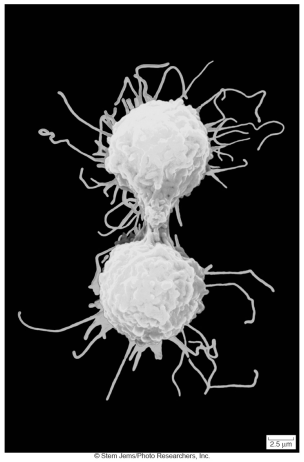
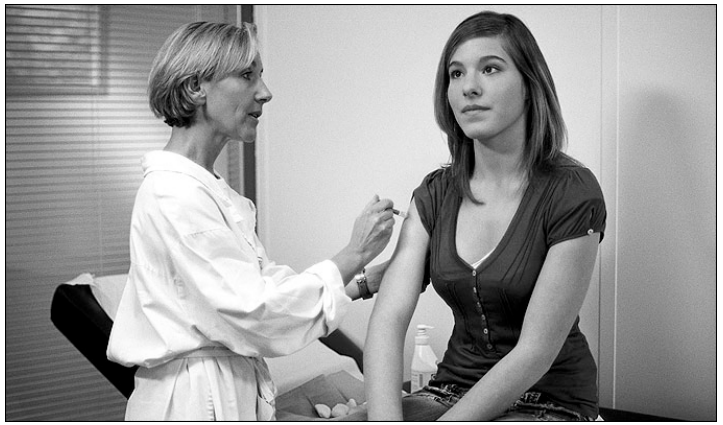
How Cells Divide

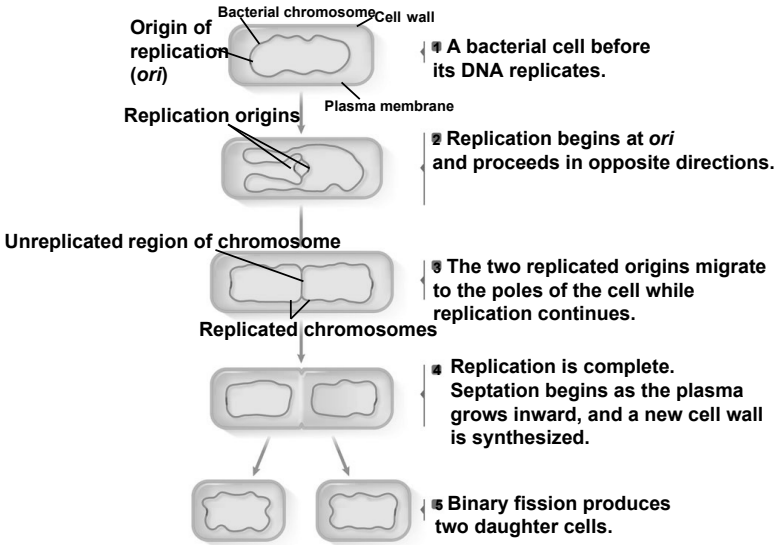
Chapter 10



Cancer and the Cell Cycle

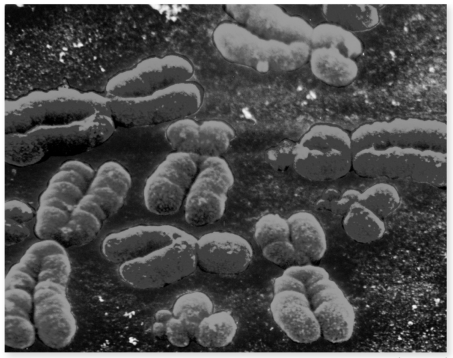


Bacterial Cell Division



Eukaryotic Chromosomes

- Every species has a different number of chromosomes
- Humans have 46 chromosomes in 23 nearly identical pairs
  - Additional/missing chromosomes usually fatal

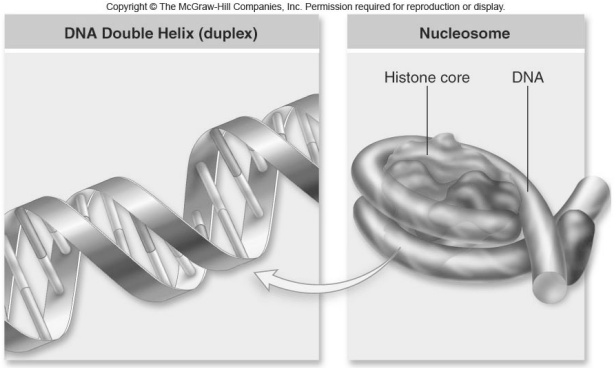


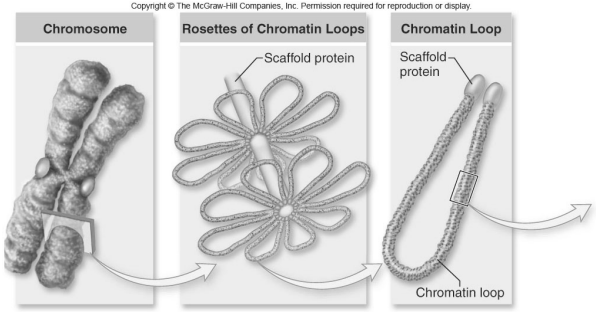
Chromosomes

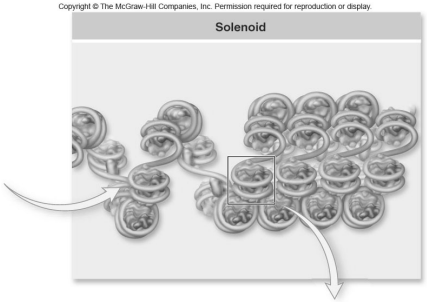
- Composed of **chromatin** – complex of DNA and protein
- DNA of a single chromosome is one long continuous double-stranded fiber
- Typical human chromosome 140 million nucleotides long
- In the nondividing nucleus
  - **Heterochromatin** – not expressed
  - **Euchromatin** – expressed

Structure

- **Nucleosome**
  - Complex of DNA (~200 bp) and 8 **histone** proteins
- Nucleosomes wrapped into higher order coils
  - Usual state of nondividing (interphase) chromatin
- During mitosis, chromatin coils arranged around scaffold of protein to achieve maximum compaction

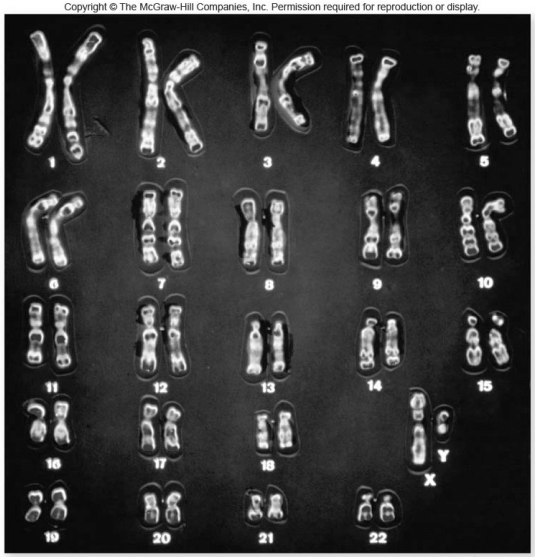






Karyotype

- Array of chromosomes from an individual organism
- Humans are **diploid** (***2n***)
  - 2 complete sets of chromosomes
  - 46 total chromosomes
- **Haploid** (***n***) – 1 set of chromosomes
  - 23 in humans
- Pair of chromosomes are **homologous**
  - Each one is a homologue



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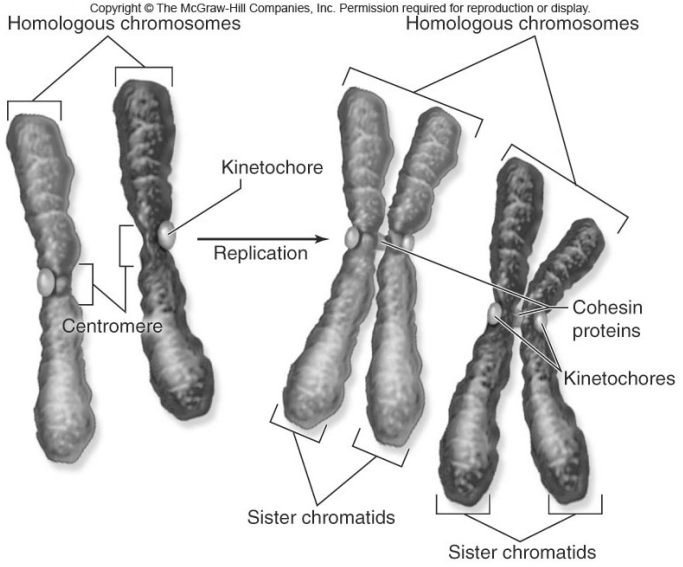
Replication

- Prior to replication, each chromosome composed of a single DNA molecule
- After replication, each chromosome composed of 2 identical DNA molecules
- Visible as 2 strands held together as chromosome becomes more condensed
  - One chromosome composed of 2 **sister chromatids**

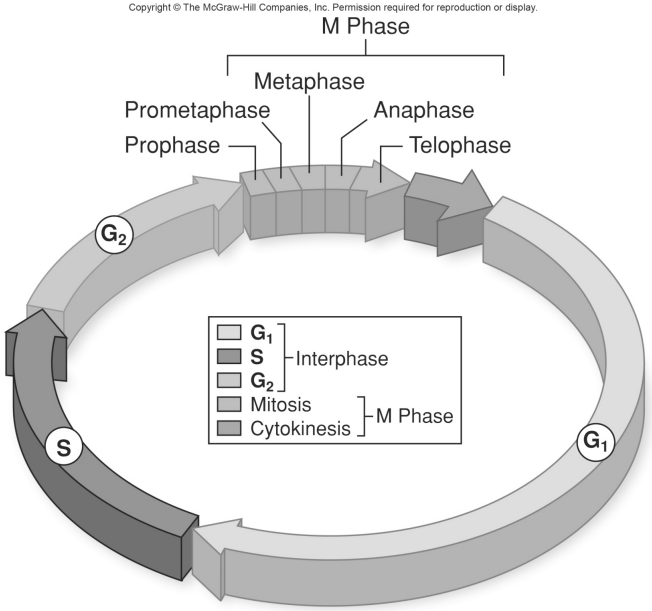


Eukaryotic Cell Cycle

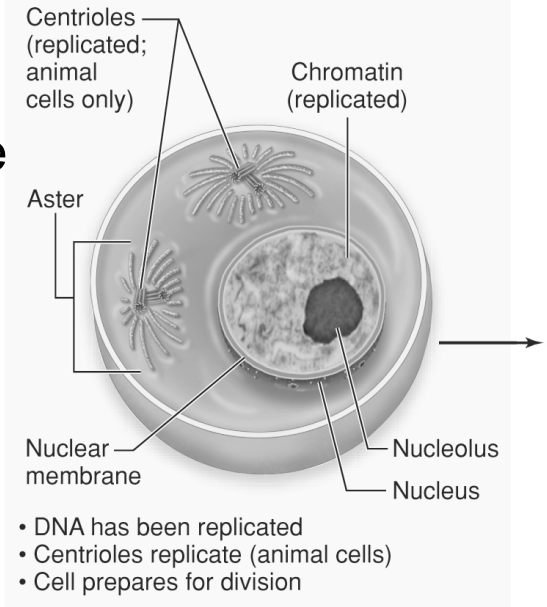
1. G_1 (gap phase 1)
   - Primary growth phase, longest phase
2. S (synthesis)
   - Replication of DNA
3. G_2 (gap phase 2)
   - Organelles replicate, microtubules organize

} Interphase

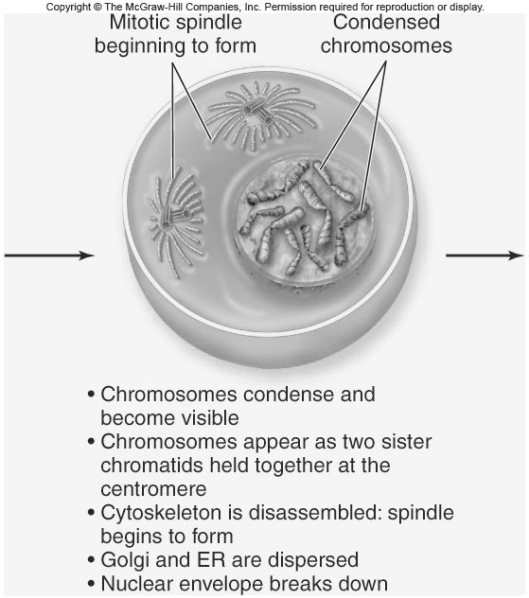
4. M (mitosis)
   - Subdivided into multiple phases
5. C (cytokinesis)
   - Separation of 2 new cells



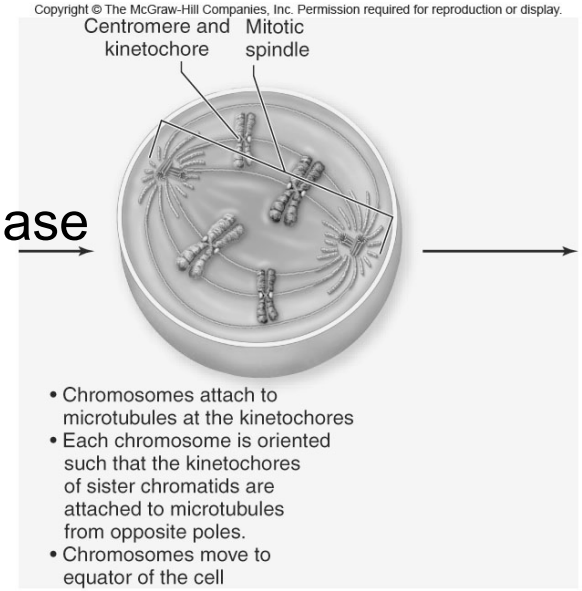
Interphase (G2)

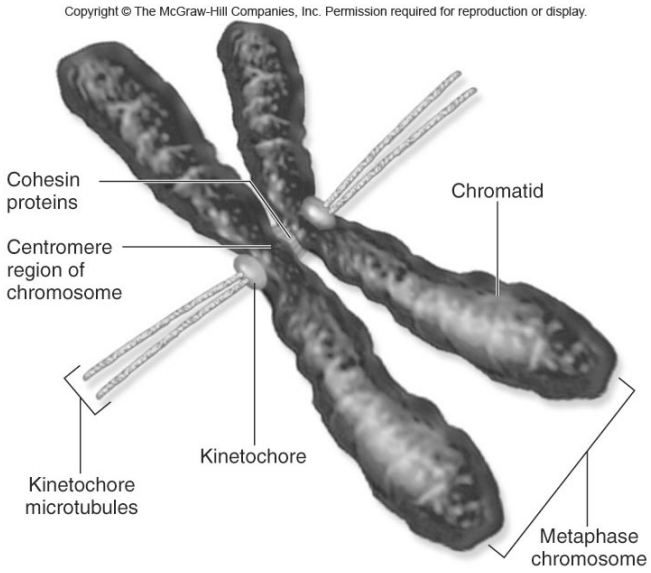


Prophase



Prometaphase





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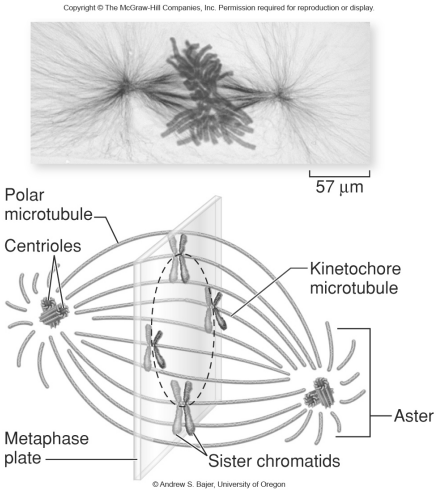
Metaphase

- Alignment of chromosomes along metaphase plate
  - Not an actual structure
  - Future axis of cell division



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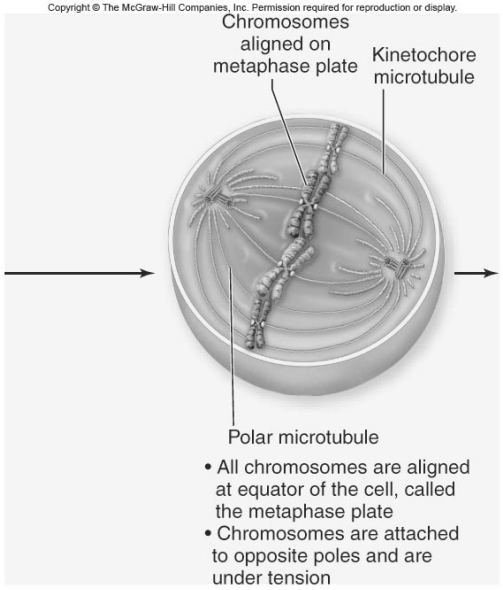
Metaphase



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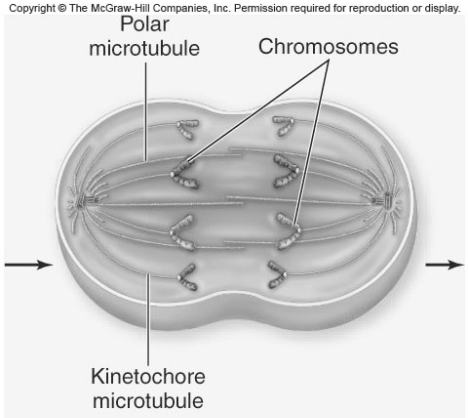
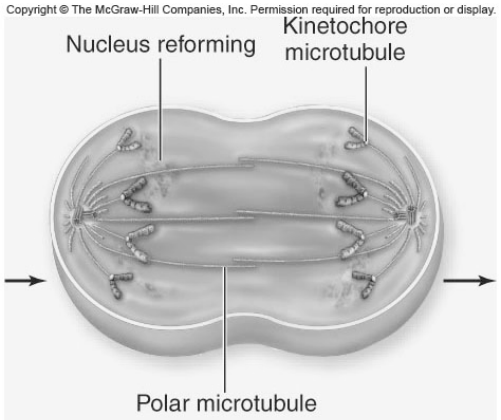
Anaphase



- Proteins holding centromeres of sister chromatids are degraded, freeing individual chromosomes
- Chromosomes are pulled to opposite poles (anaphase A)
- Spindle poles move apart (anaphase B)

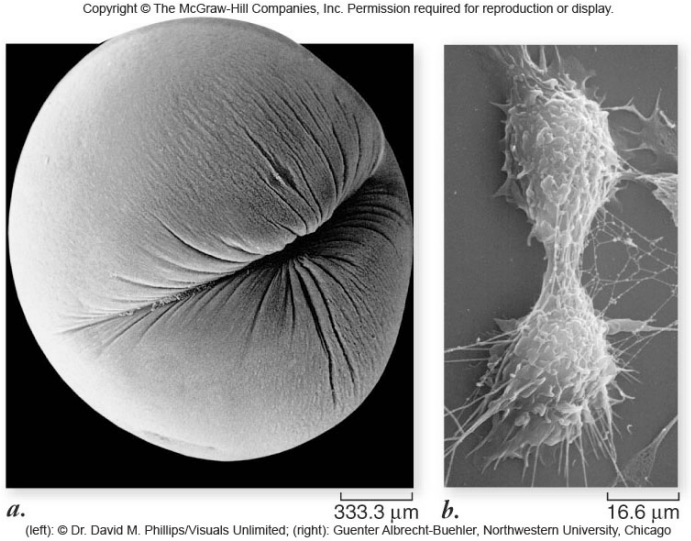
Telophase



- Chromosomes are clustered at opposite poles and decondense
- Nuclear envelopes re-form around chromosomes
- Golgi complex and ER re-form

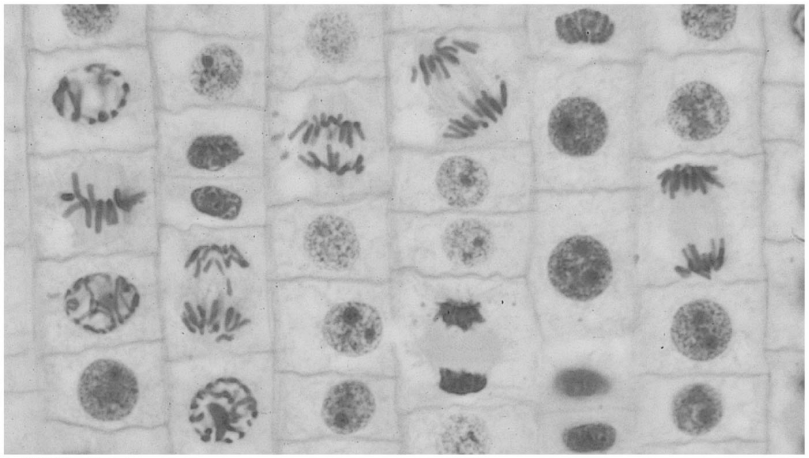
Cytokinesis

- Cleavage of the cell into equal halves
- Animal cells – constriction of actin filaments produces a cleavage furrow
- Plant cells – cell plate forms between the nuclei



(left): © Dr. David M. Phillips/Visuals Unlimited; (right): Guenter Albrecht-Buehler, Northwestern University, Chicago

Mitosis in Onion Root Tip



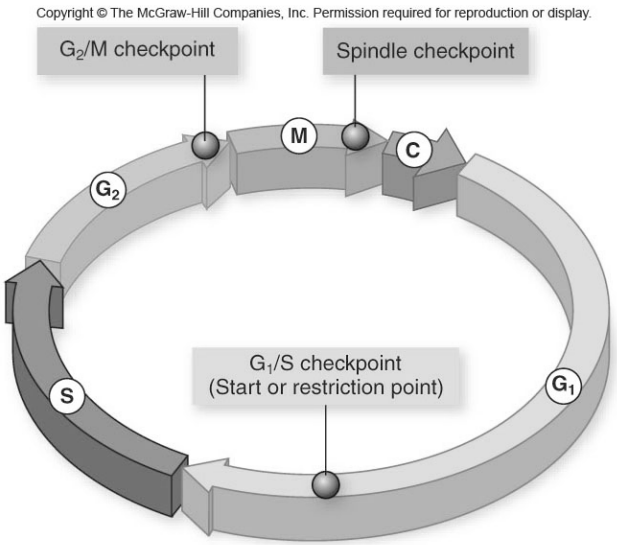
Control of the Cell Cycle

- Current view integrates 2 concepts

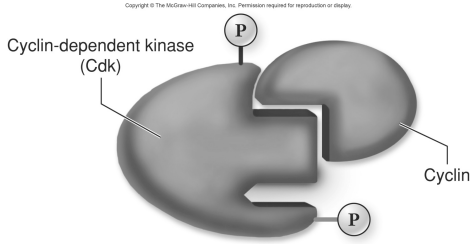
1. Cell cycle has two irreversible points
   - Replication of genetic material
   - Separation of the sister chromatids
2. Cell cycle can be put on hold at specific points called checkpoints
   - Process is checked for accuracy and can be halted if there are errors
   - Allows cell to respond to internal and external signals

Checkpoints

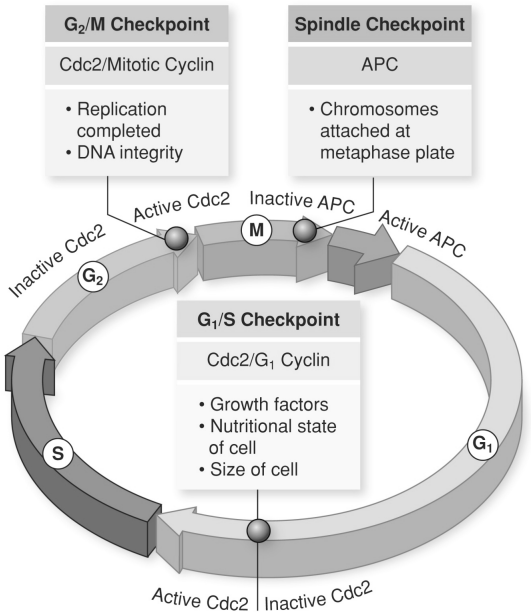
1. G_1/S checkpoint
   - Cell "decides" to divide
   - Primary point for external signal influence
2. G_2/M checkpoint
   - Cell makes a commitment to mitosis
   - Assesses success of DNA replication
3. Late metaphase (spindle) checkpoint
   - Cell ensures that all chromosomes are attached to the spindle



Cyclin-dependent kinases (Cdks)

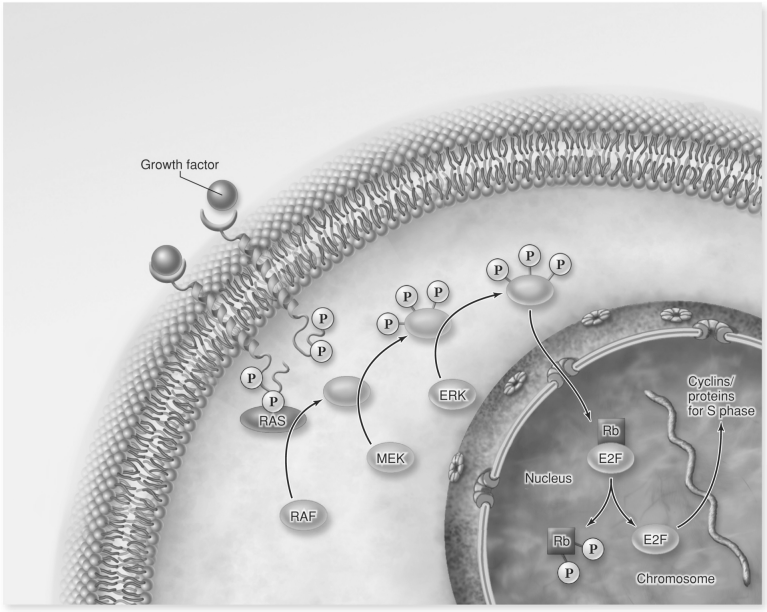


- Enzymes that phosphorylate proteins
- Primary mechanism of cell cycle control
- Cdks partner with different **cyclins** at different points in the cell cycle
- Activity of Cdk is also controlled by the pattern of phosphorylation
  - Phosphorylation at one site (red) inactivates Cdk
  - Phosphorylation at another site (green) activates Cdk



Control in multicellular eukaryotes

- Multiple Cdks control the cycle as opposed to the single Cdk in yeasts
- Animal cells respond to a greater variety of external signals than do yeast



Cancer

- Unrestrained, uncontrolled growth of cells
- Failure of cell cycle control

- Two kinds of genes can disturb the cell cycle when they are mutated

1. **Tumor-suppressor genes**
2. **Proto-oncogenes**

Tumor-suppressor genes

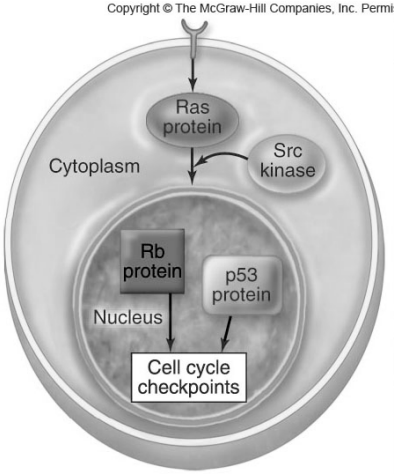
- ***p53*** plays a key role in G_1 checkpoint
- p53 protein monitors integrity of DNA
  - If DNA damaged, cell division halted and repair enzymes stimulated
  - If DNA damage is irreparable, p53 directs cell to kill itself
- Prevent the development of cells containing mutations
- *p53* is absent or damaged in many cancerous cells

Tumor-suppressor genes

- Both copies of a tumor-suppressor gene must lose function for the cancerous phenotype to develop
- First tumor-suppressor identified was the retinoblastoma susceptibility gene *(Rb)*
  - Predisposes individuals for a rare form of cancer that affects the retina of the eye
- Inheriting a single mutant copy of *Rb* means the individual has only one “good” copy left

Proto-oncogenes

- Normal cellular genes that become oncogenes when mutated
  - Oncogenes can cause cancer
- Some encode receptors for growth factors
  - If receptor is mutated in “on”, cell no longer depends on growth factors
- Only one copy of a proto-oncogene needs to undergo this mutation for uncontrolled division to take place



Mammalian cell

Proto-oncogenes

Growth factor receptor: more per cell in many breast cancers.

Ras protein: activated by mutations in 20–30% of all cancers.

Src kinase: activated by mutations in 2–5% of all cancers.

Tumor-suppressor Genes

Rb protein: mutated in 40% of all cancers.

p53 protein: mutated in 50% of all cancers.