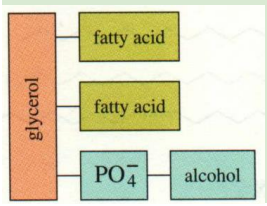
Module 4 Review

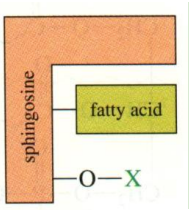
Membrane Structure

Phospholipids

- Glycero-
- G3P backbone w/ PO4 attached to C3 via pdeb
- Phosphatidic acid when replace OH w/ H
- Ether link @ C1 w/ choline makes plasmalogen



- Sphingo-
- 18C (if w/ FA = cer)
- Cer w/ phosphoethanolamine/ choline = sphingomyelin



Glycolipids

- Glycero: 1 or 2 galactose @ C3; predominant in plants (70-80% of lipids)
- Sphingo:
- Cer deriv that's abundant in neurons
- Cerebroside (cer + 1 sugar); globoside (cer+2); ganglioside (cer+3^+, req for neuron dev)

Sterols: steroid; can be esterified from FA to form cholesterol ester

Ether Lipids

- Glycerol w/ 32C @ both ends via ether bond
- Archaebacterial w/ survivability @ high pH/ temp

Asymmetry

- Outer monolayer: phosphatidylcholine and sphingomyelin
- Inner layer: phosphatidylserine and phosphatidylinositol deriv

Kinetics

- Low temp: gel phase, solid-ordered state (So) w/ lipids tightly packed and little motion
- High temp: liquid crystalline phase, liquid-disordered state (Ld) w/ more motion
    - Much cholesterol: liquid-ordered state (Lo); lipid rafts are usually in this

Protein Types

- Integral
    - Hydropathy (H) used to find which ones are Hpo (high) or Hpl (low) and if they're transmem; used for antigen targets
    - a-Helices used more bc struc flex, but B-Sheets make up more transmem bc less residues req
- Peripheral: ionic/ H interactions and mild detergent needed to dissoc (unlike integral, mem break req)
- Lipid-anchored
    - Reversible cov-linked to mem via anchor
    - Types:
        - Amide-linked myristoyl anchors: faces inside; prot (N-terminus) - Gly - lipid
        - Glycosylphosphatidylinositol anchor: faces outside; lipid - prot (C-terminus)
        - Thioester-linked (palmitoylation) & Thioether-linked prenyl anchors

Membrane Transmission

K+ Channel

- Facilitated diffusion w/ 1 Na coming per 10,000 K (high selectivity)
- Opens w/ low inner pH; H binds to C-terminus of transmem prot
- Homotetramer that is mostly Hpo (3 helices and 2 connecting loops)
- 4 K+ binding sites (K attaches to 8 Oxy inside cavity) w/ K @ S1/S3 and H2O @ S2/S4 to red repulsion, but each moves down a spot until it reaches end

Na/K Pump

- Active Transport: primary = ATP directly used; secondary = ATP indirectly used for symport/ antiport
- Na low, K high inside → 3 Na out and 2 K in via ATP hydrolysis through E-P intermed
- a-subunit (1100AA w/ half in mem, half in cyto)
    - N(ucleotide binding) domain: ATP bind in cyto & phospho P domain
    - A(ctuator) domain: prot phosphatase
    - P(hosphorylation) domain: phos of Asp376
    - T(ransport) domain: flexible helical domain where K binds
- b-subunit (300AA w/ one helix in mem, rest in ECM)
- y-subunit (50AA w/ half in mem and FXYD seq for reg)

Signal Transduction

Channel-linked Receptors

- Juxtacrine: gap jxn (connexins allow ionic flow) and mem-bound ligand (direct contacts w/ receptor)
- Paracrine: local signaling via diffusion
- Endocrine: hormone secretion via bloodstream
- High affinity (most recep full even if ligand conc low) or low (most recep full only if conc high)
- Kd (ligand conc when >50% recep full): low = high affinity, high = low affinity

Nuclear Hormone

- Cytosolic/ nuclear recep for reg of transc
- Lipidphilic endocrine sig that affects metab, repro dev, detox
- NR2B superfamily w/ two domains (DNA binding domain and highly-variable ligand binding domain)
- Dimerization (one dimer always RXR)
    - Homodimer: ligand binds to 2 same-type dimers to start fxn
    - Non-permissive heterodimer: ligand binds to one (one starts fxn, other stops)
    - Permissive heterodimer: ligand binds to either type to start fxn

GPCR

- 7TM integral prot; anchored by G prot (heterotrimeric w/ Ga holding GPCR, Gb binding to Gy, and Gy binding to lipid)
- Mechanism: Ligand → GPCR → conf change of G-prot & dissoc from GPCR → adenyl cyclase (AC), phospholipase, or ion channel activated → (Phospholipase C → IP3 or DAG) or (PKA → cAMP)
- G-prot on (GTP bound to Ga) and off (GDP bound to Ga); GAP incr GTPase activ and GEF helps release GDP
- Ga subunits: Gs (stim AC), Gi/o (inhibit AC), Gq/11 (activ phospholipase C), G12/12 (activ RhoGEF)
- IP3 for Ca release, DAG activ prot kinase C
- PKA uses neg feedback loop (as long as GTP is bound & arrestin not used)

Proteolysis (Regulated Receptor Activity)

- Transc factor reg that uses juxtacrine signaling

- Receptors: Notch 1-4; ligands: Jagged (JAG1/2) and Delta-like (DLL1/3/4)
- Mechanism: DLL activ → ubiq to Notch → proteolysis w/ irreversible S2 and S3 cleavage (S3 goes to nuc to reg transc)
- Sign on Notch from one cell downreg sig of other recep for nearby cells (reason we see neuron amongst epi cells)

Enzyme-Linked

- RTK - Recep Tyr Kinase
- Tyr Kinase-assoc Recep
- Recep-like Tyr Phosphatases
- Recep Ser/Thr Kinases
- Recep Guanylyl Cyclases

Other Signaling Pathways

- Signal Integration
- Cross-Talk