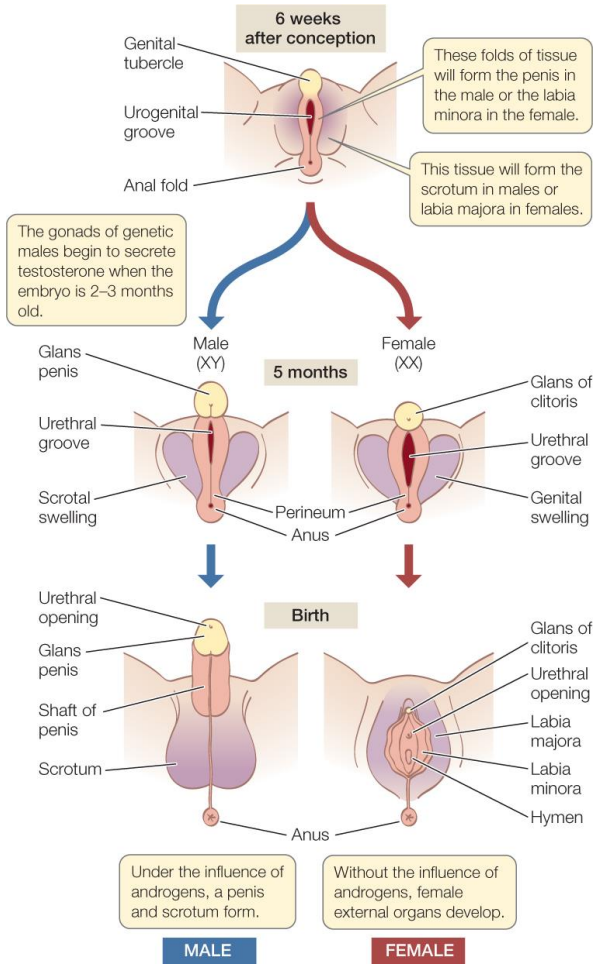
Within embryo

Among embryos

In utero factors

XY sex determination – Humans

- **2) Gonadal sex differentiation**
- For the first 7 or 8 weeks, the embryo is neither male nor female
  - Two undifferentiated gonads
  - Both male and female reproductive duct systems develop
- Depending on how key genes are expressed causes gonads to develop as testes or ovaries, establishing gonadal sex
  - Alternative pathways can produce intermediates



https://www.macmillanhighered.com/BrainHoney/Resource/6716/digital_first_content/trunk/test/hillis2e/hillis2e_ch37_2.html

XY sex determination – Humans

- Y Chromosome and testis development
- SRY gene
  - Sex-determining region of the Y chromosome
  - Located near the end of the short arm of the Y chromosome
  - Plays a major role in causing the undifferentiated gonad to develop into a testis

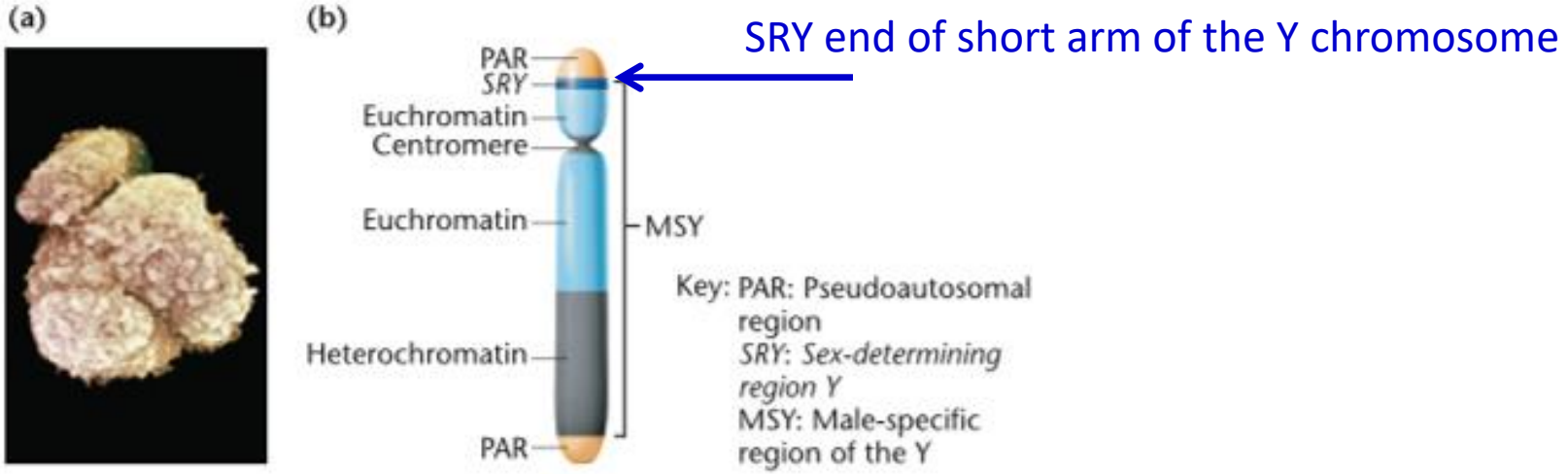
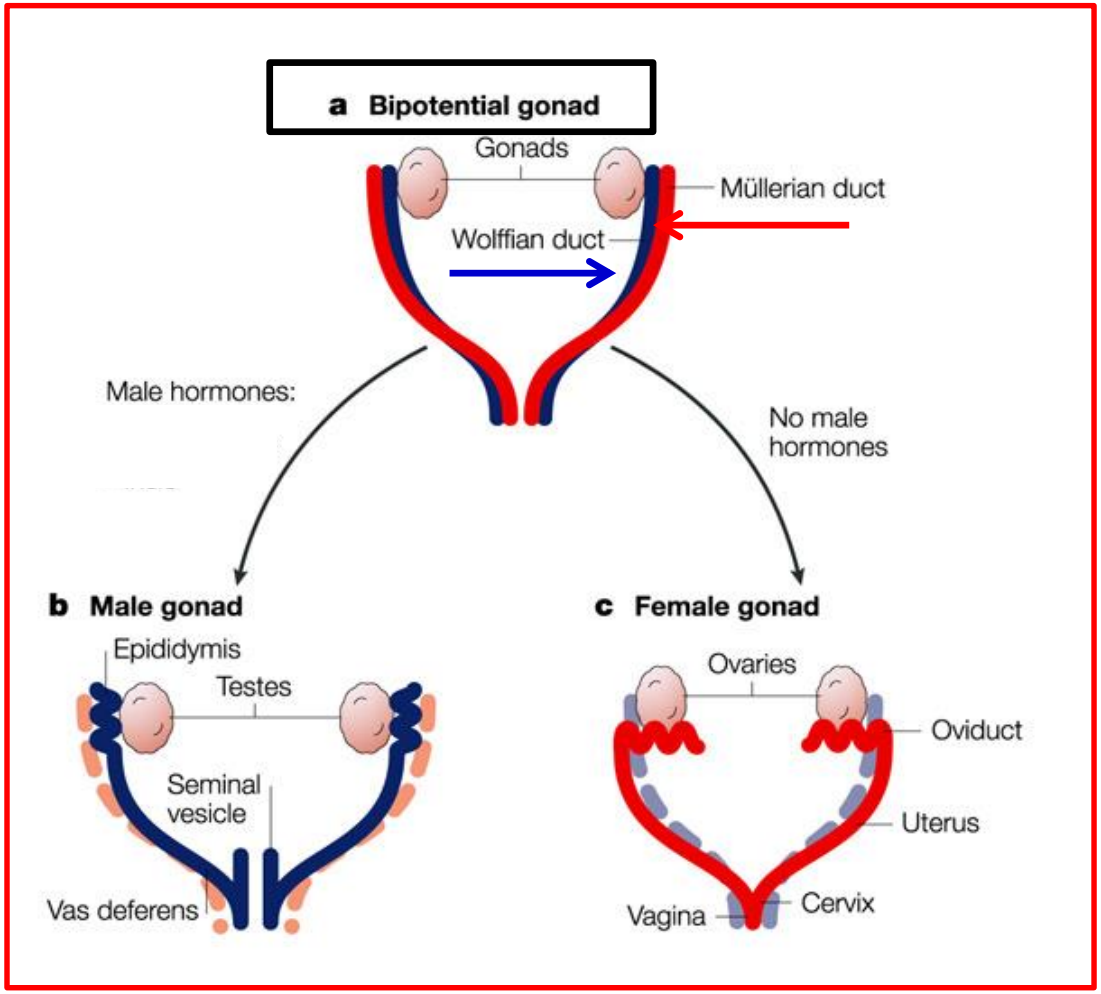


FIGURE 5.3 **(a)** Electron micrograph of the human Y chromosome (magnification × 35,000) and **(b)** regions of the Y chromosome.

XY sex determination – Humans

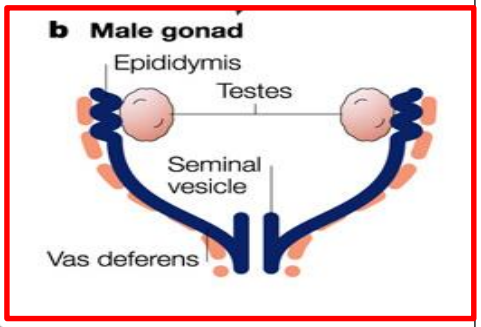
- Before sexual differentiation, both male and female embryos have **bipotentia**l gonads
- They possess both Wolffian and Müllerian ducts
- These ducts can differentiate into male or female reproductive organs according to the hormonal status of the foetus

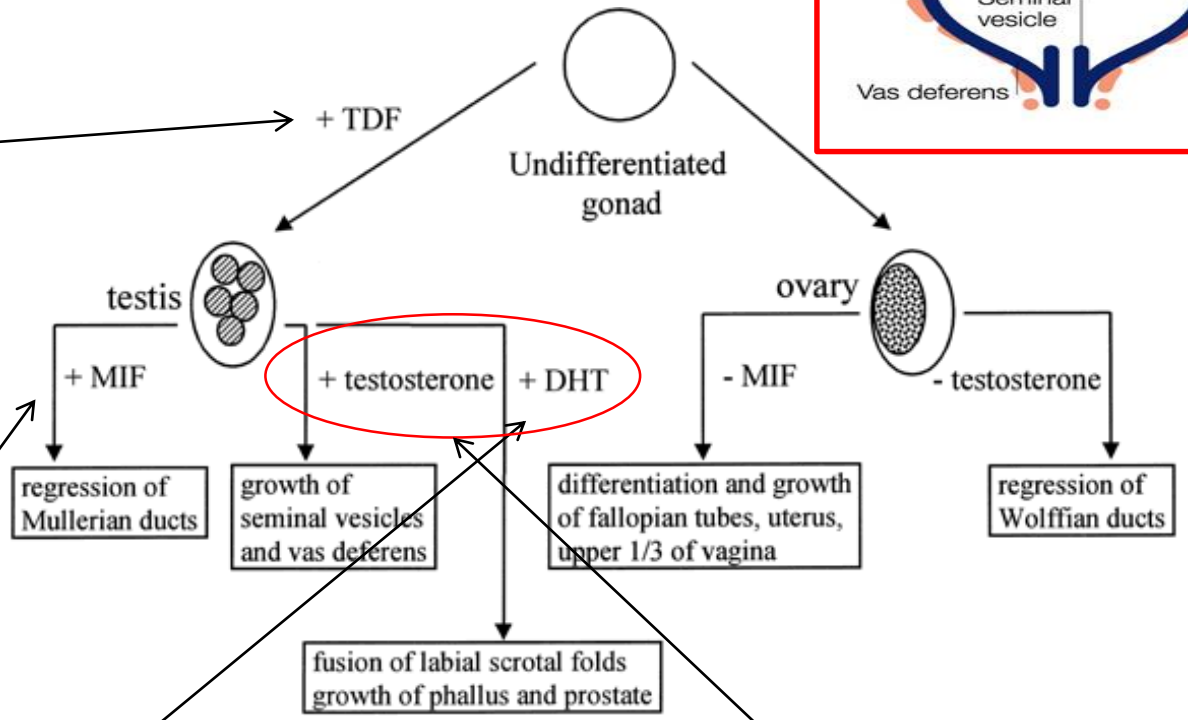


XY sex determination – Humans

Male development

Testis determining factor **(TDF) encoded by the SRY gene on Y chromosome**





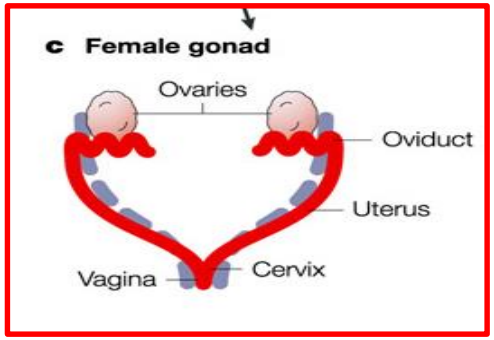
Müllerian inhibiting hormone (MIH) Hormone causes breakdown of Müllerian (female) ducts in the embryo

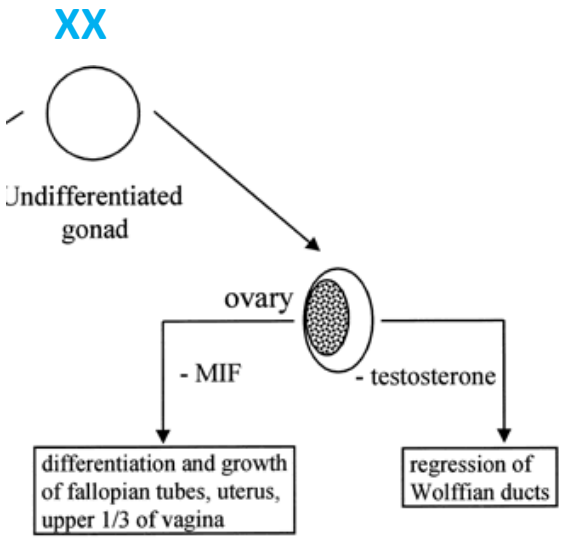
Androgen receptor, encoded by gene on X chromosome, activated by binding of testosterone or dihydrotestosterone

Dihydrotestosterone (DHT) has an essential role in the formation of the male external genitalia

XY sex determination – Humans

- **Female development**
- Requires the absence of the Y chromosome and the presence of two X chromosomes- **NO SRY gene expression**
- Embryonic gonad develops as an ovary
- In the absence of testosterone, the Wolffian duct system degenerates
- In the absence of (Müllerian inhibiting hormone) MIH, **the Müllerian duct system forms female reproductive system**





XY sex determination – Humans

- **Chromosomal sex vs. phenotypic sex**
  - **Mutations can uncouple chromosomal sex from phenotypic sex**
- A mutation in the X-linked androgen receptor gene (*AR*) causes XY males to become phenotypic females
- Testosterone is produced, but not testosterone receptors; cells develop as females
- **Androgen insensitivity**
  - An X-linked genetic trait that causes XY individuals to develop into phenotypic females

XY sex determination – Humans

- XY female with androgen insensitivity
- Santhi Soundarajan is a phenotypic female who has an XY chromosomal constitution and has androgen insensitivity
  - Body produces testosterone but **NO** receptor for it – phenotypically female

XY sex determination – Humans

- Sex phenotype can change at **puberty**
- Pseudohermaphroditism – an autosomal genetic condition that causes XY individuals to develop the phenotype of females
- Caused by mutations in several different genes
- Affected individuals have both male and female structures, but at different times of life
- At puberty, females change into males

The expression of X chromosomes

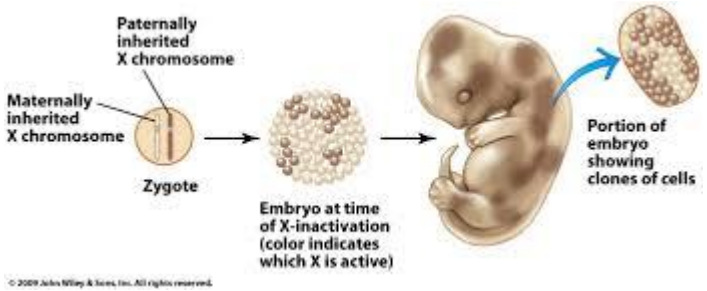
- Females have two X chromosomes, males have one; yet the amount of gene product is the same

HOW?

- Human females have one X chromosome inactivated in all somatic cells to balance the expression of X-linked genes in males and females
- Dosage compensation
  - A mechanism that regulates the expression of sex-linked gene products

The expression of X chromosomes

- **Barr bodies** and X inactivation
- **Mary Lyon hypothesis**
  - Dosage compensation in mammalian females
  - Random inactivation of one X chromosome in females equalizes the activity of X-linked genes in males and females
  - **Inactivation of X chromosome is random, occurs in somatic cells at an early stage of embryonic development and is then passed on to progeny cells by mitosis- PERMENANT**

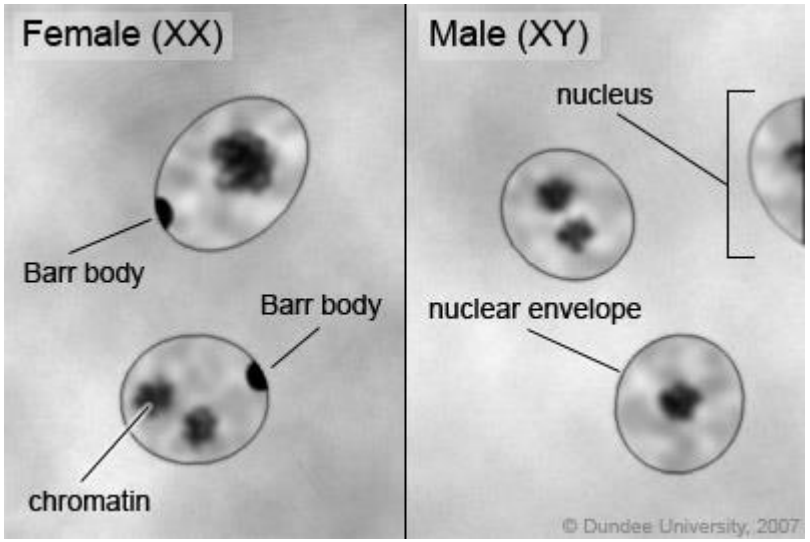


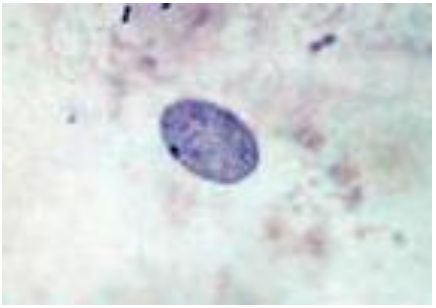
- Barr body = **An inactivated X chromosome, tightly coiled**
  - A densely staining mass in the somatic nuclei of mammalian females

http://www2.samford.edu/~djohnso2/jlb/333/sex.html

The expression of X chromosomes

- Males (46,XY) have no Barr bodies
- Normal females (46,XX) have one Barr body
- **Mutations:** female with 5 X chromosomes (49, XXXXX) has four Barr bodies
- **Rule:** The number of Barr bodies is one less than the number of X chromosomes (n-1)





https://www.sciencesource.com/archive/Barr-Bodies-in-Cheek-Cells-SS2435020.html

How many Barr bodies?

- 48, XXXX

  49,XXXXY

- 47,XXX

  48,XXXY

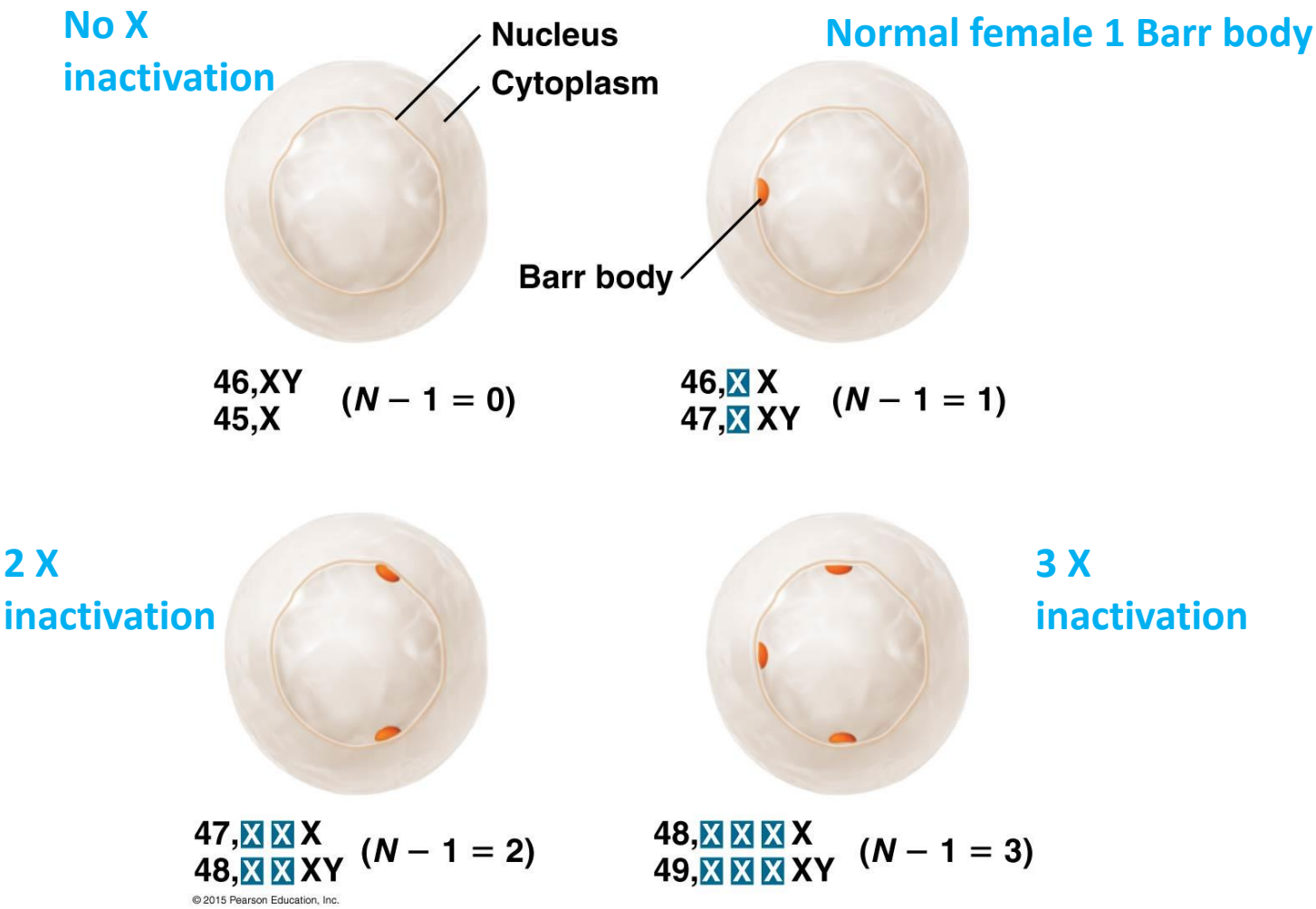
The expression of X chromosomes: All X chromosomes barring 1 inactivated

- 48, XXXX

  49,XXXXY

- 47,XXX

  48,XXXY



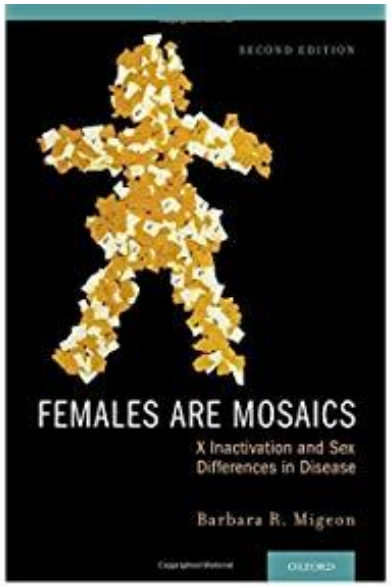
The expression of X chromosomes

- Mosaic expression in female mammals

Calico cats are always female?

https://www.youtube.com/watch?v=Y9vXhmI5FXM

6.22 min



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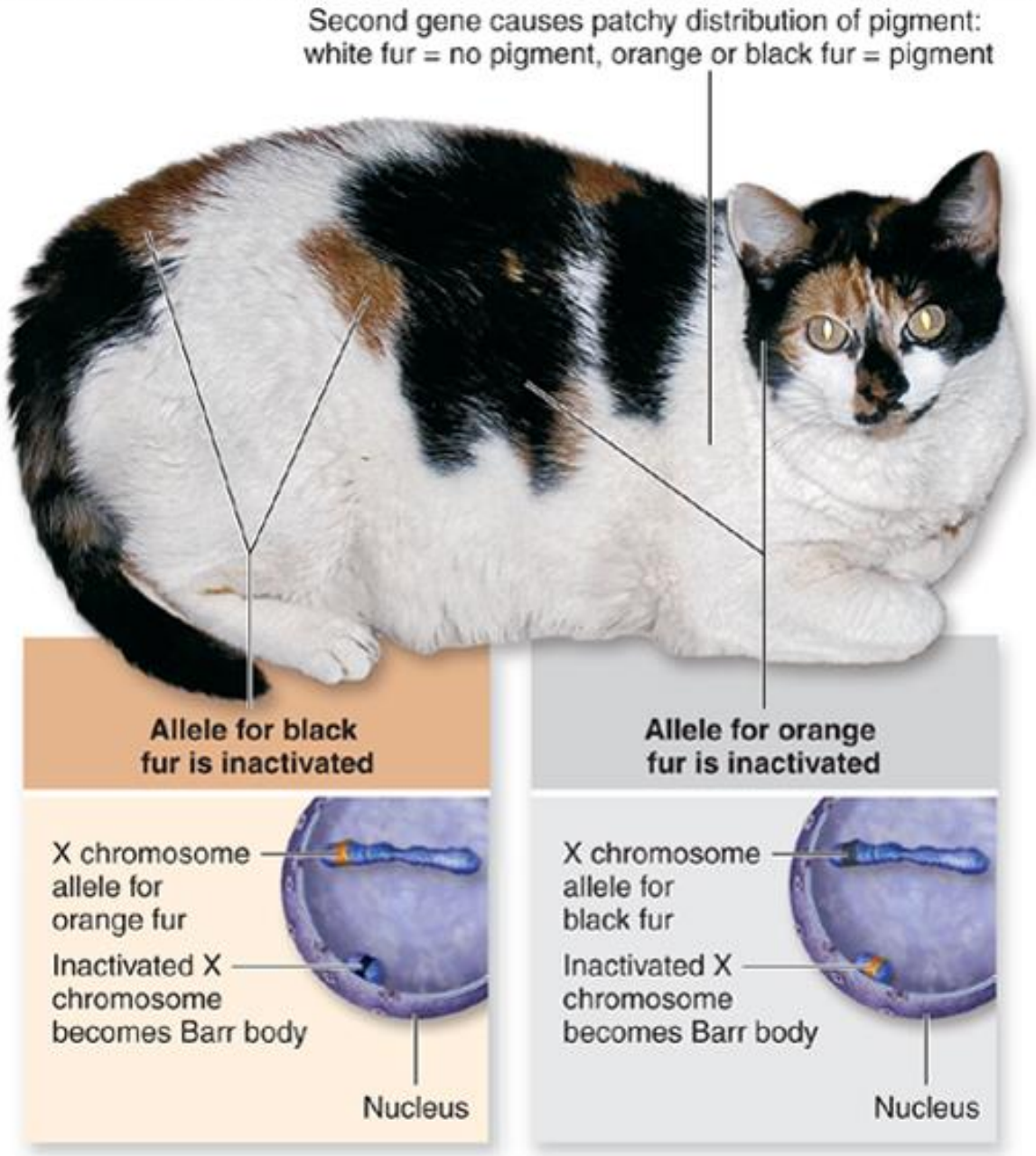


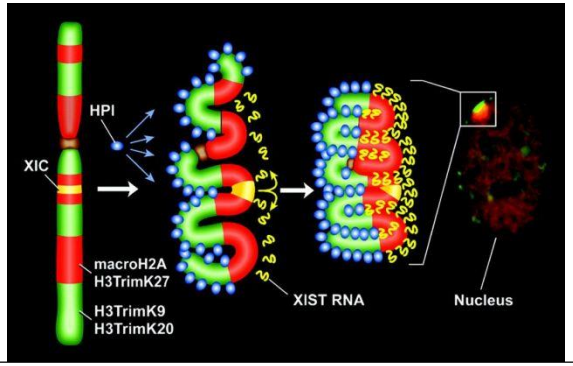
Stunning examples of X-inactivation? Or Chimeras?

The expression of X chromosomes

- X inactivation centre
  - Inactivation begins and is regulated from the X inactivation centre (Xic) of the X chromosome
- **X inactivation centre (Xic)**
  - Region on the X chromosome where inactivation begins
- Xic contains the gene *XIST* which encodes an long non-coding RNA that coats the inactive X and somehow silences it
  - Tsix (an antisense partner of Xist) and Xite

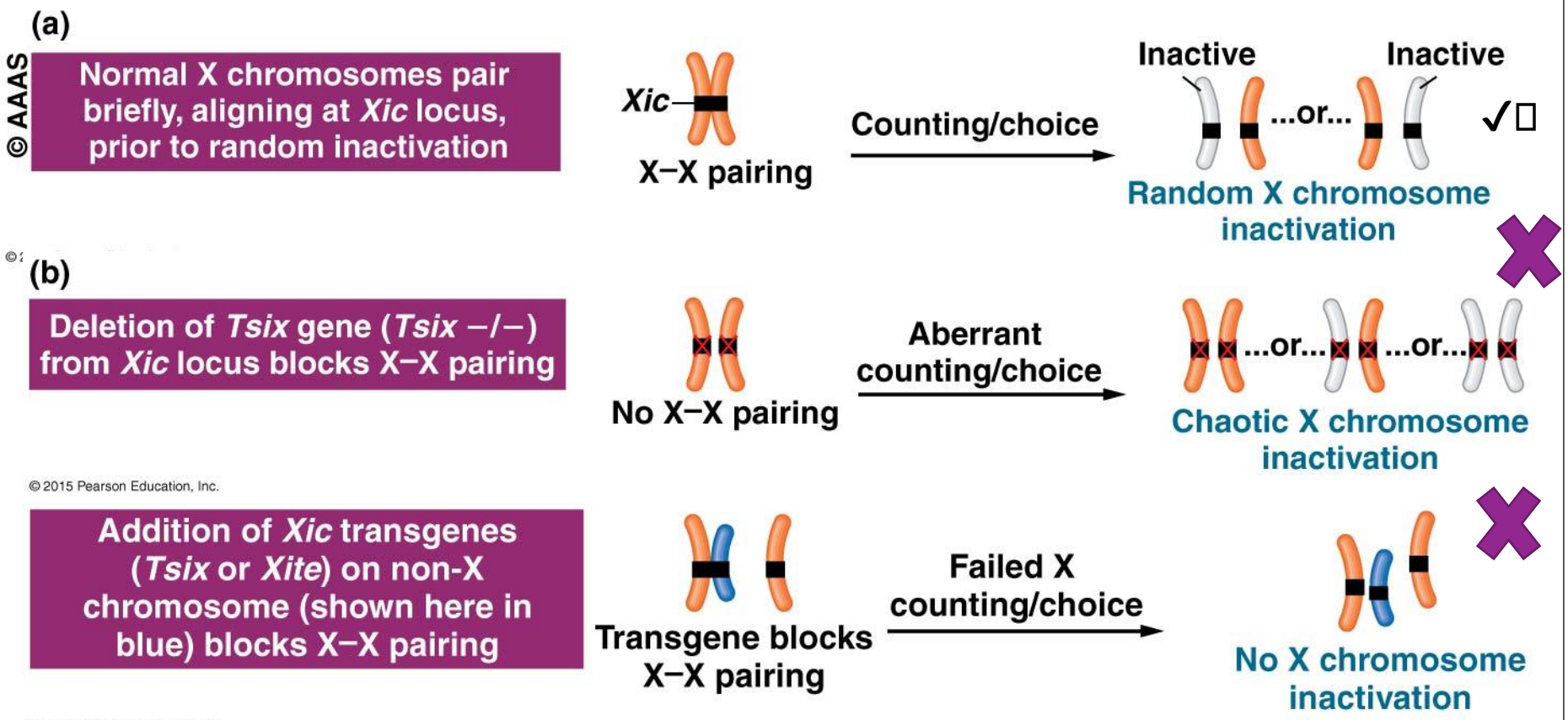
HOW DOES THIS WORK?????

How does counting of X chromosomes works???



Mechanism of X Inactivation

Brief pairing of **maternal** and **paternal** X chromosomes at Xic loci

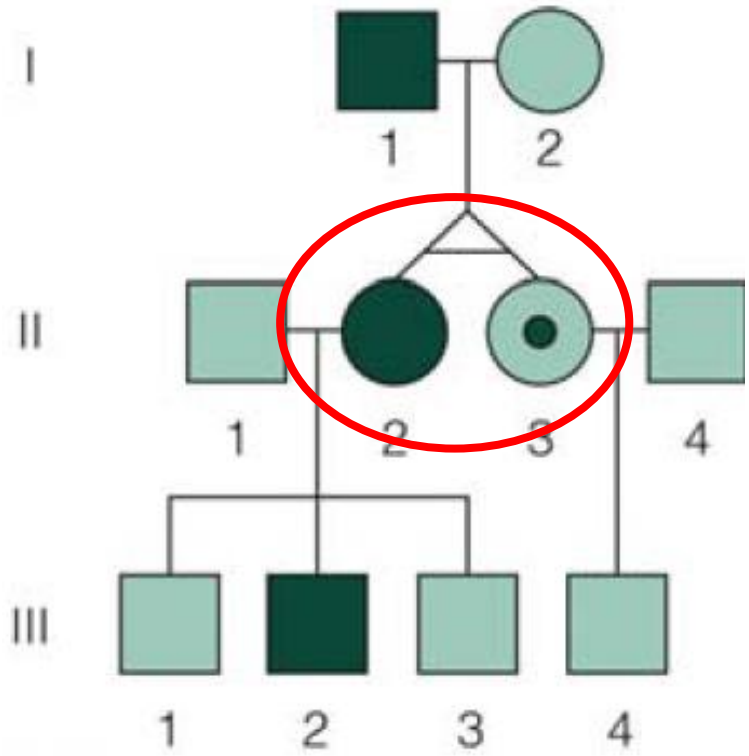


The expression of X chromosomes

- Effects of random X chromosome inactivation
- Random X inactivation can cause twins with identical genotypes to have different phenotypes

The pedigree shows identical twins who are discordant for the phenotype of colour blindness

Almost all the active Xs in the colour blind twin carry the mutant allele, and in the non colour blind twin, most of the active Xs carry the normal allele

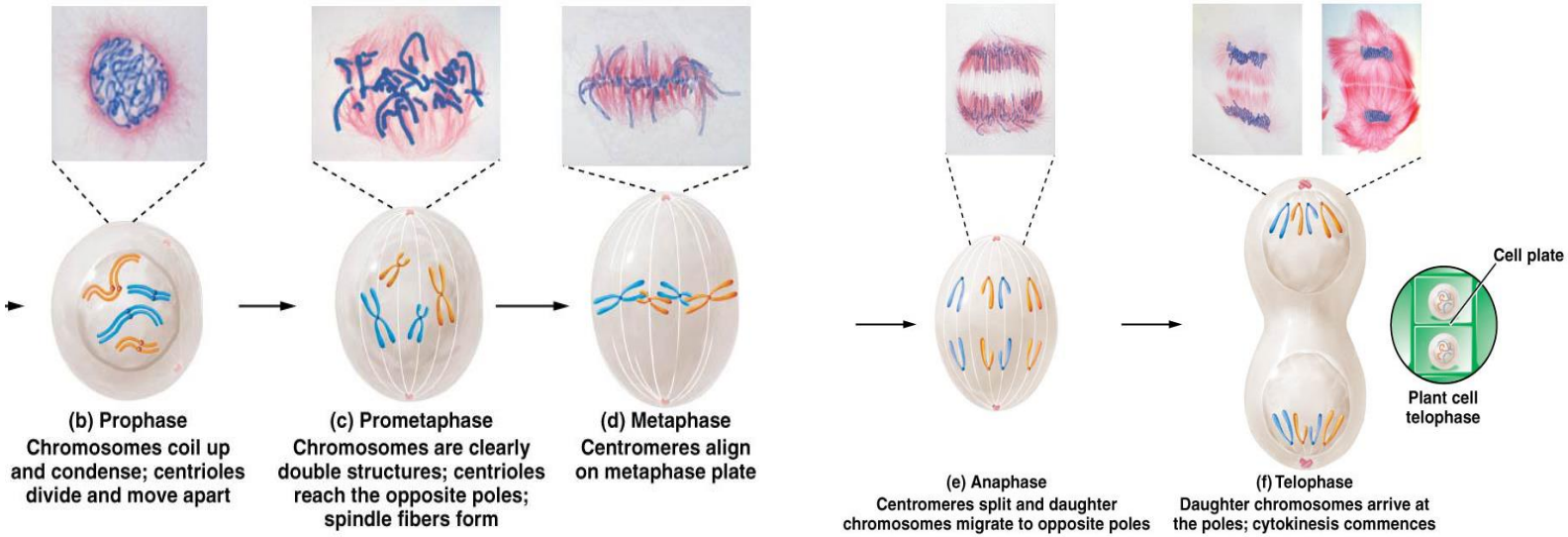


Quiz:

Genetic variation is generated through two steps during meiosis, can you name the two processes and which stages of meiosis do they occur in?

Quiz!

How many chromosomes and chromatids are present in the different stages of mitosis?



	Prophase	Prometaphase	Metaphase	Anaphase	Telophase	End of mitosis
Chromo-somes						
Chromatids						