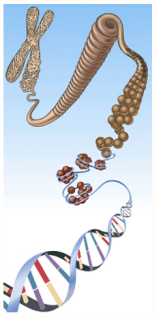
Chapter 4
Genetics and Cellular Function

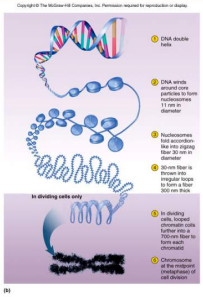
- Nucleus and nucleic acids
- Protein synthesis and secretion
- DNA replication and the cell cycle
- Chromosomes and heredity



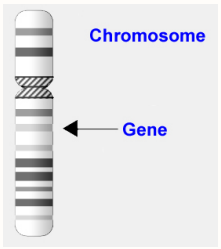
The Nucleic Acids (medical history)

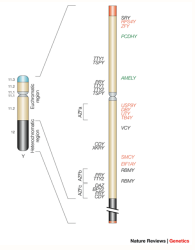
Organization of the Chromatin

- Threadlike chromatin
- Chromosomes – compacted DNA
- How many human chromosomes?
  - Fruitflies?
  - Butterflies?

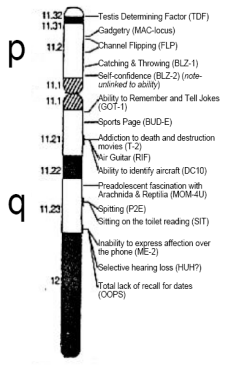


Chromosome loci

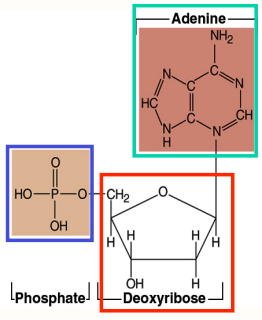




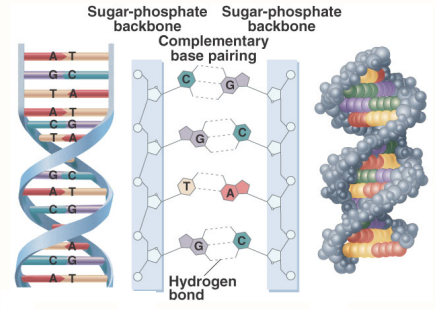
Y Chromosome



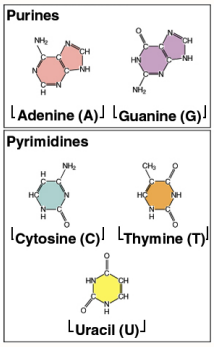
Nucleotide Structure



DNA Structure: Twisted Ladder

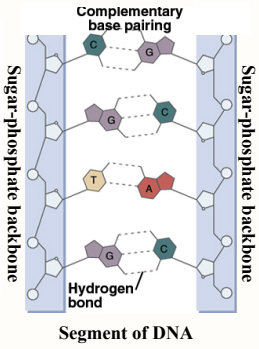


Nitrogenous Bases



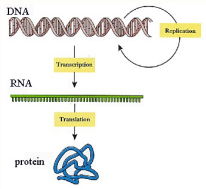
Complementary Base Pairing

- Nitrogenous bases form hydrogen bonds
- Base pairs
  - A-T and C-G
- Law of complementary base pairing
  - one strand determines base sequence of other

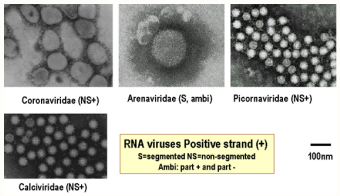


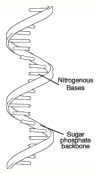
DNA Function

- Code for protein synthesis
- Gene - sequence of DNA nucleotides that codes for one protein
- Genome - all the genes of one person
  - humans have ~ 30-35,000 genes
  - 98% non-coding



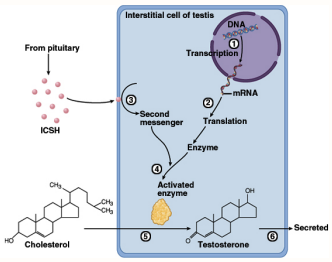
RNA: Structure and Function



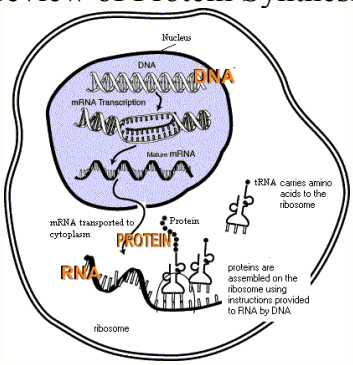


Genetic Control of Cell Action through Protein Synthesis

- DNA directs the synthesis of all cell proteins
- Different cells synthesize different proteins



Preview of Protein Synthesis

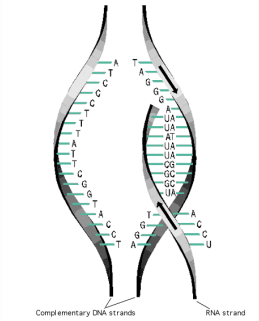


Genetic Code

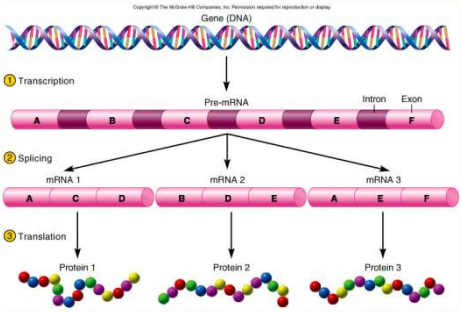
2nd base in codon

1st base in codon	U	C	A	G	3rd base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

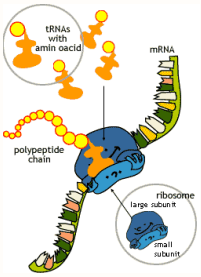
Transcription – making an RNA strand



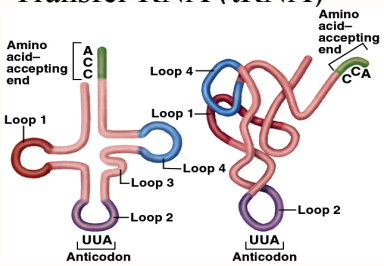
Alternative Splicing of mRNA



Translation – RNA to amino acids

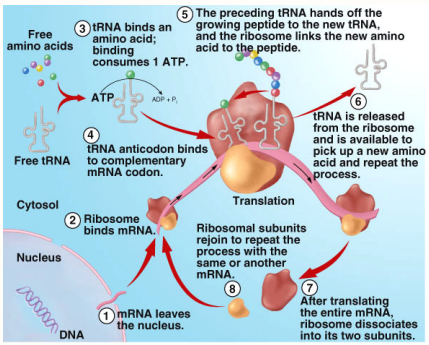


Transfer RNA (tRNA)

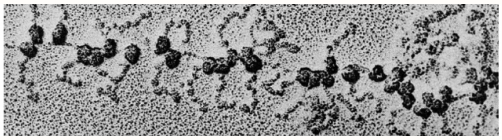


- Activation by ATP binds specific amino acid and provides necessary energy to join amino acid to growing protein molecule
- Anticodon binds to complementary codon of mRNA

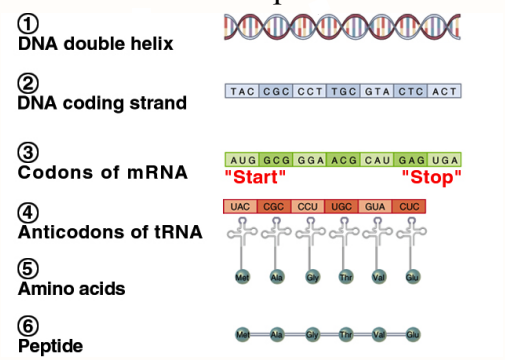
Translation of mRNA



Polyribosomes and Signal Peptides



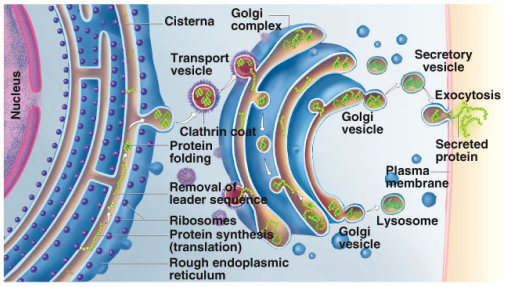
Review: DNA & Peptide Formation



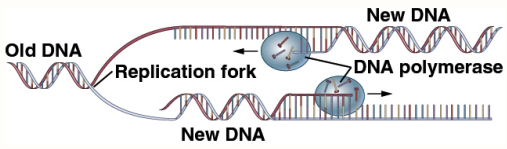
Chaperones and Protein Structure

- Newly forming protein molecules must coil, fold or join with another protein or nonprotein moiety
- Chaperone proteins
  - prevent premature folding of molecule
  - assists in proper folding of new protein
  - may escort protein to destination in cell
- Stress or heat-shock proteins
  - chaperones produced in response to heat or stress
  - help protein fold back into correct functional shapes

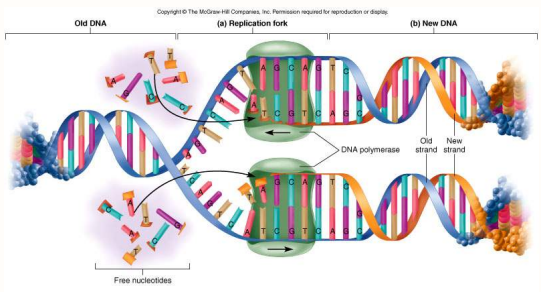
Protein Packaging & Secretion



DNA Replication



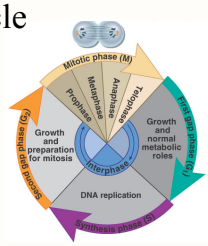
DNA Replication



DNA Replication: Errors and Mutations

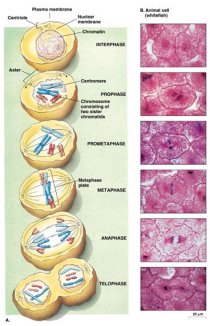
- Error rates of DNA polymerase
  - in bacteria, 3 errors per 100,000 bases copied
  - every generation of cells would have 1,000 faulty proteins
- Proofreading and error correction
  - a small polymerase proofreads each new DNA strand and makes corrections
  - results in only 1 error per 1,000,000,000 bases copied
- Mutations - changes in DNA structure due to replication errors or environmental factors
  - some cause no effect, some kill cell, turn it cancerous or cause genetic defects in future generations

Cell Cycle



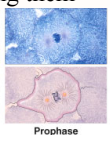
- G_1 phase, the first gap phase
- S phase, synthesis phase
- G_2 phase, second gap phase
- M phase, mitotic phase
- G_0 phase, cells that have left the cycle
- Cell cycle duration varies between cell types

Mitosis

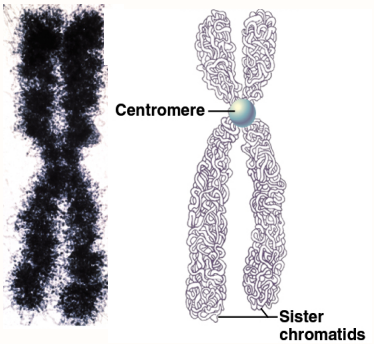


Mitosis: Prophase

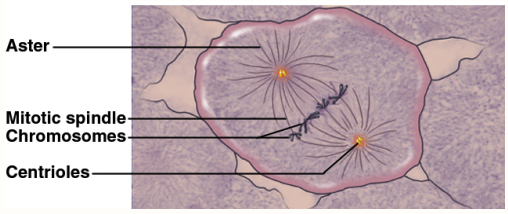
- Chromatin supercoils into chromosomes
  - each chromosome = 2 genetically identical sister chromatids joined at the centromere
  - each chromosomes contains a DNA molecule
- Nuclear envelope disintegrates
- Centrioles sprout microtubules pushing them apart towards each pole of the cell



Prophase Chromosome

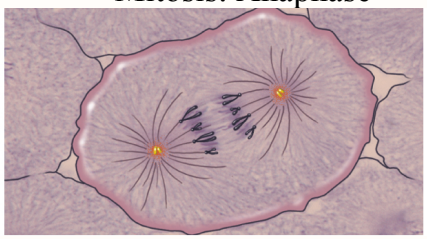


Mitosis: Metaphase



- Chromosomes line up on equator
- Spindle fibers (microtubules) from centrioles attach to centromere
- Asters (microtubules) anchor centrioles to plasma membrane

Mitosis: Anaphase



- Centromeres split in 2 and chromatids separate
- Daughter chromosomes move towards opposite poles of cells
- Centromeres move down spindle fibers by kinetochore protein (dynein)

Mitosis: Telophase

- Chromosomes uncoil forming chromatin
- Nuclear envelopes form
- Mitotic spindle breaks down

Cytokinesis

- Division of cytoplasm / overlaps telophase
- Myosin pulls on microfilaments of actin in the membrane skeleton
- Causes crease around cell equator called cleavage furrow
- Cell pinches in two
- Interphase has begun

Timing of Cell Division

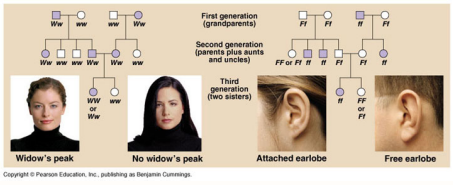
<u>Cells divide when:</u>

- Have enough cytoplasm for 2 daughter cells
- DNA replicated
- Adequate supply of nutrients
- Growth factor stimulation
- Open space in tissue due to neighboring cell death

<u>Cells stop dividing when:</u>

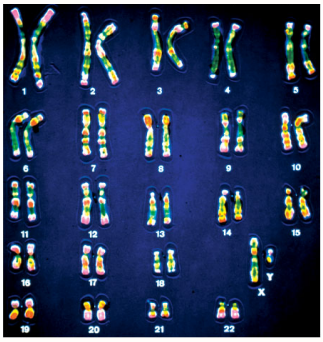
- Loss of growth factors or nutrients
- Contact inhibition

Chromosomes and Heredity



This is my son, Irvine

Karyotype of Normal Human Male

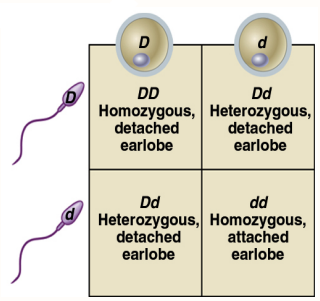


Genetics of Earlobes

Detached earlobe
DD, Dd

Attached earlobe
dd

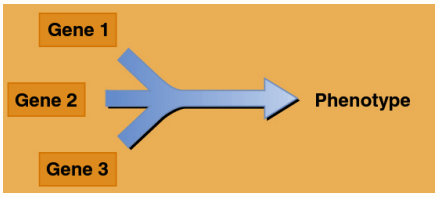
Genetics of Earlobes



Punnett square

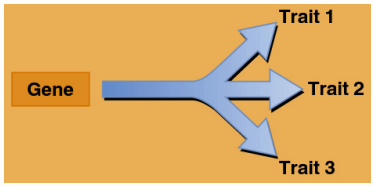
Multiple Alleles, Codominance, Incomplete Dominance

Polygenic Inheritance



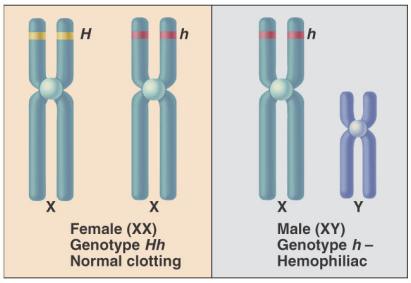
- 2 or more genes combine their effects to produce single phenotypic trait, such as skin and eye color, alcoholism and heart disease

Pleiotropy



- Single gene causes multiple phenotypic traits (ex. sickle-cell disease)
  - sticky, fragile, abnormal shaped red blood cells at low oxygen levels cause anemia and enlarged spleen

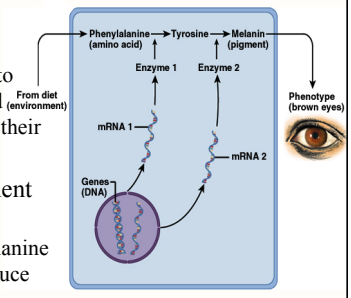
Sex-Linked Inheritance



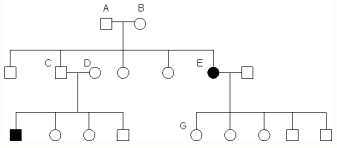
- Recessive allele on X, no gene locus for trait on Y, so hemophilia more common in men (mother must be carrier)

Penetrance and Environmental Effects

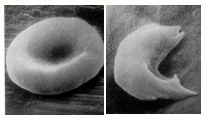
- Penetrance
  - % of population to express predicted phenotype given their genotypes
- Role of environment
  - brown eye color requires phenylalanine from diet to produce melanin, the eye pigment



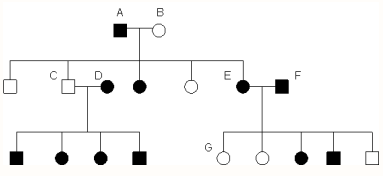
Pedigree analysis



Genetics of sickle cell anemia



Inheritance of achondroplasia



Alleles at the Population Level

- Dominance and recessiveness of allele do not determine frequency in a population
- Some recessive alleles, blood type O, are the most common
- Some dominant alleles, polydactyly and blood type AB, are rare

Cancer

- Tumors (neoplasms)
  - abnormal growth, when cells multiply faster than they die
  - oncology is the study of tumors
- Benign
  - connective tissue capsule, grow slowly, stays local
  - potentially lethal by compression of vital tissues
- Malignant
  - unencapsulated, fast growing, metastatic (causes 90% of cancer deaths)

Causes of Cancer

- Carcinogens - estimates of 60 - 70% of cancers from environmental agents
  - chemical
    - cigarette tar, food preservatives
  - radiation
    - UV radiation, α particles, γ rays, β particles
  - viruses
    - type 2 herpes simplex - uterus, hepatitis C - liver

Mutagens

- Trigger gene mutations
  - cell may die, be destroyed by immune system or produce a tumor

<u>Defenses against mutagens</u>

- Scavenger cells
  - remove them before they cause genetic damage
- Peroxisomes
  - neutralize nitrites, free radicals and oxidizing agents
- Nuclear enzymes
  - repair DNA
- Tumor necrosis factor (TNF) from macrophages and certain WBCs destroys tumors

Malignant Tumor (Cancer) Genes

- Oncogenes
  - mutated form of normal growth factor genes called proto-oncogenes
  - sis oncogene causes excessive production of growth factors
    - stimulate neovascularization of tumor
  - ras oncogene codes for abnormal growth factor receptors
    - sends constant divide signal to cell
- Tumor suppressor genes
  - inhibit development of cancer
  - damage to one or both removes control of cell division

Effects of Malignancies

- Displaces normal tissue, organ function deteriorates
  - rapid cell growth of immature nonfunctional cells
  - metastatic cells have different tissue origin
- Block vital passageways
  - block air flow and compress or rupture blood vessels
- Diverts nutrients from healthy tissues
  - tumors have high metabolic rates
  - causes weakness, fatigue, emaciation, susceptibility to infection
  - cachexia is extreme wasting away of muscle and adipose tissue