Properties of life

1. Highly organized
2. Suited to the environment
3. Respond to stimuli
4. Regulation: chemical composition differs from surroundings
   1. Homeostasis
   2. Ability to stay the same under different conditions
5. Reproduce with great fidelity (but with built in variation)
6. Grow and develop
7. Energy conversion

Feedback regulation: output feedbacks and influences process

Positive: output speeds up process

Negative: output slows down process

Autotroph: self-nourishing (plants are photoautotrophs [light autotroph])

All animals are heterotrophs

Cell theory

* All living things are composed of one or more cells
* Cells are the most basic unit of life
  + Exhibit all hallmarks properties of life
* All cells come from (preexisting) cells

DNA: unit of life

Gene: unit of heredity

Nucleotides: building blocks of DNA

All cells possess

* Genetic material (DNA)
  + Genome
  + all the necessary molecules to regulate the expression of genes
* plasma membrane (lipid bilayer)
* aqueous interior environment

Two main forms of cells

* Eukaryotic cells
  + Subdivided by internal membranes into many membrane-enclosed organelles
* Prokaryotic cells
  + Don’t have the membrane-enclosed organelles

Study of life must occur at different levels of examination (scales)

* Each level is defined by emergent properties not in the level below

Search for Similarities

* Homologous Structures
  + Structures that appear in different forms of life
  + Have anatomical (or biochemical) similarities
  + Share a common ancestor

How to study life?

1. Observation
2. Experimentation
3. Develop and test hypothesis
   * How does it grow?
   * What does it eat?
   * How does it reproduce?
   * Categorize similarities & differences

Epistemology (E-pis-te-mo-logy)

* “How do I know what I know?”
* Scientific arguments come from reasoned arguments
  + Example: What are the limits of experimental context?

Scientific Argumentation

* Deduction (deals with certainty)
  + Conclusion derived from general or universally accepted premises
  + Concluding specific outcome from general premise
* Induction (deals with probability)
  + Inferring future occurrence based on example
* Abduction (deals with reasonable guesswork)
  + Involves reasoning toward possible conclusions based on guesswork (best guess)
  + Occam’s razor

Facts: simple, basic observations shown to be true

Laws: description of phenomenon or unifying concept. Generalized observations about a relationship between two or more things in the natural world. Not explanations

Theory: broad explanation for lots of phenomenon. concise, coherent, systemic, and make predictions.

Hypothesis: limited explanation of a phenomenon rooted in data

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Laws of thermodynamics

Law 1: energy can only be converted

* Conservation of energy

Law 2: all things tend towards randomness (disorder)

* Isolated systems develop towards equilibrium
* Systems go to a more probably state

energy flows through an ecosystem (usually entering as sunlight and exiting as heat)

you are either a producer (autotroph) or a consumer (heterotroph)

Theories:

* Well-substantiated explanation
* Makes many testable predictions that are refutable
* Broader than hypotheses
* Not law

The origin of species articulated two main points

* Descent with modification
  + Contemporary species arose from a succession of ancestors
  + Phylogenetic tree (chart that shows the relationship between species to common ancestors)
* Natural selection
  + The mechanism by which descent with modification occurs (survival of the fittest)
  + Each slight variation of a trait, if useful, is preserved

Paternity tests

* Some ‘genes’ have variations that can be used for DNA testing
  + STRs (short tandem repeats)
    - Two or more nucleotides that are repeated next to each other
  + SNPs (single nucleotide polymorphisms)
    - A single nucleotide change)
* STRs can be used to exclude some alleged fathers
  + System: refers to a gene more specifically a genetic locus (specific place on a chromosome)
  + Genotype is the genetic makeup of an organism
  + Allele is a variation of a gene or locus

Alleles are different variations of genes

Experimental controls

* Experiments should have
  + Negative controls
    - D3S1358 repeats are not detected when they are absent (no false positives)
  + Positive controls
    - D3S1358 repeats can be detected precisely when present

DNA is used to make RNA that makes Protein

DNA sequences are conserved between species

* Divergent sequences indicate distant ancestral relationships
* Similar sequences indicate closer ancestral relationships

Scientific inquiries

* Hypothesis-based science (experimentation)
* Discovery science (use observation, intuition)
* Must be framed as a scientific hypothesis, must be testable and falsifiable

Three domains of life

* Eukaryotes
  + Eukarya
* Prokaryotes
  + Bacteria (eubacteria)
    - Single celled prokaryotes
    - Most diverse group
  + Archaea (archaebacteria)
  + Single celled prokaryotes that live in extreme environments)

Kingdoms of domain Eukarya

* Animalia (animals; heterotrophs)
* Plantae (plants; photoautotrophs)
* Fungi (fungi, molds, yeasts; nutrients from decomposing)
* Protista (amoebas, paramecia, etc.; mostly single-celled)

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Matter: anything that takes up space and has mass

* Elements
  + Atom: smallest unit of matter that still retains the properties of an element
  + Cannot be broken down by chemical reactions
* Compounds
  + Substances consisting of two or more elements combined in a fixed ratio
  + Characteristics different from those of its elements
* Molecules
  + Consists of two or more atoms held together by covalent bonds

Essential elements of life

96% of living humans consist of **Oxygen**, **Carbon**, **Hydrogen**, **Nitrogen**

Subatomic structure

* Proton: +1 charge, weight of 1(amu/da)
* Neutron: no charge, weight of 1(amu/da)
* Electron: -1 charge, negligible weight

Isotopes

* Different number of neutrons
* Same number of protons
* Same chemical properties
* Some are stable, some are radioactive and will decay

Radioactivity

* Spontaneous emission of particles & energy
  + α (alpha particle)
    - Helium atoms
  + β (beta particles)
    - Electrons
  + γ (gamma rays)
    - High energy electromagnetic radiation

Energy: capacity to cause change or do work

Kinetic energy: energy of motion (related to speed of motion)

Potential energy: energy matter possesses because of its location or structure (stored energy)

Biological systems use energy of possessed by electrons but not the energy of atomic nuclei

Electrons

* Electron energies represented by electron shells
  + Takes energy to jump up a shell
  + Releases energy to fall back down to ground state
* Valence electrons: electrons in the outermost shell
  + Determine the chemical behavior of the atom
  + Full shells are chemically inert
  + Bonding is one way to fill valence shells

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Bonds

* Covalent bonds
  + Share valence electrons
  + Single bond shares one pair of electrons (each atom shares one electron)
  + Double bond shares two pairs of electrons (each atom shares two electrons)
  + Triple bond shares three pairs of electrons (each atom shares three electrons)
  + Nonpolar covalent bonds: Similar electronegativities, shares electrons equally
  + Polar covalent bonds: dissimilar electronegativities, share electrons unequally
    - The separation of charge is called dipole moment signified by (δ+ or δ-)
  + Electronegativity: attraction of a particular kind of atom for the electrons in a covalent bond
    - Greater electronegativity pulls the shared electrons harder
    - Oxygen > Nitrogen > Carbon ≈ Hydrogen (relative electronegativities)
* Ionic Bonds
  + Sometimes one atom takes the electron from the other atom
  + Bonded because of difference in charge between atoms (bonded by ions)
  + Dissolves in water
* Weak chemical bonds
  + Hydrogen bonds
    - A hydrogen atom covalently bonded to one electronegative atom is attracted to another electronegative atom
  + Van der Waals interactions
  + Hydrogen bonds & Van Der Waals interactions
    - Reinforce the shapes of large molecules
    - Help molecules adhere to each other

Molecular shape and function

* Precise molecular shape is important to its function
* Molecular shape determines the specificity of interactions

Chemical reactions

* Chemical reactions make and break chemical bonds
  + Chemical reactions lead to changes in the composition of matter
  + Convert reactions to products
* All chemical reactions are reversible
* Chemical equilibrium, the rate of the forward reaction = the rate of the reverse reaction

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Water supports all life

* 75% of the earth’s surface is submerged in water
  + All living organisms require water more than any other substance
  + The abundance of water is the main reason earth is habitable
* The percentages of water on earth is ≈ to the percentage of water in living organisms

Why water is so important?

* Dipole (partial charge) allows H-bonding
  + H-bonding forms with other water molecules
  + Contributes to important emergent properties
* Emergent properties
  + Cohesion
    - H-bonding between a lot of water molecules next to each other (pulls each other up)
    - Capillary action
    - Helps pull water up through the microscopic vessels of plants
    - Surface tension
      * A measure of how hard it is to break the surface of a liquid
      * Many ordered H-bonds in the water at the air interface
  + High specific heat (moderate temperature)
    - Heat
      * Form of kinetic energy (atoms/molecules always moving [undirectedly])
      * The amount of heat possessed by an object is a measure of
        + Total amount of kinetic energy due to molecular motion
        + As a function of its volume and its temperature
    - Temperature
      * Measures the intensity of heat due to the average of kinetic energy (Average of heat due to kinetic energy)
  + Density changes
    - Becomes denser when cooled to a point then when freezing starts it becomes less dense
    - H-bonds in ice are more “ordered” (crystalize into lattices)
  + Universal solvent
    - Water is a versatile solvent due to its polarity
    - Solution: uniform mixture of 2 or more substances
    - Solvent: the one in the greater amount
    - Solute: the one in the lesser amount
    - Water breaks ionic bonds and dissolves them
      * The partial positive hydrogen side is attracted to the negative ion
      * The partial negative oxygen side is attracted to the positive ion
    - Hydrophilic substances have affinities for water (have charges, water loving)
    - Hydrophobic substances do not (neutral, water hating)

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Specific heat

* Amount of heat that must be absorbed or lost for 1 gram of that substance to change its temperature by 1˚C
  + Calories (cal)
    - 1 cal is the amount of heat required to raise the temperature of 1g of water by 1˚C
    - 1cal ≈ 4.18joules
    - Ethanol (0.57 cal/g)
    - Food calories are kilocalories (1kcal = 1000cal)
  + Allows water to minimize temperature fluctuations to within limits that permit life

Evaporation: transformation of a substance from a liquid to a gas

Heat of vaporization: quantity of heat a liquid must absorb for 1 gram of it to be converted from a liquid to gas

Evaporative cooling

* Due to water’s high heat of vaporization
* Allows water to cool a surface

Solute concentration in aqueous solutions

* A mole is the exact number of molecules of a substance in a given mass (6.02E23 molecules)
  + Calculating: #g of matter / formula weight
* Molarity (M): number of moles of solute per liter of solution

Dissociation of water

* 2H2O 🡪 H3O+ + OH- dissociates into hydronium ions and hydroxide ions (rare but important)
  + Usually only focus on the H+ and OH-

pH

* Determined by the relative concentration of hydrogen ions
* Concentration of water is 55M, when water dissociates the ions have a concentration of 10-7M
* Adding HCl: HCl 🡪 H+ + Cl- (HCl is a strong acid)
  + Increases the concentration of H+ ions lowering pH
* Adding NaOH: NaOH 🡪 Na+ + OH- (NaOH is a strong base)
  + Increases the OH- concentration, raising the pH
* pH = measurement of [H+] = -log [H+]
* Base: any substance that reduces the hydrogen ion concentration of a solution
  + Either by bonding with a H+ to form water or by attracting a proton (amine groups can ionize by bonding with a free H+)

Acid precipitation

* Burning fossil fuels is a major source of SO2 & NOx
* SO2 & NOx + H2O form strong acids
* Acid precipitation is rain, fog or snow with a pH < 5.2
* Acid precipitation damages life in lakes and streams and changes soil chemistry (generally damaging)

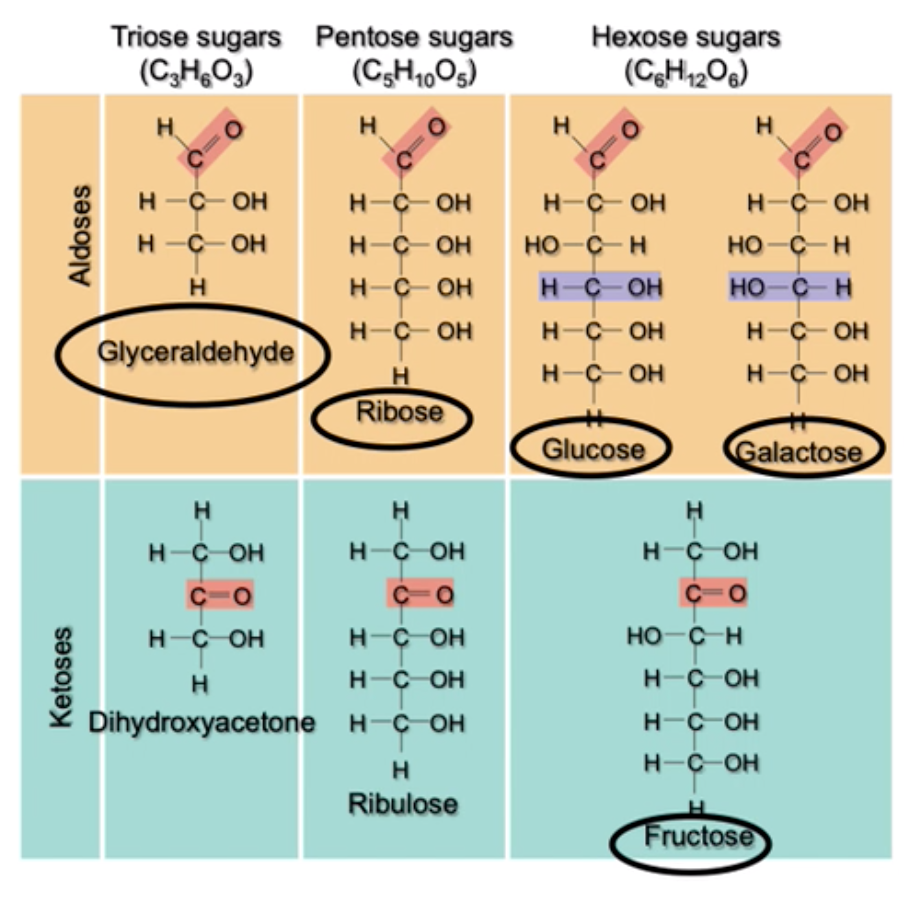
Buffers

* Generally, the internal pH of most living cells must remain close to pH 7
* Buffers
  + Substances that minimize changes to pH
  + Consist of an acid-base pair that reversibly combines with hydrogen ions
  + Acts as both an acid and base
  + CO2 + H2O <-> H2CO3 <-> HCO3- + H+

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Carbon

* The backbone of biological molecules
* All living organisms are made up of chemicals based mostly on the element carbon (organic chemistry)
* Carbon has four valence electrons (wants to gain 4 electrons of lose 4 electrons)
* Carbon chains
  + Form the skeletons of most organic molecules
  + Vary in length and shape
  + Isomers
    - Same composition, different structures
    - Structural: could have branches instead of being straight
    - Geometric (cis- or trans-): cis when functional groups are at the same side, trans when they are at opposite sides
    - Enantiomers: mirror images of compounds
* Functional groups
  + Are the parts of molecules involved in chemical reactions
  + Are chemically reactive groups of atoms within an organic molecule
  + Hydroxyl group
    - -OH or HO-
    - Polar because of the oxygen
  + Carbonyl group
    - >C=O
    - Commonly found in sugars
    - If in the middle, it’s a ketone
    - If at the end, it’s an aldehyde
  + Carboxyl group
    - -COOH
    - Acts as an acid (the H at the end of OH can be donated)
  + Amino group
    - -NH2
    - Acts as a base
    - Compound name: amine
  + Sulfhydryl group
    - -SH or HS-
    - Can make disulfide bridges that help stabilize a protein
    - Compound name: thiol
  + Phosphate group
    - -OPO32-
    - Can act as an acid (very electronegative, can release H+ ions)
    - When attached, can react with water to release energy
    - Compound name: organic phosphate
  + Methyl group
    - -CH3
    - Affects the expression of genes
    - Affects the shape and function of sex hormones
    - Hydrophobic compound
    - Compound name: methylated compound



Macromolecules

* Polymers made of monomers
* All organisms share the same limited number of monomer types (≈40-50)
* Each organism is unique because of the unique arrangements of monomers into polymers
* 3 of 4 classes (formed with unique monomers)
  + Carbohydrates
    - Monomer: monosaccharide
    - When a straight chain of them is put into water, they tend to isomerize into a cyclical molecule
  + Proteins
    - Monomer: amino acid (acts as a buffer)
    - Has an amine group on one side and a carboxyl group on the other, has a hydrogen at the bottom, and a R group (distinguishing figure) on the other side
    - Has an alpha carbon in the middle
    - 3 classes of amino acids
      * Nonpolar: The R group is nonpolar
      * Polar: The R group is polar
      * Charged (acidic/basic): The R group either acts as an acid or base
  + Nucleic acids
    - Monomer: nucleotide
    - Nucleotide is made of phosphate group, pentose sugar, nitrogenous base
    - Purines are the nitrogenous bases that are longer
    - Pyrimidines are the nitrogenous bases that are shorter
    - DNA: GC AT, RNA: GC AU
    - The 5’ carbon is connected to the phosphate group
  + (Lipids)
    - Three classes
      * Fats (triacylglycerides)
      * Phospholipids
      * Steroids

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Polymers formed by condensation reactions

* 2 subunits join with loss of a small molecule (if the molecule is water it is a dehydration reaction)
* Requires energy

Polymers can be disassembled by hydrolysis

* Water is added to the molecule to break the bond between two subunits
* Releases energy

Polymer properties – carbohydrates

* α and β glyosidic linkages, the glucose molecules can from with the hydroxyl group pointing up or down respectively
* α all face the same way when they link
* β alternate which way they are facing when they link
* α forms corkscrew shapes and form amylose (amylopectin when it branches) in plants, and glycogen in animals (they tend to be energy stores)
* β pack tightly and form cellulose (they tend to be structural)

Polymer properties – proteins

* Primary structure
  + Groups of 3 with different names (20 amino acids)
* Secondary structure
  + Form a helix (α helix) when they hydrogen bond with itself
  + Form β strands that hydrogen bond with other strands (β pleated sheet)
* Tertiary structure
  + Wraps around and fold into a 3D shape
  + Formed by hydrogen bonds, ionic bonds, disulfide bridges, and hydrophobic interactions and van der Waals interactions (hydrophobic sections fold into each other to better avoid water)
* Quaternary structure
  + How individual protein subunits interact with other protein subunits
* All those structural folding eventually determine how it functions
  + Sickle-cell disease
* When a protein unravels it is denatured
* When a protein when it folds back into shape it is renatured
* Proteins that assist in protein foldings are chaperonins
* Protein-folding problems
  + Most proteins go through many intermediate states before they reach their final form
  + Misfolded proteins can cause more misfolded proteins

Determination of protein structure

* Nuclear Magnetic Resonance (NMR aka MRI)
* X-ray crystallography (X-rays sent through a protein crystal are refracted onto photopaper)

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Polymer properties – nucleic acids

* RNA is a polar molecule
  + Conceptually single stranded
  + Order of nucleotides (nitrogenous bases) is key
  + Read from 5’ to 3’
* DNA is a polar molecular
  + Typically, an antiparallel double-stranded helix (strands are facing opposite ways)
  + Base pairing
    - A-T (2 hydrogen bonds)
    - G-C (3 hydrogen bonds)

Molecular properties – lipids

* Fluidity and Tm (Temperature of melting)
  + Length of fatty acid chains (longer = it’s harder to melt because of Van Der Waal interactions)
  + # and location of double bonds (causes the fatty acid chain to bend outwards and push at another lipid making it harder to stick to each other using Van Der Waal interactions)
* Water solubility
  + Fatty acid chains are hydrophobic, and they will try to stick together to avoid water
  + Biological fats, steroids and PLs are amphipathic (have hydrophobic and hydrophilic regions)
* Lipid-water interactions
  + They form a lipid bilayer so none of the hydrophobic tails interact with water

Functions – carbohydrates

* Monosaccharides & disaccharides
  + Fuel
  + Source of carbon
* Polysaccharides
  + Starches and starch-like molecules
    - Stores α-glucose (fuel)
  + Insoluble fibers
    - Cell walls (β-glucose)
    - Exoskeleton (chitin) (β-Ν-acetylglucosamine)

Functions – proteins

* Structure
  + Nuclear lamina (lines the inner nuclear envelope)
  + Keratins (helps protect the outer layer of skin from stress)
  + Silk
  + Collagen
* Transport
  + Hemoglobin (carriers)
  + Ion channels (portals)
  + Kinesins, dyneins, myosins (motor proteins)
* Contraction and movement
  + Microtubules
  + Microfilaments
* Communication and responding to environmental cues
  + Hormones, signaling molecules, receptors
    - Insulin and its receptor/progesterone and its receptor
  + Small G-proteins (ras, ran, rac, rho)
* Energy storage
  + Ovalbumin (eggs)
  + Casein (milk)
  + Seed proteins
* Defense
  + Antibodies/anti-bacterial peptides
* Enzymes
  + Catalytic proteins (speed up chemical reactions)

Functions – nucleic acids

* DNA (encodes hereditary information [genes])
* RNA
  + Products of gene expression
  + Critical for protein synthesis

Function – lipids

* Fuel source: triglycerides in fat cells (adipose tissue)
* Component of cell membranes: phospholipids & cholesterol
* Provides surfaces for lipophilic reactions: internal membranes of cells (e.g. endoplasmic reticulum, plasma membrane)
* Sex and other steroid hormones (cholesterol derivatives)
* Aid in digestion: bile salts (aid in digestion), emulsifiers
* Local mediators and signaling molecules (prostaglandin synthesis-promote fear and inflammation)

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How cell biologists study cells

* Biochemical approaches
  + Take tissue, homogenize them, centrifuge to separate it into a pellet and everything else. (the pellet is made of nuclei (won’t work on prokaryotic cells)), then take out the not pellet then spin it faster, repeat to separate out stuff. Then study the part that you want to study
* Genetic approaches
  + Breed animals with the mutation to study the mutation
* Pharmacological approaches
  + Study chemicals to find medical uses
* Microscopy
  + Cytology: study of cell structure

Parameters of microscopy

* Contrast
  + Differences in color, luminescence
* Magnification
  + Enlargement
* Resolution
  + Minimum distance two points can be separated and distinguished as two separate points
  + D = (0.61λ)/NA
  + Wavelength (λ)
    - Shortest λ visible light ≈ 390 nm (electron is ≈ 0.005nm)
  + Numerical aperture (NA) 10 X .25
    - Measure of the quality of the objectives and light path

Microscopy

* Light microscopes illuminate specimens with visible light
  + Brightfield: doesn’t manipulate light, doesn’t work well with living cells (unstained cells), works better with stained cells (usually dead)
    - Vital dyes can stain cells without killing them, histological stains kill cells
  + Phase contrast and DIC/Nomarski microscopy manipulate light paths
    - Allows for details with live cells that are unstained
    - Phase contrast looks sharpied
    - DIC/Nomarski looks grey and 3D-ish
  + Fluorescence
    - Inject dyes that binds with what you want to see that glows when excited by light
    - Inject thing you want to investigate into a rabbit to get rabbit antibodies for that thing, then inject the rabbit antibody into a goat to get antibodies for the rabbit antibody, attach a fluorescent molecule to the goat antibody, then put them into the cell to track the specific thing
    - Green fluorescent protein (GFP)
      * Put the gene near a protein of interest to track it in a living cell
  + Confocal, Deconvolution removes out of focused light
    - Confocal: focuses light at multiple points then layers them to make a clearer image
    - Deconvolution does the same as confocal except with computer software to do it
  + Super-resolution: has a super high resolution
* Electron microscopes illuminate specimens with electrons
  + Scanning electron microscopy
    - Sees the outside of the structure (topological image)
  + Transmission electron microscopy
    - Cuts the samples into very thin sections with something like a diamond knife, stain them with metal
    - Sees the inside of the structure

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Prokaryotic cell

* Lack organelles
* Nucleoid: area where bacterial chromosomes reside
* Ribosome: large functional RNA and proteins that synthesize proteins
* Cytoplasm: contains cytosol that has all the stuff dissolved in it and all the stuff floating in it
* Plasma membrane: lipid bilayer that contains the cytoplasm
* Cell wall: made of carbohydrates and protein, provides protection from the outside (different from eukaryotic cell walls)
* Flagella: tentacle like structure that help the cell move (different from eukaryotic flagella)
* Fimbriae: hair like structures that help the bacteria attach
* Pili: hair like structures that help the bacteria attach, also help transfer plasmid DNA
* Plasmid (episome): cyclical DNA that can be transferred between prokaryotes

Eukaryotic cell

Nucleus: Nuclear envelope (consists of inner and outer nuclear membrane), stores the host genome, regulates gene expression, contains the nucleolus

* + Inner nuclear membrane: lined with nuclear lamina, contains the nucleoplasm (cytoplasm for inside the nucleus)
  + Outer nuclear membrane: continuous with the ER and can be studded with ribosomes like the rough ER

How DNA is arranged in the nucleus

* They all have their own territories, where the territories of DNA meet, is where they are turned on and off
* When they are dividing
  + Histones form nucleosomes (makes DNA look like beads on a string (with short spacers in between))
  + ^ is then layered on top of each other and packed even tighter, and so on and so on
* Chromatin (DNA packaged by proteins)
  + Comes in condensed (heterochromatin) or decondensed (euchromatin) forms
  + Condensed chromatin is DNA that isn’t used in a specific cell, decondensed is used
  + Entire DNA in condensed form is called chromosome
* Nucleolus
  + Only obvious intra-nuclear structure
  + Location of genes encoding ribosomes
  + Primary function is to synthesize ribosomes
* Ribosomes
  + Made of rRNA and proteins
  + Carry out protein synthesis (translation)
  + Are either attached to the rough ER (bound ribosome) or just floating in the cytosol (free ribosome)
* Transcription: process of synthesizing protein
  + DNA is transcripted to Pre-mRNA
  + Pre-mRNA is processed into mRNA
  + mRNA leaves the nucleus to a ribosome to be turned into a protein (translation)
* Free cytosolic ribosomes
  + Translates proteins that go to the (nucleus, nucleolus, peroxisomes, mitochondria, chloroplasts, cytosol)
* How to know where to transport proteins
  + They have markers that say where they belong

Nuclear envelope

* Separates sites of transcription and translation
* mRNA leaves nucleus through the nuclear pore complexes (NPCs)

Peroxisomes

* Break down fatty acids
* convert H2O2 to H2O
* Generates hydrogen peroxides when breaking down fatty acids
* Cholesterol synthesis
* Photorespiration
* Fat storage in plants

Components of the cytoskeleton

* Microtubules
  + Hollow tubes made of α and β tubulin
  + Maintains cell shape (deals with compression forces)
  + Helps cells move (cilia or flagella)
  + Helps chromosomes move during cell division
  + Helps move organelles
* Microfilaments
  + Made of two intertwined strands of actin (actin is made of actin subunits)
  + Maintains cell shape (deals with tension forces)
  + Changes in cell shape (muscle contraction)
  + Cytoplasmic streaming
  + Helps in cell movement (pseudopodia)
  + Helps with cell division (cleavage furrow formation)
* Intermediate filaments
  + Fibrous proteins supercoiled into thick cables (can be different proteins like keratin)
  + Maintains cell shape (deals with tension forces)
  + Holds nucleus and some other organelles in place
  + Is what the nuclear lamina is made of
* Function of the cytoskeleton
  + Structure and architecture (all)
  + Promote motility (microtubules, microfilament)
    - Movement of cells
      * Cilia and flagella (microtubule)
    - Movement of organelles (microtubules, micro filaments)
    - Movement of macromolecules and big complexes (microtubules, microfilaments)
    - Contraction of muscles (microfilament)
    - Movement of chromosomes during division (microtubules)
  + Organization and localization (microtubule, microfilament)
    - Position of organelles, enzymes, etc.
* Intermediate filaments
  + Usually 10 nm thick
  + 1˚ functions
    - Maintain cell shape
    - Load bearing
    - Architectural
  + Examples
    - Nuclear laminas (only one in the nucleus)
    - Keratins
    - Neurofilaments
* Microtubules
  + Made of hollow tubes of a spiral of alpha and beta tubulin
* Centrosome (microtubule organizing centers)
  + – end is connected to centrosome, the + end is growing outwards
  + Bulk of microtubules are organized in most cells
  + Contains a pair of centrioles (not essential to function)
  + Generally found next to the nucleus
* Microtubules provide movement
  + Cell movement
    - Cilia
    - Flagella
    - ^ both share a common ultrastructure
  + Intercellular movements
    - Microtubular lengthening and shortening
    - Tracks for motor proteins
      * Kinesin (move from – end to + end) (outward)
      * Dynein (move from + end to – end) (inward)
* Microfilaments (actin filaments)
  + Highly conserved (means important)
  + Maintenance of cell shape
  + Muscle contraction
  + Cytoplasmic streaming
  + Smallest diameter
  + Made with actin
  + Associated with myosin motors
  + Cell division
  + Provide support (to increase the surface area of the plasma membrane)
  + Can move stuff
  + Adapted to absorb nutrients efficiently
  + Microfilaments function in cellular motility
    - Motor protein myosin + actin
    - Amoeboid movement
    - Surrounding the central vacuole (in plants) (cytoplasmic streaming)
  + Microvilli
    - Increases surface area of the plasma membrane to do more transferring (makes it look like a brush)

Endoplasmic reticulum

* Proteins have to go through the ER before going to the Golgi bodies
* Rough ER
  + Initial site of proteins that enter endomembranous system
  + A protein recognizes a signal peptide and stops translation, brings it over to the ER
    - The protein gets translated into the ER and cannot return to the cytosol
  + Proteins are modified by carbohydrates
  + Studded with ribosomes
  + Protein synthesis
  + Protein folding
  + Protein modification (carbohydrates)
  + Quality control
* Smooth ER
  + No ribosomes
  + Synthesizes lipids, steroids, phospholipids
  + Carbohydrate metabolism (glycolipids)
  + Stores calcium
  + Metabolizes drugs
* Endomembrane system
  + Regulates protein and lipid traffic
  + Performs metabolic functions in the cell
  + Endomembrane system
    - ER
    - Golgi apparatus
    - Transport vesicles
    - Lysosomes
    - Endosomes

Golgi apparatus

* Flattened membranous sacs called cisternae
* Shipping and receiving center
* Receives transport vesicles produced in rER
* Receives from the cis side, ships out from the trans side
* Will modify proteins as it moves through it

Lysosomes

* Intracellular catabolism
* Gets stuff from 2 places
  + Outside of cell
    - Endocytosis, food
  + Biosynthetic factory (ER)
    - Source of catabolic enzymes
    - Catabolism is the breakdown of complex molecules to smaller ones
    - Opposite of catabolism is anabolism
* Digestive compartments
  + Carry out intracellular digestion following endocytosis
  + Contains hydrolytic enzymes that can digest all kinds of macromolecules
* Endocytosis
  + Phagocytosis (cellular eating) (uses endosomes)
  + Pinocytosis (cellular drinking) (uses small vesicles)
  + Receptor mediated endocytosis
* Autophagy
  + Lysosomal degradation (senescent organelles get surrounded with a vesicle and a lysosome merges with it to breakdown the senescent organelle)

Vacuoles

* A plant or fungal cell (may have one or more)
* Endosomes (formed by phagocytosis/endocytosis)
* Contractile vacuoles (pump excess water out of protist cells)
* Central vacuoles
  + Found in plants
  + Hold reserves of inorganic compounds and water

Cells

* Bounded by a plasma membrane
* Contains a semifluid substance called the cytosol (water-based)
* Contained chromosomes (nucleic acids + proteins)
* Have ribosomes

Membrane models

* Model system
  + Mammalian red blood cell plasma membranes
* Composed of lipids and proteins
  + Carbohydrates are present but modify lipids and proteins
  + Phospholipids often most abundant
    - Are amphipathic, containing both hydrophobic and hydrophilic parts

E.Gorter and F.Grendel

* Reasoned that cell membranes must be a phospholipid bilayer two molecules thick.

Models of membrane structure

* Sandwich model (davson-danielli)
  + There are proteins that cover the bilayer because water interacted a lot
* Fluid mosaic model (singer and Nicholson)
  + Proteins have hydrophobic regions in the middle and hydrophilic regions on either end, and they are imbedded into the plasma membrane
  + To test it, they froze cells and fractured it to try to break it causing the phospholipid layer to separate and then look at it under an electron microscope (bumpy means this model is true)
  + To test it they also fused cells with different florescent proteins and saw after an hour, the proteins diffused (membrane is fluid)

Cholesterol

* It is a buffer for the fluidity of cellular membranes.
* Prompts microdomain formation

Plasma membrane

* Functions as a selective barrier (allows sufficient passage of nutrients & waste)
* Surface to volume ration
  + A smaller cell has a higher surface to volume ratio
    - Surface area increases at a rate of x2
    - Volume increases at a rate of x3
  + Larger cells have to have more surface area to exchange more stuff
* The membrane is selectively permeable ()
  + Small non-polar has no issues
  + Small polar molecules are mostly blocked (by hydrophobic layer)
  + Large polar molecules are blocked even more (larger size requires more energy to get through)
  + Ions cannot get through (lots of water tries to h-bond with it making it impossible to pass the hydrophobic region)
* Membrane proteins
  + Penetrate the hydrophobic core of the lipid bilayer
  + Often transmembrane proteins, completely spanning the membrane
  + Peripheral membrane protein
    - Loosely bound to the surface of the membrane
  + Major functions
    - Transport
      * Diffusion
        + Movement down a gradient without any help (small non-polar molecules)
        + Osmosis (diffusion of water)

Tonicity (environment)

Hypotonic: lower concentration than cell, water will try to rush in (plants will be turgid)

Isotonic: same as cell, water will move in at the same rate that it moves out

Hypotonic: higher concentration than cell, water will rush out (plants will shrivel)

* + - * Facilitated diffusion
        + Movement down a gradient with help (larger molecules/polar molecules)
        + Carriers and channels do this
      * Active transport
        + Requires sources of energy to move solutes against their concentration gradients
    - Enzymes
      * Active transport
      * ATP synthase
      * Kinases involved in cell communication
    - Signal transduction (cell communication)
      * G-protein coupled receptors
      * Receptor tyrosine kinases
      * Channels
    - Cell-cell recognition
      * Membrane glycoproteins help cells distinguish one type of neighboring cell from another
    - Intercellular joining
      * Plants
        + Plasmodesmata

Large channels that perforate plant cell walls

Share cytoplasm

* + - * Animals
        + Gap junction

Small pores that only allow for ions and small molecules to pass

* + - * + Tight junction

Impermeable junctions

* + - * + Adherens junctions & desmosomes

Basically cellular rivets

Joins the cytoskeletal structures of one cell with those of another

* + - Attachment to the cytoskeleton and extracellular matrix (ECM)
      * Integrins
      * Extracellular matrix
        + Made of glycoproteins and other macromolecules
        + Functions: support, adhesion, movement, regulation

Cellular energy

* Metabolism
  + Totality of an organism’s chemical reactions
  + Transforms matter and energy
  + Subject to the laws of thermodynamics
  + Coordinated and regulated reactions
* Energy
  + Capacity to cause change
  + Exists in various forms, some that can be used to do work
  + Catabolic pathways (mitochondria)
    - Break down complex molecules into simpler compounds
    - Release energy (exergonic reaction)
    - ΔG = Gfinal – Ginitial where ΔG is negative
    - Spontaneous
  + Anabolic pathways (chloroplasts)
    - Build complicated molecules from simpler ones
    - Consume energy (endergonic reaction)
    - ΔG = Gfinal – Ginitial where ΔG is positive
  + Change in free energy (ΔG) (Gibbs free energy)
    - ΔG = ΔH - T ΔS
    - Where ΔH is total energy (enthalpy) and TΔS is the amount of disorder (S specifically is entropy)
    - T (temperature) stays constant
    - For a reaction to occur spontaneously
      * ΔH has to go down
      * TΔS has to go up
      * Or both
      * Basically -ΔG is exergonic and spontaneous

Energy coupling: how cells manage their energy to do work

ATP

* Powers cellular work by coupling exergonic reactions to endergonic reactions
* ΔG = -7.3 kcal/mol
* Energy is released when the third phosphate at the end of the chain breaks
* Regenerated by catabolic pathways

Activation energy: the amount of energy needed for an exergonic reaction to spontaneously occur

Enzyme: catalyzes a reaction, lowering its activation energy

Enzyme lowers EA

* Orienting substrates correctly
* Straining substrate bonds
* Providing a favorable microenvironment
* Covalently bonding to the substrate

Impacts to enzyme activity

* Temperature
* pH
* Cofactors
  + Inorganic factors (ions)
* Coenzymes
  + Organic factors

Enzyme regulation

* Competitive inhibitor (binds with the active site of the enzyme physically blocking the substrate)
* Noncompetitive inhibitor (allosteric inhibition)
  + Binds with a different part of the enzyme, causing its activation site to change shape, preventing the enzyme from working
  + An enzyme can shift between active and inactive forms, an activator keeps it in the active form, an inhibitor keeps it in the inactive form
  + Cooperativity: substrate acts as an allosteric activator (one binds to a section and stabilizes other active sites)
* Where enzymes are active
  + Inside organelles
  + In membranes
  + Into complexes

Redox reactions (reduction-oxidation)

* Catabolic pathways yield energy due to the transfer of electrons
* Transfer of electrons from one reactant to another (loses energy)
  + Losing an electron (oxidized) (called the reducing agent)
  + Gaining an electron (reduced) (called the oxidizing agent)
* Many redox reactions change electron sharing in covalent bonds (they don’t always ionize)

Oxidation of organic fuel by cellular respiration

* During cellular respiration, glucose is oxidized and oxygen is reduced
* Stepwise energy harvest (NAD+ and electron transport chains)
  + Cellular respiration
    - Oxidizes glucose in a series of steps
    - Gradual, controlled release of energy (like a car using gas)
    - Energy release controlled in part by electron carriers
      * Nicotinamide adenine dinucleotide (NAD+) helps control energy release
        + NAD+ is oxidized, NADH is reduced
        + Electrons from organic compounds are usually firs transferred to NAD+ , a coenzyme
      * Flavin adenine dinucleotide (FAD) is also an electron carrier

Cellular respiration (3 stages)

* Three metabolic stages of cellular respiration
  + Glycolysis
    - Occurs in the cytosol
    - Produces a little ATP via substrate-level phosphorylation
    - “splitting of sugar”
    - Breaks down glucose into pyruvate (oxidation)
    - Need to invest 2 ATP at the start to generate 4 ATP, 2NADH and 2 pyruvates at the next step
    - Net reactions
      * Glucose -> 2 pyruvate + 2 H2O
      * 4 ATP formed – 2 ATP used -> 2 ATP
      * 2 NAD+ + 4e- + 4H+ -> 2 NADH + 2 H+
    - Steps that happen but don’t need to be memorized
      * The 1 ATP turn glucose into glucose 5-phosphate which increases the potential energy and traps glucose in the cell
      * Glucose 6-phosphate turns into fructose 6-phosphate
      * A 2nd ATP turns fructose 6-phosphate into fructose 1,6-biphosphate
      * Fructose 1,6-biphosphate splits into glyceraldehyde 3-phosphate and dihydroxyacetone phosphate
      * Dihydroxyacetone phosphate changes into glyceraldehyde 3-phosphate
      * The two glyceraldehyde 3-phosphate lose high energy H+ ions and gain
      * another phosphate group (generates 2 NADH)
      * They lose the phosphate group (generates 2 ATP)
      * They are then transformed a bunch and, in the end, lose the two phosphate groups (generates another 2 ATP)
  + The citric acid cycle (Krebs cycle)
    - Occurs in the mitochondria (mitochondria matrix)
    - Produces a little ATP via substrate-level phosphorylation
    - Pyruvate goes from the cytosol into the mitochondria (while this happens, it is changed into acetyl CoA)
    - As it goes through the cycle, electrons are removed from Acetyl CoA and put into NAD+ forming NADH, generating some ATP and the electrons are also put into FAD making FADH2
  + Oxidation phosphorylation
    - Occurs in the mitochondria
    - Produces lots of ATP via oxidative phosphorylation
    - Cytochromes syphon off energy from the electrons and at the end oxygen accepts the oxygen
    - The protein complexes on the inner mitochondrial membrane pump protons into the intermembrane space by using energy from the electrons before passing the electron onwards
    - Chemiosmosis: as protons go down it’s concentration gradient, it goes through ATP synthase and converts ADP and a P group into ATP (can run in reverse)
    - Summary
      * NADH and FADH2
        + Donate their electrons to the electron transport chain
        + Donates them in a controlled manner
      * Electron transport chain
        + Electrons from NADH and FADH2 pump H+ ions to create a gradient
      * Chemiosmosis
        + ATP synthase uses that gradient to produce ATP
  + Terms
    - Substrate-level phosphorylation: takes a phosphate from a substrate and moving it onto an ADP producing an ATP
  + ATP and Citrate are inhibitors for phosphofructokinase (slowing down glycolysis and the whole cycle)
  + AMP (ATP with only 1 phosphate group) stimulates the process

Mitochondria

* Origins (endosymbiosis)
  + long ago an ancestral eukaryote cell engulfed non-photosynthetic eubacteria, and that became the mitochondria (a relationship where both benefit but one is inside the other)
  + because of this, mitochondria have DNA and ribosomes
* Found in nearly all eukaryotic cells
* Enclosed by two membranes
  + Smooth outer membrane
  + Folded inner membrane called cristae

Fermentation: allows some cells to produce ATP without oxygen

* Alcohol fermentation
  + Pyruvate becomes acetaldehyde that becomes ethanol
* Lactic acid fermentation
  + Pyruvate becomes lactate

Anaerobes

* Obligate anaerobes
  + Rely on fermentation
  + Can’t survive in the presence of O2
* Facultative anaerobes
  + Using either fermentation or cellular respiration
  + Pyruvate is a fork in the metabolic road
  + Yeast and many bacteria

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Photosynthesis

* Process that converts solar energy into chemical energy
  + Occurs in autotrophs (plants. Algae, some protists and some prokaryotes)
* Chloroplasts
  + Leaves of plants are major sites of photosynthesis
    - Stomata open to allow for gas exchange
  + Three membranes
    - Thylakoids
      * Flattened sacs
    - Grana
      * Stacks of thylakoids
  + Substances that absorb visible light
    - Chlorophyll A: main photosynthetic pigment
    - Chlorophyll B: accessory pigment
    - Carotenoids
  + Exited electrons
    - Lose energy (heat)
    - Fluoresce
    - Resonate (don’t need to know)
    - Exchange e- with other molecules
* Photosynthesis is a redox process (reverse of respiration)
  + Energy + 6CO2 + 6H2O 🡪 C6H12O6 + 6O2
  + (reduced) (oxidized) (reduced) (oxidized)
  + Endergonic (energy comes from the sun)
  + Takes the oxygen from water (grew a photosynthetic plant in radioactive water (radioactive oxygen) and a different plant in radioactive carbon dioxide (radioactive oxygen))
* Two stages
  + The light reactions
    - Occurs in the grana
      * Splits water
      * Releases O2, ATP, NADPH (reduced form of NADP)
    - Chloroplasts convert solar energy to ATP and energy stored in e-
    - Wavelength of light determines electromagnetic energy (wavelength and energy are inversely proportional)
    - In the thylakoid membrane
      * There are two photosystems (II, I)
      * Composed of a reaction center surrounded by light-harvesting complexes (photosystems)
    - Models of light reactions
      * Noncyclic electron flow (linear electron flow)
        + Noncyclic electron flow

Primary pathway of energy transformation in the light reactions

Produces NADPH, ATP and O2

Energy from the sun is collected and transferred to a chlorophyll (chlorophyll is being oxidized) and the electron from the chlorophyll is taken by the primary acceptor chlorophyll then oxidizes water to regain its electrons. The electrons taken by the primary acceptor are transferred to an electron transport chain to produce ATP and the electrons are transferred to photosystem I (the chlorophyll). Energy from the sunlight is transferred to this new chlorophyll causing the chlorophyll to lose its electron to another primary acceptor which uses that energy to make NADPH

Proton motive force is much stronger in chloroplasts than in mitochondria (4-8 vs 7-8)

* + The Calvin cycle (C3 plant)
    - Occurs in the stroma
    - Produces sugar
    - Requires CO2, ATP, NADPH (reducing power)
    - Three phases
      * Carbon fixation
        + RuBisCo takes 3 CO2 and turns 3 5-carbon molecules (1 phosphate at either end) into 3 6-carbon molecules (1 phosphate at either end)
        + The 3 6-carbon molecules are unstable and quickly break down to 6 3-carbon molecules (1 phosphate molecule at one end)
      * Reduction
        + ATP is used and the 6 3-carbon molecules
      * Regeneration of the CO2 acceptor
        + ATP is used and 5 30carbon sugars become 3 5-carbon sugars
    - RuBisCO is the key enzyme
      * It is an inefficient enzyme
      * It can interact with both CO2 and O2

Chemiosmosis occurs in both chloroplasts and oxidative phosphorylation

Special organization

* Mitochondria
  + H+ in intermembrane space
* Chloroplast
  + H+ in thylakoid membrane

Stomata

* When open
  + Gas exchange
  + Water loss (transpiration)
* Under hot and dry environments
  + Stomata closes (slows down photosynthesis) because if it stays open the plant would wilt

Photorespiration (C3 plants)

* CO2 entry is limited, and water is conserved
* RuBisCo uses O2 instead
* ^ creates useless 2 carbon molecules which is converted by peroxisomes and mitochondria to make CO2 (wastes a lot of ATP)

C4 adaptation

* PEP carboxylase fixes CO2 efficiently (4 carbon intermediate)
* Cellular adaptations
  + Mesophyll cell
    - It fixes CO2
  + Bundle sheath cell
    - Calvin cycle

CAM plants

* Pineapples
* CO2 fixed at night (stomata open)
* Temporal adaptation
* Calvin cycle occurs during the day because it needs high energy electrons, ATP and NADPH

Cell communication

* Coordinates cell activity within a population of cells
  + Tissues and organs (fight of flight)
  + Seen in single cells
* Communication pathways are generally conserved throughout evolution
* Pathways may have combinatorial effects
* Types of signaling
  + Long distance
    - Endocrine (hormones)
      * Glands (pituitary, thyroid, adrenal, etc.)
      * Organs (pancreas, ovary, testes, etc.)
  + Short distance
    - Paracrine (secreted signals don’t travel through the circulatory system)
      * Autocrine (self-signaling)
      * Synaptic signaling (signaling something really close)
  + Local signaling
    - Paracrine (short distance signal release)
    - Autocrine (self-signaling)
    - Cell contact
      * Signal through junctions
      * Signal through cell-cell contact
    - Extracellular matrix
* Reception: signal is produced and received and recognized by target cell (signaling molecule binds to a receptor on the plasma membrane) (receptors are generic)
  + 3 membrane receptors
    - G protein-coupled receptors
      * G protein is a receptor protein
        + GDP bonded to it means it’s off
        + GTP bonded to it means it’s on
      * When the signaling molecule bonds to the receptor, the receptor changes shape and makes GDP leave the G protein and allows GTP to bind activating the G protein
      * The activated G protein then binds to its enzyme and lose a phosphate group and activation a cellular response
    - Receptor tyrosine kinases
      * Trigger multiple signal transduction pathways at once
      * Abnormal RTK F(x) associated with many cancers
      * Signal molecule makes the two separate parts into one molecule that phosphorylates the tyrosines in its structure that i
    - Ion channel receptors
      * Signaling molecule binds to the ion channel receptor to open it causing ions outside the cell to rush in to activate a cell response
  + Intracellular receptor
    - Receptor for steroids (testosterone, progesterone, glucocorticoid, estrogen)
    - They bind hydrophobic molecules that diffuse through the cell
* Transduction: the receptor changes shape and releases relay molecules in a signal transduction pathway (signal gets amplified)
  + Happens in multiple steps
    - Often involving protein shape change
    - Often involves protein phosphorylation
      * Protein kinase: enzyme that phosphorylates a protein substrate (on switch)
      * Protein phosphatase: enzyme that removes phosphates from a protein substrate (off switch)
    - Amplifies signal
    - Coordination of different pathways
    - Phosphorylation cascade
      * Allows many different proteins to be activated and inhibited by phosphorylation (amplification)
      * Provides many points where the signal can be regulated
    - Transduction use 2nd messengers
      * Small, nonprotein, water-soluble molecules/ions
        + Cyclic AMP
        + Cyclic GMP
        + Calcium ions
        + Inositol trisphosphate (IP3)
        + Spread by diffusion
      * Participate downstream from
        + G protein-coupled kinases
        + Receptor tyrosine kinases
* Response: cell reacts to the transduced signal and deactivates the signal response
  + One signal can lead to 1 response, multiple responses, or different responses in different cells
    - Two receptors can cause one pathway to activate or prevent activation
  + Responses to signals
    - May trigger gene expression
    - Regulate the cell activity of enzymes
    - Change cell structure/function
    - Trigger apoptosis
      * Programmed (controlled) cell deaths
      * Prevents enzymes from leaking out of a dying cell and damaging neighboring cells
      * Activation of proteases (caspases)
      * Implicated with disease (Alzheimer’s, Parkinson’s, cancer)

Cell division

* How unicellular organisms reproduce
* How multicellular organisms use cell division
  + Development from a fertilized cell
  + Growth
  + Repair
* Cell division cycle
  + Includes cell division and events prior to division (duplicating genomes)
  + Interphase
    - G1 (decides if it is ready to commit to cell division)
      * Active in transcription & translation, no DNA synthesis, deciding whether to commit to cell division, cell growth
    - S phase (DNA synthesis)
      * Active in transcription & translation, DNA synthesis, committed to divide, cell growth
    - G2 (decides if it is ready to actually divide)
      * Active in transcription & translation, no DNA synthesis, deciding whether it is ready to enter M phase, cell growth, checking for DNA damage
  + M phase
    - Mitosis: division of the nucleus
      * G2 of interphase: two centrosomes and chromatin is duplicated
      * Prophase: chromosomes are condensed, and the centrosomes begin to migrate to opposite sides of the cell forming the mitotic spindle, apart and transcription begins to stop
      * Prometaphase: nuclear envelope breaks down; microtubules try to connect to the centromeres and the chromosomes align in the middle of the cell
      * Metaphase: all the chromosomes are aligned at some arbitrary point called the metaphase plate (the chromosomes have to line up before the next step)
        + The back and forth pull between the microtubules causes them to line up
      * Anaphase: chromosomes split into chromatids that go into daughter cells
        + Anaphase A: sister chromatids separate, and the kinetochore microtubules start shortening at the end connecting to the chromatids
        + Anaphase B: astral microtubules shrink pulling everything into the daughter cell
      * Telophase: chromosomes begin to be enveloped by a nuclear envelope and after they are enveloped, they begin to decondense
      * Cytokinesis: microfilaments create a cleavage furrow causing the giant cell to split into two daughter cells.
        + A ring of microfilaments form a ring and contract forming a cleavage furrow until the cell splits into two
    - Cytokinesis: division of the cytoplasm
    - There is translation but very limited transcription
  + Mitosis results in genetically identical daughter cells
  + DNA is replicated and chromosomes are condensed
  + Each duplicated chromosome has two sister chromatids which separate during cell division (held together by a centromere)
    - Is split during mitosis into sister chromatids (they have chromatids where the centromere was)
  + Cell division cycle regulation
    - Molecules present in the cytoplasm regulate progress through the cell cycle
      * tested by fusing a G1 phase cell to a S phase cell and found that the G1 phase cell entered the S phase and the experiment was repeated with an M phase cell and showed that there is something in the S and M phase cells that causes a cell to enter different phases
      * MPF was transferred from a dividing cell to a nondividing cell ^
  + Cell cycle clock
    - MPF
      * Activity exhibits cell division cycle behavior
      * Consists of two proteins
    - Cyclin-dependent protein kinases (CDKs)
      * Kinases are enzymes that add phosphate groups onto substrates
      * Protein kinases do that to proteins (CDKs are an example of this)
    - Mitotic CDK (MPF: M-phase promoting factor)
      * Cyclins are regulatory subunits of CDKs (Cyclin and MPF activity are correlated)
    - There are other CDKs and cyclins that are important for controlling passage through G1, S, and M phase (they control the orderly, clock-like progression through the cycle)
    - Cell cycle control system (are controlled by CDKs can be influenced by outside factors)
      * G1 checkpoint: checks if there are enough resources to divide (if it fails this then it enters the G0 phase)
      * G2 checkpoint: checks if the DNA is fully replicated/damaged, if it isn’t fully replicated/damaged the cell will try to fix it (if it fails it will commit apoptosis)
      * M checkpoint: checks if all the chromosomes are lined up at the metaphase plate before continuing to anaphase. (if it fails it will commit apoptosis)
* External factors that impact cell growth
  + The cells have to be attached to something (must be attached to substratum to divide)
  + Density-dependent inhibition (crowded cells stop dividing)
* Cancer cells
  + They don’t respond normally to the body’s control mechanisms and from tumors
* Mitotic spindle
  + Astral microtubules connect to the cell membrane
  + Kinetochore microtubules connect to chromosomes
  + Polar miccmbvmcmcmmmcrotubules (go from one side of the cell to the other)
* G0: if a cell stops and stay at G1 for long periods of time it is said to be in G0
* Meiosis
  + Sex cells produce gametes (sperm and egg cells)
  + Reduces the number of chromosomes in half
  + Differences between meiosis and mitosis
    - Prophase I: homologous chromosomes will stick together (creating tetrads) and portions of them will switch places (synapsis holds homologous chromosomes together and allow swapping). This process is called recombination
    - Metaphase I: tetrads are lined up in the middle
    - Anaphase I: tetrads are split
    - Telophase I and cytokinesis: nuclear envelope forms and they are split into 2 different cells
    - Prophase II onwards: nuclear envelope breaks down, chromosomes align at the metaphase plate, they split, and a new nuclear envelope forms and splits into 4 cells
  + In males the 4 gametes are the same size
  + In females all the resources go into 1 cell (the egg) and the remaining 3 become polar bodies
* Comparison of mitosis and meiosis
  + Meiosis
    - Produces daughter cells that are genetically distinct from the parent and sister cells
    - Diploid is reduced to haploid
  + Mitosis
    - Produces daughter cells that are genetically identical to the parent and sister cells
    - Cells remain diploid
* Eukaryotic chromosomes
  + Consist of chromatin, a complex of DNA and protein that condenses during cell division
  + Somatic cells (diploid) have two sets of chromosomes (body cells)
  + Gametes (haploid) have one set of chromosomes (reproductive cells)
* Mitosis in a plant cell
  + Everything is the same as an animal cell until the telophase where a cell plate will form that will eventually become part of the cell wall
* Prokaryotes
  + Binary fission
    - Bacterial chromosomes replicates
    - The two daughter chromosomes actively move apart

Heredity: transmission of traits from one generation to the next

* Genetics is the study of heredity

Inheritance: offspring acquire genes from parents by inheriting chromosomes

* Genes (units of heredity)
  + Segments of DNA made of specific sequences of DNA nucleotides (dATP (A), dTTP (T), etc.)
  + Each gene is an organism’s DNA has a specific locus (where a specific gene is located on a chromosome) on a certain chromosome

Transmission of hereditable traits

* Precise DNA replication
* Plants & animals use vehicles for gene transmission (gametes (pollen/sperm and ova))
  + Gametes fuse with each other (fertilization)
* Asexual reproduction
  + One parent produces genetically identical offspring by mitosis
  + Common in single celled organisms or budding organisms (yeast, hydra)
* Sexual reproduction
  + Two parents give rise to offspring that have unique combinations of genes
  + Unique combinations are created by meiosis
  + Human example
    - Somatic cells have 46 chromosomes (23 pairs of chromosomes)
    - One set comes from each parent (22 autosomes and 1 sex chromosomes)
  + Sex chromosomes
    - Distinct from each other (x and y)
    - Determines the sex of the individual (xx = female, xy = male)
    - Xy is the nomenclature when the homogametic sex is female
    - Wz is used when homogametic sex is male (zz)
  + Life cycles
    - Generation-to-generation sequence of stages in reproductive history
    - Mitosis and meiosis alternate in sexual cycles
    - In animals, the haploid (gamete) is short lived
    - In most fungi and some protists,
    - In plants and some algae,
* Genetic variation
  + Descent with modification (due to meiosis)
    - Independent assortment (gene/chromosome shuffling)
      * When tetrads line up at the metaphase plate during metaphase I the positioning of the organization of the chromosomes are random (chromosomes of one parent can lined up on one side or swapped with the position of the other parent)
      * Crossing over: produces recombinant chromosomes that carry genes derived from two different parents
    - Random fertilization/gamete fusion
      * What genes the gamete that happens to fertilize the egg caries
    - Mutations
      * Original source of genetic variation

Mendelian genetics

* Blending hypothesis vs particulate hypothesis
  + Blending: all the genetic material from the two parents’ mixes
  + Particulate: parents pass on discrete heritable units (genes)
* Mendel used peas
  + They were available in many varieties
  + They were easy to control their mating
    - Peas were “true-breeding” (characteristics were either-or)
* Terminology
  + Character: a heritable feature (like flower color)
  + Trait: a variant of a character (like purple or white flowers)
  + Alleles: different versions of genes that account for variation
  + Phenotype: what we see
  + Genotype: the actual genes
  + Homozygous: having the same alleles
  + Heterozygous: having different alleles
  + Hybridization: interbreeding different varieties
  + True-breeding: homozygous for every trait
  + P generation: parent generation
  + F1 generation: 1st filial generation (1st generation after p generation)
  + F2 generation: 2nd filial generation (2nd generation after p generation)
* Law of segregation (different alleles can be packaged into different gametes)
  + In Mendel’s f1 generation, all the plants were purple (blow to blending because all the flowers were purple)
  + In the f2 generation, there was a ratio of 3:1 of purple: white flowers (blow to blending because white flowers shouldn’t be possible anymore)
  + Punnett square
    - To account for the 3:1 ration, he determined that the P generation was homozygous (purple being dominant, white being recessive)
    - The F1 generation was heterozygous
    - The F2 generation yielded 1 homozygous dominant, 2 heterozygous purple, 1 homozygous recessive
  + Alleles were assumed to account for the variation
    - If two alleles at the locus differ (diploid organisms inherit two alleles (one from each parent))
      * Dominant allele determines appearance, recessive has no noticeable effect
  + Alleles from heritable character separate (segregate) during gamete formation and end up in different gametes
* Testcross
  + Monohybrid cross: mating a plant with one unknown genotype with a plant with the recessive genotype to figure out the unknown’s genotype. (regular Punnett square)
  + Dihybrid cross: a cross that illustrates the inheritance of two characters (if the traits are linked then it’s a regular Punnett square, if they aren’t linked, then it’s a 4x4 Punnett square)
* Laws of Probability govern mendelian inheritance
  + The multiplication rule: the probability of two or more different events occurring is the product of the probabilities (chance of flipping heads twice, ½ \* ½ = ¼)
  + The addition rule: the probability that any one of two or more mutually exclusive events will occur is calculated by adding together the probabilities (chance of getting 2 sons or 2 daughters, ¼ + ¼ = ½)
  + Example of use: in a trihybrid cross (AsBbCc x AaBbCc) assuming independent assortment, what is the probability of getting an offspring with aaBBcc genotype?
    - Make a Punnett square for each of the traits (Aa x Aa, Bb x Bb, Cc x Cc)
    - aa is ¼, BB is ¼, cc is ¼, so the probability is ¼ \* ¼ \* ¼ = 1/64

beyond mendelian genetics

* sometimes an allele is not completely dominant or recessive
  + incomplete dominance
  + codominance
* when a gene has more than two alleles
* when a gene produces multiple phenotypes
* Spectrum of dominance
  + Complete dominance: the F1 generation’s phenotype is entirely the dominant
  + Incomplete dominance: the F1 generation’s phenotype is somewhere between both phenotypes
  + Codominance: two dominant alleles affect the phenotype in separate, distinguishable ways.
    - An example is is human blood group LM and LN alleles (encodes the M or N antigen)
* With multiple alleles
  + Blood type can have antigen genotypes of A, I, B where A and B are dominant, and I is recessive. If the genotype is AA or AI, the phenotype will be A; if the genotype is BB or BI, the phenotype will be B; if the genotype is AB, then the phenotype will be AB; and if the genotype is II, then the phenotype will be O.

Pleiotropy: genes have multiple phenotypic effects (a defective ion pump can impact many parts of the body)

Polygenic inheritance: many genes impact one phenotype (like height) (if there is a spectrum, then it’s probably polygenic)

Epistasis: a gene at one locus alters the phenotypic expression of a gene at another locus

Nature and nurture

* Environment can impact phenotype appearing to alter simple mendelian inheritance
* The norm of reaction is the phenotypic range of a particular genotype that is influenced by the environment
* Multifactorial characters: characteristics that are influenced by both genetic and environmental factors (examples include cancer and heart disease) (Mendel’s fundamental laws still apply)
  + Multifactorial disease: diseases that impacted by both genetics and the environment (like cancer and heart disease)

Inheritance patters of particular traits can be traced and described using pedigrees

Recessively inherited disorders (only show up with homozygous recessive)

* Carriers: people who carry one recessive allele but are phenotypically normal

Dominant disorders

* Dwarfism and achondroplasia are not lethal so they can be dominant and still exist
* Huntington’s disease, is lethal but doesn’t kill until late in life (after reproduction)

Chromosomal theory

* Mendelian inheritance has its physical basis in the behavior of chromosomes
  + Genes are located on chromosomes
  + Behavior of chromosomes during meiosis accounts for Mendel’s laws
* Morgan’s experimental evidence
  + He bred red eyed flies with recessive white eyed flies (got a new generation of red eyes)
  + He then bred the F1 generation with themselves (got a 3:1 ratio of red:white)
  + But in the F2 generation all the white eyed flies were male

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X inactivation in female mammals

* Gene dosage (number of copies of that gene present), for females there are 2 x chromosomes
* One of the two x chromosomes are randomly disabled during embryonic development
  + The deactivated x chromosome is condensed into heterochromatin (this is specifically called a Barr body)

Linked genes

* Each chromosome has hundreds or thousands of genes
* Linked genes tend to be inherited together because they are near each other on the same chromosome
* Linked genes exhibit recombination frequencies less than 50% (recombination frequency can’t be greater than 50%)

Genetic maps

* An ordered list of the genetic loci along a particular chromosome
  + Based on recombination frequencies, DNA breakpoints, cytogenic staining (physical map), nucleotides (physical map)

Alteration of chromosome number or structure

* Nondisjunction
  + Pairs of homologous chromosomes do not separate (can occur in meiosis I and II)
  + Gametes contain two copies or no copies of a particular chromosome
  + Causes aneuploidy (offspring have abnormal number of one chromosome)
    - Like trisomy (three copies of a particular chromosome) and monosomy (one copy of a particular chromosome)
    - Klinefelter syndrome (an extra chromosome in a male, producing XXY individuals)
    - Turner syndrome (monosomy X, producing an X0 karyotype)
  + Polyploidy
    - More than two complete sets of chromosomes in an organism
    - Diploid, triploid, tetraploid
* Deletion: segments can be deleted
* Duplication: segments can be duplicated
* Inversion: segments can break off and flip around
* Translocation: segments can move to a different chromosome
  + Reciprocal translocation: segments from two different chromosomes swap locations

Some inheritance patters are exceptions to the standard chromosome theory

Normal exceptions to mendelian genetics

* Genes located in the nucleus
  + Genomic imprinting
    - Silencing of certain genes that are “stamped” with an imprint during gamete production
    - Imprints are created during gametogenesis (imprints prevent certain gene expression)
      * Imprinting method is consistent from generation to generation in species
    - Imprints erase each generation
* Genes outside of the nucleus
  + Organellar inheritance
    - Chloroplast & mitochondrial inheritance
      * Chloroplasts are randomly separated, so one side could get more of one chloroplast than another
      * Mitochondria is inherited from the maternal parent so any issues with the maternal parent’s mitochondria will be passed onto her offspring

Chemical basis of genes

* During the previous century, scientists believed that chromosomes were the source of heritable information used by cells
* Chromosomes are made of proteins, DNA, and a small amount of RNA
* Bacterial transformation
  + Mice were given a bacteria with a shell and they died, mice were given a shell-less strain of the bacteria and they lived, mice were given a heat-killed version of the shelled bacteria and survived, mice were given a mixture of the shell-less strain and heat-killed version of the shelled bacteria and the mice died but shelled version of the bacteria was found
  + Avery, McCarty and MacLeod build upon ^ and tested three different cases, one where protein was broken down, one where RNA was broken down, and one where DNA was broken down. Where the DNA was still present, the shells were present but when DNA was missing the shelled bacteria were not there
  + Alfred Hershey and Martha Chase convinced everyone of ^ when they performed an experiment where a phage (T2) had its DNA marked with radioactive chemicals and another one with its proteins marked with radioactive chemicals and learned that it injected the DNA not the protein
* Genetic Transformation
  + A change in genotype and phenotype due to the assimilation of external DNA by a cell
* Chargaff’s rule
  + DNA compositions vary from one species to the next
  + %G = %C, %A = %T
* X-ray crystallography
  + Maurice Wilkins and Rosalind Franklin used to study molecular structure
    - Discovered that DNA was antiparallel (the backbone faces opposite directions)
    - There was a sugar-phosphate backbone on the outside
    - Nitrogenous bases paired in DNA’s interior
  + With Franklin’s and Wilkin’s work, Watson & Crick figured out Chargaff’s rule
    - Figured out that G bonded to C and A bonded to T
    - Figured out that G triple bonded to C and A double bonded to T
* DNA Replication
  + Watson & Crick predicted semi-conservative replication
    - Predicted that when DNA was replicated, DNA would split and become templates for the synthesis of the daughter strands of DNA
    - Meselson and Stahl designed an experiment to test ^
      * They grew bacteria in a culture with nitrogen-15 and they transferred those bacteria to a medium with nitrogen-14 where they allowed one round of DNA replication and took a sample then allowed another round of replication and took a sample then centrifuged the samples
      * They predicted that the results would be the semiconservative model, where after one round of replication, each of the DNA molecules would consist of one parent strand (N-15) and one daughter strand (N-14) and all the DNA would be of equal density, then after another round of replication, there would be 2 similar DNA molecules and 2 DNA molecules made entirely of N-14
      * Or Conservative model where the parental DNA would act as a template but come back together creating 1 heavy (N-14) DNA and 1 light (N-13) DNA after the first replication
      * Or Dispersive model where DNA is replicated in several small chucks so after every replication, the DNA would become slightly lighter every time
      * They ended up observing that the Semiconservative model was correct
  + Replication beings at origins
    - Eukaryotic chromosomes have hundreds of replication origins
    - Two strands separate from each other exposing the template where DNA replication begins (replication bubble)
    - Helicase separates the two base pairs of a strand of DNA
    - Topoisomerase breaks DNA to release tension that gets built up as helicase separates DNA then fixes the DNA
    - Single-strand binding proteins prevent the parental strands from binding together again
    - Primase synthesizes the first portion for DNA synthesis making an RNA primer
  + Elongating a new DNA strand
    - DNA replication occurs at the replication fork
      * Catalyzed by DNA dependent DNA polymerases
      * They only add nucleotides to the 3’ end of a growing strand
  + Priming DNA synthesis
    - DNA polymerase can’t start DNA replication
      * They can only add nucleotides to the 3’ end (daughter strand grows in the 3’ direction)
    - The initial nucleotide strand synthesis has to begin with
      * RNA primer
      * Or existing DNA strand
  + Antiparallel elongation
    - One RNA primer is needed for the leading strand, because DNA depended DNA polymerase is traveling in the 3’ direction
    - Multiple RNA primers are needed for the lagging strand, because helicase opens DNA in the direction of 5’ so a RNA primer is needed for DNA dependent DNA polymerase to start and it travels until it reaches a RNA primer then it stops, a different DNA polymerase removes the primer and adds in DNA nucleotides, and DNA ligase binds the phosphate-sugar backbone together
  + DNA has many repair mechanisms (happens during G2 phase)
    - Nucleotide excision repair
      * DNA doesn’t fit correctly (a bump forms), so nuclease removes a section of DNA and DNA polymerase replaces the nucleotides and DNA ligase binds the phosphate-sugar backbone
  + End replication problem of linear chromosomes
    - At the end of chromosomes, on the lagging strand, the RNA primer is removed but there is nothing to the right for DNA polymerase to connect to in order to fill in the gap making each successive cell division lose more DNA
    - To deal with this issue, the end of DNA molecules have nucleotide sequences called telomeres (prevents erosion of genes at the end)
    - Telomerase lengthens the telomeres in germ cells
      * It is an RNA dependent DNA polymerase (uses RNA to make DNA through the use of “reverse transcriptase”)

Transcription: RNA synthesis

Translation: protein synthesis

Gene Expression

* DNA directs protein synthesis through transcription and translation
* Garrod
  + Genes dictate phenotypes through enzymes
* Beadle and Tatum
  + One gene leads to one enzyme
  + Designed a test where they grew some wild-type cells on a bare minimum medium and mutated the cells and found that the mutant cells could not grow and divide in the same medium
  + Through this experiment they separated the mutants into 3 classes of mutations
    - Class I: all the mutations are in gene A that coded for enzyme A
    - Class II: all the mutations are in gene B that coded for enzyme B
    - Class III: all the mutations are in gene C that coded for enzyme C
  + People recognized that some genetic diseases were not caused by enzymes and changed it to one gene leads to one protein
  + People then learned that proteins are made of polypeptides and changed it to one gene leads to one polypeptide
    - mRNA encodes polypeptides
  + Genes may code RNAs that don’t code protein (like rRNA, tRNA, miRNA, lncRNA)

Basic principles of transcription and translation

* Transcription
  + Synthesis of RNA under the direction of DNA
  + Produces mRNA that encode proteins (can also produce RNAs that don’t encode protein)
* Translation
  + Synthesis of a polypeptide, which occurs under the direction of mRNA
  + Mediated by ribosomes
* In prokaryotes
  + Transcription and translation are coupled together, translation begins the same time transcription occurs
* In eukaryotes
  + The two processes are separated by a nuclear envelope
  + mRNA is modified before it becomes true mRNA

The genetic code

* Genetic information is encoded on codons (sequences of 3 nucleotides)
  + Codons come from the mRNA sequence which are formed based on a DNA template (like a long segment of RNA primer)
* mRNA codons
  + They encode amino acids and the translation stop signal (there is a lot of redundancy)
  + All coding sequences start with AUG which codes for methionine and is the start signal

Molecular components of transcription

* RNA synthesis
  + Catalyzed by DNA dependent RNA polymerase
    - It opens DNA strands, and joins RNA nucleotides, it also doesn’t need a primer.
  + It follows DNA base pairing rules except that U replaces T
* Stages of transcription are
  + Initiation (all the steps needed to bring RNA polymerase to the start site)
    - RNA polymerase is recruited by promoters (cis- sequences)
      * The promoter is the DNA sequence that the RNA polymerase binds to (contains the start point)
      * Signal initiation
      * One promoter is called the TATA box
    - Enhancers (silencers)
      * DNA sequences that are further upstream that regulate expression (both up and down)
      * They are also cis- sequences
      * They recruit transcription factors
    - Transcription factors (trans-)
      * Bind to enhancers & promoters
      * They bind to create an environment that recruits or inhibits RNA polymerase’s ability to bind to the site
      * Can also bind to other sequences that are associated to the gene and can help recruit RNA polymerase to the site
  + Elongation (RNA polymerase opens DNA and creates a transcription bubble and starts synthesis on one of the templates (it’s start defines the start of a gene))
    - Nucleotides are added to the 3’ end of the growing RNA molecule
      * Doesn’t need a primer or helicase to separate the two strands
      * Instead of T it uses U (A-T and G-C)
    - A gene can be transcribed simultaneously by several RNA polymerases
  + Termination (The stop signal (defines the end of a gene))
    - In bacteria
      * The polymerase stops transcription at the end of the terminator
      * mRNA is translated without further modification
    - In eukaryotes
      * RNA polymerase II transcribes the polyadenylation signal sequence (signals for a separate protein to add a poly-a tail which is just a lot of adenine nucleotides)
        + The poly-a tail increases the chance of the mRNA to be synthesized
      * Transcript is only released after 10-35 nucleotides after the polyadenylation sequence
* Eukaryotic transcription unit: mRNA processing
  + The 3’ end gets a poly-a tail
  + The 5’ end receives a modified nucleotide cap (modified guanine nucleotide)
  + Split Genes and RNA splicing
    - Introns: sections of pre-mRNA that are removed
    - Exons: the remaining sections that are joined together to from mRNA
    - Spliceosomes help remove introns
      * snRNPs are made of small nuclear RNA (snRNA) and proteins
      * Spliceosomes are made of snRNPs and other proteins
    - Ribozymes
      * Catalytic RNA molecules function as enzymes and can splice RNA

Translation

* Components of translation
  + Messenger RNA (mRNA)
    - The message that is to be translated
  + Transfer RNA (tRNA)
    - Deliver amino acids to ribosomes
      * each amino acid has its own tRNA
      * each has an anticodon on the other end that determines the amino acid it carries
    - it is an 80 nucleotide strand of RNA that hydrogen bonds with itself
    - Aminoacyl-tRNA synthetase
      * Senses the anticodon on a tRNA and binds the correct amino acid to it
  + Ribosomal RNA (rRNA)
    - Facilitate the specific coupling of tRNA anticodons with mRNA codons during protein synthesis
    - It is made of a large subunit and a small subunit
    - Subunits are made of proteins and RNA molecules
    - It had three binding sites
      * P site
      * A site
      * E site
    - The translation doesn’t begin at the start (begins with AUG)
* Building a polypeptide
  + Initiation (requires initiation factors)
    - The anticodon of a tRNA binds with the AUG of the mRNA at the P site
  + Elongation (requires elongation factors)
    - A tRNA with the correct anticodon enters at the A site
    - The amino acid is transferred to the tRNA in the A site
    - The mRNA shifts over and the tRNAs move over one site
    - The tRNA at the E site (now without an amino acid) then leaves
  + Termination (requires termination factors)
    - Ribosome reaches a stop codon in the mRNA (the stop codon is now in the A site)
    - A Release factor binds to the A site and causes the polypeptide to be released by splitting the two subunits of the rRNA
* Polyribosomes
  + A number of ribosomes simultaneously translate a single mRNA molecule
    - This forms a polyribosome (polysome)

After the polypeptide is freed, it can undergo many modifications after translation (in most cases the first polypeptide which was the start signal is removed)

Mutations

* Changes in the genetic material of a cell
* Impacts protein structure and function
* Types of mutations
  + Point mutation: changes in just one base pair of a gene
    - Missense: the change changes one amino acid with another
    - Nonsense: the change changes one amino acid into a stop codon
    - Silent mutation: the change causes no change because the change leads to the same amino acid
  + Insertion and deletions: additions or losses of nucleotide pairs in a gene
    - Frame shift mutation: the new, or missing, nucleotide causes the codons to be read wrong and have the wrong amino acids to be added
    - Insertion/deletion: the reading frame stays the same, but a codon is added/removed
* Mutagens
  + Spontaneous mutations: can occur during DNA replication, recombination, or repair
  + Mutagens: physical or chemical agents that can cause mutations

Regulation of bacterial gene expression

* The product of the protein synthesis inhibits the gene expression and enzyme activity
* Operons
  + In an operon like the trp operon
    - Genes are clustered together based on function
    - The promoter and all the related genes (cistrons)
    - When transcribed, the single mRNA codes for multiple genes
    - The operator (part of the promoter), is controlled by a regulatory gene upstream
      * The separate gene creates a mRNA that codes for a repressor protein that needs to be activated before it binds to the operator
  + In an operon like the lac operon
    - Just like the trp operon except that the repressor is always active except when allolactose (a modified version of lactose) is present and inactivates the repressor
    - Prokaryotes generally prefer glucose, but when glucose levels are low, cAMP is released and binds to a CAP protein is activated and recruits more RNA polymerase
      * When glucose and lactose is present, CAP is inactive and transcription of the lac operon is slow

Eukaryotic gene expression

* Chromatin (DNA has control over if it’s tightly wound up or not)
  + Heterochromatin
    - Constitutive
      * Wound tightly, doesn’t have very many genes that are expressed
    - Facultative
      * Open?
  + Euchromatin
    - Loosely packed, open DNA that can be read
* Histone modifications and the histone code (understand that different modifications can promote or inhibit gene expression)
  + Acetylation
    - Promotes gene expression
  + Methylation
    - Generally, a repressor but is complex
  + Phosphorylation
    - Can
  + DNA methylation
    - Usually has an inhibiting function
* Epigenetic inheritance
  + The inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence (something else that impacts the packing of DNA happens to block the expression of the gene)
    - DNA methylation associated with imprinting
    - Histone modifications
* Transcriptional regulation
  + Control elements stimulate binding of transcriptions factors (general vs. specific)
    - Promoters (general)
      * TATA box
      * CCAAT box
    - Enhancers, repressors (silencers)
      * May act at a distance
      * May act in a tissue specific manner (specific)
      * Different cell types have different activators available that control what genes are expressed (genes require multiple different activators to express)
* Coordinately controlled genes in eukaryotes
  + Co-expressed eukaryotic genes are not organized in operons (with a few minor exceptions)
  + These genes can be scattered over different chromosomes, but each has the same combination of control elements
  + Copies of the activators recognize specific control elements and promote simultaneous transcription of genes
* Post-transcriptional processing
  + Transcription alone does not account for gene expression
  + Regulatory mechanisms can operate at various stages after transcription
  + Such mechanisms allow a cell to fine-tune gene expression rapidly in response to environmental changes
  + Mechanisms of post-transcriptional regulation
    - The cap increases the chance the mRNA translation starts
    - The poly-a-tail makes the mRNA stable (prevents it from degrading so quickly)
    - Splicing (removing of introns and splicing of exons)
      * Differential splicing (a gene is spliced differently at different places)
* Noncoding RNAs play multiple roles in controlling gene expression
  + Only a small fraction of DNA codes for proteins and a very small fraction of the non-protein-coding DNA consists of genes for RNA such as rRNA and tRNA
  + A significant amount of the genome may be transcribed into noncoding RNAs (ncRNAs)
  + Noncoding RNAs regulate gene expression at two points: mRNA translation and chromatin configuration
* Effects on mRNAs by microRNAs (miRNA) and small interfacing RNAs (siRNA) (are the same in this class)
  + They base pair with mRNAs and begin to either degrade the mRNAs or physically block translation
  + microRNA is produced by the cell and can bind with lots of different mRNAs
  + siRNA usually come from viruses or someone editing genes
  + at least half of all human genes may be regulated by them
  + siRNAs can block gene expression (this is called RNA interference RNAi)
  + RNAi is used in labs to study the gene function
* Chromatin remodeling by ncRNA
  + Some ncRNA act to bring about remodeling of chromatin structure
  + In some yeast species, siRNA re-from heterochromatin at centromeres after chromosome replication
  + Small ncRNAs called piwi-associated RNAs (piRNAs) induce heterochromatin, blocking the expression of parasitic DNA elements in the genome, known as transposons
  + RNA-based regulation of chromatin structure is likely to play an important role in gene regulation
* Proteasome (breaks proteins into amino acids)

Change in gene definition over time

* Inheritable unit
* Chromosomes encoding enzymes (DNA not protein)
* One gene-one enzyme
* One gene- one polypeptide
* One gene-one transcription unit (gene-splice variants, start variants)

Penetrance: Proportion of individuals carrying a particular variant (allele) of a gene that also express an associated trait (the phenotype) [a lot of genes are not completely penetrant]

Expressivity: Proportion of individual carriers of a genotype for a trait who show the trait to a specifiable extent (differences in severity)

Coordinated gene expression

* Cell differentiation is the process by which cells become specialized in structure and function (after many cycles of cell division, cells in an area become more specialized)
* The physical process that give an organism its shape constitute morphogenesis
* Differential gene expression results from genes being regulated differently in each cell type
* Materials in the egg set up gene regulation that is carried out as cells divide

Cytodeterminants

* Cells with different concentrations of different molecules may decide what that cell becomes (like a green molecule that drives the cells to secrete a signal that causes other cells to express genes that are not expressed in the originating cell)
* An egg’s cytoplasm contains RNA, proteins, and other substances that are distributed unevenly in the unfertilized egg
* Cytoplasmic determinants are material substances in the egg that influence early development
* As the zygote divides by mitosis, cells contain different cytoplasmic determinant, which lead to different gene expression

Induction: environment causes transcriptional changes in nearby target cells

Cell identity

* A protein is highly concentrated (like Bicoid where higher concentration leads to one side being the head and where Bicoid has a lower concentration leads to the other side being the butt)
  + When Bicoid was removed completely, a head didn’t develop
  + When Bicoid was placed in the middle, a head developed in the middle

Gene expression can be coordinated using a master regulatory gene (a single regulatory gene when turned on, turns itself on and other genes that would lead to its cell type)

How cancer is made

* Proto-oncogene can be moved to a new area that happens to be next to a promoter which then causes the gene to be expressed a lot
* Proto-oncogene can be duplicated multiple times which causes the gene to be expressed a lot
* Proto-oncogene can be mutated in a way that keeps it on/not degrade (keeps on or prevents it from breaking off) or the control element of the gene is mutated, and the protein is expressed a lot

Check <https://wrightstate.hosted.panopto.com/Panopto/Pages/Viewer.aspx?id=2b49b8b9-c868-47c3-a219-ab1700e4ff66> for when the test is