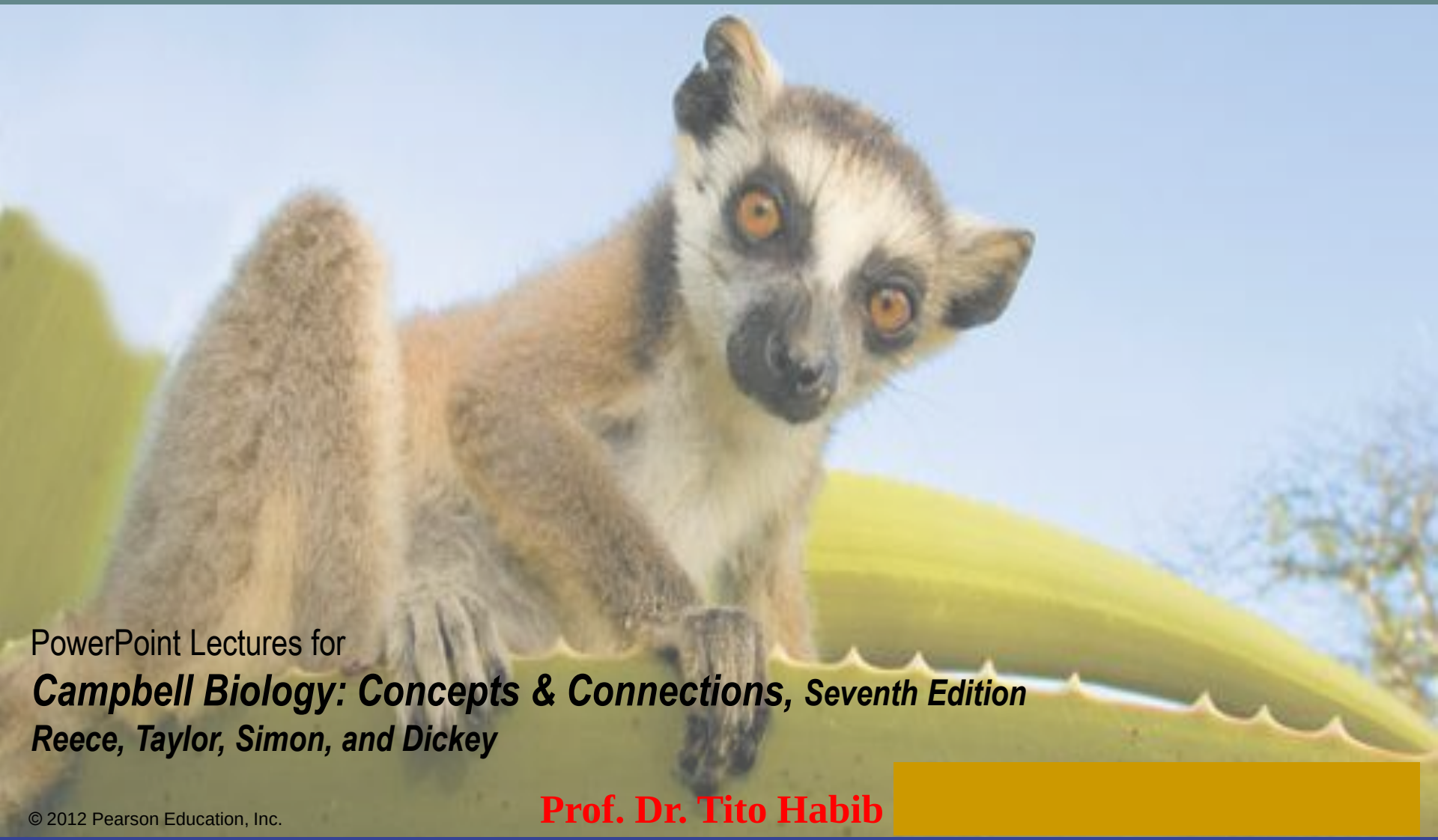
Genetic Diseases

Chapter 2



PowerPoint Lectures for

***Campbell Biology: Concepts & Connections*, Seventh Edition**

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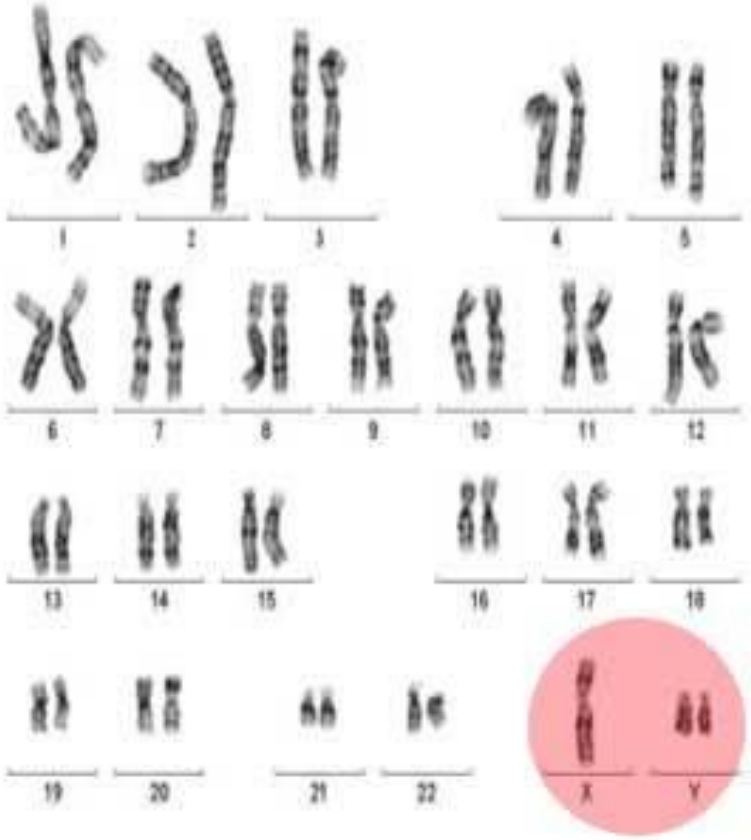
What is a genetic disorder?

A genetic disorder is a disease that is caused by a change, or mutation, in an individual's DNA sequence.

What is a mutation?

Small scale/ gene

Large scale/ chromosome



Types Of Genetic Disease

- Single gene disorders
- Chromosomal disorders
- Multifactorial/Polygenic disorders
  - Complex/Common diseases

Inherited human disorders show either

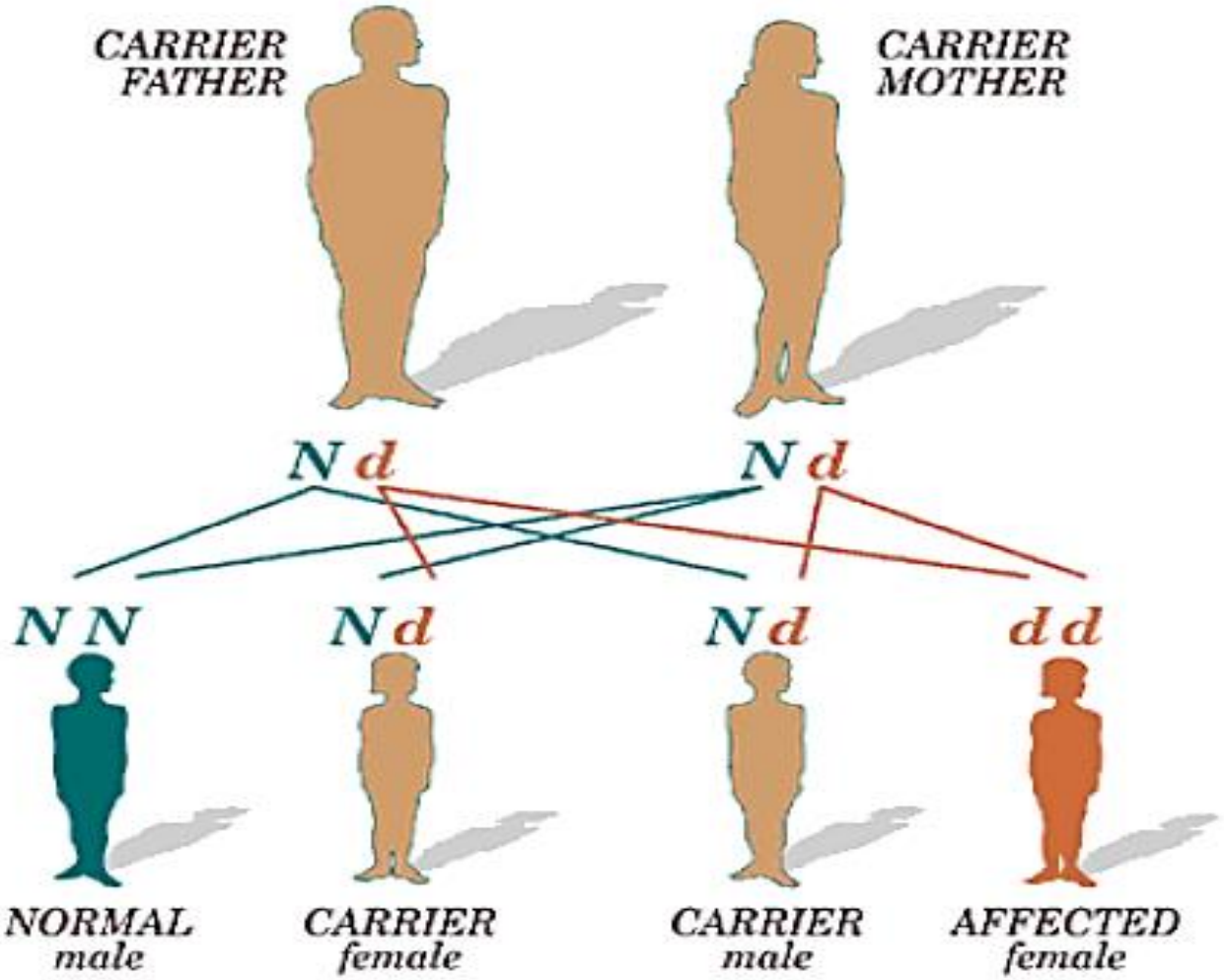
recessive inheritance in which

- two recessive alleles are needed to show disease,
- heterozygous parents are carriers of the disease-causing allele, and
- the probability of inheritance increases with **inbreeding**, mating between close relatives.

dominant inheritance in which

- one dominant allele is needed to show disease and
- dominant lethal alleles are usually eliminated from the population.

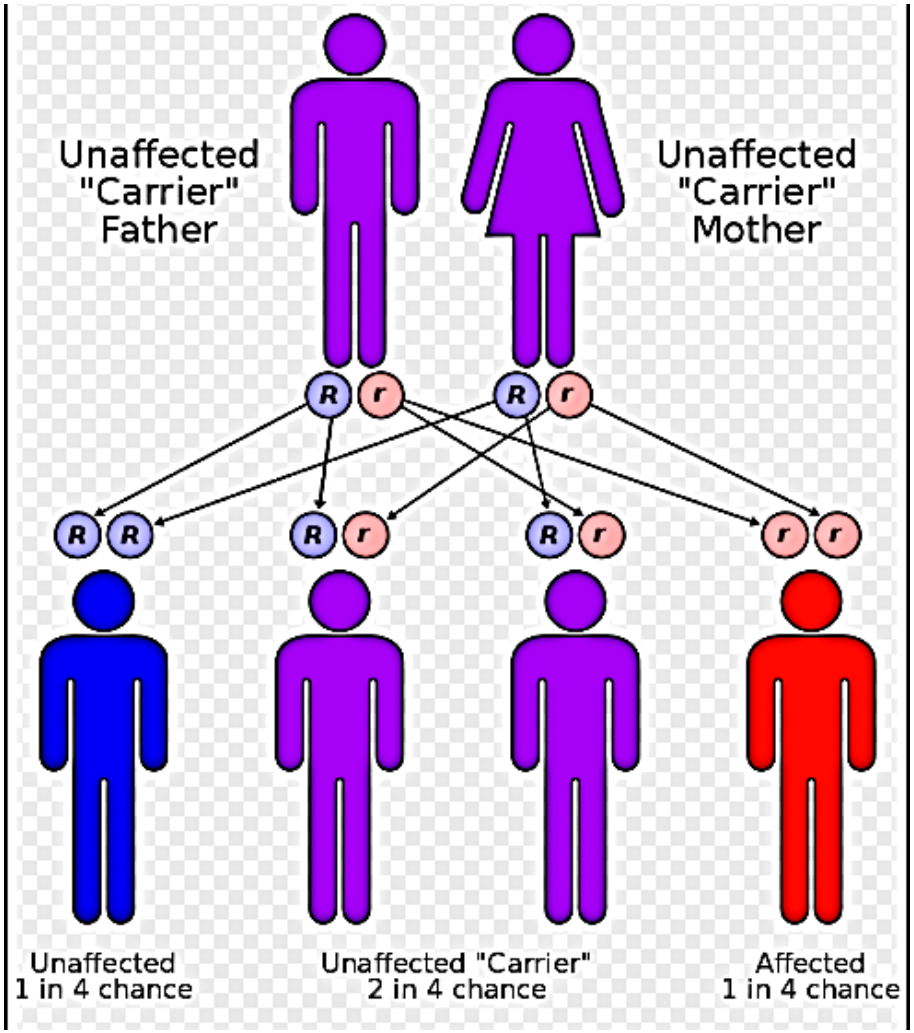
Autosomal Recessive Disorders



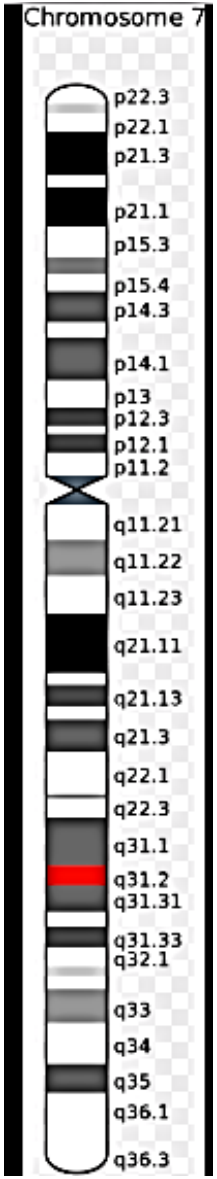
9.9 CONNECTION: Many inherited disorders in humans are controlled by a single gene

recessive inheritance

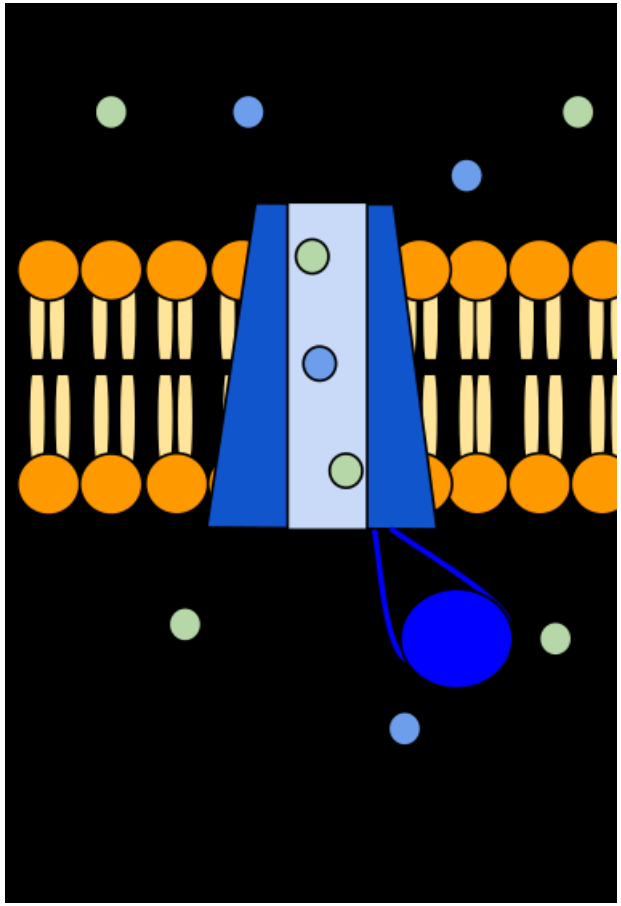
- The most common fatal genetic disease in the United States is **cystic fibrosis** (CF), resulting in excessive thick mucus secretions. The CF allele is
  - recessive and
  - carried by about 1 in 31 Americans.

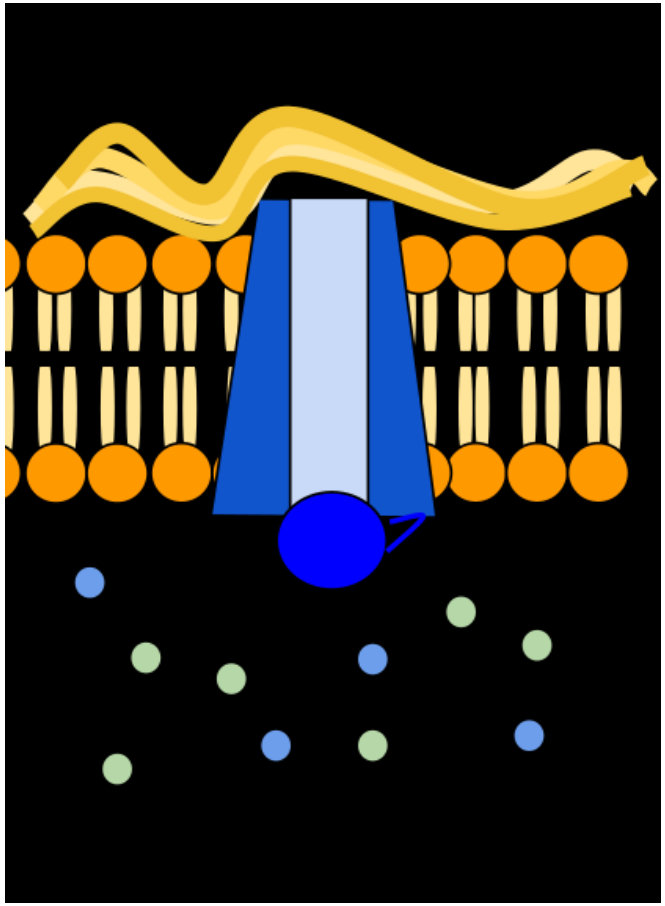


Cystic fibrosis has an autosomal recessive pattern of inheritance.

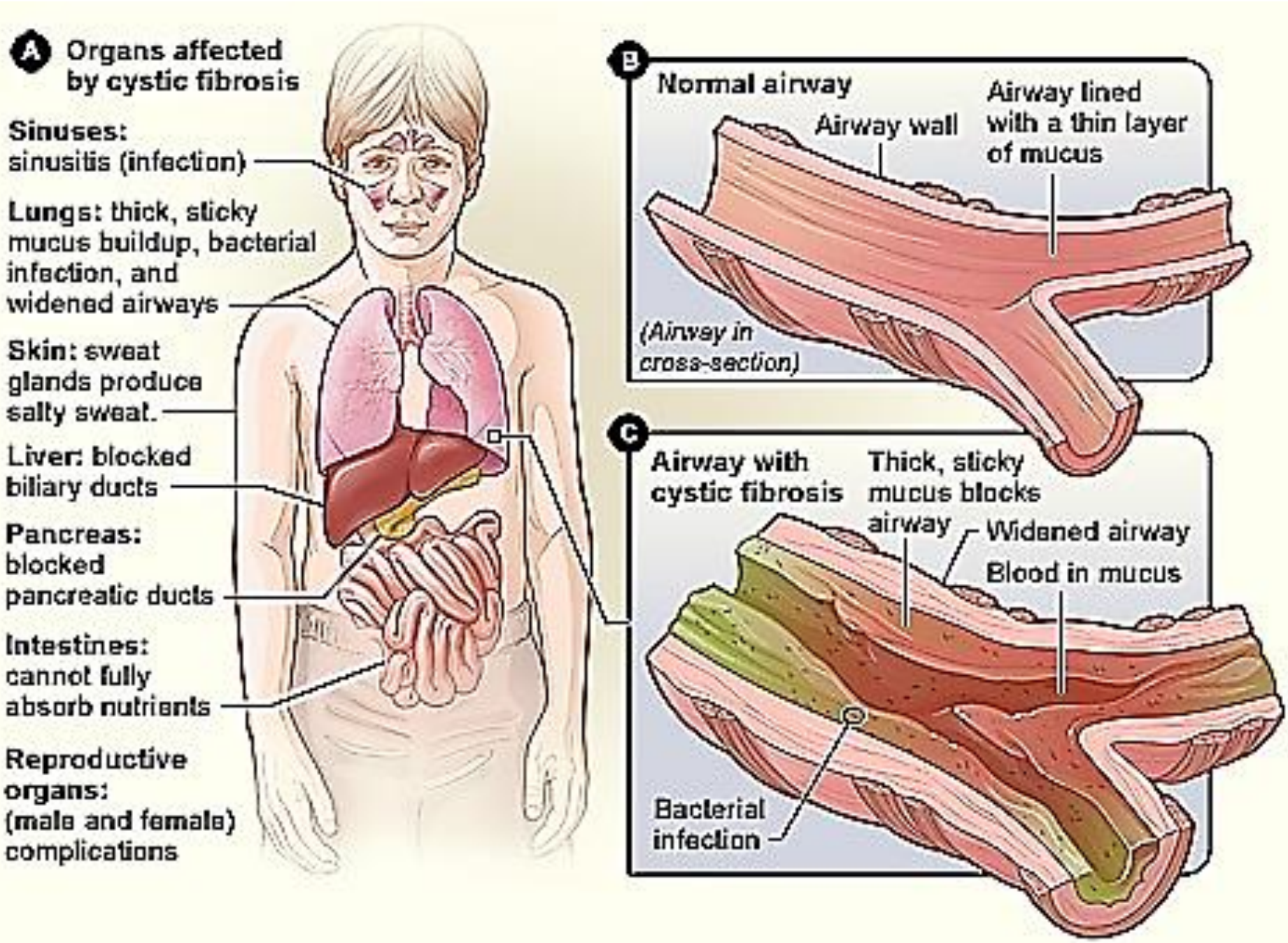


The *CFTR* gene at the 7p31.2 locus of chromosome 7 .

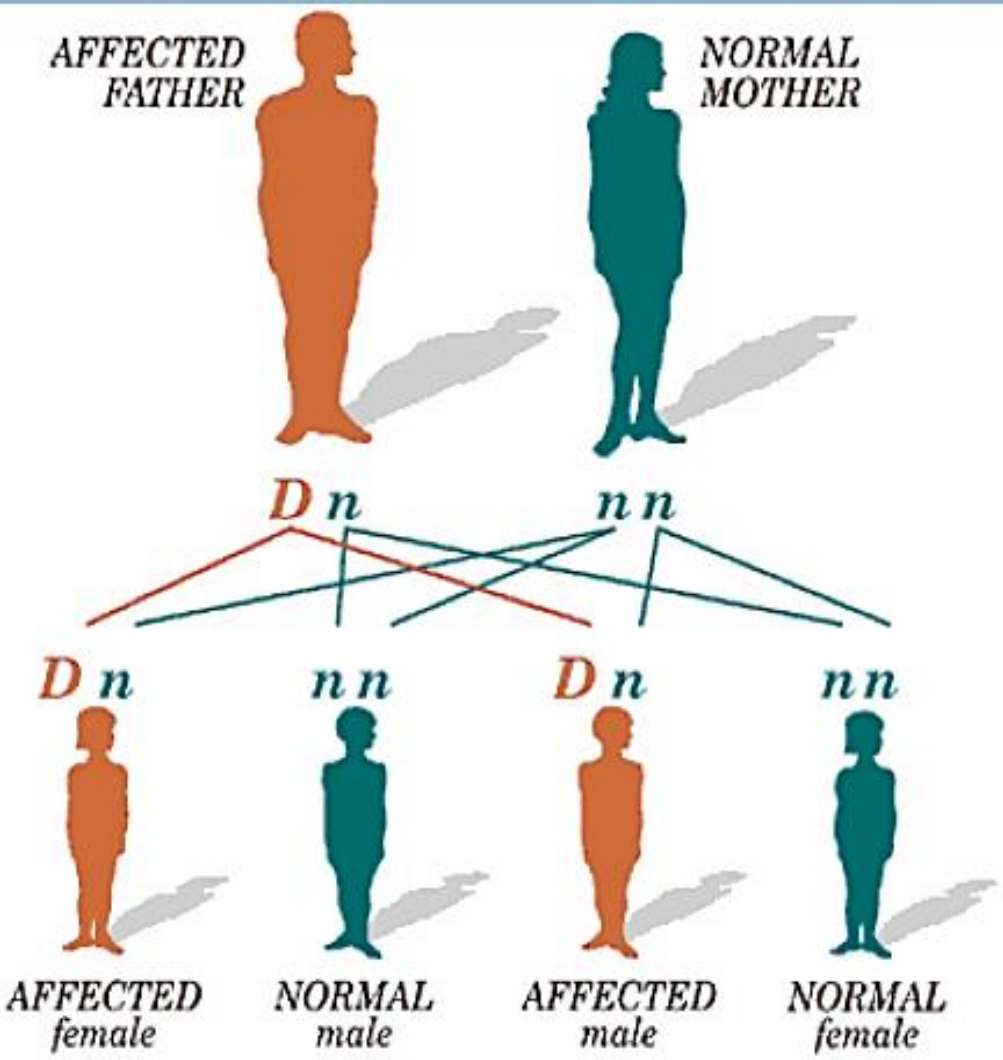




The CFTR protein is a channel protein that controls the flow of H_2O and Cl^- ions in and out of cells inside the lungs. When the CFTR protein is working correctly, ions freely flow in and out of the cells. However, when the CFTR protein is malfunctioning, these ions cannot flow out of the cell due to a blocked channel. This causes cystic fibrosis, characterized by the buildup of thick mucus in the lungs.


A Organs affected by cystic fibrosis
Sinuses: sinusitis (infection)
Lungs: thick, sticky mucus buildup, bacterial infection, and widened airways
Skin: sweat glands produce salty sweat.
Liver: blocked biliary ducts
Pancreas: blocked pancreatic ducts
Intestines: cannot fully absorb nutrients
Reproductive organs: (male and female) complications
B Normal airway
Airway wall
Airway lined with a thin layer of mucus
(Airway in cross-section)
C Airway with cystic fibrosis
Thick, sticky mucus blocks airway
Widened airway
Blood in mucus
Bacterial infection

Autosomal Dominate Disorders

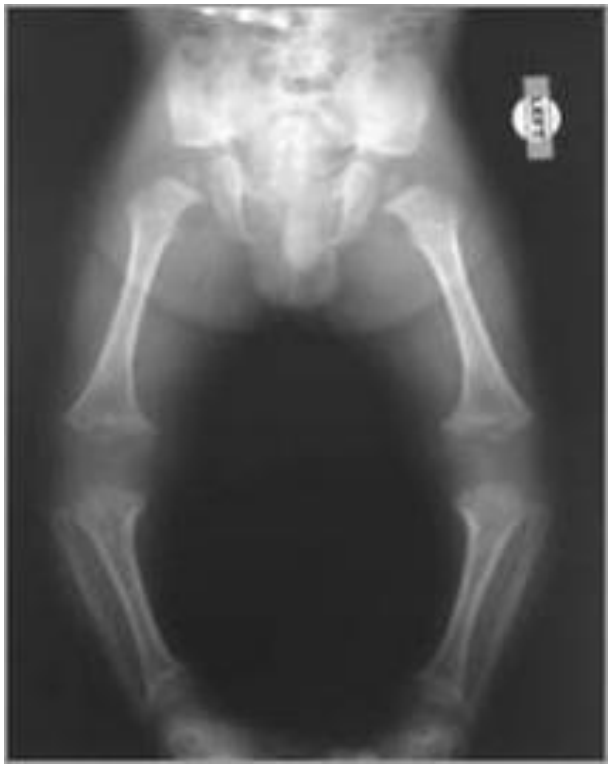


9.9 CONNECTION: Many inherited disorders in humans are controlled by a single gene

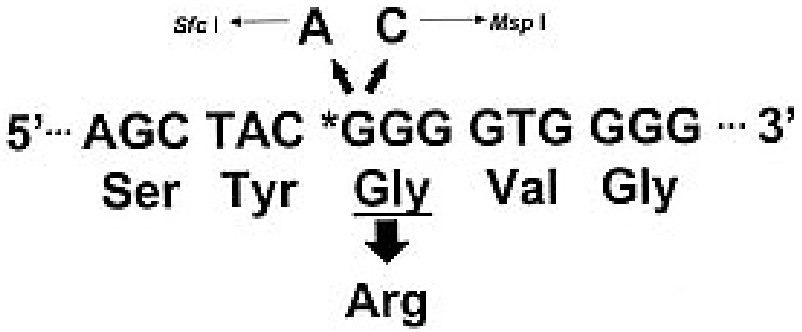
dominant inheritance

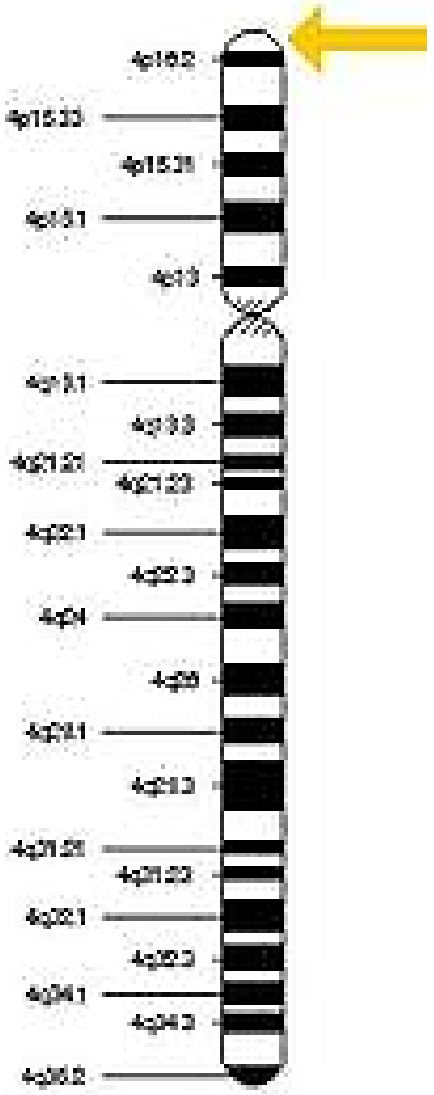
- Dominant human disorders include
  - **achondroplasia**, resulting in dwarfism, and
  - **Huntington's disease**, a degenerative disorder of the nervous system.

Achondroplasia



Achondroplasia

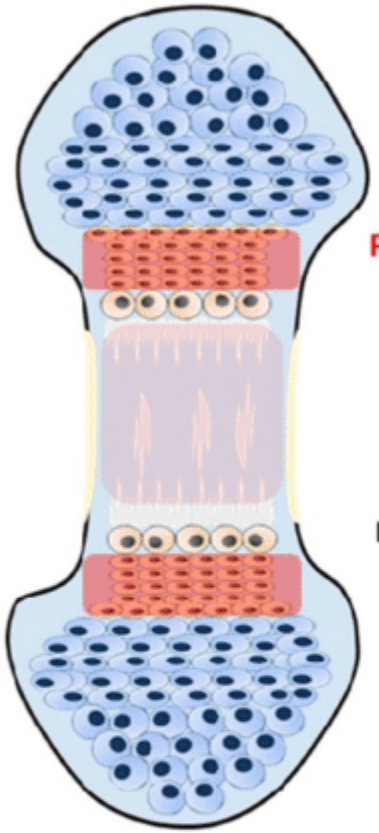




FGFR3 (fibroblast growth factor receptor 3) gene on Chromosome 4q16.3

Bone Development

Bone Repair



FGFR3

Resting zone

Prehypertrophic zone

Osteoblast
Osteocyte
Osteoclast

Hypertrophic zone

Proliferating zone

Expression

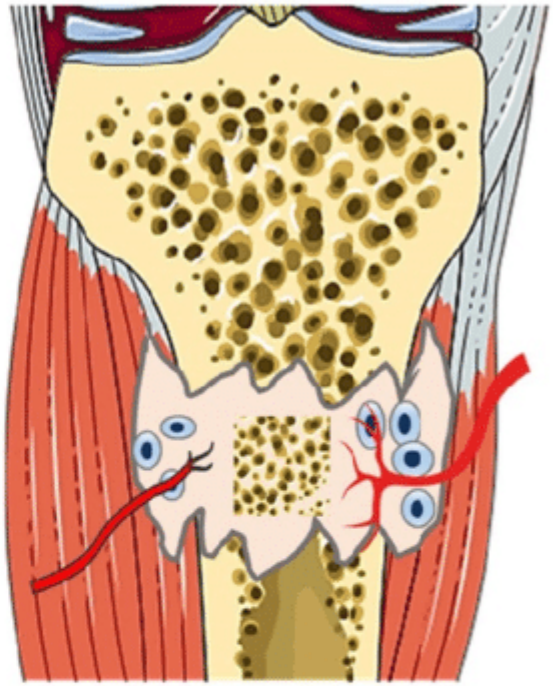
Resting chondrocytes

Prehypertrophic chondrocytes

osteoblasts

periosteum

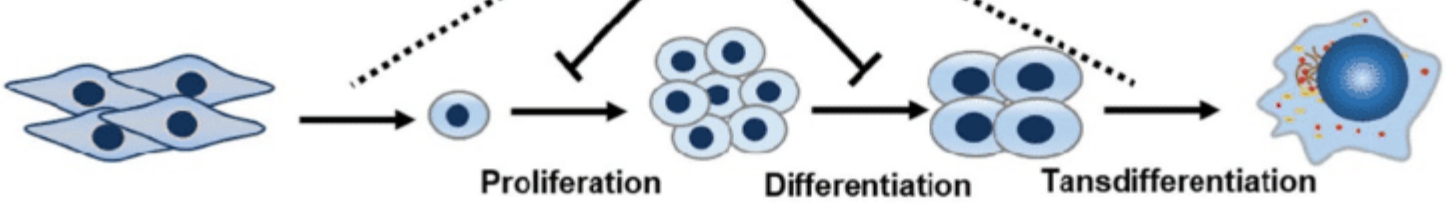
Osteoclast



ECM synthesis

FGFR3

ECM degradation



Mesenchymal cells

Chondrocytes

Osteoblasts

Dominantly Inherited Disorders

- Some human disorders
  - Are due to dominant alleles
    One example is
    achondroplasia
  - A form of dwarfism that is lethal when homozygous for the dominant allele (DD)

	D	d
D	DD	Dd
d	Dd	dd

Figure 14.15

ACHONDROPLASIA

(One kind of Dwarfism)

CAUSE: AUTOSOMAL DOMINANT gene

1 in 25,000 births

DD = lethal
Dd = dwarf phenotype
dd= = normal height

200,000 "little people" worldwide

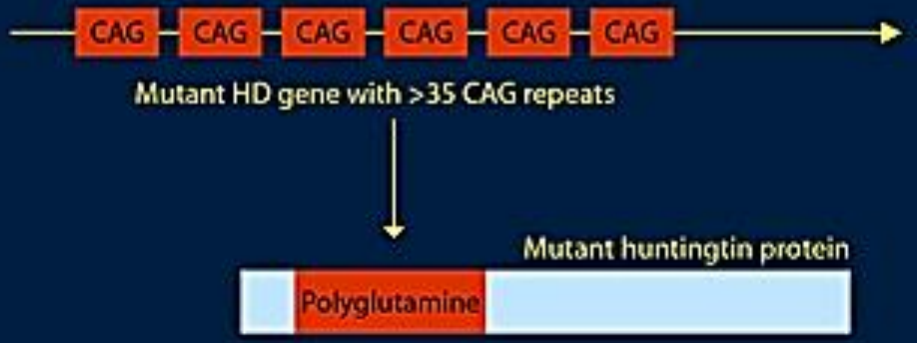
One of oldest known disorders – seen in Egyptian art

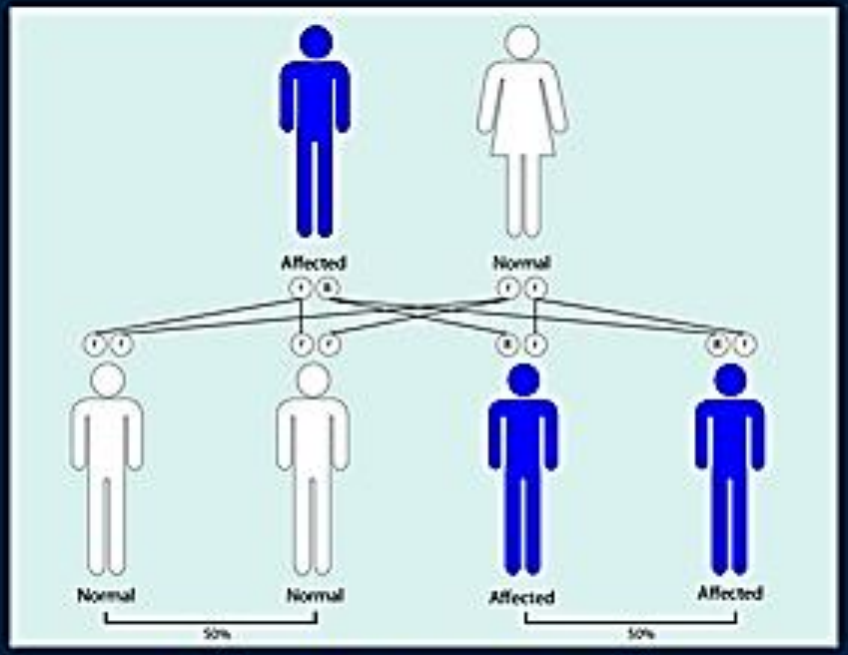

HUNTINGTON'S
DISEASE

Huntington's disease

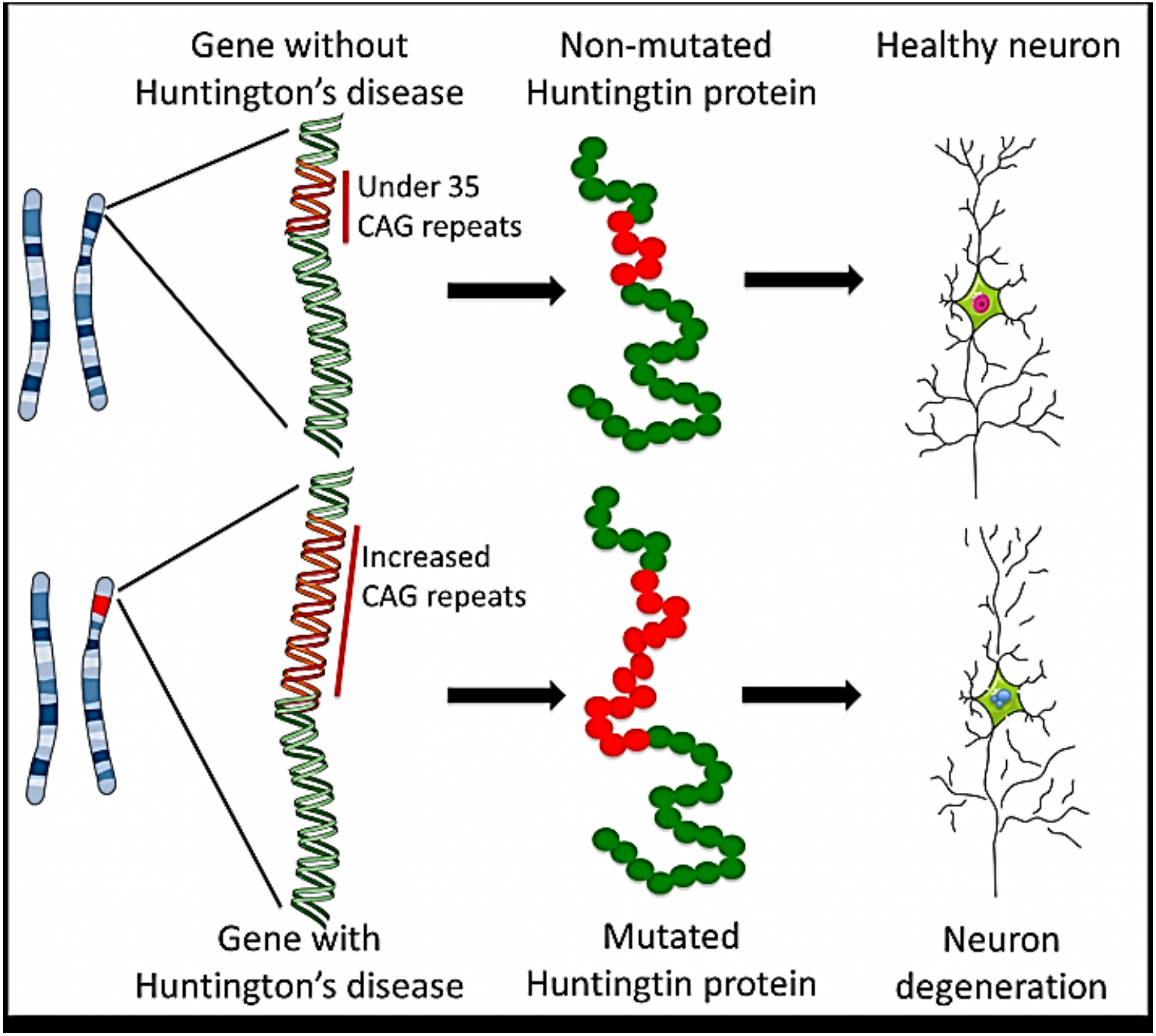
HD gene/*HTT* gene (4p16.3)

Chromosome 4





Autosomal Dominant Inheritance


Gene without
Huntington's disease
Non-mutated
Huntingtin protein
Healthy neuron
Under 35
CAG repeats
Increased
CAG repeats
Gene with
Huntington's disease
Mutated
Huntingtin protein
Neuron
degeneration

MRI findings in HD

HD

Normal

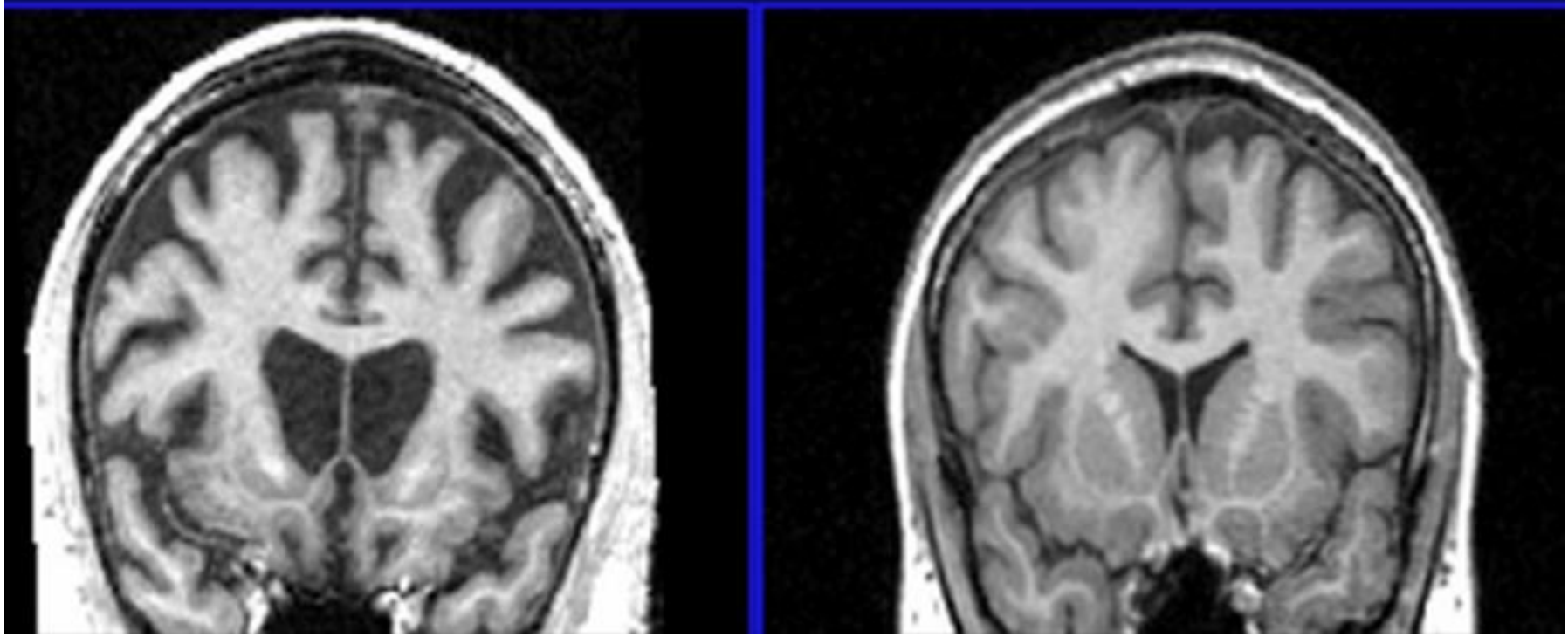


TABLE 9.9 SOME AUTOSOMAL DISORDERS IN HUMANS

Disorder	Major Symptoms	Incidence		Comments
Recessive disorders				
Albinism	Lack of pigment in the skin, hair, and eyes	1/22,000		Prone to skin cancer
Cystic fibrosis	Excess mucus in the lungs, digestive tract, liver; increased susceptibility to infections; death in early childhood unless treated	1/2,500	Caucasians	See Module 9.9
Galactosemia	Accumulation of galactose in tissues; mental retardation; eye and liver damage	1/100,000		Treated by eliminating galactose from diet
Phenylketonuria (PKU)	Accumulation of phenylalanine in blood; lack of normal skin pigment; mental retardation	1/10,000	in U.S. and Europe	See Module 9.10
Sickle-cell disease	Sickled red blood cells; damage to many tissues	1/400	African-Americans	See Module 9.13
Tay-Sachs disease	Lipid accumulation in brain cells; mental deficiency; blindness; death in childhood	1/3,500	Jews from central Europe	See Module 4.10
Dominant disorders				
Achondroplasia	Dwarfism	1/25,000		See Module 9.9
Alzheimer's disease (one type)	Mental deterioration; usually strikes late in life	Not known		Familial (inherited) Alzheimer's is a rare form of the disease
Huntington's disease	Mental deterioration and uncontrollable movements; strikes in middle age	1/25,000		See Module 9.9
Hypercholesterolemia	Excess cholesterol in the blood; heart disease	1/500	are heterozygous	See Module 9.11