Review II: Cell Biology

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Outline
- Cell Cycle
- Signal Transduction

Cell Cycle
- Four phases of the cell cycle:
  - M: cell division; each cell gets 1 copy of the genome
  - G1: cell growth; preparation for DNA replication
  - S: DNA synthesis (replication)
  - G2: preparation for M phase
  - M phase animation:
- A fifth “phase”: G0 (quiescence)

Cell Cycle Phases
Chromatin Packaging

- Why does DNA in interphase "look" different from DNA in mitosis?
- Higher order of packaging
- Mitotic phase: DNA packaged into chromosomes
- Interphase: DNA present as chromatin
- "beads-on-a-string"
- beads = nucleosomes
- nucleosomes = DNA wrapped around histones

Mitotic chromosomes = transcriptionally inactive (heterochromatin)

Interphase chromatin = transcriptionally active (euchromatin)

Mitosis animations:
- www.cellsalive.com/mitosis.htm
- www.biology.arizona.edu/cell_bio/tutorials/cell_cycle/cells3.html

Cell Cycle Control

- Web animation (www.cellsalive.com/cell_cycle.htm)
- Checkpoints controlled by proteins
- Important group of checkpoint proteins are the cyclins
- Cyclin levels "cycle" during different phases
- Cyclins, by themselves, are inactive
- Associate with cyclin-dependent kinases (cdk)
- Cdk levels invariant throughout the cell cycle
- G1 cyclin — cyclin D (cdk4)
- S-phase cyclins — cyclins A and E (cdk2)
- G2 cyclins — cyclin B (cdc2 (cdk1))

Cyclins and cdks

- Cyclins
  - G1 cyclin (cyclin D)
  - S-phase cyclins (cyclins E and A)
  - Mitotic cyclins (cyclins B and A)

- Cdk
  - G1 Cdk (cdk4)
  - S-phase cdk (cdk2)
  - M-phase cdk (cdc2 (Cdk1))
**Cell Cycle Checkpoints**

- **G1**
  - Cyclin B-cdc2
  - Nuclear envelope breakdown; assembly of mitotic spindle; activation of APC
- **G2**
  - Cyclin A-cdk2
  - In molecular terms, passing G1 is the phosphorylation of the retinoblastoma protein, Rb. Unphosphorylated Rb binds the transcription factor, E2F; the phosphorylated form cannot bind E2F, thereby allowing E2F to modulate gene expression
- **M**
  - Cyclin A-cdk2
  - Dissociation of APC; exit from M

**Regulation via Phosphorylation**

- Phosphorylation and dephosphorylation regulate many key events
- Cell cycle control
- Signal transduction
- Transcription

**Signal Transduction**

- Ensures that a signal is converted from one form to another
- From the exterior of the cell to the interior
- Retain original signal content

**Steps in Signal Transduction**

- Signal is sent. e.g. hormone, non-steroid ligand (epinephrine)
- Recognition of the signal by the cell via a receptor
- Receptors can be present on the cell membrane or in the cytosol
- Internal signaling molecules transduce and amplify the signal
- Carried out via a signaling cascade, with multiple regulatory steps
- E.g. Glycogen breakdown in response to epinephrine
Cell Receptors

- **Ion-channel linked**: involved in rapid synaptic signaling between excitable cells; mediated by neurotransmitters
- **Enzyme-linked receptors**: when activated, either function directly as enzymes or are associated with enzymes.
- **G-protein coupled receptors (GPCR)**

GPCRs

- Largest family of cell-surface receptors
- Biological functions include smell, taste, vision, blood pressure neurotransmission, embryogenesis, cell growth, development
- Rhodopsin is the only GPCR with a known 3D structure
- Contains 7 membrane traversing α helices (7TM)
- N terminal – outside cell, C terminal – inside cell
- Ligand binding outside cell induces conformational change detected inside cell
- Mediating molecule is a G protein (hence the name GPCR)
- Heterotrimeric GTP-binding regulatory protein (α, β, γ)
- Activated G protein transmits signal by binding to other proteins (e.g. adenylate cyclase: converts ATP to cAMP)
Signal effects

Regulation by reversible phosphorylation and dephosphorylation

Signal reception

Signal mediation and amplification

Additional Reading

- Biochemistry, 5th ed., Berg, Tymoczko, Stryer
- Biochemistry, 3rd ed., Voet & Voet