

# Chromosomes and Human Genetics

## The Philadelphia Story

A. The first abnormal chromosome to be associated with cancer was named the Philadelphia chromosome after the city in which it was discovered.

1. Karyotyping revealed that the abnormal chromosome is number nine to which a piece of number twenty-two is attached.

2. The altered genes specify an abnormal protein that stimulates unrestrained division of white blood cells—leukemia.

B. The modern study of genetics began with the rediscovery of Mendel's work in 1884.

1. By 1882, Flemming observed threadlike chromosomes in the nuclei of dividing cells.

2. By 1887, Weismann suggested that meiosis halves the number of chromosomes when gametes are made.

3. By 1900, Mendel's work was finally appreciated—namely, his view that diploid cells have two units for each trait and the units segregate during gamete formation.

## I. The Chromosomal Basis of Inheritance—An Overview

### A. Genes and Their Chromosome Locations

1. *Genes* are units of information about heritable traits, with particular locations on particular chromosomes.

2. In humans, one homolog of each chromosome is inherited from each parent.

3. Pairs of chromosomes that are similar in structure and function are called *homologous chromosomes*.

4. *Alleles* are slightly different forms of the same gene.

5. Gene exchange between homologs is called *crossing over* resulting in *genetic recombination*.

## B. Autosomes and Sex Chromosomes

1. Gender is determined by sex chromosomes.

a. Human females have two X chromosomes.

b. Human males have one X and one Y chromosome.

2. All nonsex-determining genes are the same in males and females and are called autosomes.

## C. Karyotype Analysis

1. Chromosomes are visualized in a lab preparation called a karyotype.

2. Chromosomes are identified and arranged by their characteristic size, shape, centromere location and staining patterns.

## II. *Focus on Science*: Karyotyping Made Easy

### III. Sex Determination in Humans

#### A. Karyotype analysis reveals:

1. All normal human eggs carry only one X chromosome.

2. Half of the sperm carry an X, the other half carry a Y.

#### B. Gender of human offspring are determined thus:

1. If an X-bearing sperm fertilizes an X-bearing egg, a female results.

2. If a Y-bearing sperm fertilizes an X-bearing egg, a male results.

#### C. The Y chromosome carries a male-determining gene that is Y-linked.

D. There are also genes on the sex chromosomes that code for nonsexual traits.

### IV. Early Questions About Gene Locations

#### A. Linked Genes: Clues to Inheritance Patterns

1. Morgan's work with fruit flies led to the discovery of X-linked genes.

2. The older term "sex-linked genes" has been replaced with more precise terms: X-linked genes and Y-linked genes.

3. Several linked genes on each type of chromosome is called a linkage group.

#### B. Crossing Over and Genetic Recombination

1. Linkage can be disrupted by crossing over.

a. Crossing over is an exchange of parts of homologous chromosomes.

b. The probability that crossing over will lead to the separation of two genes on a chromosome is proportional to the distance between them; that is, the farther apart two genes are, the greater their frequency of crossing over.

2. Crossing over introduces variations in genotypes and phenotypes and provides for the selection process necessary to evolution.

#### V. Human Genetic Analysis

##### A. Constructing Pedigrees

1. Human genetics is difficult to study.

a. We live under variable conditions in diverse environments.

b. Humans mate by chance and may, or may not, choose to reproduce.

c. Humans live as long as those who study them.

d. The small family size characteristic of human beings is not sufficient for meaningful statistical analysis.

2. The analysis of family pedigrees provides data on inheritance patterns through several generations.

##### B. Regarding Human Genetic Disorders

1. *Genetic abnormality* is a term applied to a genetic condition that is a deviation from the usual, or average, and is not life-threatening.

2. *Genetic disorder* is more appropriately used to describe conditions that cause medical problems.

3. A *syndrome* is a recognized set of symptoms that characterize a given

disorder.

## VI. Inheritance Patterns

### A. Autosomal Recessive Inheritance

1. Either parent can carry the recessive allele on an autosome.
2. Heterozygotes are symptom-free; homozygotes are affected.
3. Two heterozygous parents have a 50% chance of producing heterozygous children and a 25% chance of a homozygous recessive child. When both parents are homozygous, all children can be affected.
4. Galactosemia (the inability to metabolize lactose) is an example of autosomal recessive inheritance in which a single gene mutation prevents manufacture of an enzyme needed in the conversion pathway.

### B. Autosomal Dominant Inheritance

1. A dominant allele is always expressed and if it reduces the chance of surviving or reproducing, its frequency should decrease; mutations and postreproductive onset work against this hypothesis.
2. Achondroplasia (dwarfism) is a benign abnormality, but Huntington disorder is serious degeneration of the nervous system with an onset from age 40 onward.

### C. X-Linked Recessive Inheritance

1. X-linked recessive inheritance has these characteristics:
  - a. The mutated gene occurs only on the X chromosome.
  - b. Heterozygous females are phenotypically normal; males are affected because they have only one allele for the trait (on the X chromosome) and it can be recessive.
  - c. A normal male mated with a female heterozygote has a 50% chance of producing carrier daughters and a 50% chance of producing affected sons. In the case of a homozygous female and a normal male, all daughters will be carriers and all sons affected.
2. Color blindness is an example of an X-linked recessive trait that is not very serious at all.

3. A serious X-linked recessive condition is hemophilia A, the inability of the blood to clot because the genes do not code for the necessary clotting agent(s); fragile X syndrome is a recessive disorder that causes mental retardation in males.

## VII. *Focus on Health*: Too Young To Be Old

## VIII. Changes in Chromosome Structure

### A. Major Categories of Structural Change

1. *Duplication* occurs when a gene sequence is in excess of the normal amount.

2. An *inversion* alters the position and sequence of the genes so that gene order is reversed.

3. A *translocation* occurs when a part of one chromosome is transferred to a nonhomologous chromosome; an example is a form of cancer where a segment of chromosome #22 is on #9 (Philadelphia chromosome).

4. A *deletion* is the loss of a chromosome region by viral attack, chemicals, irradiation, or other environmental factors; for example, the loss of a portion of chromosome #5 causes a disorder called cri-du-chat.

### B. Does Chromosome Structure Ever Evolve?

1. Changes in chromosome structure tend to be selected against rather than conserved over evolutionary time.

2. However, gene regions for the polypeptide chains of hemoglobin have duplicated to produce different hemoglobins with different oxygen transporting efficiencies.

## IX. Changes in Chromosome Number

### A. Categories and Mechanisms of Change

1. Aneuploidy, one extra or one less chromosome, may affect one of every two newly fertilized eggs.

2. Polyploidy, three or more of each chromosome, is common in plants but is lethal to the zygote if it occurs in humans.

3. *Nondisjunction* at anaphase I or anaphase II frequently results in a change in chromosome number.

a. If a gamete with an extra chromosome ( $n + 1$ ) joins a normal gamete at fertilization, the diploid cell will be  $2n + 1$ ; this condition is called trisomy.

b. If an abnormal gamete is missing a chromosome, the zygote will be  $2n - 1$ : monosomy.

## B. Changes in the Number of Autosomes

1. Down syndrome results from trisomy 21; 1 in 1,100 live newborns in North America are affected.

2. Most children with Down syndrome show mental retardation, and 40% have heart defects.

3. Down syndrome occurs more frequently in children born to older women.

## C. Changes in the Number of Sex Chromosomes

### 1. Turner syndrome

a. Turner syndrome (designated XO) involves females whose cells have only one X chromosome, mostly due to nondisjunction in the father.

b. A vast majority of XO embryos and fetuses are spontaneously aborted.

c. Affected individuals are sterile and have other phenotypic problems such as premature aging and shorter life expectancy.

### 2. Klinefelter syndrome

a. Nondisjunction (mostly in the mother) results in an extra X chromosome in the cells (XXY) of these affected males.

b. These individuals are taller than average, usually are sterile, and may show some mental slowness.

### 3. XYY condition

a. The extra Y chromosome in these males does not affect fertility, but they are taller than average and are slightly mentally retarded.

b. Erroneous correlations have linked these persons with predisposition to crime.