

Review III: Cellular Processes

Judy Wieber

BBSI @ Pitt 2007

Department of Computational Biology
University of Pittsburgh School of Medicine

May 25, 2007

Outline

- Metabolism
- Cell cycle
- Transcription and RNA processing
- Translation: protein synthesis
- Signal transduction
- Immune response
- Disease states

Metabolism

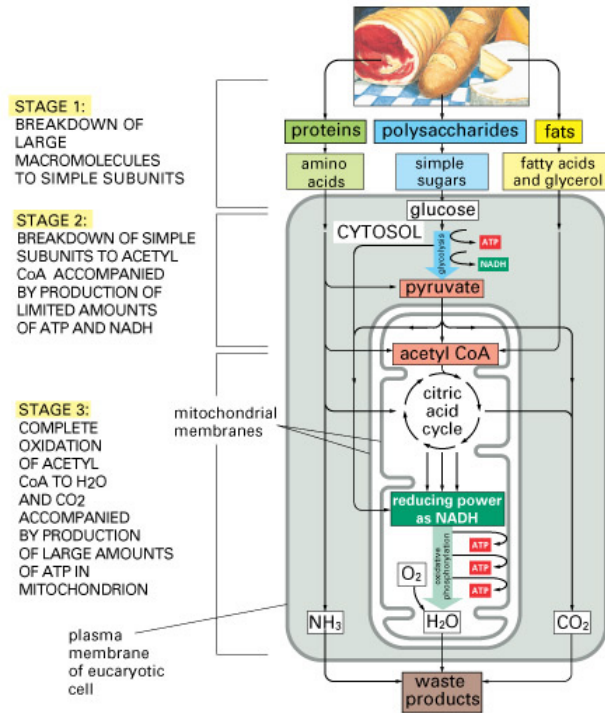
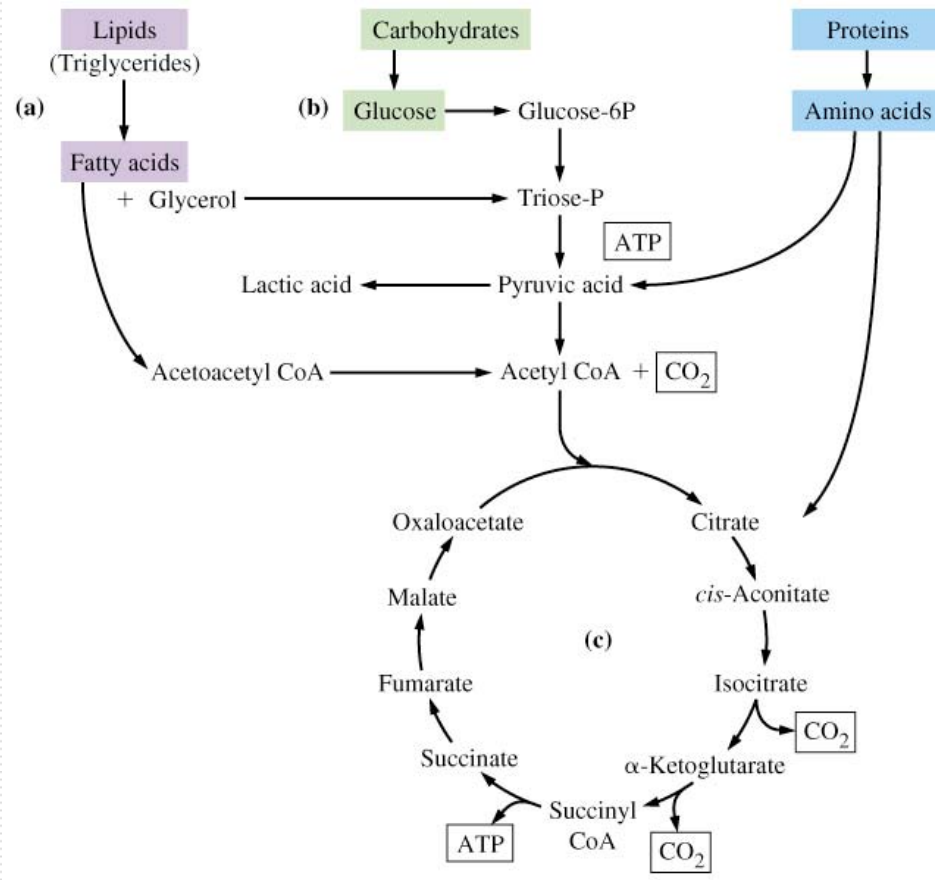


Figure 13-2 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Metabolism (continued)



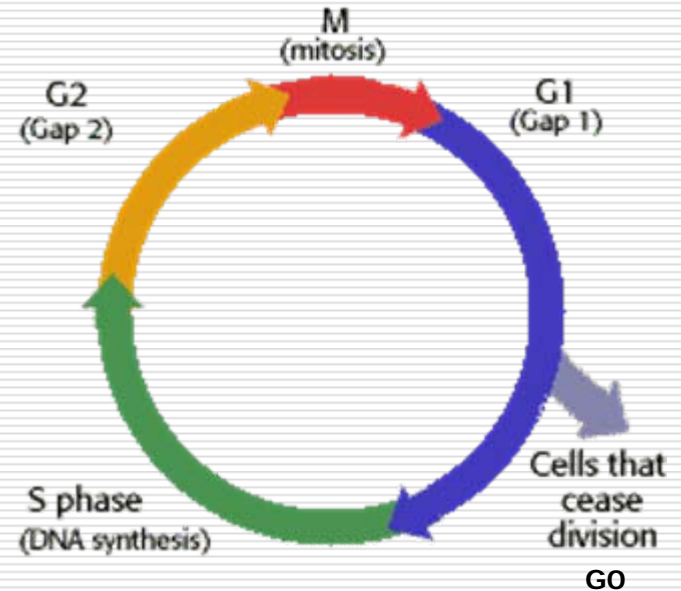
(ATP formation)

Regulation via Phosphorylation

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

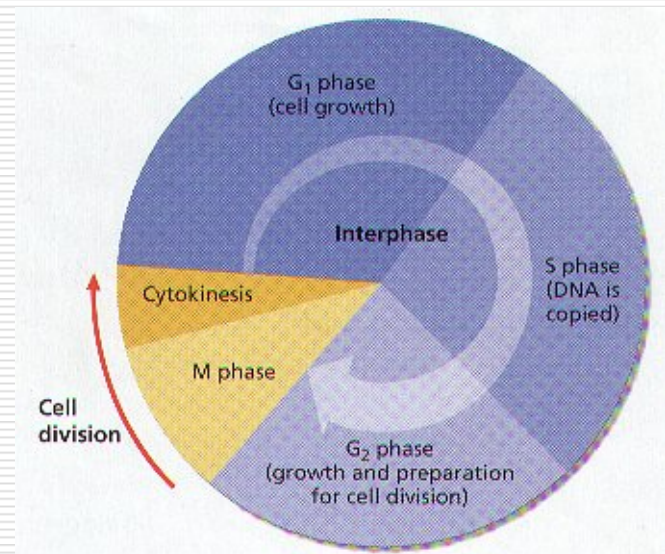
Cell Cycle

- ❑ Four phases of the cell cycle:
- ❑ Mitosis (M phase)
- ❑ Gap 1 (G1 phase)
- ❑ DNA Synthesis (S phase)
- ❑ Gap 2 (G2 phase)
- ❑ A fifth "phase": G0 (quiescence)



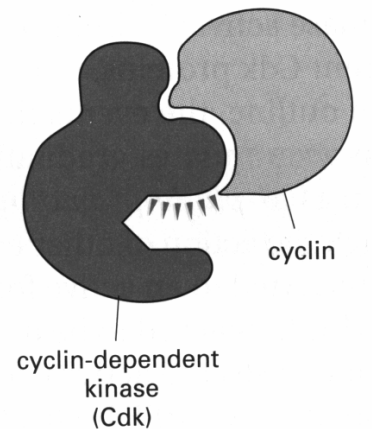
Cell Cycle Phases

- ❑ 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 animations: ([1](#)) ([2](#))



Cell Cycle Control

- ❑ Web animation ([link](#))
- ❑ 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)

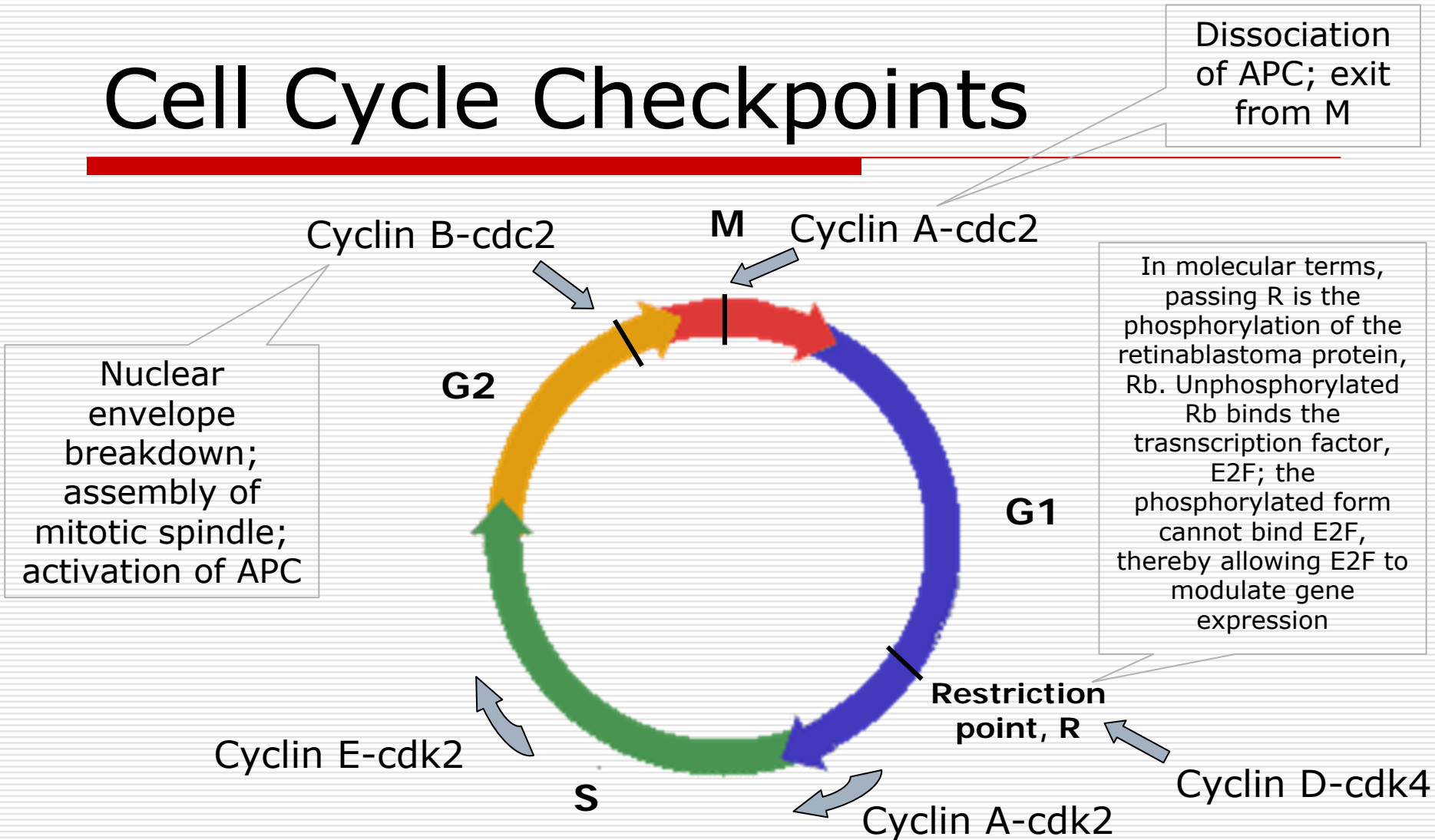
Cdks

G1 Cdk (cdk4)

S-phase cdk (cdk2)

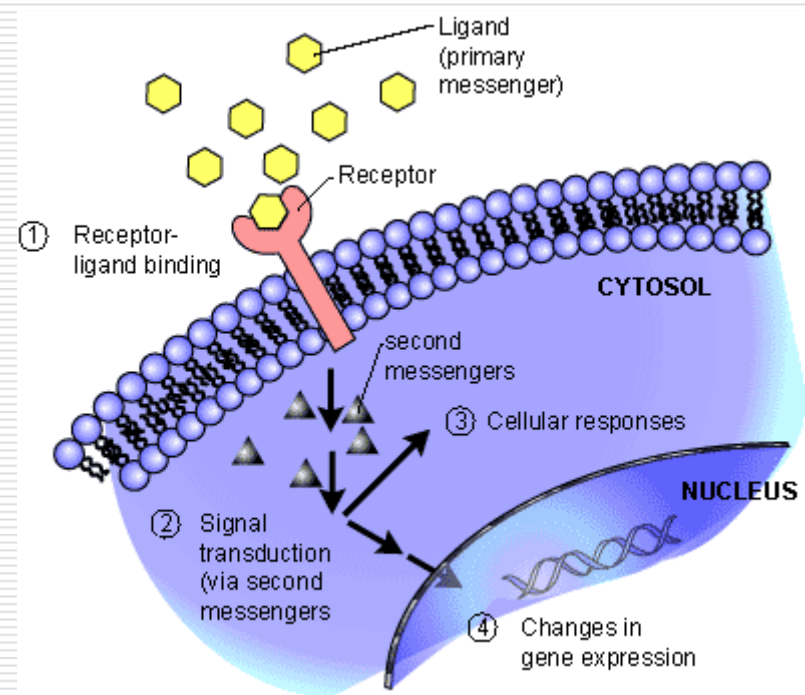
M-phase cdk (cdc2 (Cdk1))

Cell Cycle Checkpoints



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

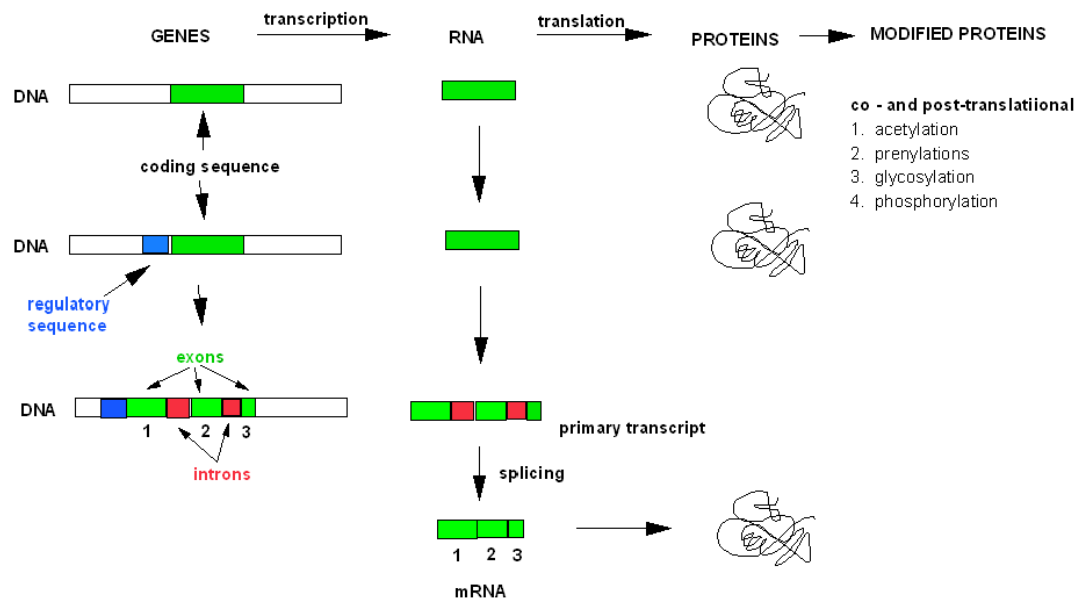


Steps in Signal Transduction

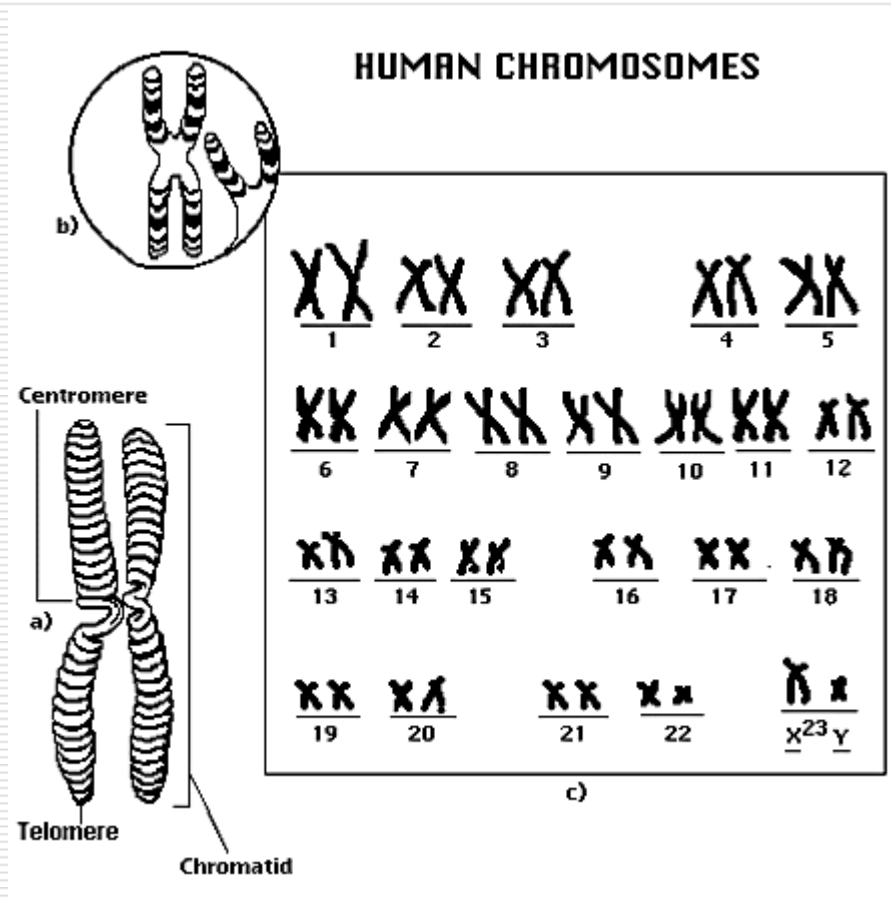
- ❑ Signal is sent. e.g. hormone, non-steroid ligand (epinephrine)
- ❑ Recognition of the signal by the cell via a *receptor*.
- ❑ Receptors can be present on the cell membrane or in the cytosol
- ❑ *Internal signaling molecules* transduce and amplify the signal
- ❑ Carried out via a *signaling cascade*,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

Genes, RNA, and Proteins

GENES, RNA, AND PROTEINS: FROM SIMPLICITY TO COMPLEXITY



Chromosomes

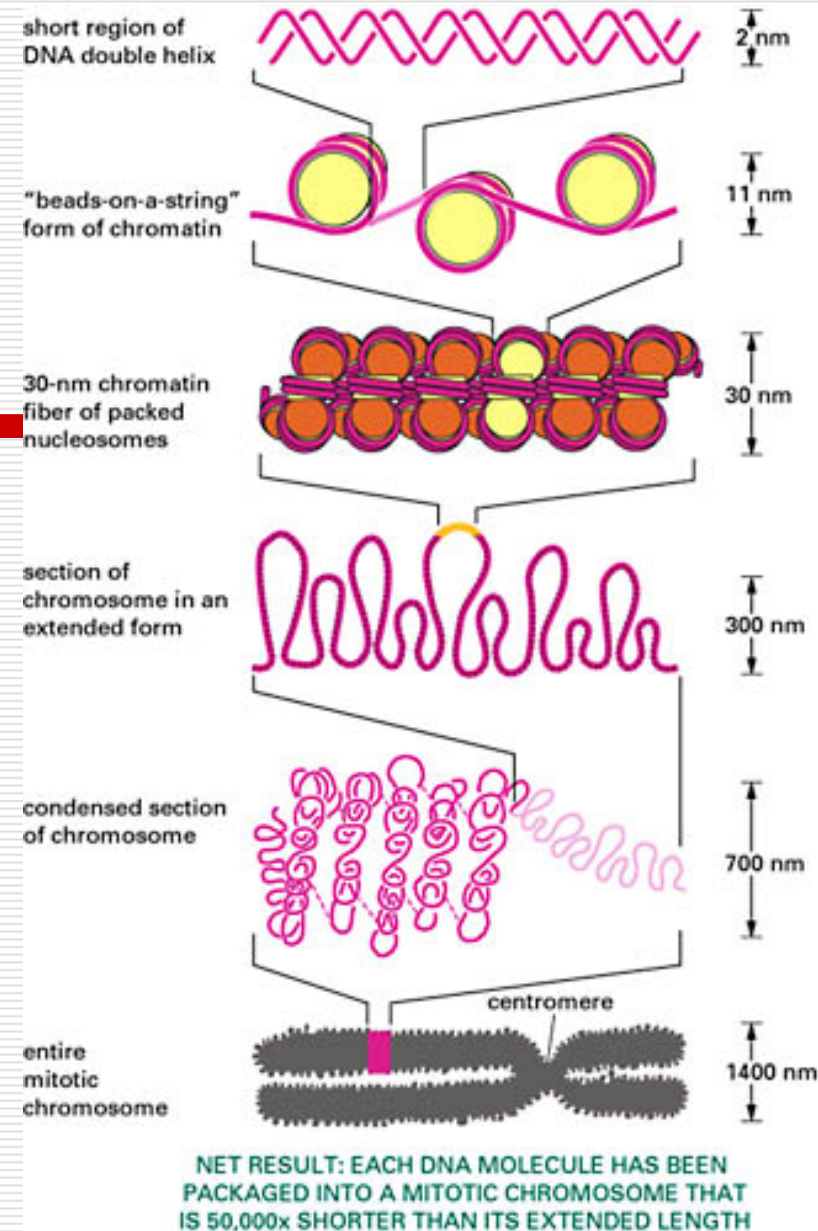


Mitosis

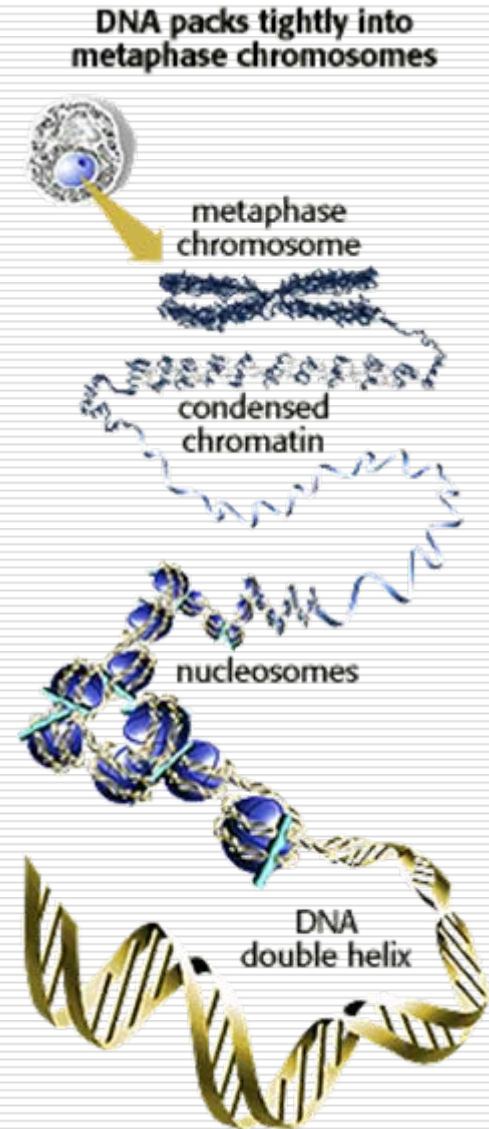
(Mitosis with music)

Chromatin Packaging

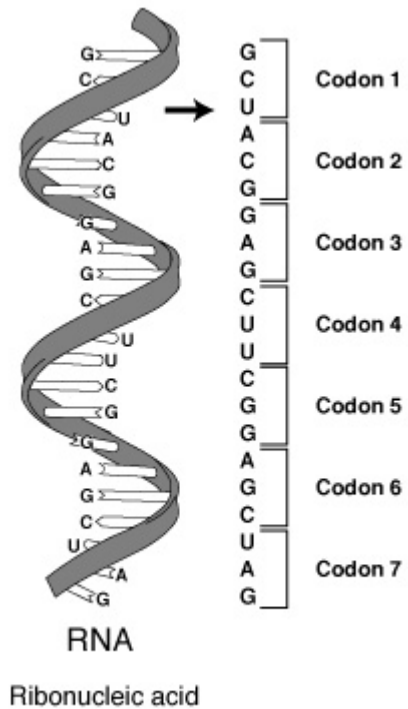
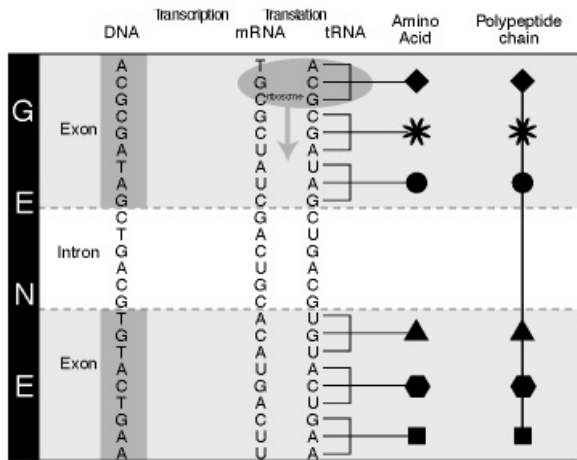
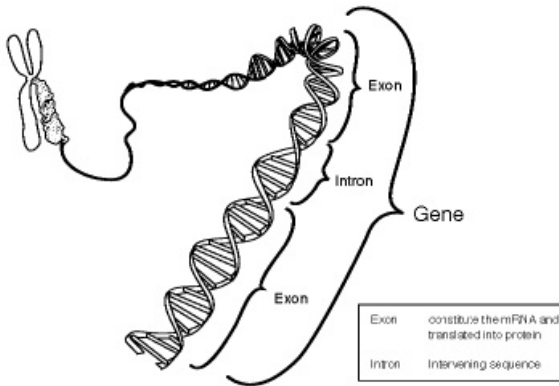
- ❑ Why does DNA in interphase “look” different from DNA in mitosis?
- ❑ Higher order of packaging
- ❑ Mitotic phase: DNA packaged into chromosomes
- ❑ Interphase: DNA present as chromatin
- ❑ “beads-on-a-string”
- ❑ beads = nucleosomes
- ❑ nucleosomes = DNA wrapped around histones



- ❑ Mitotic chromosomes = transcriptionally inactive (heterochromatin)
- ❑ Interphase chromatin = transcriptionally active (euchromatin)



Exons, Introns, Codons

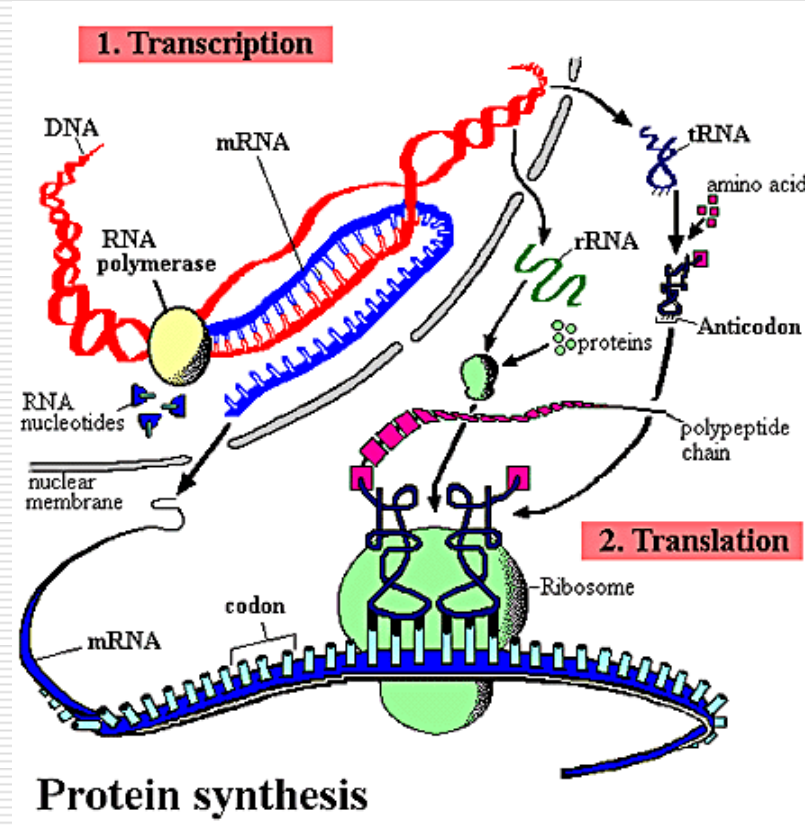


The Genetic Code

The Genetic Code

		Second base			
		U	C	A	G
First base	U	UUU } Phe UUC } UUA } Leu UUG }	UCU } Ser UCC } UCA } UCG }	UAU } Tyr UAC } UAA } Stop UAG } Stop	UGU } Cys UGC } UGA } Stop UGG } Trp
	C	CUU } Leu CUC } CUA } CUG }	CCU } Pro CCC } CCA } CCG }	CAU } His CAC } CAA } Gln CAG }	CGU } Arg CGC } CGA } CCG }
	A	AUU } Ile AUC } AUA } Met AUG }	ACU } Thr ACC } ACA } ACG }	AAU } Asn AAC } AAA } Lys AAG }	AGU } Ser AGC } AGA } Arg AGG }
	G	GUU } Val GUC } GUA } GUG }	GCU } Ala GCC } GCA } GCG }	GAU } Asp GAC } GAA } Glu GAG }	GGU } Gly GGC } GGA } GGG }

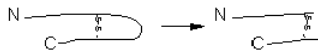
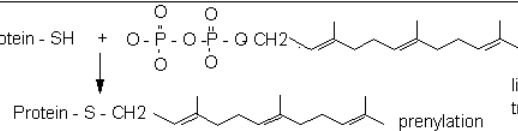
Transcription and Translation



([Translation](#))

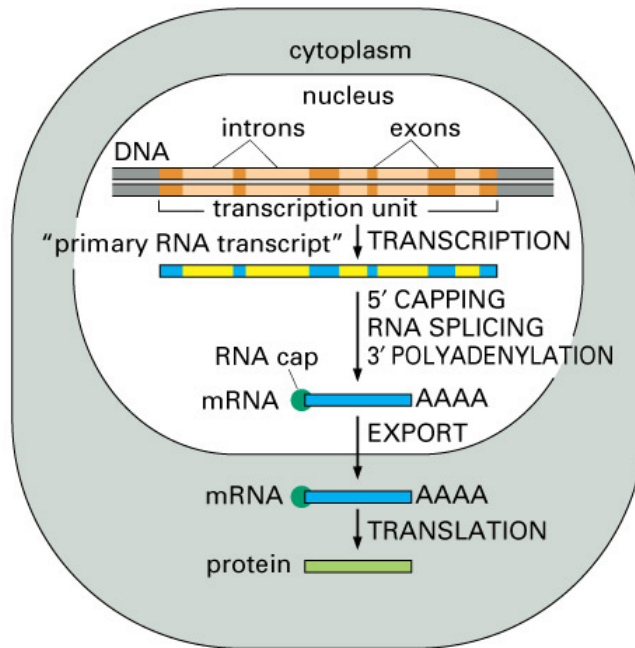
Post-translational Modification

POST-TRANSLATIONAL MODIFICATION OF PROTEINS: EXAMPLES

MODIFICATION	REACTION EXAMPLES	ENZYME	PURPOSE
1. proteolysis		proteases	"activation of enzymes; targeting of proteins
2. acetylation; acylation	$\text{H}_2\text{NR} + \text{CH}_3\overset{\text{O}}{\parallel}\text{C}-\text{SCoA} \longrightarrow \text{CH}_3\overset{\text{O}}{\parallel}\text{C}-\text{NHR}$	acetylase, acylase	chang charge; binding; protection
3. phosphorylation/ dephosphorylation	$\begin{array}{l} \text{Ser-OH} \xrightarrow{\text{ATP}} \text{Ser-OPO}_3 \\ \text{Thr-OH} \xrightarrow{\text{ATP}} \text{Thr-OPO}_3 \\ \text{Tyr-OH} \xrightarrow{\text{ATP}} \text{Tyr-OPO}_3 \end{array}$	kinases phosphatases	change charge, binding; regulation
4. lipid attachment	$\text{Protein-SH} + \text{O}-\overset{\text{O}}{\parallel}\text{P}-\text{O}-\overset{\text{O}}{\parallel}\text{P}-\text{O}-\text{CH}_2-\text{C}_{15}\text{H}_{31}$  prenylation or + 14:0, 16:0, or PI attachment to amino acid	lipid transferases	anchor proteins to membrane, regulation
5. glycosylation	$\begin{array}{l} \text{Asn-NH}_2 \\ \text{Ser-OH, Thr-OH} \end{array} \longrightarrow \begin{array}{l} \text{Asn-NH}_2\text{-sugar (N-linked)} \\ \text{Ser-OH-sugar (O-linked)} \\ \text{Thr-OH-sugar (O-linked)} \end{array}$	glycosyl transferases	recognition increased t1/2 targeting

Eukaryotes vs. Prokaryotes

(A) EUCARYOTES



(B) PROCARYOTES

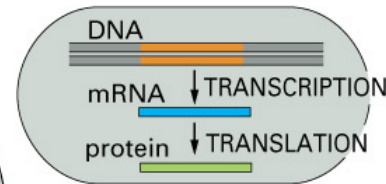


Figure 7-20 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Immune Response

(Cells of the immune system)

(The cellular immune response)

Disease States

- Diabetes
- Cancer
- AIDS

Diabetes

([Insulin and glucose regulation](#))

([Type II Diabetes video](#))

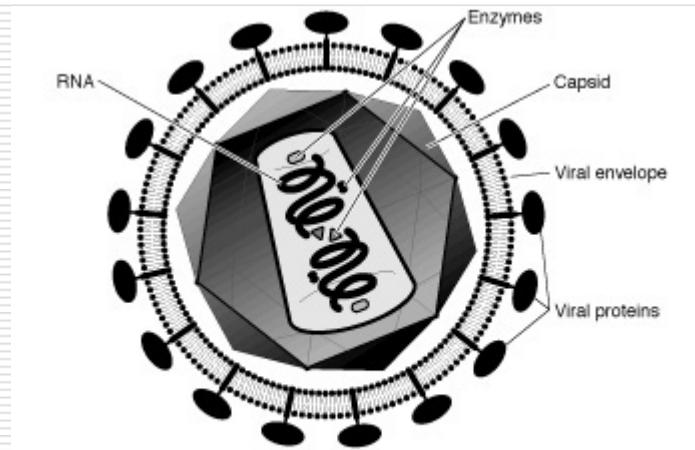
Cancer

(Oncogenes)

(p53's role)

(Nova - cancer programs)

AIDS



Structure of Human Immunodeficiency Virus (HIV)

([AIDS video - Kaiser](#))

([HIV lifecycle - Johns Hopkins](#))

Additional Reading

- ❑ Molecular Biology of the Cell, 3rd ed., Alberts *et al.*
- ❑ Biochemistry, 5th ed., Berg, Tymoczko, Stryer
- ❑ Biochemistry, 3rd ed., Voet & Voet