Chromosomal determination of sex

Females and males are readily distinguished by many differences in their internal and external phenotypes, behavior, and metabolism. In humans, as with most other animals, the sex is determined chromosomally.

Female cells contain two X chromosomes, while male cells have one chromosome X and one Y. The presence of the Y chromosome determines the direction of the embryonic development to male. In other words, if Y is not present, embryo development is set to female. It is in concordance with the sex of Turner (X0, girl) and Klinefelter (XXY, boy) syndromes.

In fact, it is not the chromosome Y itself, but its small section called the **SRY** (sex determining region), or the TDF (testis determining factor), which encodes a small protein with a transcription factor function. **Its presence leads to the development of the testes.** If chromosomal rearrangement occurs and SRY is translocated to chromosome X, then such chromosome X behaves as Y, although some other Y specific sequences are necessary for the full development of a male individual. Among them, for example, the TSPY1 gene cluster. The TSPY1 protein (encoded by TSPY1 gene; Testis-specific Y-encoded gene) is found only in testicular tissue and is involved in spermatogenesis.

Testes form and secrete two major hormones:

- **MIS (Müllerian-inhibiting substance)**, or the AMH (anti-Müllerian duct hormone) (https://en.wikipedia.org/wiki/Anti-Müllerian_hormone), which interferes with the Müllerian duct progression
- **Testosterone**, which leads to fetal masculinization (the penis, scrotum, and other male anatomy formation; the secondary sex characteristics development)

Testosterone is produced by Leydig cells in the interstitial space of the testis. Its function is mediated by binding to the **androgen receptor** (*AR* encoded on the X chromosome). While testosterone signaling is not required for spermatogenesis induction in germ cells, it plays a critical role in the surrounding Sertoli cells to support male germ cell development and survival.

Human sex chromosomes

- Heterogametic sex: male XY
- Homogametic sex: females XX

The human X and Y chromosomes are derived from homologue autosomes. From the evolutionary point of view, it was beneficial to accumulate genes that are key to one sex and to separate them from genes that are advantageous for the other sex. This naturally had to lead to the degeneration of one chromosome. Y chromosome evolution is thus characterized by massive gene decay. Lack of recombination over most of its length leads to the male-limited transmission of the non-recombining segment.

Y chromosome

- Small chromosome (group G) but without satellite sequences.
- Rich in repetitive sequences and segmental duplications (50.4%).
- Two short pseudoautosomal regions sharing homology with chromosome X - PAR1 and PAR2 (a place where recombination occurs in male meiosis).
- Traits that are inherited solely by Y chromosome are called holandric traits (Y-linked).

X chromosome

- Medium size submetacentric chromosome (group C).
- In females, one of the two X chromosomes is randomly and permanently inactivated, by so called X-inactivation or Lyonization (Cytogenetically recognizable as Barr body.).
- Two short pseudoautosomal regions sharing homology with chromosome Y - PAR1 and PAR2.
- Traits that are inherited via X chromosome are called X-linked.