The chromosomal basis of sex varies with the organism

- In human and other mammals, there are two varieties of sex chromosomes, X and Y.
  - An individual who inherits two X chromosomes usually develops as a female.
  - An individual who inherits an X and a Y chromosome usually develops as a male.
- This X-Y system of mammals is not the only chromosomal mechanism of determining sex.
- Other options include the X-0 system, the Z-W system, and the haplo-diploid system.
- In the X-Y system, Y and X chromosomes behave as homologous chromosomes during meiosis.
  - In reality, they are only partially homologous and rarely undergo crossing over.
- In both testes (XY) and ovaries (XX), the two sex chromosomes segregate during meiosis and each gamete receives one.
  - Each egg receives an X chromosome.
  - Half the sperm receive an X chromosome and half receive a Y chromosome.
- Because of this, each conception has about a fifty-fifty chance of producing a particular sex.
- In humans, the anatomical signs of sex first appear when the embryo is about two months old.
- In individuals with the *SRY* gene (sex determining region of the Y chromosome), the generic embryonic gonads are modified into testes.
  - Activity of the SRY gene triggers a cascade of biochemical, physiological, and anatomical features because it regulates many other genes.
  - In addition, other genes on the Y chromosome are necessary for the production of functional sperm.
- In individuals lacking the SRY gene, the generic embryonic gonads develop into ovaries.

Sex-linked genes have unique patterns of inheritance

- In addition to their role in determining sex, the sex chromosomes, especially the X chromosome, have genes for many characters unrelated to sex.
- These *sex-linked* genes follow the same pattern of inheritance as the white-eye locus in *Drosophila*.
- If a sex-linked trait is due to a recessive allele, a female will have this phenotype only if she is homozygous.
    - Heterozygous females will be carriers.
- Because males have only one X chromosome (*hemizygous*), any male receiving the recessive allele from his mother will express the trait.
- The chance of a female inheriting a double dose of the mutant allele is much less than the chance of a male inheriting a single dose.
- Therefore, males are far more likely to inherit sex-linked recessive disorders than are females.
- Several serious human disorders are sex-linked.
- **Duchenne muscular dystrophy** affects one in 3,500 males born in the United States.
    - Affected individuals rarely live past their early 20s.
    - This disorder is due to the absence of an X-linked gene for a key muscle protein, called dystrophin.
    - The disease is characterized by a progressive weakening of the muscles and loss of coordination.
- **Hemophilia** is a sex-linked recessive trait defined by the absence of one or more clotting factors.
    - These proteins normally slow and then stop bleeding.
- Individuals with hemophilia have prolonged bleeding because a firm clot forms slowly.
    - Bleeding in muscles and joints can be painful and lead to serious damage.
- Individuals can be treated with intravenous injections of the missing protein.

- Although female mammals inherit two X chromosomes, only one X chromosome is active.
- Therefore, males and females have the same effective dose (one copy) of genes on the X chromosome.
    - During female development, one X chromosome per cell condenses into a compact object, a **Barr body.**
    - This inactivates most of its genes.
- The condensed Barr body chromosome is reactivated in ovarian cells that produce ova.
- Mary Lyon, a British geneticist, has demonstrated that the selection of which X chromosome to form the Barr body occurs randomly and independently in embryonic cells at the time of X inactivation.
- As a consequence, females consist of a mosaic of cells, some with an active paternal X, others with an active maternal X.
    - After Barr body formation, all descendent cells have the same inactive X.
    - If a female is heterozygous for a sex-linked trait, approximately half her cells will express one allele and the other half will express the other allele.
- In humans, this mosaic pattern is evident in women who are heterozygous for a X-linked mutation that prevents the development of sweat glands.
    - A heterozygous woman will have patches of normal skin and skin patches lacking sweat glands.
- Similarly, the orange and black pattern on tortoiseshell cats is due to patches of cells expressing an orange allele while others have a nonorange allele.
- X inactivation involves the attachment of methyl (CH_3) groups to cytosine nucleotides on the X chromosome that will become the Barr body.
- One of the two X chromosomes has an active *XIST* gene (X-inactive specific transcript).
    - This gene produces multiple copies of an RNA molecule that almost cover the X chromosome where they are made.
    - This initiates X inactivation, but the mechanism that connects *XIST* RNA and DNA methylation is unknown.
- What determines which of the two X chromosomes will have an active *XIST* gene is also unknown.