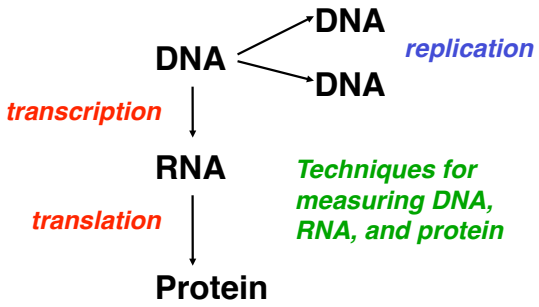
Molecular Biology: The Central Dogma



DNA contains basic units of heredity = gene

1 gene = blueprint for 1 protein

Polymers (generic type of large molecule)

Poly **= many,** ***mer*** **= part**

- **monomer = 1 unit**
- **dimer = 2 units**
- **trimer = 3 units**
- **oligomer = several units (1 or 2 dozen)**
- **polymer = many units (1000s)**

units joined by covalent bonds

Uses of Polymers

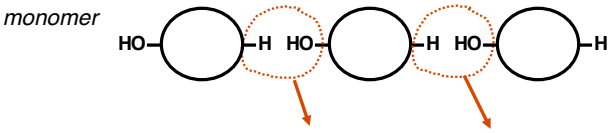
Energy Storage: **starch** *(glucose polymer)*
To make a covalent bond between monomers takes energy
To break covalent bonds within a polymer releases energy
So polymers allow energy storage.

Physical Structure: **wood, hair, skin, etc.**

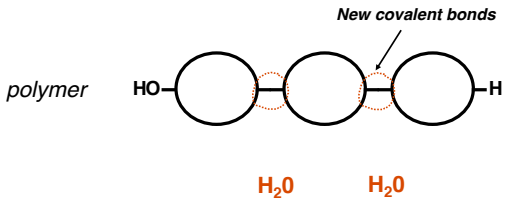
Chemical Reactions: **enzymes** *(amino acid polymers)*

Information Storage: **DNA & RNA** *(nucleic acid polymers)*

Making a polymer:



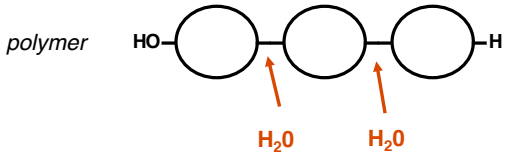
Making a polymer:



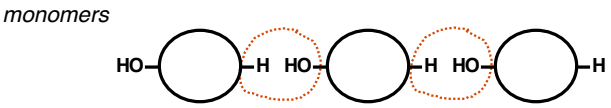
Condensation or dehydration reaction

(because water is lost)

Breaking a polymer:

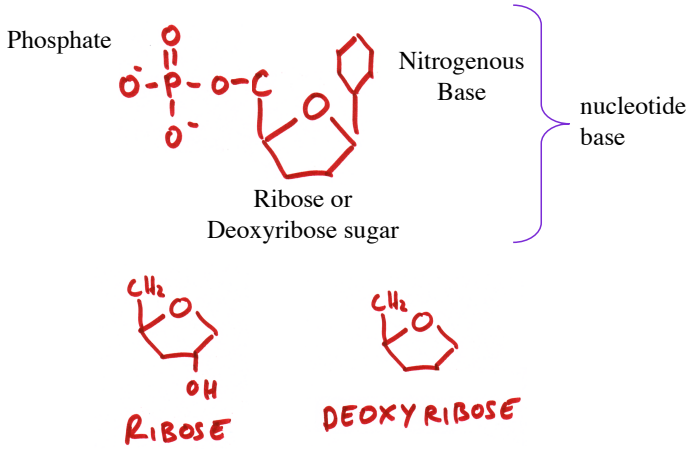


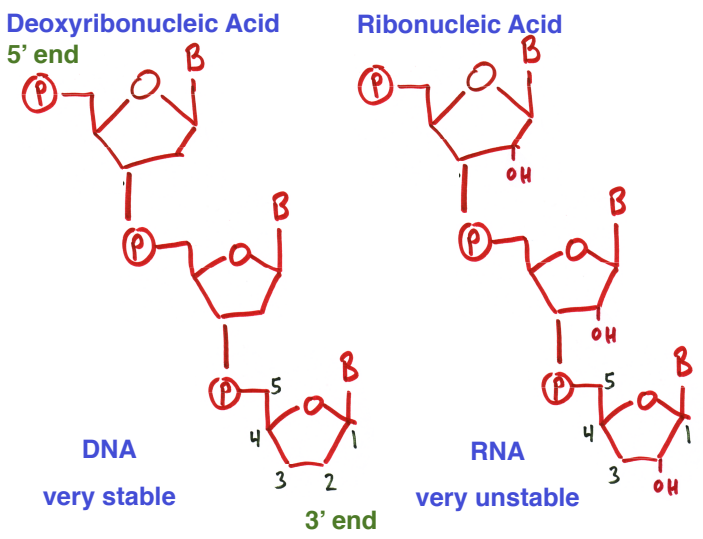
Breaking a polymer:



Hydrolysis (to break-up with water)

Nucleic Acids: Polymers of nucleotide bases





dC, dT, dG, dA if used in DNA

(i.e. deoxycytosine)

cytosine
thymine (in DNA)
adenine
guanine
uracil (in RNA)

C, U, G, A if used in RNA

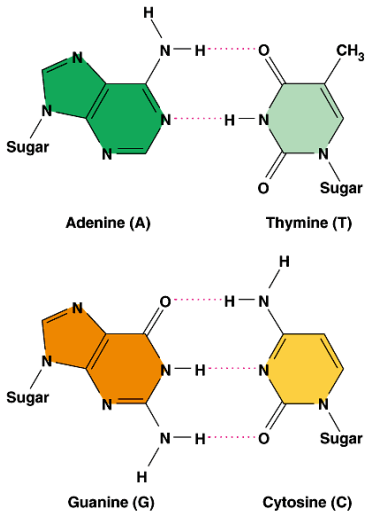
Bases can pair up by hydrogen bonding:

C - G **G - C**

T - A **A - T**

U - A **U - A**

Figure 16.6 Base pairing in DNA



Purines

Pyrimidines

The two strands of the double helix are antiparallel.

```
5′----ACTTCGCTA----3′
3′----TGAAGCGAT----5′
```

```
 5′-D-O-G- 3′
,ε -⊥-∀-Ↄ-,ς
```

Nucleic Acids code for protein and control protein synthesis:

- **dsDNA in nucleus = genetic code replicated when cells divide.**
- **mRNA (messenger RNA) in cytoplasm is transcribed from DNA genes.**
- **Proteins in the cytoplasm are translated from nucleic acid primary sequence of the mRNA.**

CENTRAL DOGMA

DNA → **RNA** → **protein**

transcription ***translation***

DNA and information Storage

2 Levels of Analysis:

Heredity and Genetics:
study the transmission of characteristics and genes within breeding populations

vs.

Biochemical Reactions:
Study the structure of DNA and the enzymatic reactions that replicate it during reproduction and protein synthesis

DNA and information Storage

The genetic material must have 4 properties:

1. **Encode a blueprint so new proteins can be synthesized on demand.**
2. **Store the blueprint in every cell in a concise fashion, so don't have to store copies of every protein, lipid, and carbohydrate.**
3. **Use genetic information to pass the traits of one generation to the next during reproduction (of cells or organisms).**
4. **Allow some variation so that generations can change slowly over time and adapt to new environments.**

Storage of Information that defines the organism

not the actual chemicals of the organism

homunculus in sperm that "inflates" when united with egg

more efficient to store the sequence of amino acids for:
- **composition of structural proteins**
- **enzymes that synthesize/digest other macromolecules**
- **enzymes that store energy or perform work**

interaction of enzymes and other chemicals
-> construction of body

Gene = Unit of Heredity

Information is stored in genes.

At cellular level, genes are made of DNA = code for protein synthesis.

Genetic code translated into 1° structure of protein.

Protein could be an enzyme, or a pigment (e.g. eye color), or a hormone, etc.

The collection of genes you have determines your genotype.

Example: Alkaptonuria

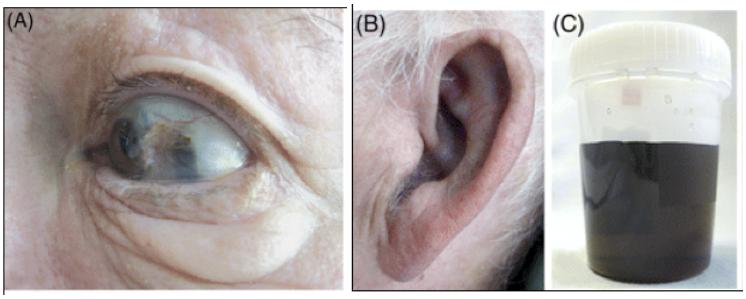
Inherited genetic disease of metabolism

Patients have black urine; trait appears to be inherited.

Conclusions in 1900 when metabolic pathways were beginning to be understood:

- **Families inherit the ability to make enzymes.**
- **Families with alkaptonuria inherit a defective ability to make one enzyme.**
- **one gene = one protein.**
- **(one bad gene = one bad protein.)**
- **At the time, not known how plans for making an enzyme are passed down generations**
- **(i.e. what a gene is made of…)**

Alkaptonuria

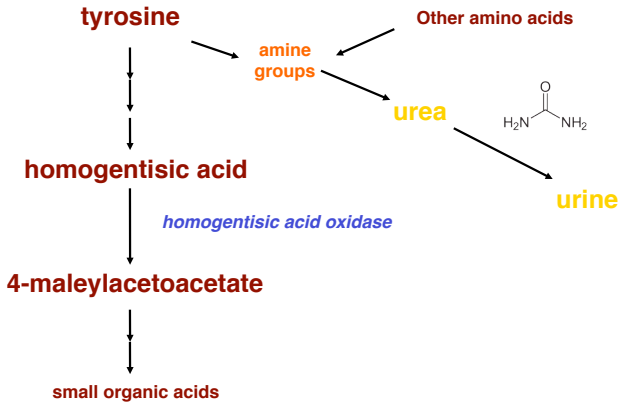


urine sample

European Heart Journal, Cover, Volume 29, Number 4, February 2008

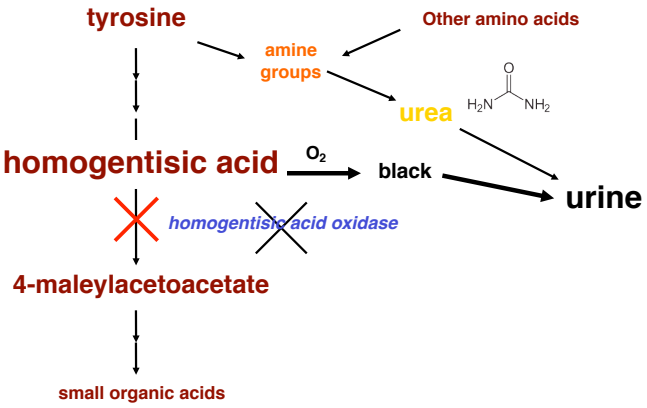
Alkaptonuria

Normal families



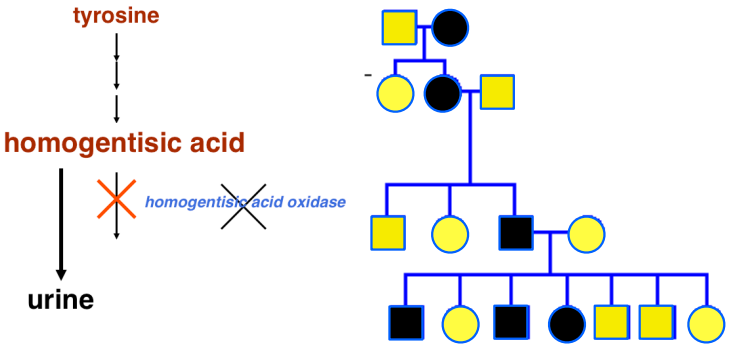
Alkaptonuria

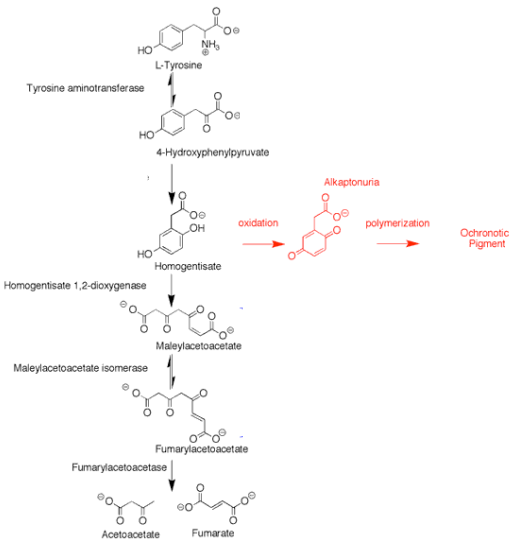
Diseased families



Alkaptonuria

Pedigree of affected family:

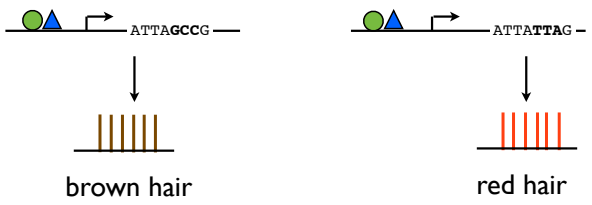




Gene Expression underlying variation

variation in coding region

same promoter, so same level of expression in 2 different people
different coding regions, so different protein variants are expressed



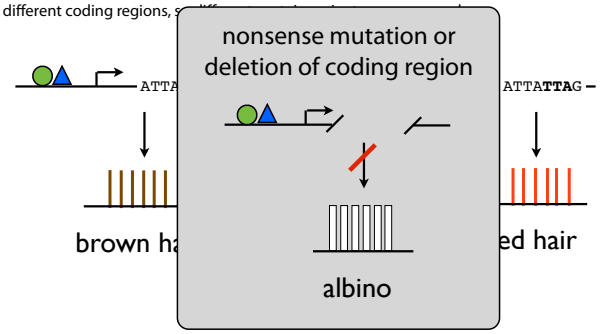
variation in hair pigment genes

(actually enzymes that synthesize eumelanin vs. pheomelanin pigments)

Gene Expression underlying variation

variation in coding region

same promoter, so same level of expression in 2 different people
different coding regions, s



Beadle and Tatum:
Neurospora mold mutants

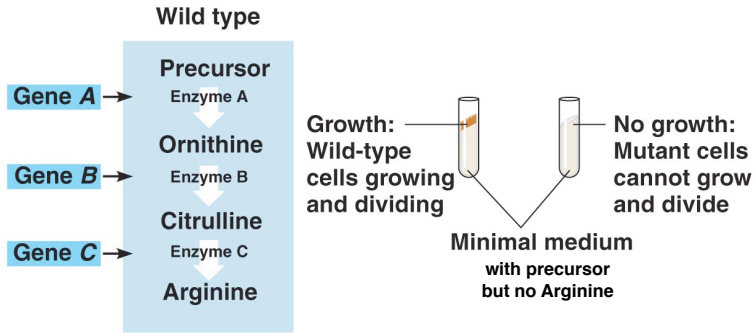
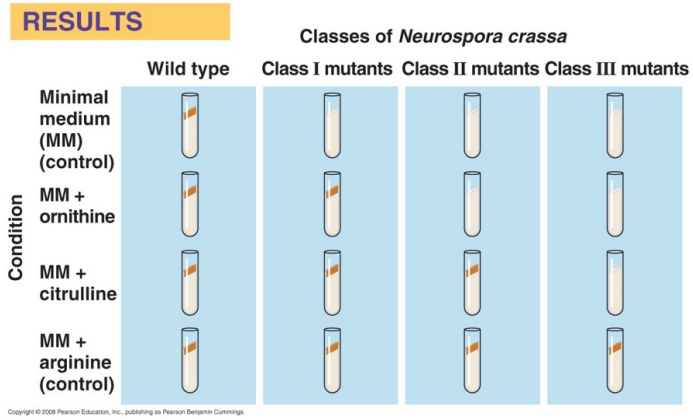
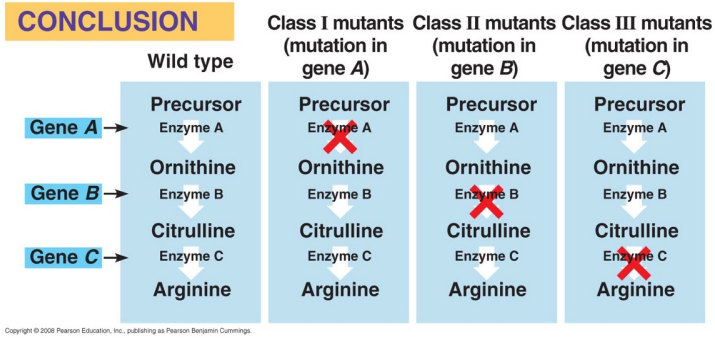


Fig 17.2



Beadle and Tatum:
Neurospora mold mutants



Genotype and Phenotype

Genotype is type of gene you have:
normal enzyme gene *vs.* defective enzyme gene.

Phenotype is observable trait as a result of genes:
a. outward appearance (normal skin vs. black patches)
b. color of urine (yellow *vs.* black)
c. ability to break down tyrosine (yes *vs.* no)
d. the enzyme characteristics (functional *vs.* inactive)

Phenotype can be due to single gene, or be **polygenetic**:
e.g. height (caused by genes for growth hormone, bone growth, nutritional enzymes, etc.)

Genotype and Phenotype

The **genome** is the collection of all the genes in an organism.

Estimated to be 30,000 to ~~100,000 (2000) 50,000 (2003)~~ 24,000 (2004) genes in human genome. Consortium researchers have confirmed the existence of 19,599 protein-coding genes in the human genome and identified another 2,188 DNA segments that are predicted to be protein-coding genes.

The specific versions of all these genes
= **genotype** of a specific human.

The end product of all these proteins
= **phenotype** of the specific human.

DNA is the physical manifestation of the genome.

Topics:

1. DNA in chromosomes

2. Replication of DNA during Division (replication) of Prokaryotic and Eukaryotic cells
(reviewed in Chapter 12)

3. Four classic experiments establishing DNA as hereditary material
(Chapter 16 part 1)

Chromosomes

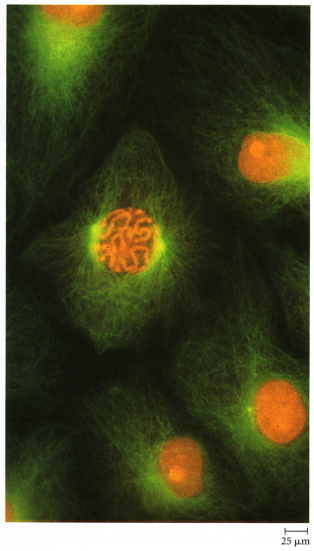
DNA is subdivided into chromosomes: a long fiber of double-stranded DNA, coated with various DNA binding proteins.

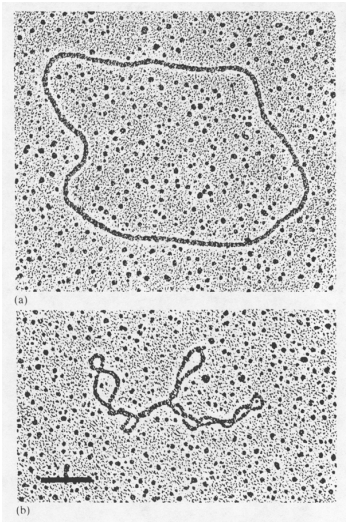
Prokaryotes:
DNA is free-floating: in 1 circular chromosome

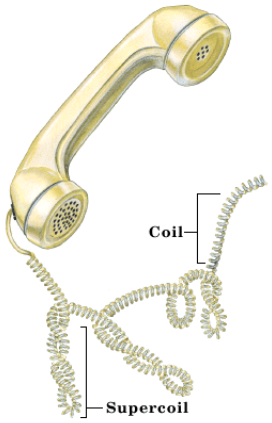
Eukaryotes:
DNA is localized in the chromatin of the nucleus in several linear chromosomes

Different genes for different proteins can be on different chromosomes.

Different species have different numbers of chromosomes
Humans have 46 chromosomes per cell (all cells in one person have copies of same DNA (except sperm and eggs))



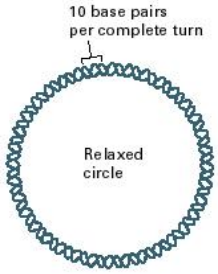




Dr. Leng, Florida International University.

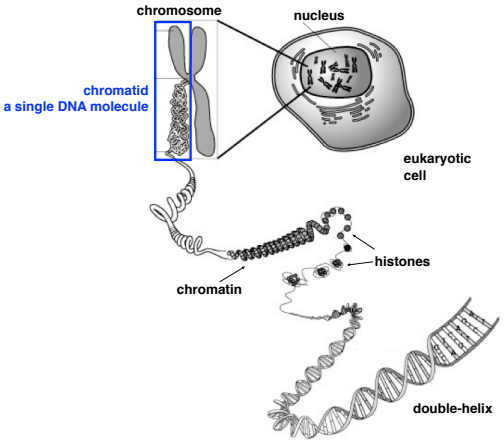
Prokaryotes (Bacteria): One Circular Chromosome

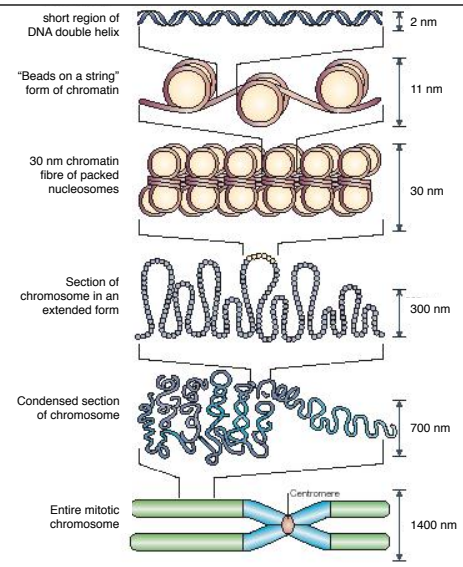
circle of DNA coiled in a double helix



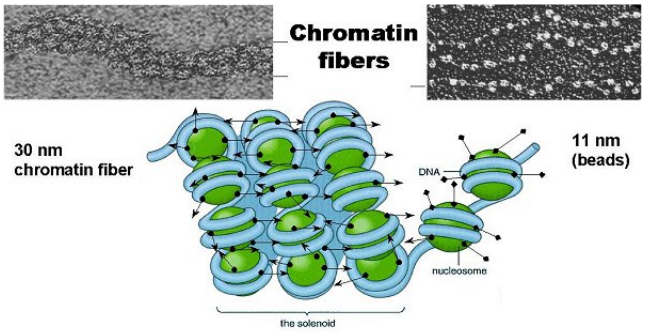
supercoil of coiled DNA

Eukaryotes: Many Chromsomes
linear DNA molecules wound around proteins





Nature Reviews Immunology
(Vol 3, No. 11, pp 890-899(2003)



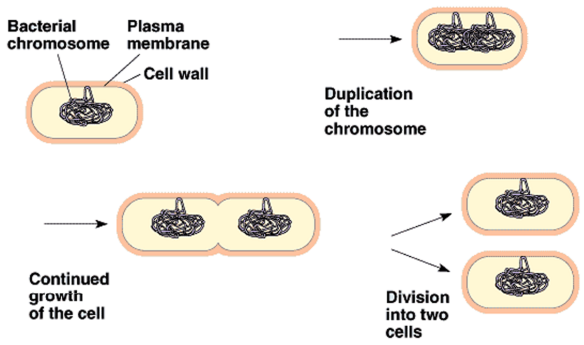
All somatic cells (not gametes = eggs, sperm) in the human body have copies of all the chromosomes.

So each cell contains all the genes, i.e. the blueprints for all proteins.

But different cells use different genes to make different proteins.

So liver cell and lung cell have same DNA, same genes, but express different sets of those genes.

Binary Fission in Bacteria



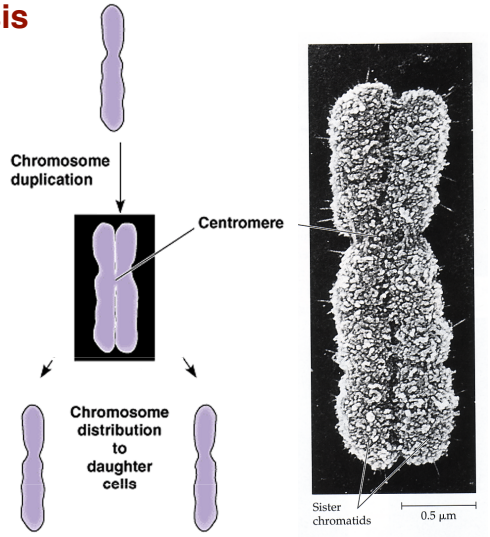
Mitosis

Duplication of DNA and division of the nucleus in a cell, followed by cytokinesis resulting in 2 cells.

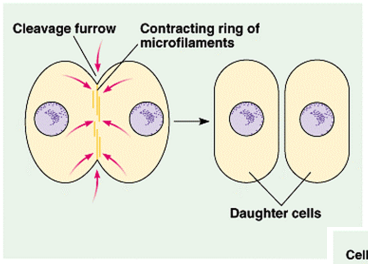
The cells of human tissues have to divide to replace damaged or dead cells.

(Cancer is special case of out-of-control cell division, leading to tumors.)

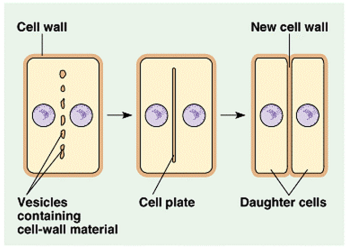
Mitosis



Cytokinesis



(a) Cleavage of an animal cell



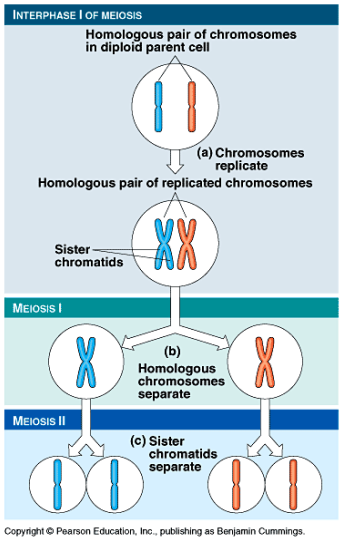
(b) Cell plate formation in a plant cell

Meiosis

Division of the nucleus without duplication of the DNA

Leads to production of sperm or egg cells.

(sex is special case of cell division and merger to mix and match chromosomes of two individuals)



Human Chromosomes

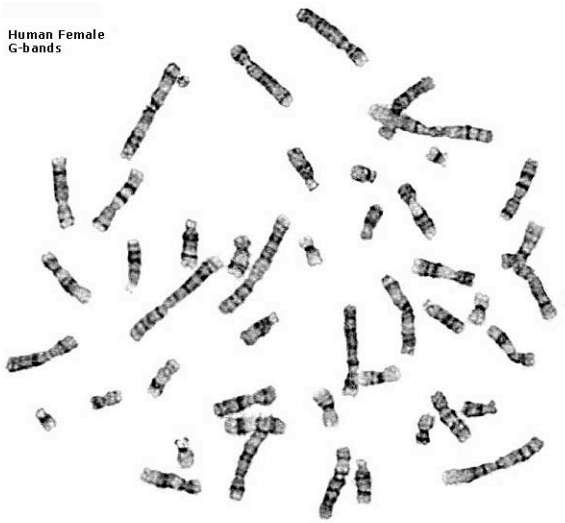
In humans total of 46 chromosomes:
22 pairs of autosomal chromosomes and 1 pair of sex chromosomes

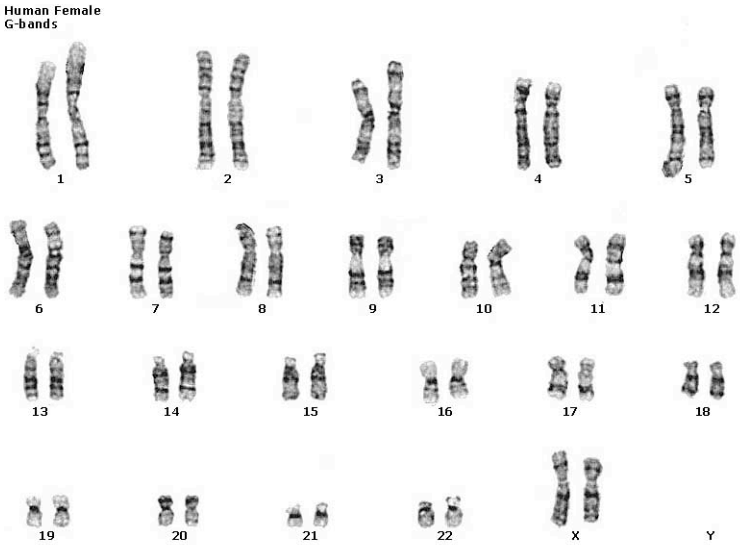
Autosomal pairs have identical genes on them (with slight variations).

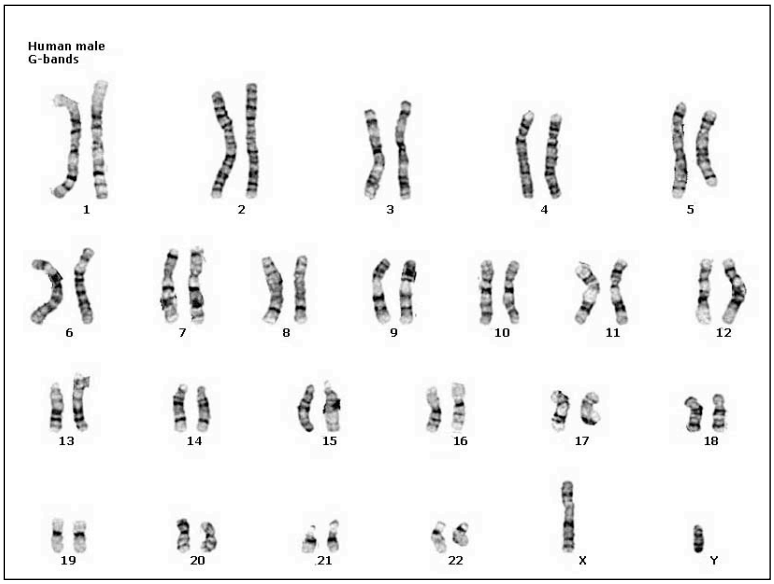
Sex chromosome pairs are either:
XX = female, or
XY = male

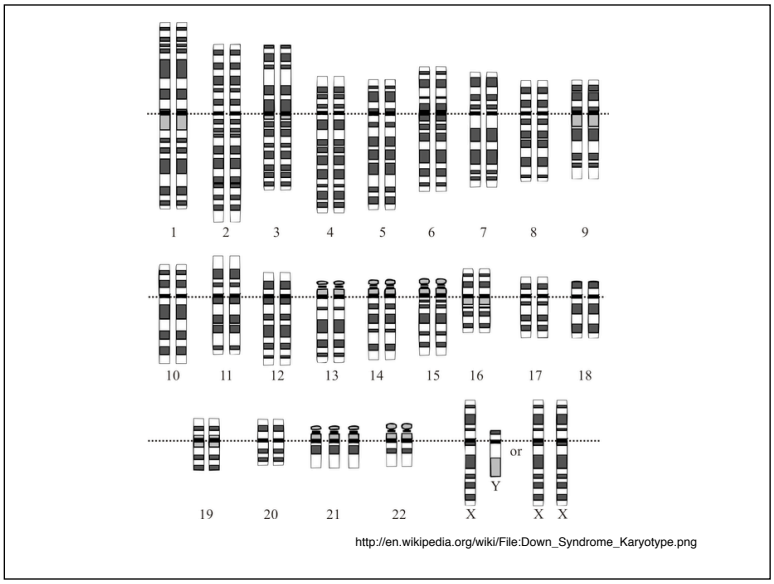
So you get 1 chromosome of each autosomal chromosome from each parent (either your grandmother's or grandfather's: which one you get is random).

And 1 sex chromosome from each parent. (which one you get is random – but can only get X from mother, either X or Y from father).









http://en.wikipedia.org/wiki/File:Down_Syndrome_Karyotype.png

Sources of DNA in the body

- **10 Trillion *somatic* cells in the human body**
  - **i. Chromosomes (2 x 23 /cell)**
    - 3 billion base pairs; 20,000 proteins
    - half from Father, half from Mother
  - **ii. Mitochondrial Chromosome (1000s/cell)**
    - 15,000 base pairs; 13 proteins
    - derived from Mother
- **Bacteria (100 trillion / person)**
  - 1000s of different species
  - millions of different genes
- ***DNA of whatever you last ate....***