Aula 6. Determinação do sexo. Mamíferos

1677 Anton van Leeuwenhoek → espermatozoides

1827 Carl Ernest von Baer → óvulo

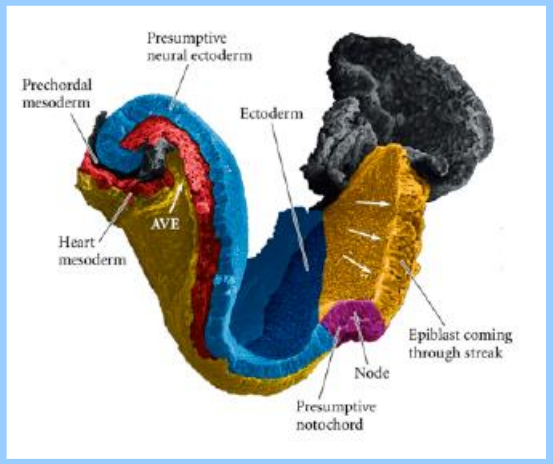
1902 Clarence McClung → cromossomos “acessórios”

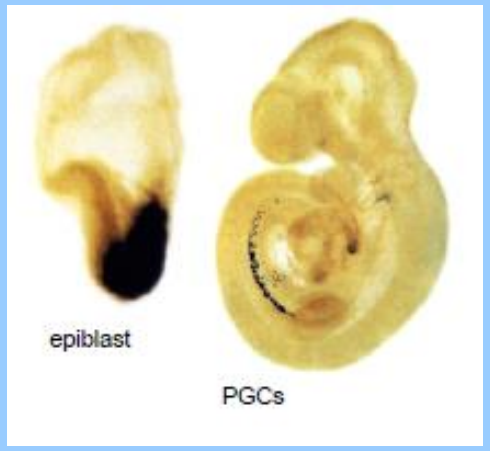
1947 Alfred Jost → diferenciação do trato reprodutório

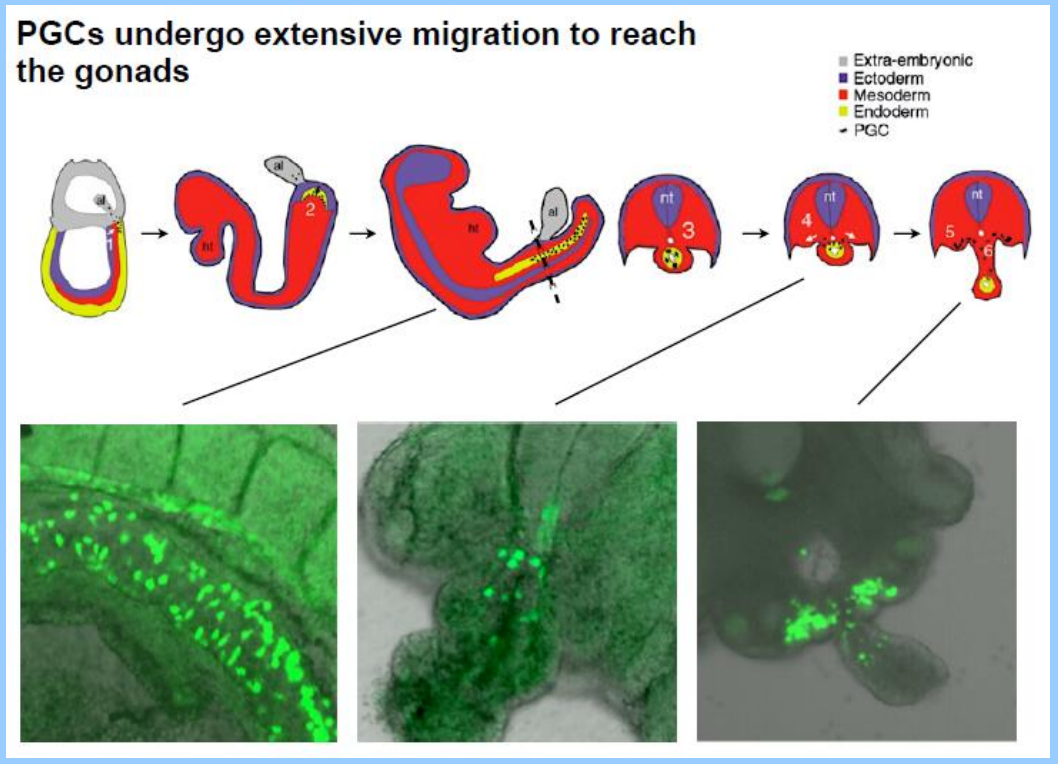
1959 Welshons & Russell → papel do cromossomo Y

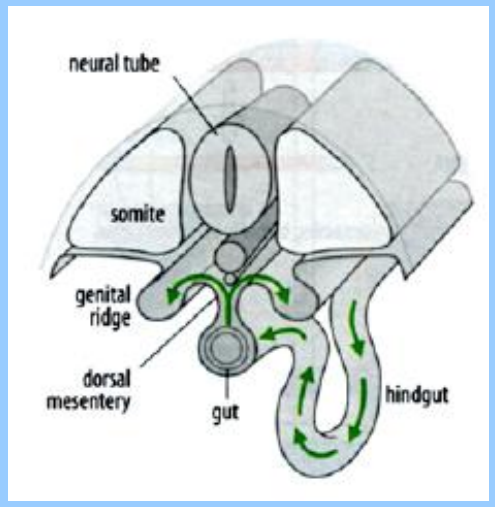
1989-1991 Lovell-Badge et al. → descoberta do gene SRY
- machos XX e fêmeas XY examinadas
- isolamento de 35 kb do cromossomo Y
Sex-determinig Region of the Y

Origem das células germinativas



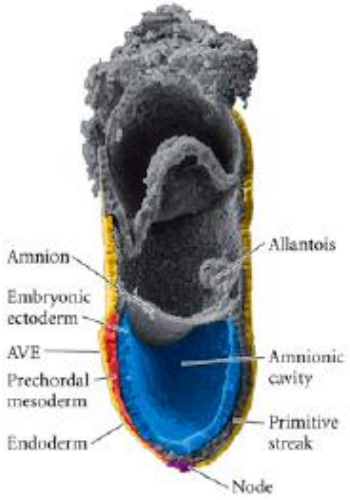


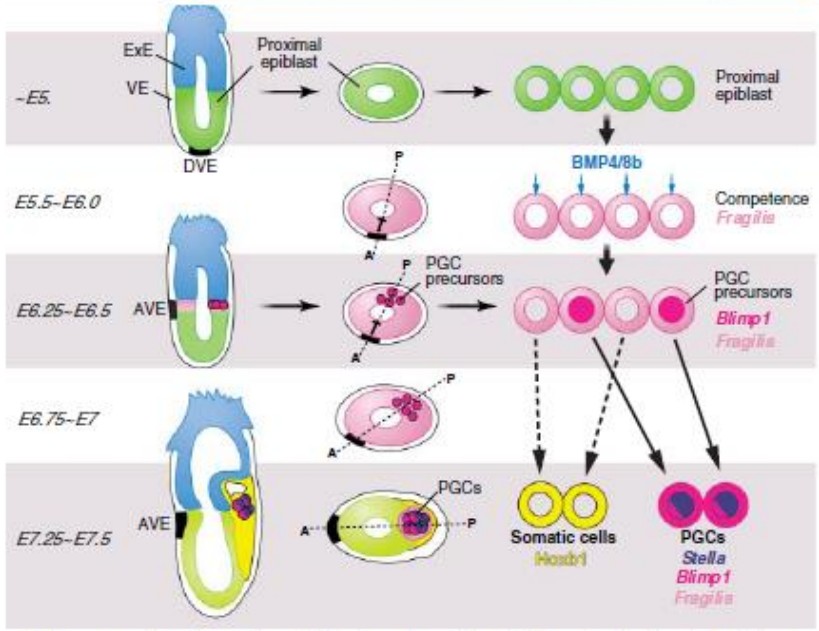




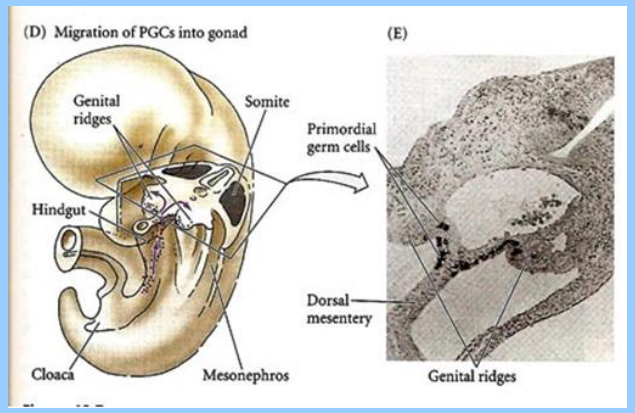
Primordial germ cell specification in mouse

- no distinct germ plasm
- PGCs induced by bmps at posterior of epiblast, near primitive streak
- cells competent to form PGCs express *fragilis* transmembrane protein
- ~20 cells express transcriptional repressor *blimp1* (*B lymphocyte-induced maturation protein 1*) and are committed PGCs
- transcriptional repression program blocks drift towards somatic fates





ExE = extraembryonic ectoderm, VE = visceral endoderm, AVE = anterior visceral endoderm



Fgf9 / Wnt4 Signals

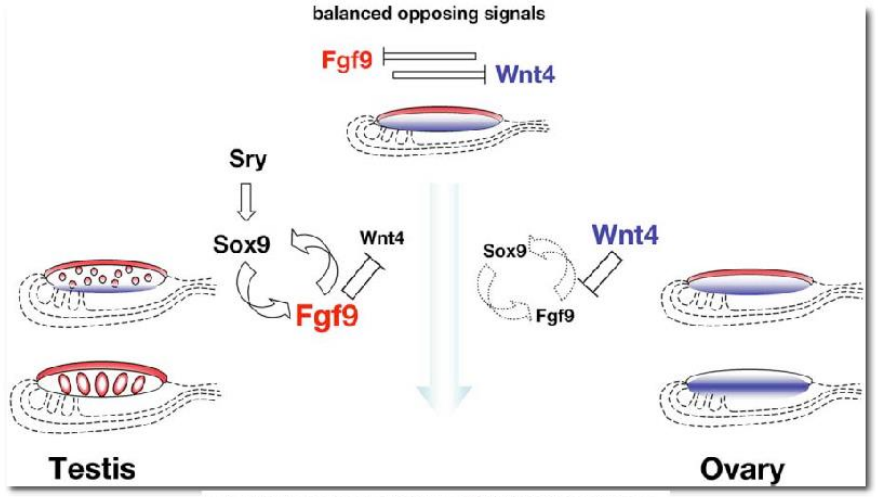


Fig. 3. Model of balanced opposing signals between *Fgf9* and *Wnt4*. In XY gonads, *Sry* upregulates *Sox9* to establish a feed-forward loop that upregulates *Fgf9* and silences *Wnt4*. In XX gonads, *Wnt4* dominates and silences *Fgf9* and *Sox9*.

Kim & Capel, Develop Dynamics 235:2292–2300, 2006

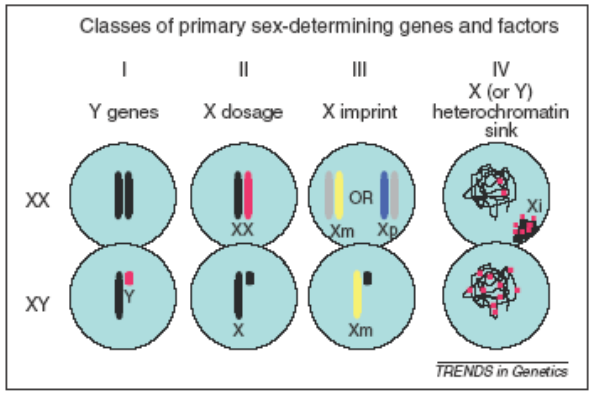
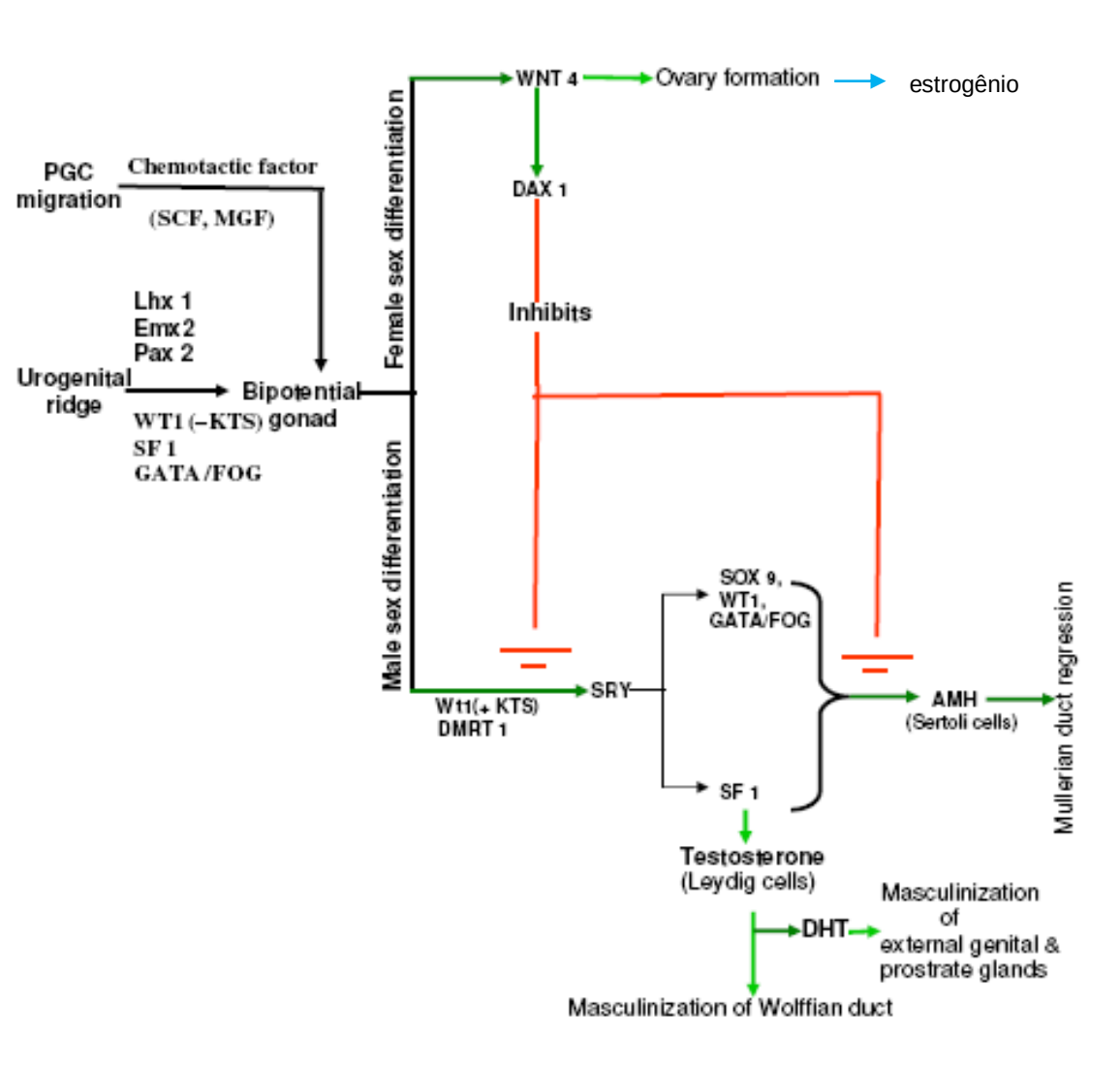


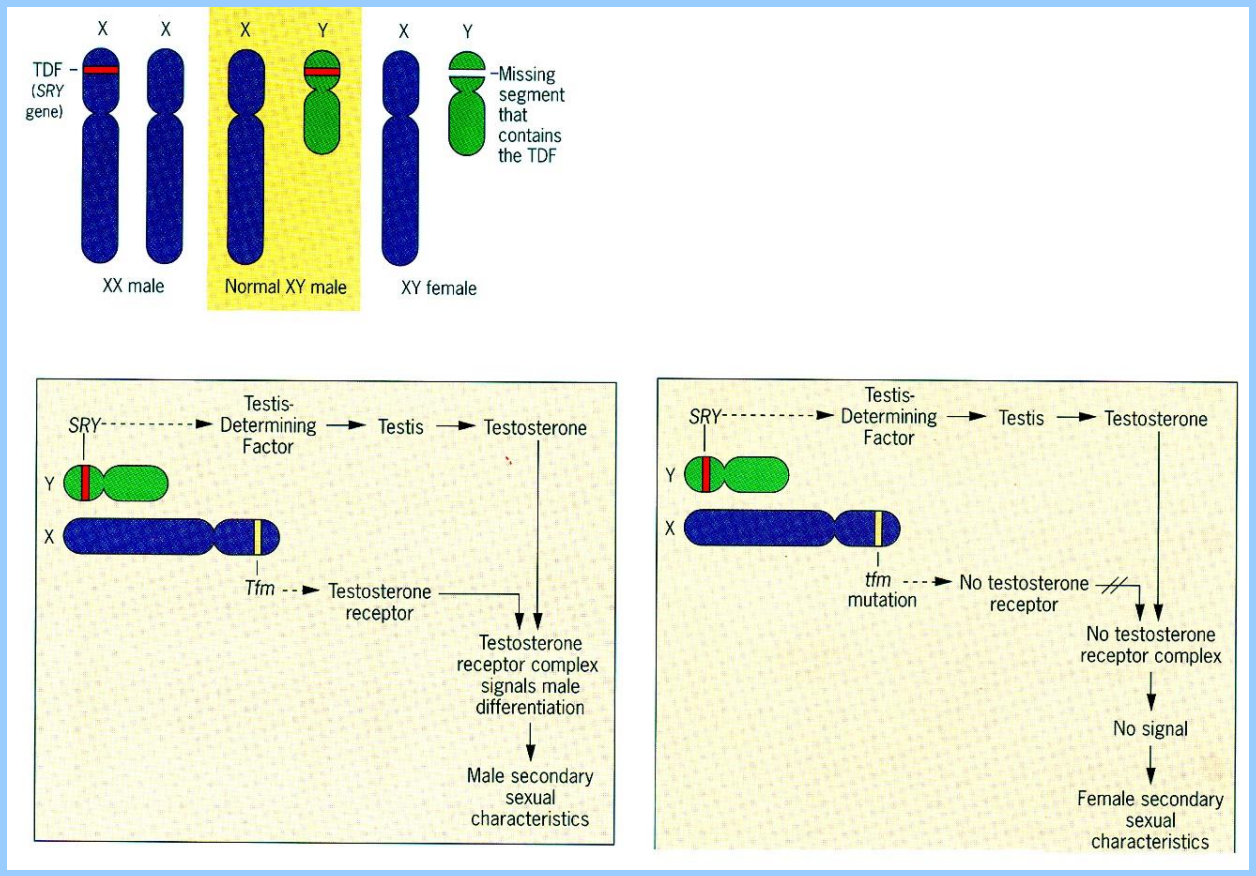
Figure 1. Four possible classes of primary sex-determining factors are recognized. Class I comprises Y genes that have a male-specific effect in one or more tissues, such as *Sry* and Y genes required for spermatogenesis. Class II are X genes that are expressed at a higher level in females than in males by virtue of the 2:1 ratio in the number of X chromosomes. Class III are X genes that receive a parental imprint. The X chromosome receiving a maternal imprint (Xm, yellow) is active in half of XX cells and all of XY cells, whereas the X chromosome receiving a paternal imprint (Xp, blue) is active in half of XX cells and no XY cells. Class IV are proposed regions of sex chromosome heterochromatin [the heterochromatic inactive X (Xi) is illustrated here] that act as sex-specific sinks for factors (red dots) that regulate the amount of euchromatin and/or heterochromatin at interphase and, therefore, affect gene expression throughout the genome. To date, specific members of only Class I have been identified (*Sry* and spermatogenesis genes [9–11]). Although evidence indicates that the number of X chromosomes leads to some sex differences in phenotype [49], the specific genes or chromosome regions that explain these X effects have not yet been identified. Class IV is particularly speculative at present because it is based on a limited number of studies. Future studies are likely to expand the importance of Classes II–IV.

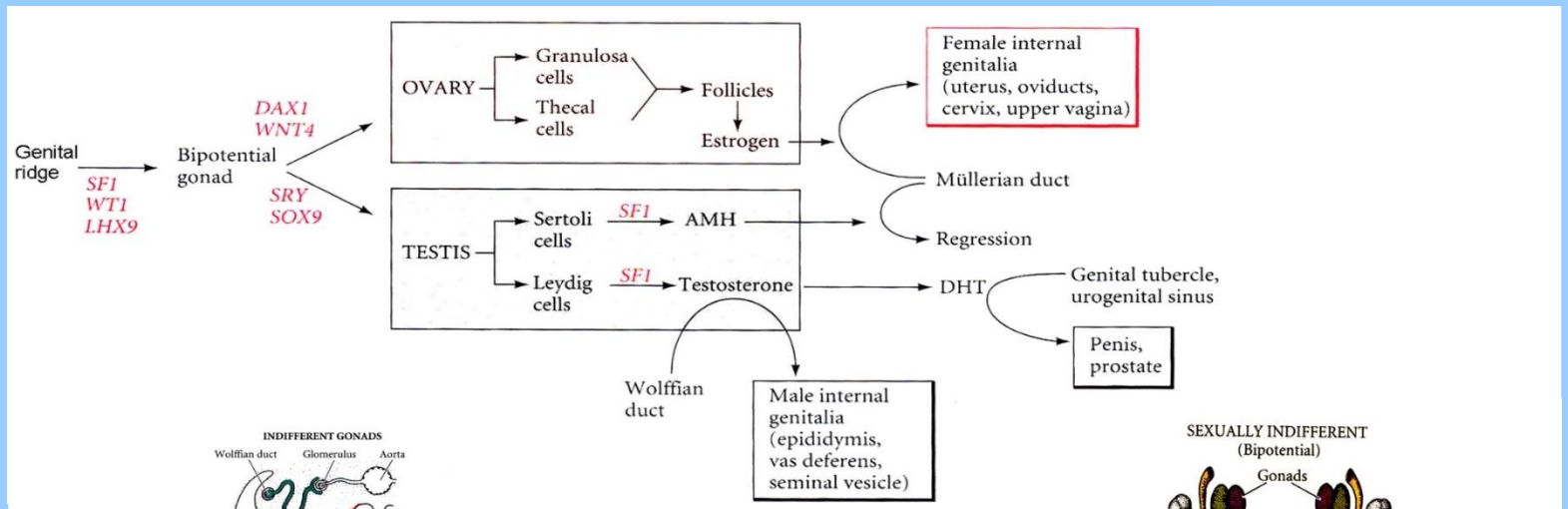
Arnold (2012) Trends in Genetics 28: 55-61

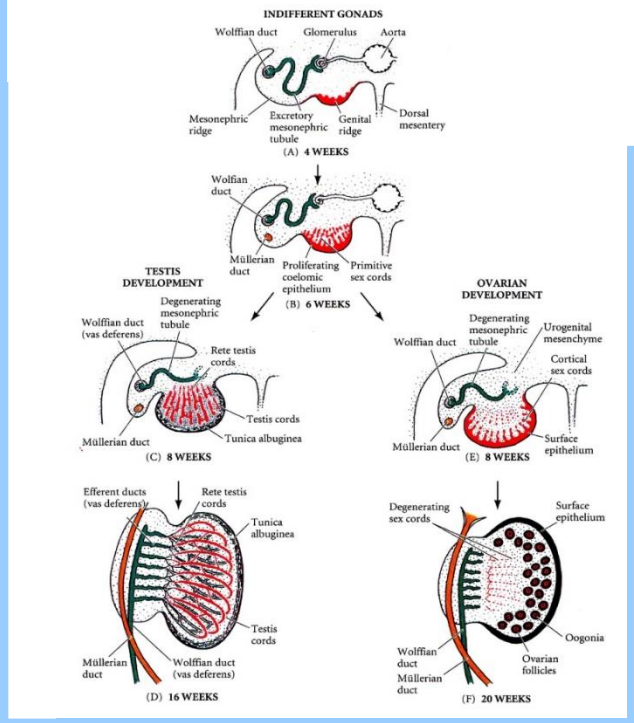
Determinação do sexo: interação genética

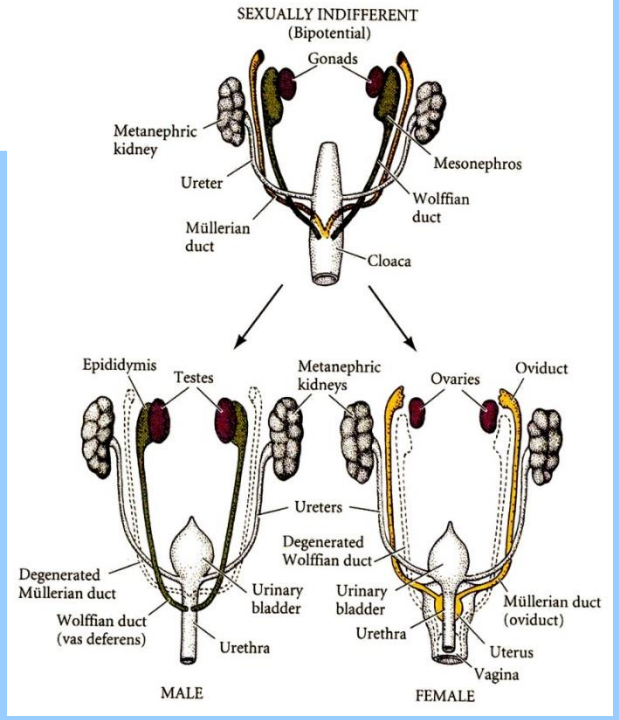


Alterações na determinação genotípica do sexo









Gilbert, Developmental Biology, 7 th edition