What are genetic disorders?

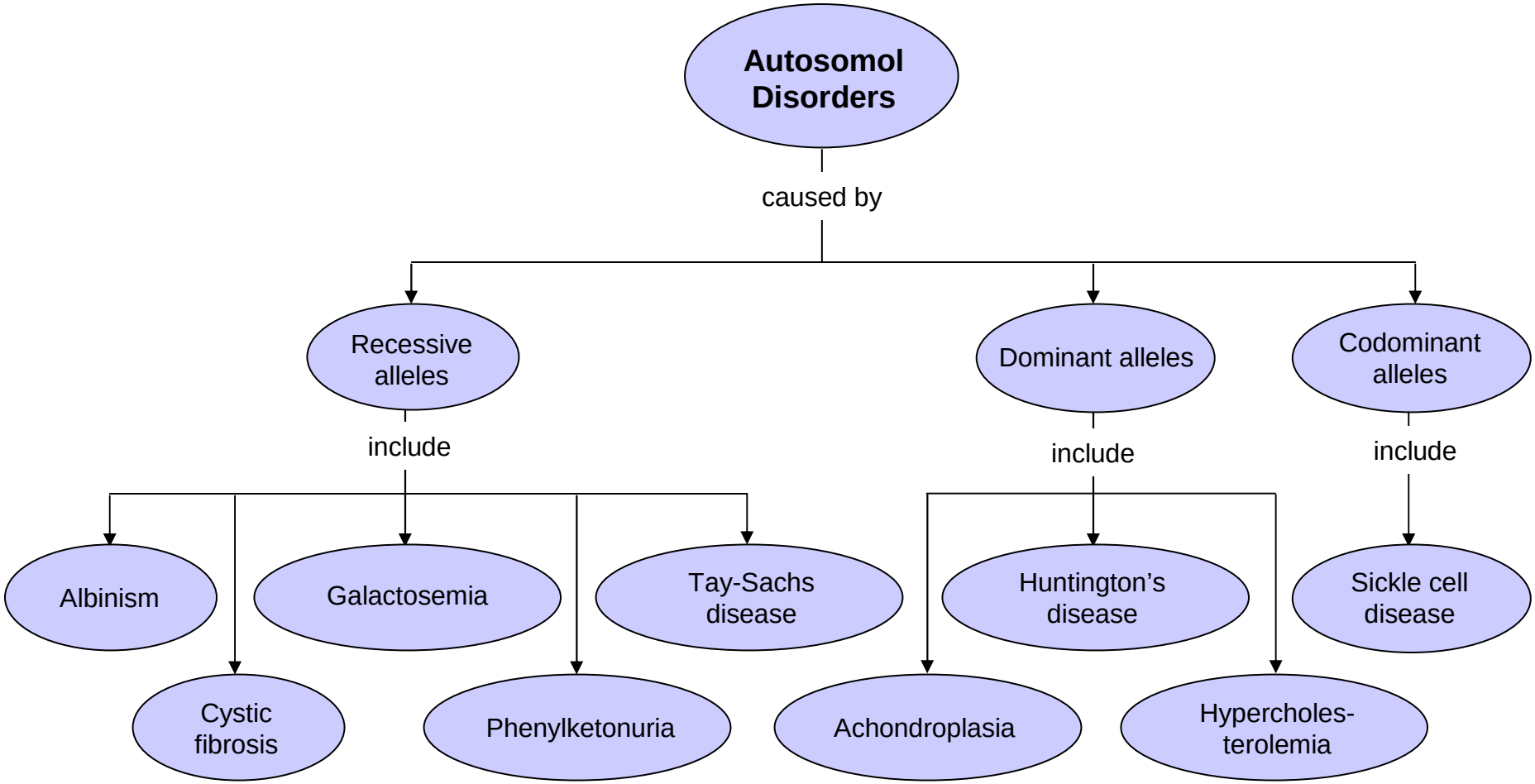
- A disease caused by abnormalities in an individual's genetic material (genome)
- There are four types of genetic disorders
  1. Single-gene (also called Mendelian or monogenic)
  2. Multifactoral (also called complex or polygenic)
  3. Chromosomal
  4. Mitochondrial

Single-gene Disorders

- Caused by mutations in the DNA sequence of one gene.
- This can affect the production of a protein which can lead to a disorder.
- There are more than 6,000 known single-gene disorders.
- They occur in about 1 out of every 200 births.

Examples of Single-gene Disorders

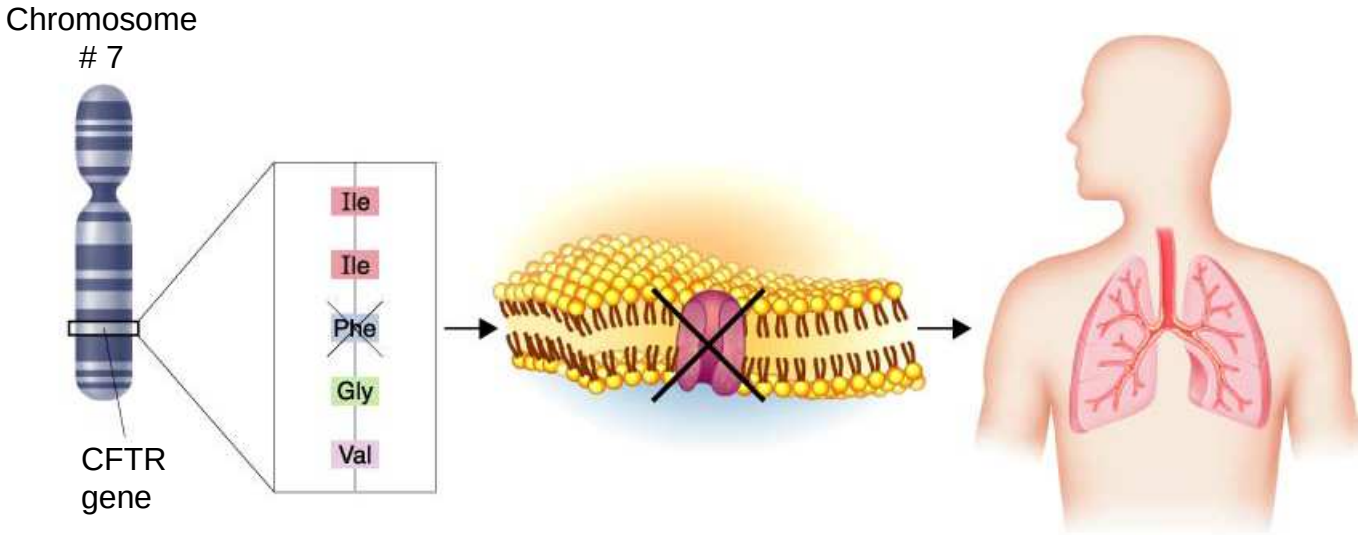
- Cystic Fibrosis
- Sickle cell anemia
- Huntington’s disease
- Marfan Syndrome


Autosomol Disorders
caused by
Recessive alleles
Dominant alleles
Codominant alleles
include
include
include
Albinism
Galactosemia
Tay-Sachs disease
Huntington's disease
Sickle cell disease
Cystic fibrosis
Phenylketonuria
Achondroplasia
Hypercholes-terolemia

Cystic Fibrosis

- Controlled by a recessive allele.
- Causes mucus to build up in the lungs
  - More susceptible to infection
  - Usually only live to early twenties
- 1 out of 2500 whites of European decent.
  - More rare in other groups
- 1 out of 25 (4%) is a carrier
- Disrupts a membrane protein that transports chloride ions

Cystic Fibrosis



A The most common allele that causes cystic fibrosis is missing 3 DNA bases. As a result, the amino acid phenylalanine is missing from the CFTR protein.

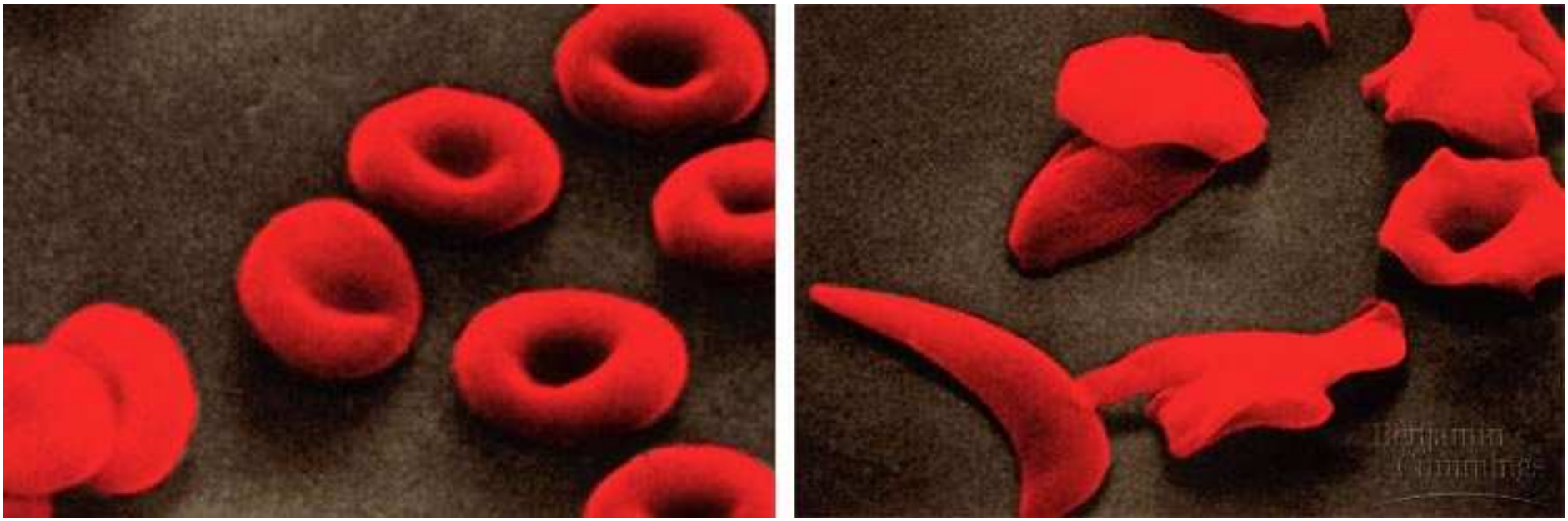
B Normal CFTR is a chloride ion channel in cell membranes. Abnormal CFTR cannot be transported to the cell membrane.

C The cells in the person's airways are unable to transport chloride ions. As a result, the airways become clogged with a thick mucus.

Sickle-cell disease

- Caused by the substitution of a single amino acid in the hemoglobin protein in red blood cells.
  - Red blood cells take on a sickle shape.Fig.
  - Clumping of cells causes clogging of small blood vessels
- Affects 1 out of 400 African-Americans.

Figure 23.12x Normal and sickled cells



Tay-Sachs Disease

- Caused by a disfuncitonal enzyme that fails to break down brain lipids. Recessive allele
  - Seizures, blindness, degeneration of motor and mental skills
- High incidence among Jewish people whose ancestors lived in central Europe
  - 1 out of 3600 births. 100 times higher than among non-Jews or Mediterranean Jews

Multifactorial (polygenic) Disorders

- Caused by a combination of environmental factors and mutations in multiple genes.
- Example, different genes that influence breast cancer susceptibility are on chromosome 6,11,13,15,17, and 22.
- Most common chronic disorders are multifactorial disorders.

Examples of Multifactorial Disorders

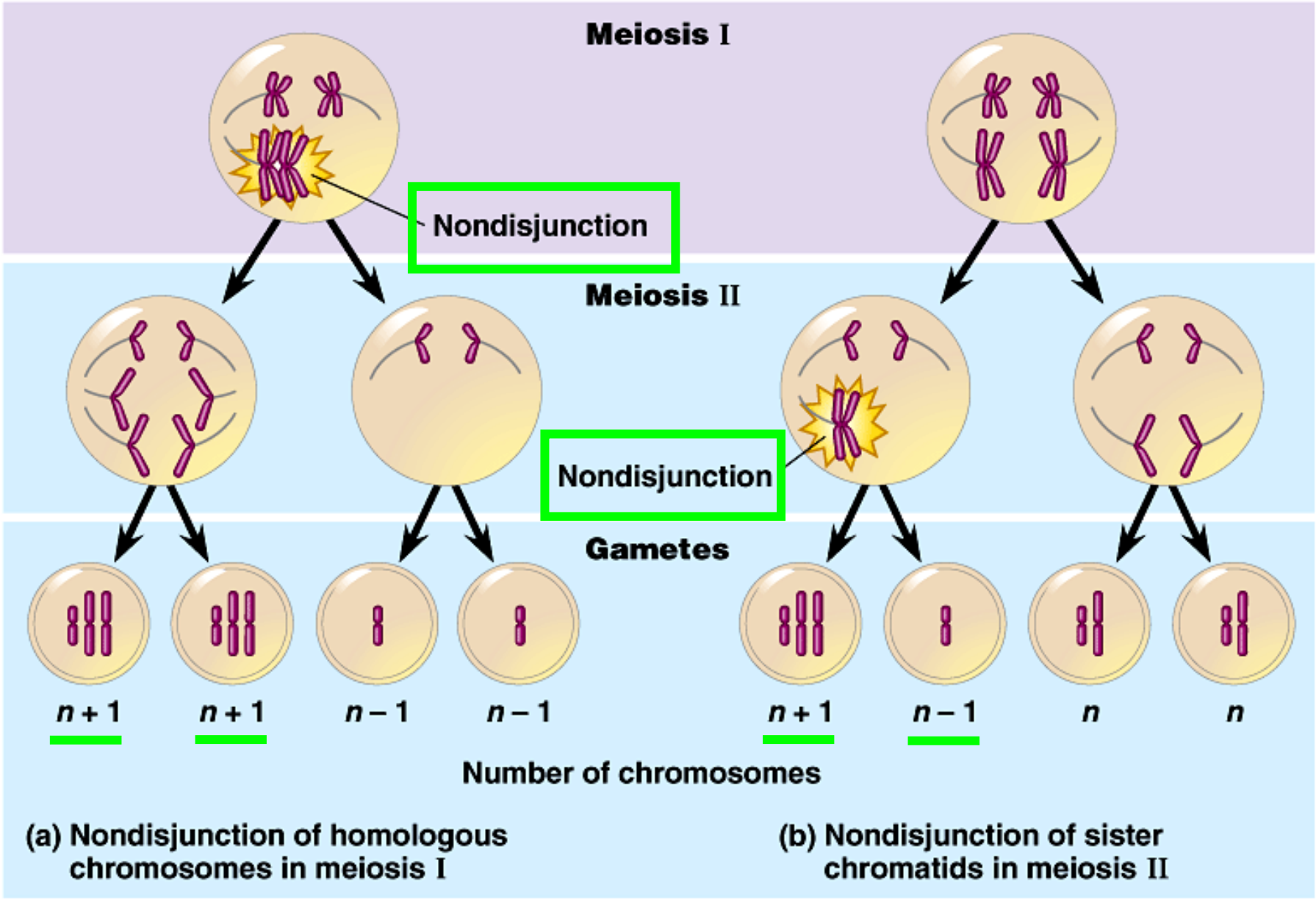
- Heart disease
- High blood pressure
- Alzheimer's disease
- Arthritis
- Diabetes
- Cancer
- Obesity

Chromosomal Disorders

- Caused by chromosomal mutations
  1. Deletions
  2. Duplications
  3. Inversions
  4. Translocations
  5. Extra copies

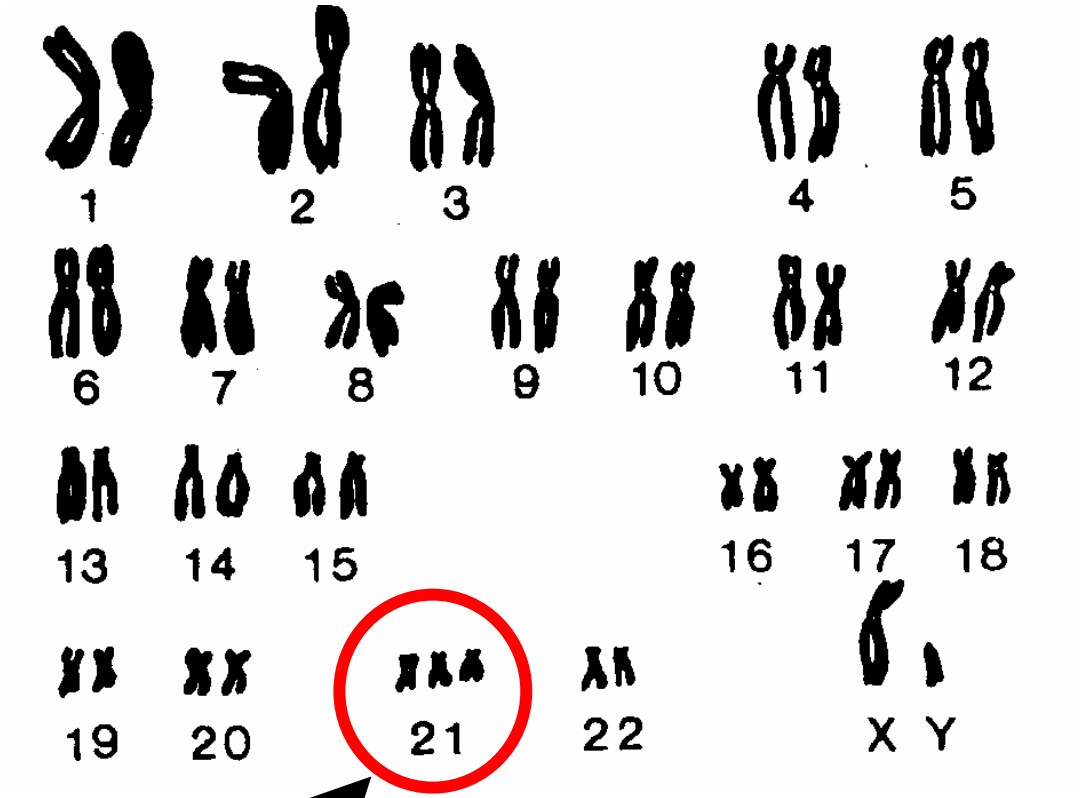
Down syndrome

- 1 out of 700 children born in the US
- Results from an extra chromosome 21
  - Trisomy 21
  - Each body cell has 47 chromosomes
- Trisomy 21 severely alters the individuals phenotype
  - Facial features, short stature, heart defects, susceptibility to respiratory infections and mental retardation.
- Caused by non-disjunction during gamete formation



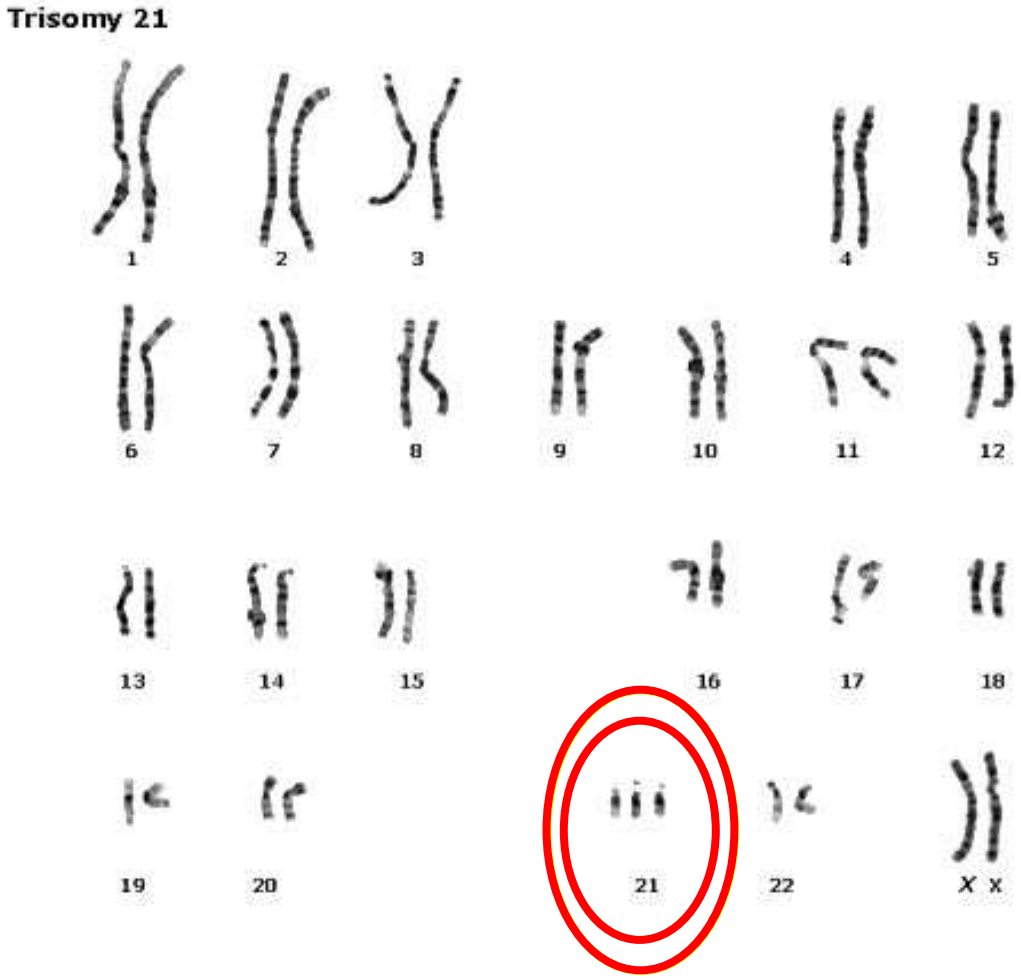
Down Syndrome

An individual
with Down Syndrome
has 47 chromosomes
in every body cell



Trisomy 21

Down Syndrome



Caused by non-disjunction during meiosis

Karyotyping

- A way of looking at the chromosome makeup of an individual.
- During mitosis the chromosomes condense and become visible.
- A photo can be taken
- A karyotype can be made from the photo by arranging the chromosomes into homologous pairs.

Karyotyping

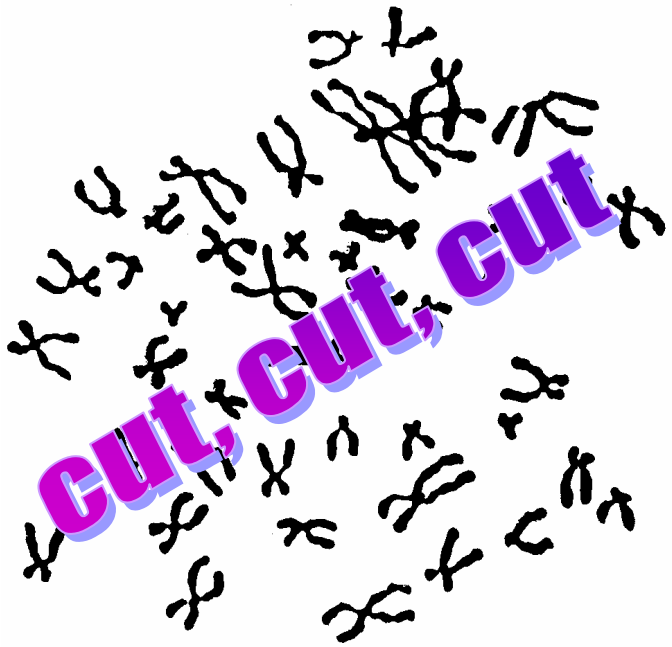
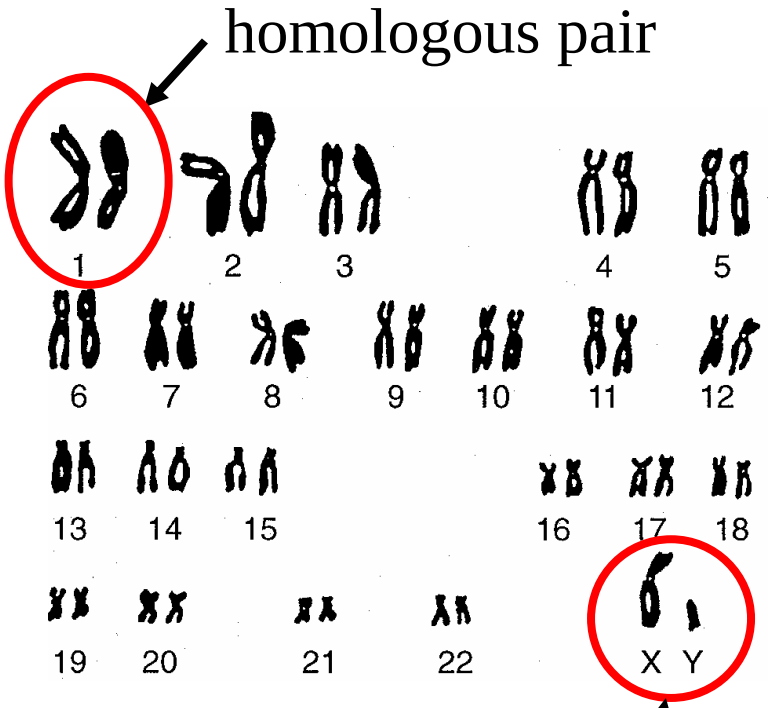


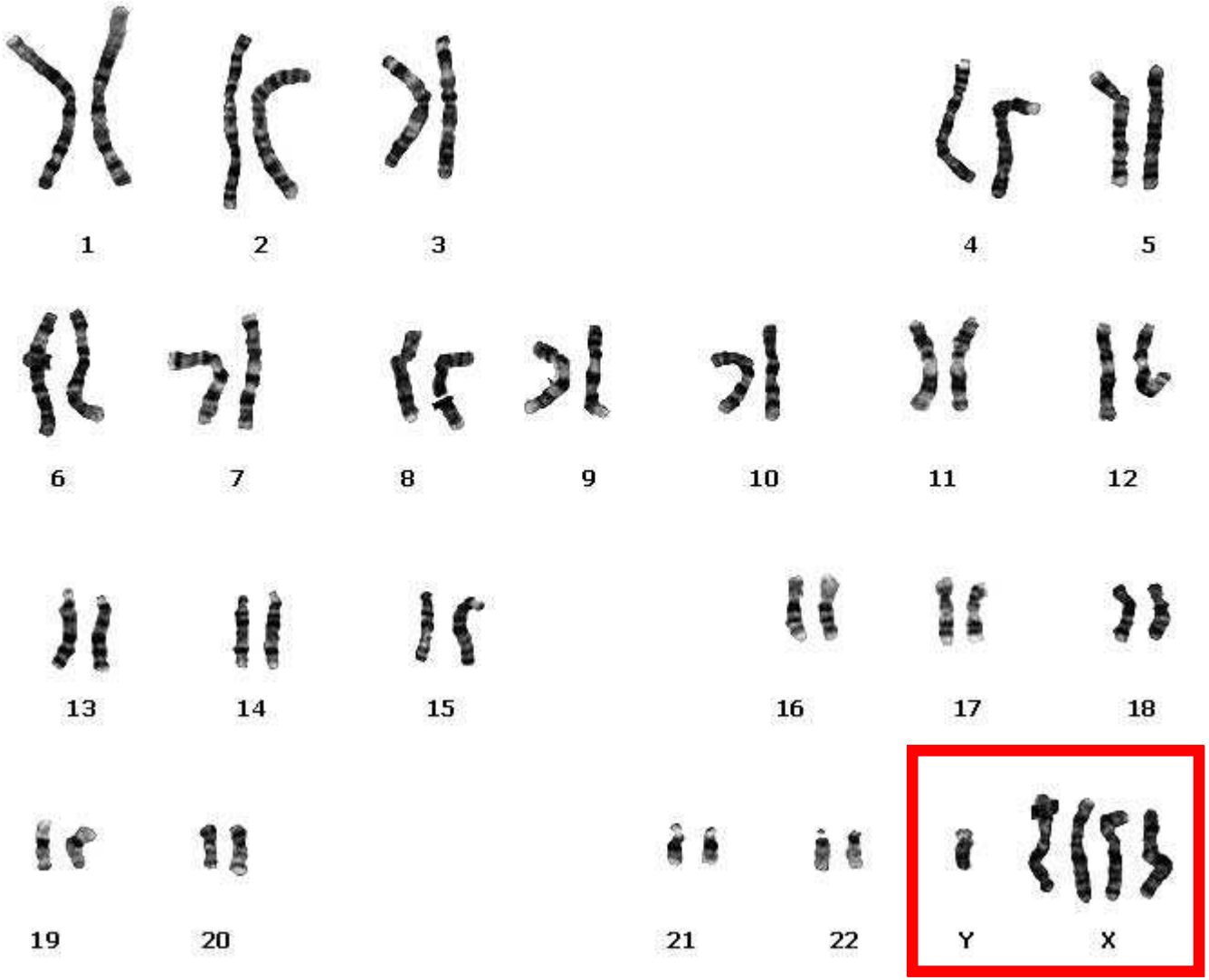
photo of chromosomes

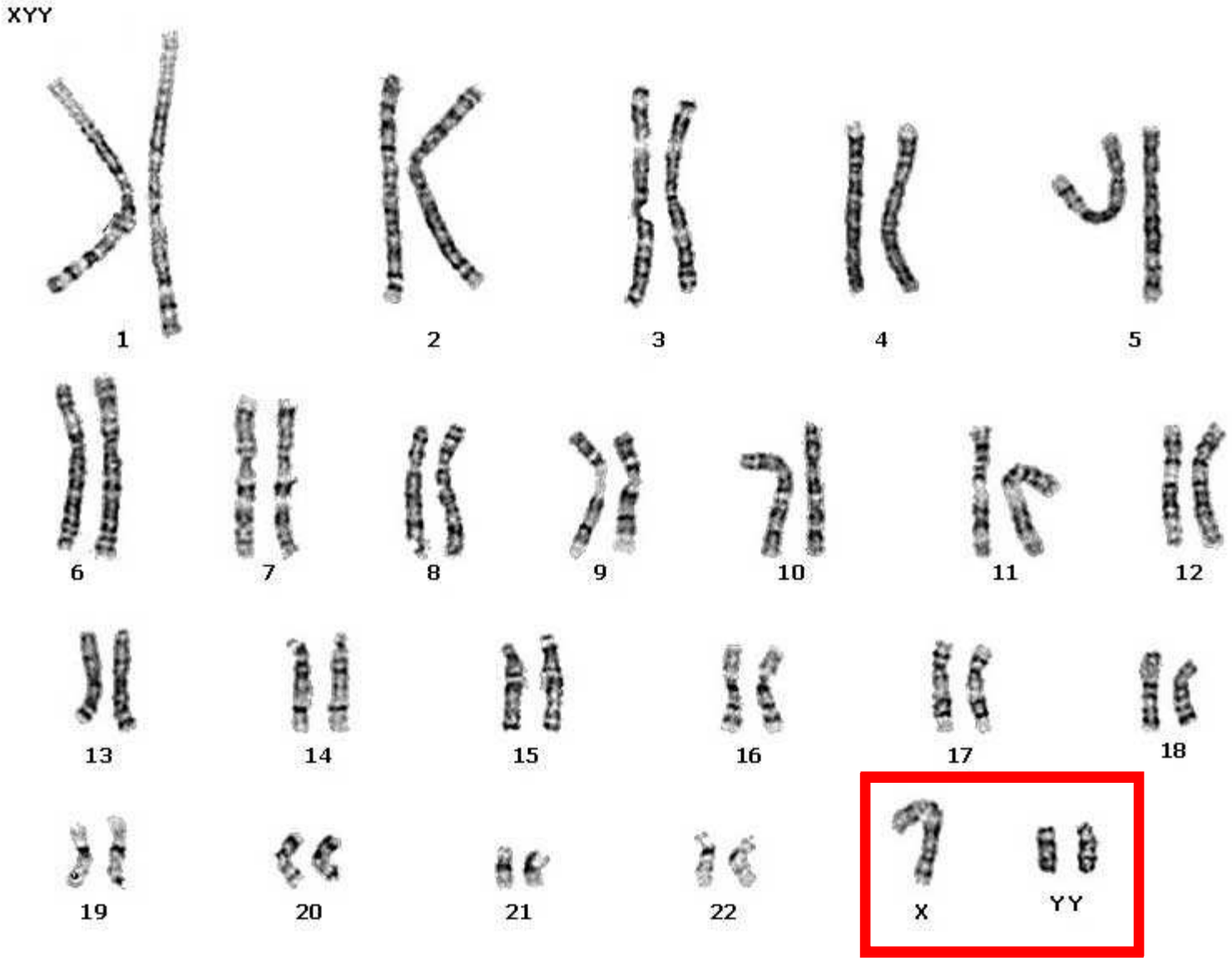


arranged karyotype

sex chromosomes

XXXXY, Klinefelter's Syndrome

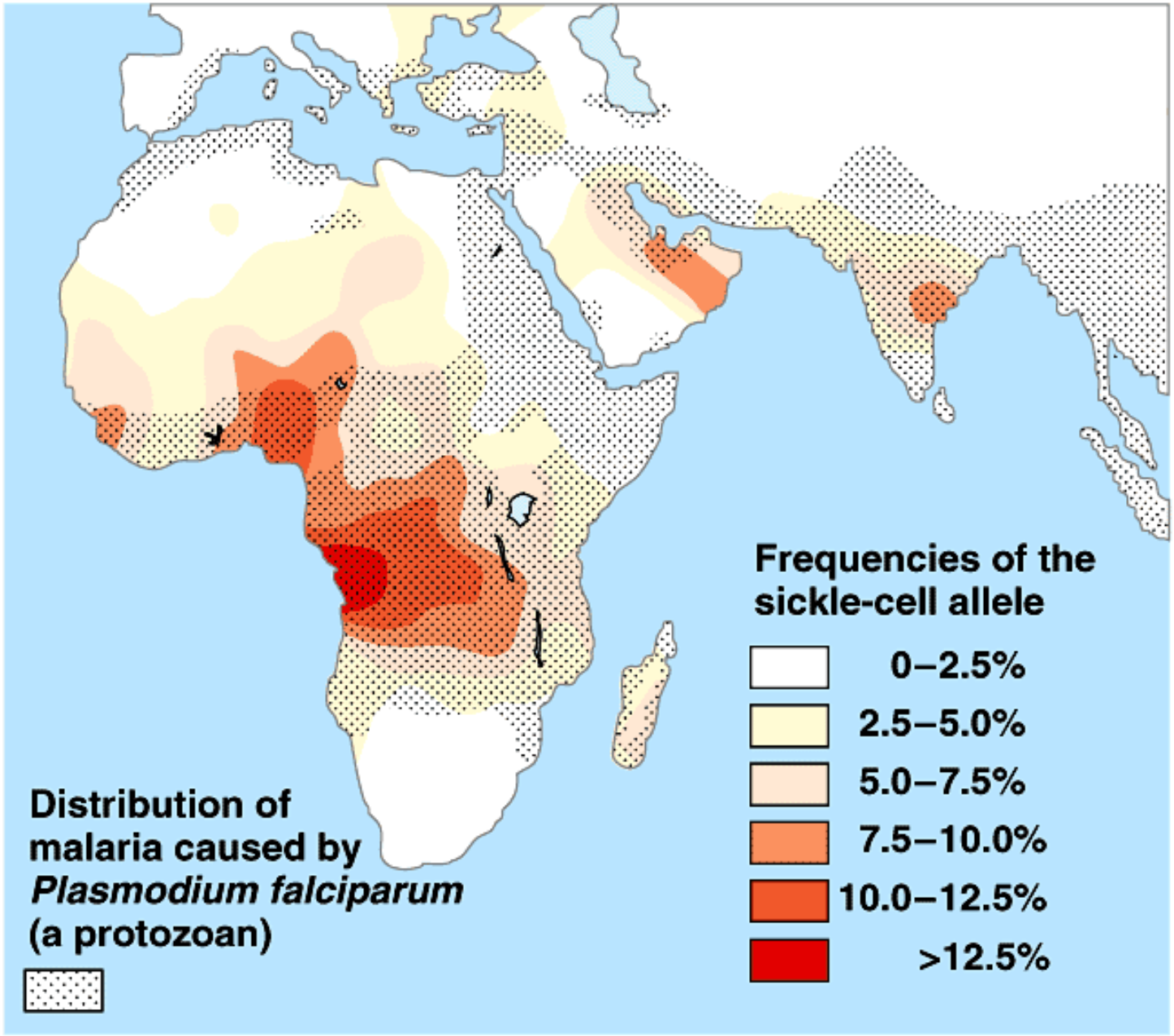



XYY
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
YY

Mitochondrial Disorders

- Relatively rare type of genetic disorder caused by mutations in the nonchromosomal DNA of mitochondria.
- Each mitochondrion may contain 5 to 10 circular pieces of DNA.

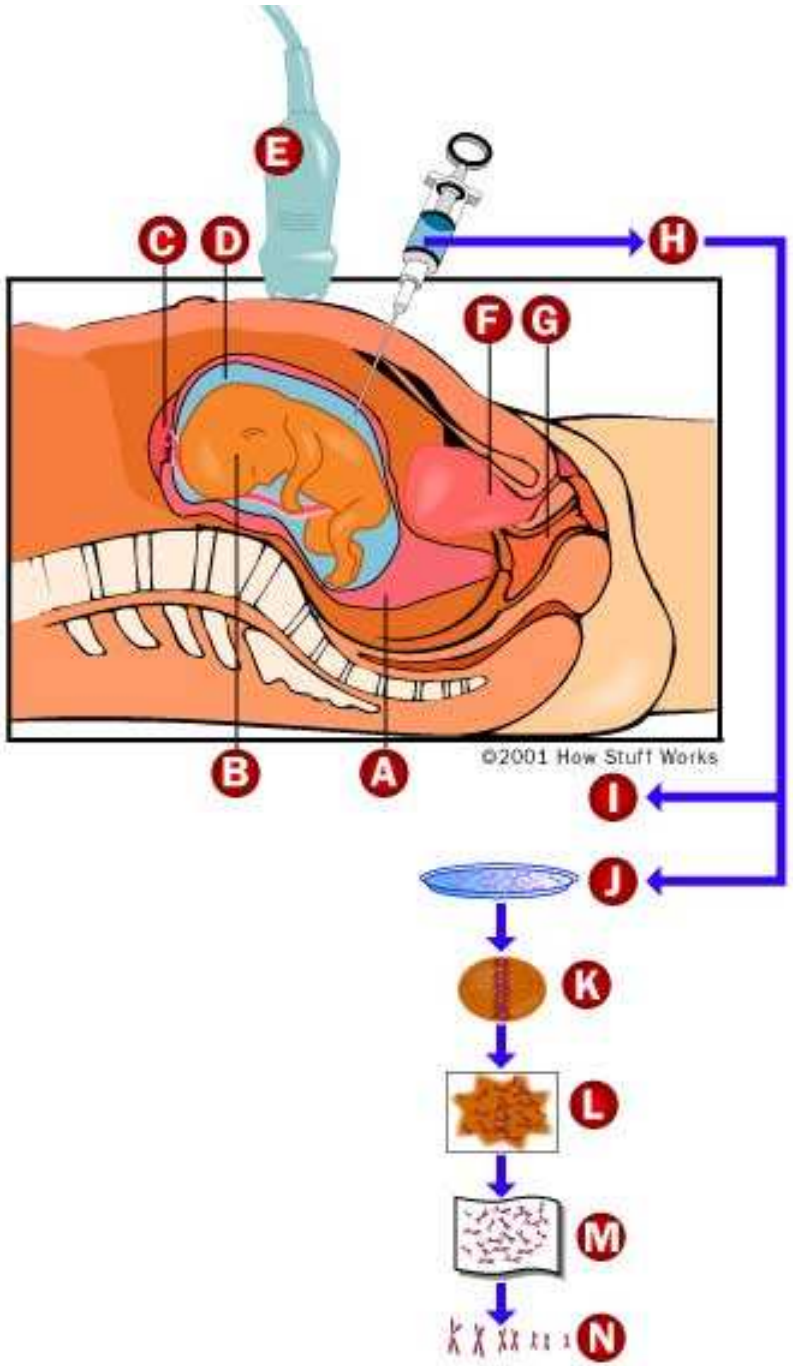
Figure 23.10 Mapping malaria and the sickle-cell allele



Fetal Testing

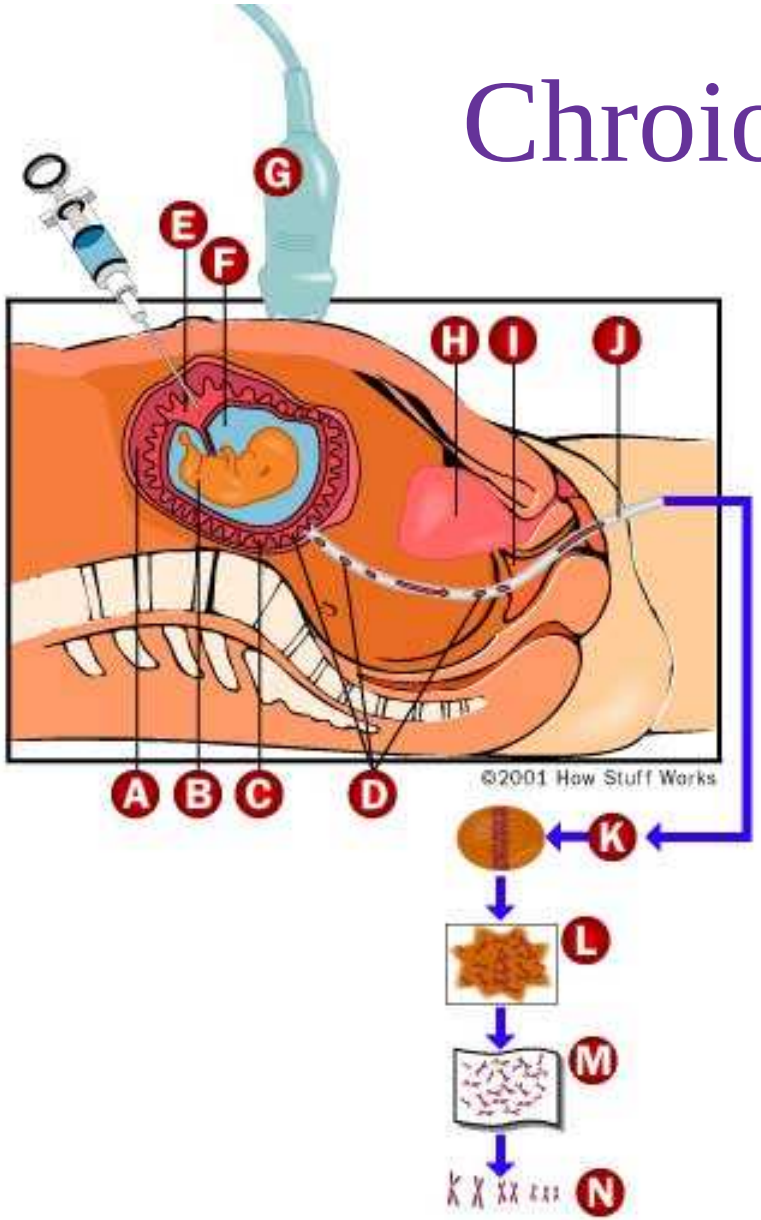
- Amniocentesis
  - Needle is inserted into the uterus and 10ml of amniotic fluid is extracted
  - Tests can be done on the cells that are in the fluid extracted.
- Chorionic villus sampling (CVS)
  - Small amount of fetal tissue is taken from the placenta
  - Tests are done on the cells in this tissue.

Amniocentesis



- A Uterus
- B Fetus
- C Placenta
- D Amniotic sac
- E Ultrasound probe
- F Bladder
- G Vagina
- H Sample of amniotic fluid removed
- I Analysis of chemicals in amniotic fluid
- J Cells from amniotic fluid grown in culture
- K 2-3 weeks of cell growth
- L Treated cells are squashed on a microscope slide
- M Chromosomes are photographed
- N A karyotype is prepared

Chroionic Villus Sampling

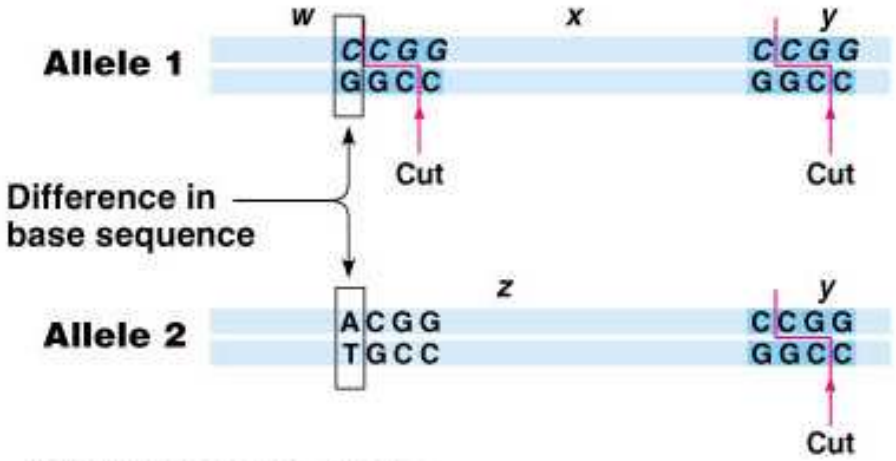


A Uterus
B Fetus
C Chorion
D Chorionic villi
E Placenta
F Amniotic fluid
G Ultrasound probe
H Bladder
I Vagina
J Sampling tube
K Next day
L Treated cells are squashed on a microscope slide
M Chromosomes are photographed
N A karyotype is prepared

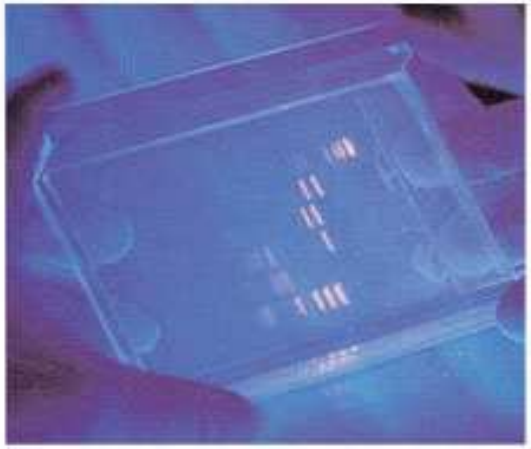
Testing for Alleles

- If two prospective parents suspect they might be carrying recessive alleles for a genetic disorder such as cystic fibrosis or Tay-Sachs disease, how could they find out for sure?
- It is possible to get a genetic test to see if the recessive allele is present in an individuals DNA (genetic code)

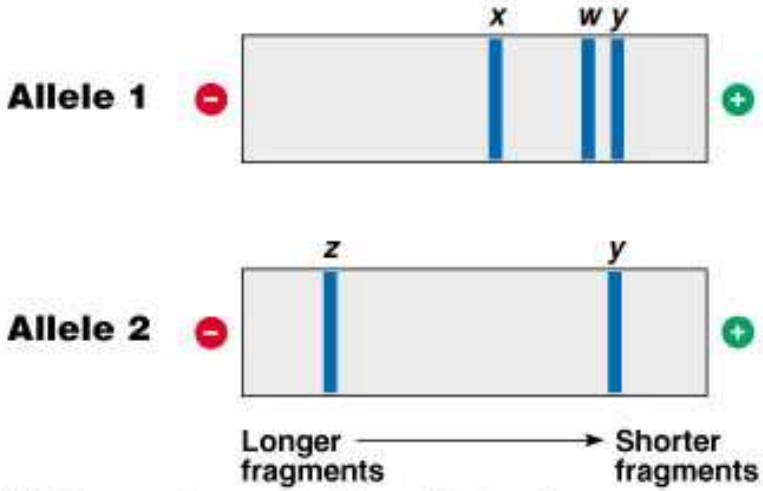
Figure 20.9 Using restriction fragment patterns to distinguish DNA from different alleles



(a) DNA from two alleles



(c) Completed gel



(b) Electrophoresis of restriction fragments

Gene Therapy

- The process of changing a gene that causes a genetic disorder
- An absent or faulty gene is replaced by a normal, working gene
- The body can then make the correct protein, usually an enzyme it needs.
- This eliminates or lessens the disorder

Gene Therapy

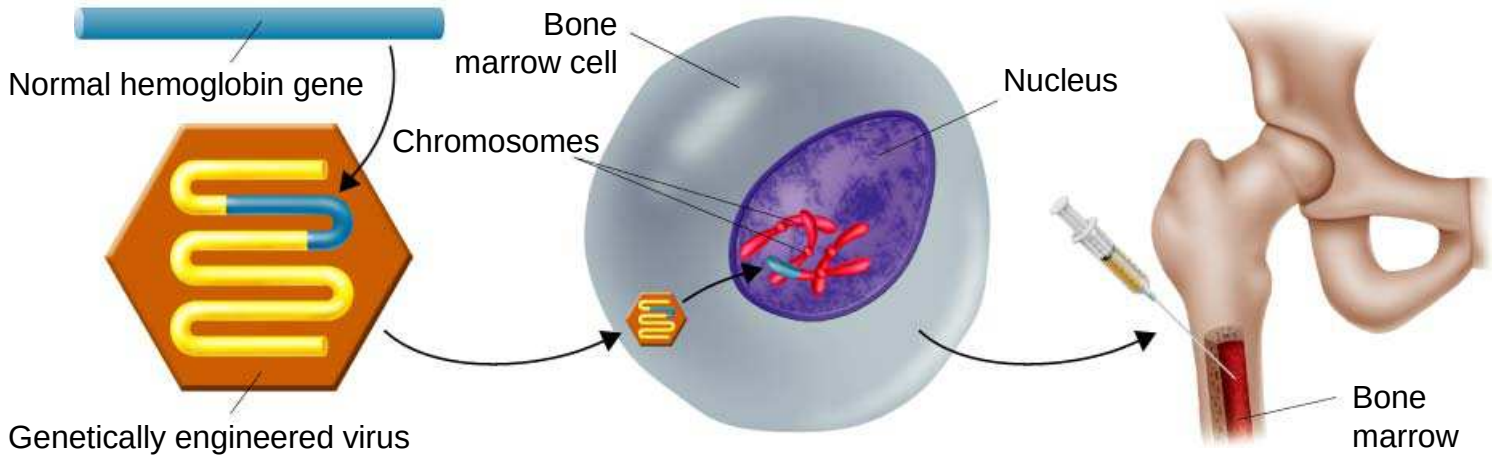
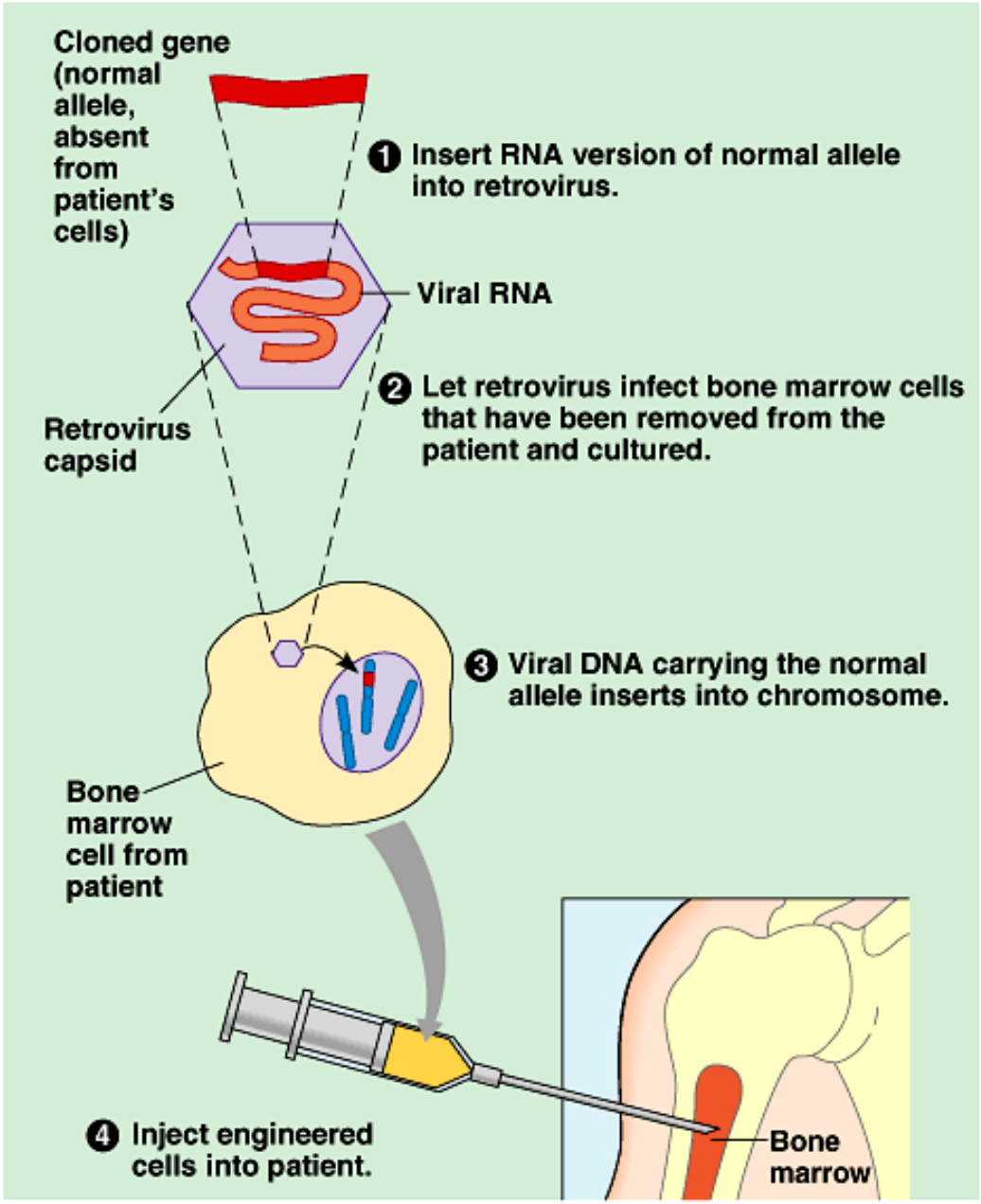


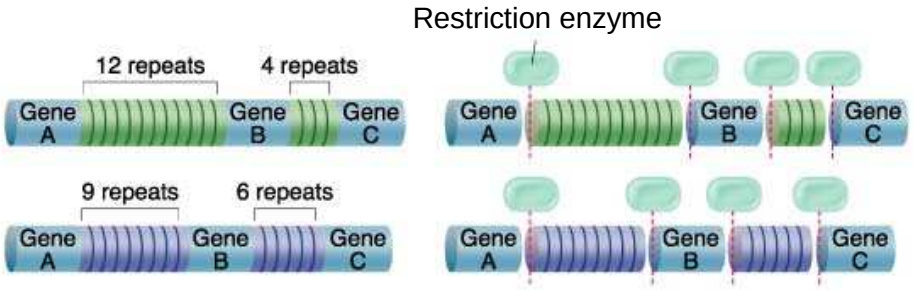
Figure 20.16 One type of gene therapy procedure

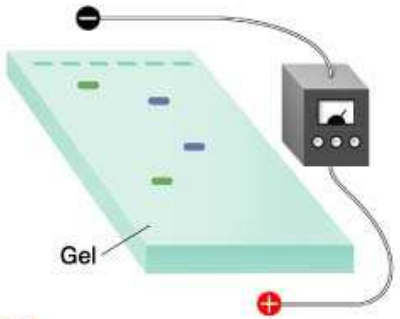


DNA Fingerprints

- Used to identify individuals. Like an actual fingerprint.
- DNA is cut with restriction enzymes and then the fragments are separated using gel electrophoresis.
- Every individual has a unique band pattern

DNA Fingerprinting



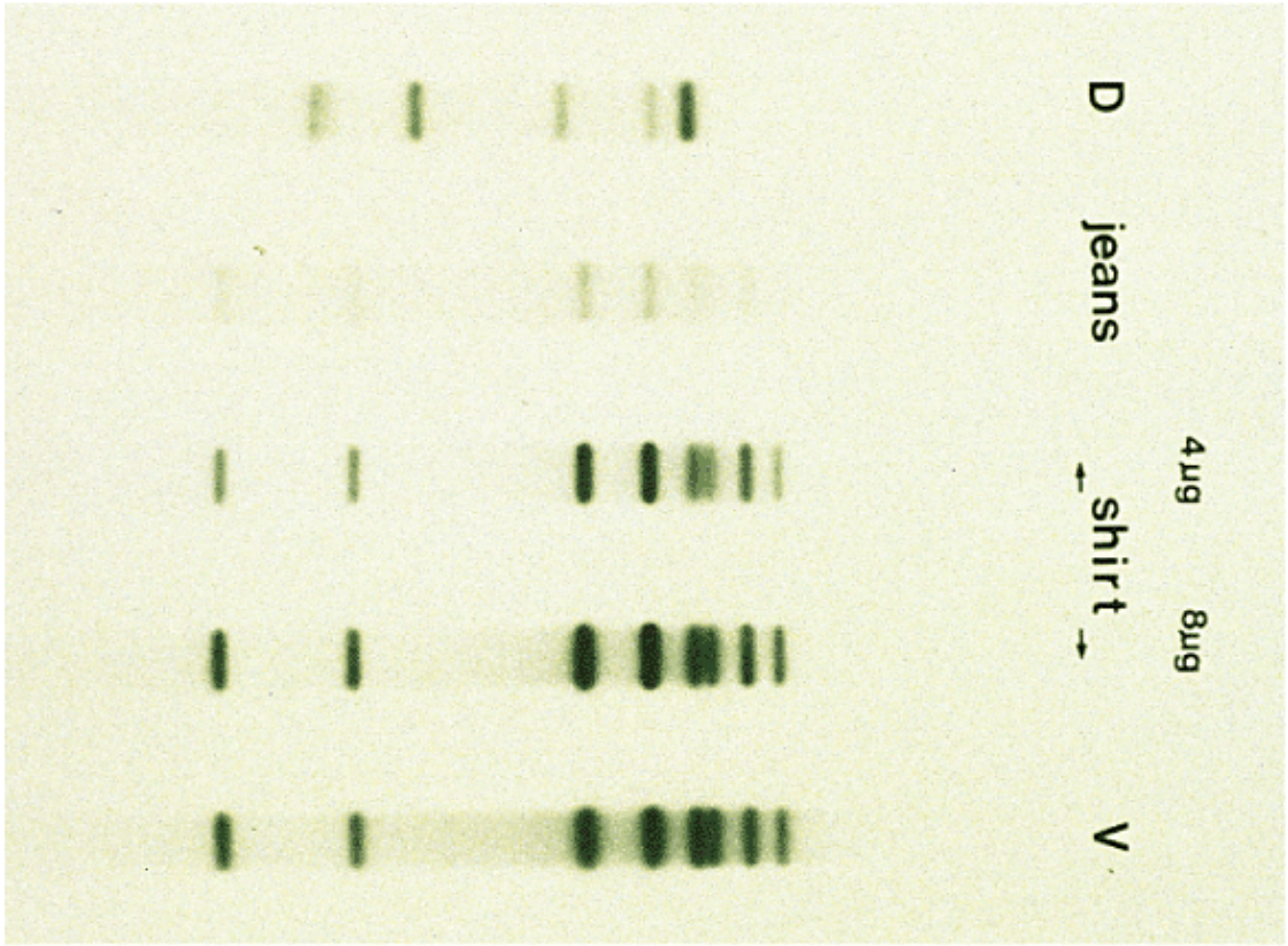


A Chromosomes contain large amounts of DNA called repeats that do not code for proteins. This DNA varies from person to person. Here, one sample has 12 repeats between genes A and B, while the second sample has 9 repeats.

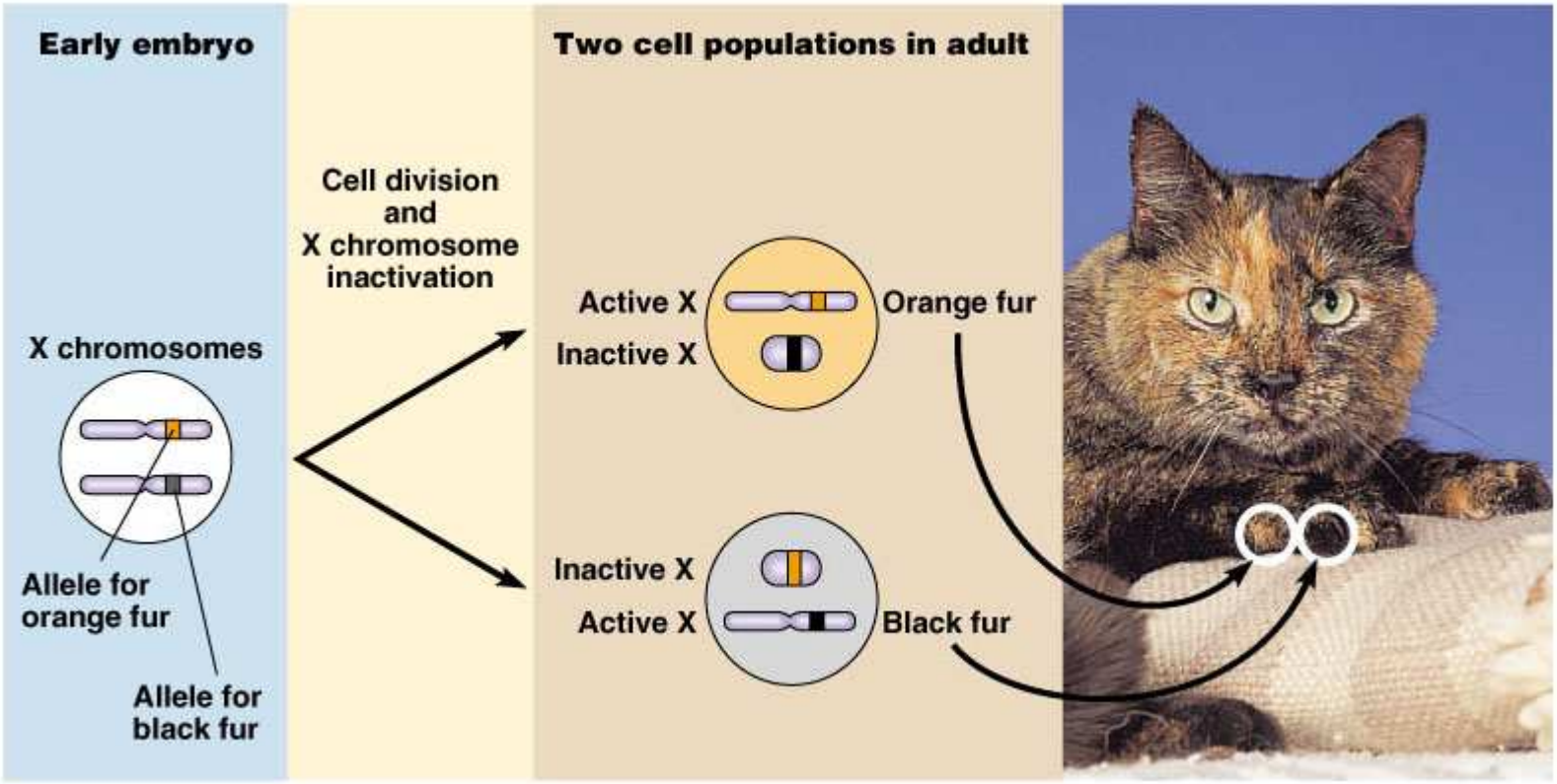
B Restriction enzymes are used to cut the DNA into fragments containing genes and repeats. Note that the repeat fragments from these two samples are of different lengths.

C The DNA fragments are separated according to size using gel electrophoresis. The fragments containing repeats are then labeled using radioactive probes. This produces a series of bands—the DNA fingerprint.

Figure 20.17 DNA fingerprints from a murder case

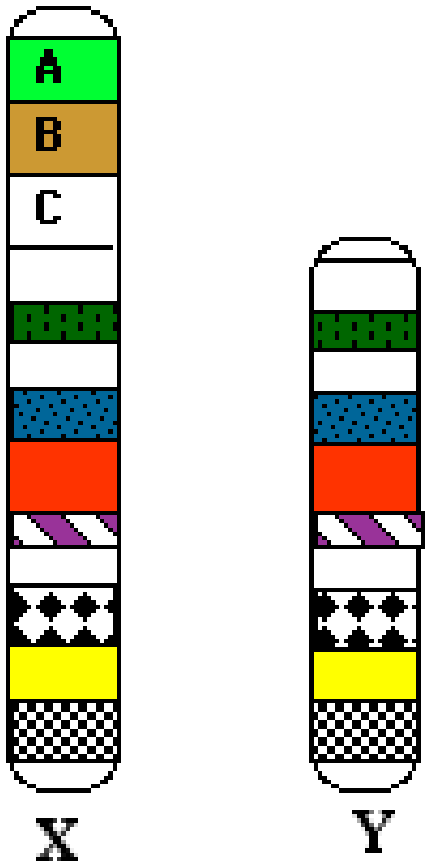


X chromosome inactivation



X chromosome inactivation

Sex Linked Traits



The Y chromosome is missing this section of the X chromosome. The lower sections of both chromosomes contain the genes for the same traits.

Red-Green Colorblindness

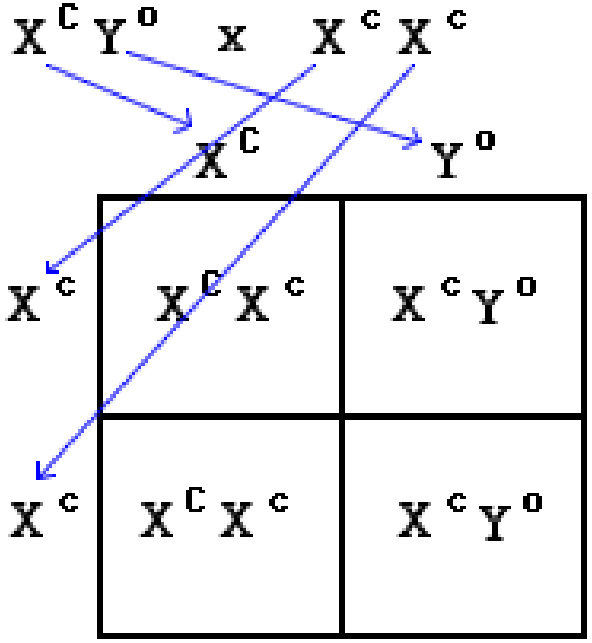
Phenotypes	Genotypes
Normal Vision Male	$X^C Y^o$
Colorblind Male	$X^c Y^o$
Normal Vision Female	$X^C X^C$
Normal Vision Female (carrier)	$X^C X^c$
Colorblind Female	$X^c X^c$

Parents' Phenotypes:

Normal Vision Father X Colorblind Mother

Parents' Genotypes:

$X^C Y^o$ x $X^c X^c$



Phenotypes of Offspring:

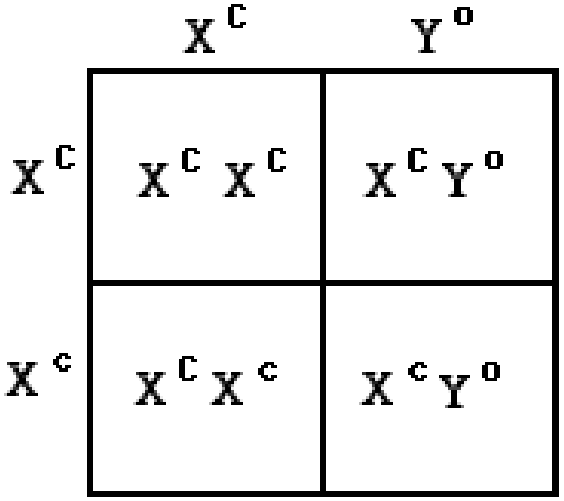
100% Normal Vision Daughters
100% Colorblind Sons

Parents' Phenotypes:

Normal Vision Father X Normal Vision Mother (no colorblindness in her big family)

Parents' Genotypes:

$X^C Y^o$ x $X^C X^C$



Phenotypes of Offspring:

100% Females Normal Vision
50% Males Normal Vision
50% Males w/ Colorblindness

Sex Linked Genes

- Red-green color blindness
  - X-linked: color vision deficiency
- Hemophilia
  - X-linked: normal blood clotting factors are not produced
  - Results in prolonged bleeding
- Muscular dystrophy
  - X-linked: gradual irreversible wasting of skeletal muscle
- Fragile X Syndrome
  - X-linked: causes mental retardation

Ethical Issues in Human Genetics

Ethical Issues in Human Genetics

- Changing height, hair color etc.?
- Custom designed humans?
- Cloning?

- Society will have to decide how this new knowledge and understanding of human genetics should be used