BIOCHEMISTRY

covalent	"legit" bonds	H:1, O:2, N:3, C:4
ionic	+/- attract	nonpolar: carbon/hydrogen ONLY, symmetrical, diatomic
hydrogen	H + FON	
hydrophobic	nonpolar in polar	acid: gives up H^+ in condens. rxn
vDW	everything else	base: gives up OH^- in cond→lysis rxn

functional groups: quizlet

- condensation: formation of polymers (requires energy)
- hydrolysis: releases energy

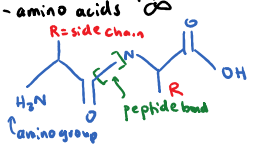
Macromolecules

① Lipids
- hydrophobic/water insoluble
- triglyceride = glycerol + fatty acid
- phospholipid = phosphate + fatty acid
- unsaturated: double bonds (plants)
- saturated: no double bonds
- lipid bilayer (cell wall!)

② Carbohydrates
$C_m H_{2n} O_n$
- look like a "ring" formed by glycosidic linkages in condensation rxns
- covalently bond to proteins and lipids on cell surface

③ Nucleic Acids
Phosphate group 5 carbon sugar + base
- add to carbon 3' → condensation reaction = phosphodiester bond

④ Proteins
- amino acids — peptide bonds, condensation rxns + carboxyl



- zwitterionic: both acid and base
1. sequence of amino acids
2. α-helix, β-sheet
3. Folding ← "denaturing"
4. Other proteins

Reactions

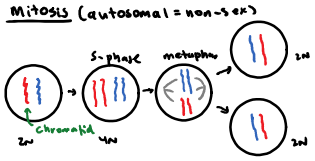
exergonic: lets off energy
endergonic: requires energy
free energy: energy that can do work
- controlled by catalysts and inhibitors
enzyme: protein catalyst that lowers activation energy
- inhibitors: allosteric, competitive
  - noncomp. (other site)
  - uncomp. (enzyme-substrate complex)

The Cell

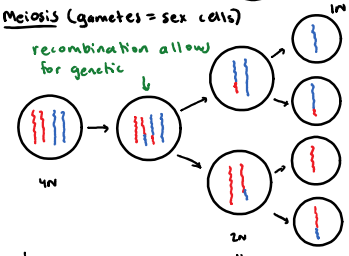
① Cell membrane: lipid bilayer, endocytosis/exocytosis
② Cytoskeleton: keeps cellular structure, + ECM
③ Nucleus: contains genetic information, has double membrane in eukaryote
④ Mitochondrion: energy conversion, endosymbiont theory
⑤ Endomembrane system:
ribosomes (free or attached) + Golgi Body + Lysosomal ER (stacked tubules, protein synthesis)

GENETICS

Mitosis (autosomal = non-sex)



Meiosis (gametes = sex cells)



Crosses

M1 M2

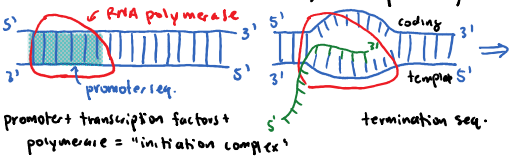
Monohybrid cross — two parents, one trait
Self cross — cross something with itself
Dihybrid — independently assorted, unlinked
Test cross — cross w/ double recessive

$\frac{\text{recombinant}}{\text{total}} \times 100 = \text{cM}$ (distance apart of genes)

MOLECULAR BIOLOGY

Transcription

DNA → RNA (75% transcribed); needs promoter, enhancer

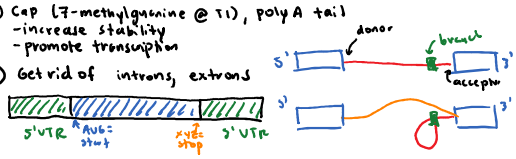


promoter + transcription factors + polymerase = "initiation complex"

RNA processing

① Cap (7-methylguanine @ 5'), poly A tail
- increase stability
- promote transcription

② Get rid of introns, extrons

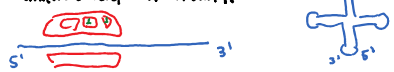


Translation

- begins at "start" codon (AUG)

① Initiation: ribosome binds to mRNA, moves to "start" codon and then begins translation

② Elongation: tRNA binds to codon, peptide bonds between amino acids, mRNA shifts



③ Termination: stop codon triggers separation of amino acid chain from codon

Gene Expression Regulation

- mutations at DNA level
  - silent: no amino acid change
  - missense: amino acid change
  - nonsense: amino acid → stop
  - frameshift: insertion or deletion
- transcription:
  - splicing, methylation, transcription factors, phosphorylation, acetylation
- protein: tag w/ ubiquitin for degradation

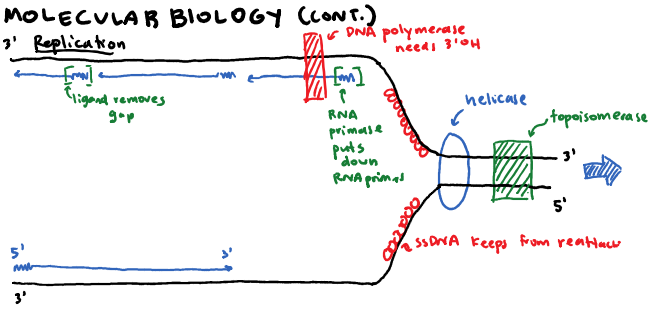
DNA Proofreading

- original DNA methylated
- mistakes create "bubbles"

① DNA polymerase: 3' to 5' exonuclease looks for mistakes and then "chews back"
② Mismatch repair: shortly after S-phase → swaps out single BP
③ Excision repair: any time, small mutations only

MOLECULAR BIOLOGY (CONT.)

Replication



① Helicase "unzips", topoisomerase uncoils (at ORI, recognized by ORI RC) AATTT
② Leading → continuous, a) RNA primase b) DNA polymerase
Lagging → multiple primers, polymerase goes in chunks, gap filled by ligase
③ Telomerase → 3' end, prevents degradation

unzip → prime → polymerase → ligate (if necessary) → telomerase

A = T C ≡ G antiparallel strands

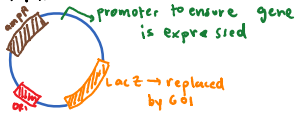
- adds to 3'OH
- can denature and renature

RECOMBINANT DNA

Cloning

- making many copies of one piece of DNA

① Use restriction enzymes to cut from larger strand of DNA. ("sticky" if an overhang.
② Ligate to vector (plasmid or phage)
③ Transform (add the vector to bacteria)



④ Selection (grows in ampicillin) / Screening (LacZ)

Restriction Mapping

- after you amplify, cut at asymmetric location w/ restriction enzymes
- look to make sure same length (gel electrophoresis)

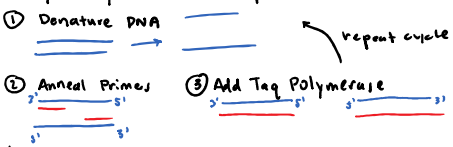
DNA Sequencing

- synthesize DNA w/ dNTPs and ddNTPs
  *ddNTP stops at N
- put DNA in gel electrophoresis and "count up" from bottom

Polymerase Chain Reaction

- way of exponential DNA amplification in lab

① Denature DNA
② Anneal Primes
③ Add Taq Polymerase



Libraries

Genomic: genes, promoters, enhancers
① Open cells, extract DNA
② Cut with restric, insert into vector
③ Transform → bacteria
④ Screen with colony hybridization

cDNA: made from mRNA reverse transcriptase, used to make coding seq.
① Open cells, extract RNA
② Reverse transcribe with polyaT prime
③ cDNA → vectors, transform
④ Screen to find DNA of interest (colony hybridization)

Expression Library: mRNA → protein coding seq.
① Open cells, extract RNA
② Synthesize double stranded DNA
③ Insert into vector
④ Transform
⑤ Screen with labelled antibody to find bac w/ GOI

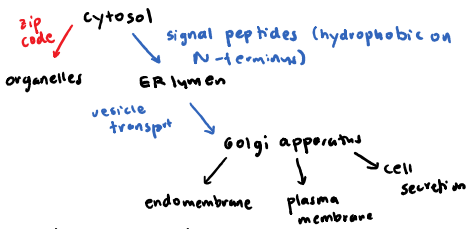
CELL BIOLOGY

Protein Folding

chaperones help:
- * fold proteins
- * fix misfolded proteins
- * prevent proteins from aggregating together

- peptide bonds are planar

Protein Localization



- protein is folded in ER, sugars attached
- Nuclear Localization Sequence → nucleus

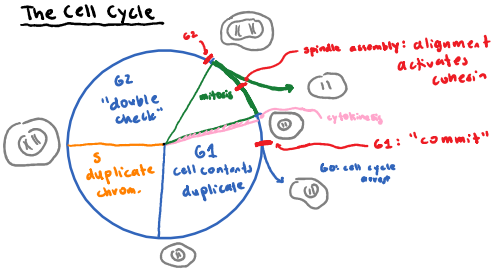
Cell-Cell Signaling

autocrine: signal affects own cell
juxtacrine: signal affects adjacent cells
paracrine: affects nearby cells (not touching)
endocrine:
- kinase phosphorylation → activation of enzyme
- membrane receptors
  - * ion channels: allow ions to enter or leave
  - * protein kinase receptors: ligand
    - ligand binds
    - recruits G-protein

(GTP = active, GDP = inactive)

CANCER

The Cell Cycle



G1 factors: nutrients, cell size, growth factors
spindle assembly: correct tension → cohesin
G2: correctly duplicated chromosomes
- regulated by cyclin, CDK
  - * cyclin regulated by TF and proteasome (multi-ubiquitin chain)
- use yeast for observation because we can see (morphology) stage of cell cycle
  - * permissive, nonpermissive temp (denature)
- apoptosis: programmed cell death

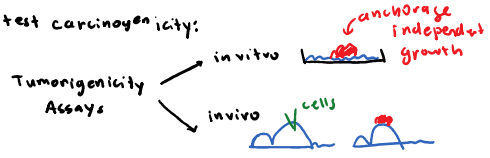
Tumor Progression

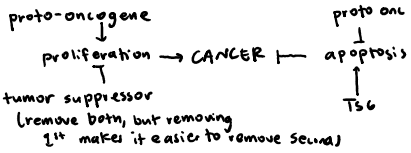
① Normal cells
② Hyperplasia: too many, but properly differentiated cells
③ Benign tumor (adenoma, polyp) — NOT CANCER
④ Malignant tumor — CANCER
  - * aneuploidy, karyotyping, structure
  - * invading surrounding tissue → musc. tissue → blood
⑤ Metastasic tumor = second tumor elsewhere

Carcinogens

- mutagen that causes cancer
- to test mutagenicity, you
  ① Incubate cell culture in liver extract
  ② Grow in His⁻ culture

- to test carcinogenicity:





DEVELOPMENTAL BIOLOGY

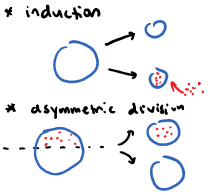
Cell Type Formation

- fate = specialized function of cell
- combinatorial code = the genes that control cell type

egg + sperm (n) → zygote (2n) totipotent → ESC pluripotent → committed unipotent → differentiated

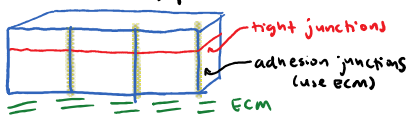
① Undecided / Uncommitted / Undetermined
② Decided (expression of regulatory genes)
③ Differentiated

controlled via:
- * induction — morphogen = determinants if autonomous
- * asymmetric division



Cell Functions and Junctions

Mesenchymal: singular cells, can move
Epithelial: cell sheets, polar

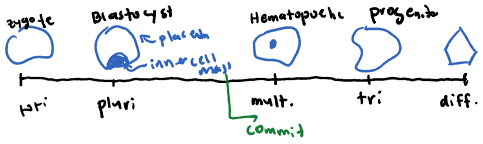


can change shape — EMT → MET / MET → EMT
- * epiboly = "stretch"
- * convergent extension/intercalation
- * radial intercalation
- * delamination

cytoskeleton: cell structure, migration

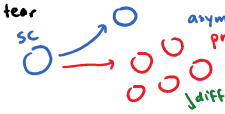
Organogenesis

① Blastula: ball of cells form after first cell division
② Gastrula: undifferentiated cells distinguished, starting tumor
③ Neurula: onset of differentiation

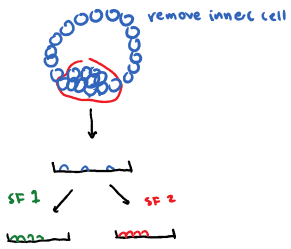


Stem Cells

- relatively undifferentiated and self-renewing
- adult stem cells
  - * perform maintenance for normal wear and tear

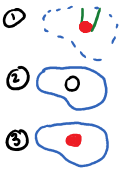


- embryonic stem cells



- iPSC's: take fully differentiated cell and turn it into stem cell by introducing 3-4 transcription factors

Somatic Cell Nuclear Transfer



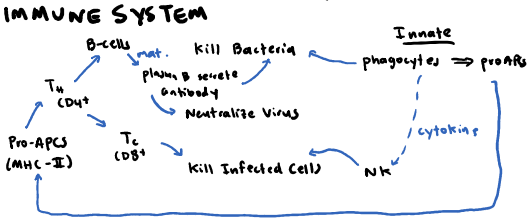
Regeneration

"reforming" of damaged organ, blastema = leading edge

Tissue Engineering

- cells
  - * must have correct potency
  - * ES or iPS, organ-derived SC, patient-derived iPSC
- culture
  - * signal factor
  - * 3D: cell-cell interaction, adhesion, signaling

IMMUNE SYSTEM



T helper = help other immune cells coordinate efforts
- * select B-cells w/ correct VDJ

T cytotoxic = kill cells presenting MHC-I

TCR interfaces with MHC I, produces antibody that prevent cell from surviving

Pro APC → Th → B cell → ~~Plasma~~ eventually killed
→ memory B-cells
↻ self-improve

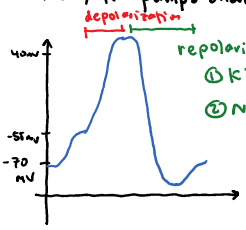
NEUROLOGY

Out ↑↑↑Na⁺ ↑Cl⁻ ↑Ca²⁺ +
In ↑↑K⁺ −

① Reach threshold potential
② Depolarize → action potential
③ Signal propagation down axon
④ Repolarize

NEUROBIOLOGY (CONT'D)

- depolarize because Na^+ move to the inside
- Na^+/K^+ pumps enable depolarization/repolarization



myelin sheath:
- prevents ion leakage
- gives ion longer range
- speeds up propagation (non myelinated nodes)

Synapses

① Electrical
* direct ion flow
* gap junctions
* fast
* uncommon b/c unregulated

② Chemical
* ligands, receptors, signalling
* slow → diffusion
* ability to be regulated

Excitatory:
* ion channels or ion flow
* RP closer to threshold

Inhibitory:
- Cl^- influx, K^+ efflux

Idea of summation:
- changes in membrane potential added over time and space

Regulated by:
① Neurotransmitters (synthesis, degradation, reuptake)
② Receptor on post-synaptic neuron
- LTP/LTD (Long Term Potentiation/Depression)
  - incoming signal the same, but neuron changes response
* changed by:
  - expression of receptor
  - affinity to neurotransmitter

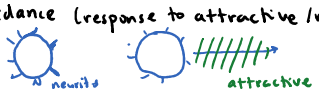
(these changes take a long time)

Circuits

input → sensory neuron → interneuron(s) → motor neuron → output

- genetic or experimental
- motifs = subunits of signaling
  * excitatory or inhibitory

Form either:
① Randomly (useful stay, useless die)
② Guidance (response to attractive/repulsive cues)



- long range: secreted protein gradient
- short range: physically touching, surface signals
  * tested via stripe assays

Growth cone = thing at end of axon
* actin, microtubules
  (G-actin → unpolymerized monomer, F-actin) filamentous, polymerized

Neurological Disorders

hyperactive	hypoactive
- epilepsy: interneurons that have lots of connections with overactive APs	- neurodegenerative = neurons dying, type depends on neurons dying

Optogenetics

- light-activated channel proteins
  (-) ions Cl^- specific → further polarize
  (+) ions Na^+ specific → depolarize
- turn on or off neurons

EVOLUTION

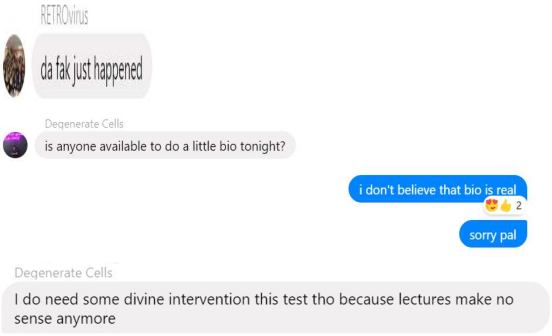
mutations → (natural selection) → → → → evolution

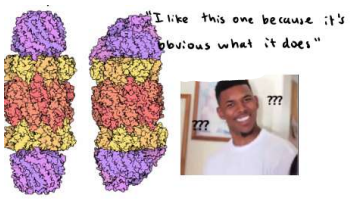
Cryptic Mutations

- genetic variations that are not controlled by a phenotype
- can be revealed by stress

homolog: gene that has similar sequence b/w species
paralog: duplicate genes
orthologs: same function

"heck bio"
- a compilation





Lecture 33
Wednesday, May 9, 2018 11:31 AM

did not attend lecture

Lecture 36
Wednesday, May 16, 2018 11:09 AM

nice one delia