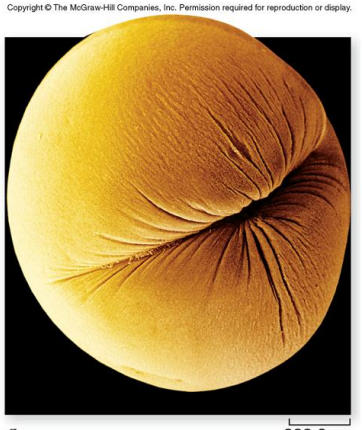
How Cells Divide

Chapter 10



Eukaryotic Chromosomes

Eukaryotic chromosomes –

-linear chromosomes

-every species different number of chromosomes

-**chromatin** – complex of DNA & proteins

  -**heterochromatin** – not expressed

  -**euchromatin** – expressed regions

Eukaryotic Chromosomes

Chromosomes: very long & must be condensed to fit within nucleus

-**nucleosome** – DNA wrapped around a core of 8 **histone proteins**

-nucleosomes spaced 200 nucleotides apart along DNA

-further coiling creates **30-nm fiber** or **solenoid**

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Eukaryotic Chromosomes

Solenoid further compacted:

-radial loops held in place by scaffold proteins

-scaffold of proteins aided by a complex of proteins called **condensin**

karyotype: particular array of chromosomes of an organism

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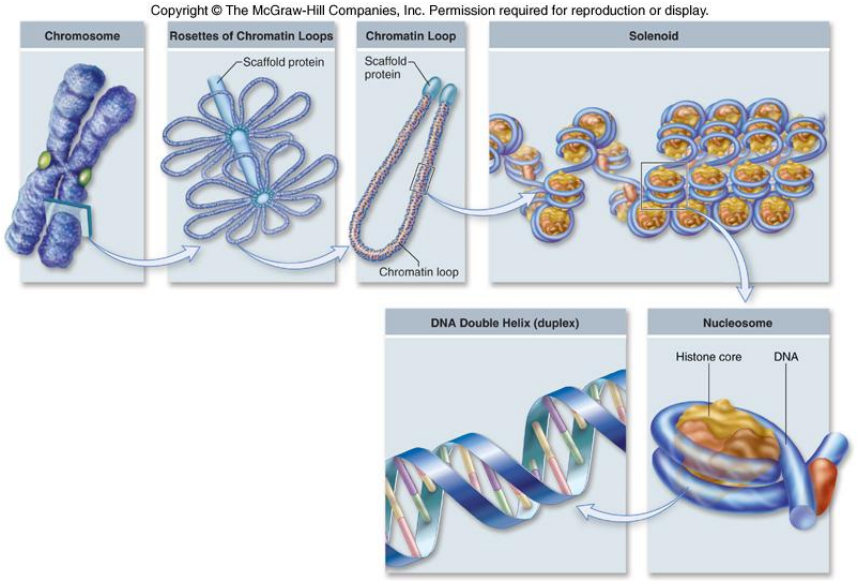

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Karyotype

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Eukaryotic Chromosomes

Chromosomes replicated before cell division

-Replicated chromsomes connected to each other at their **kinetochores**

-**cohesin** – complex of proteins holding replicated chromosomes together

-**sister chromatids**: 2 copies of chromosome within replicated chromosome

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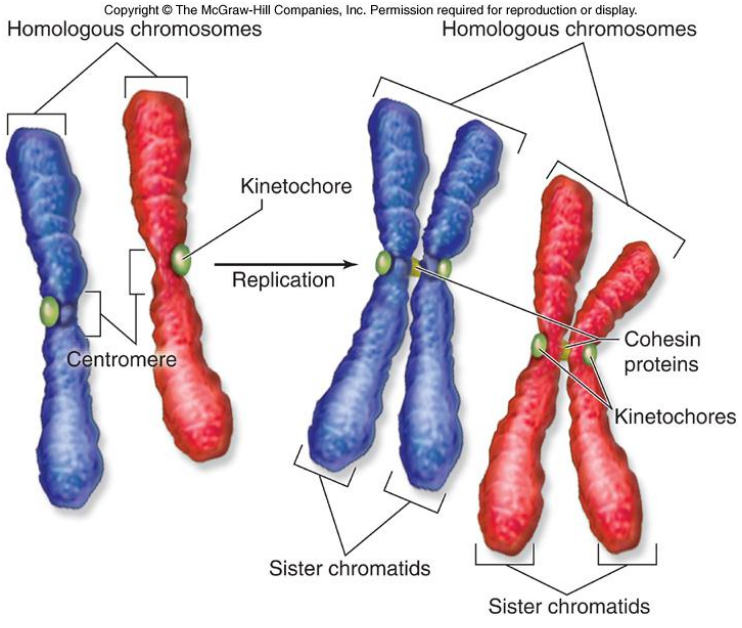

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Eukaryotic Cell Cycle

Eukaryotic cell cycle has 5 main phases:

1. G_1 (gap phase 1)
2. S (synthesis)
3. G_2 (gap phase 2)

} **interphase**

4. M (mitosis)
5. C (cytokinesis)

Length of complete cell cycle varies greatly among cell types (18-22 hrs for human cells)

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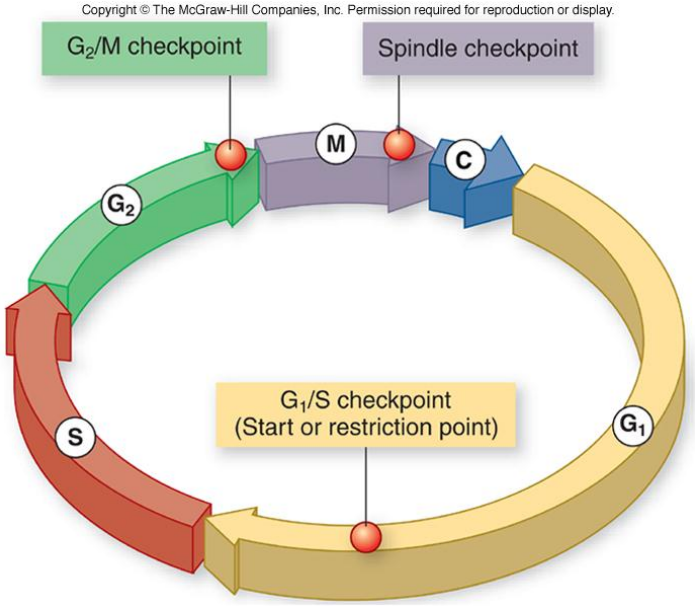
Cell Cycle



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Interphase

Interphase composed of:

G_1 (gap phase 1) – time of cell growth
-RNA/protein synthesis
S phase – synthesis of DNA (DNA replication)
- 2 sister chromatids produced

G_2 (gap phase 2) – chromosomes condense
-protein synthesis for mitosis

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Interphase

Following S phase, sister chromatids appear to share centromere

Centromere replicated but 2 centromeres held together by cohesin proteins

Proteins of kinetochore attached to centromere

Microtubules attach to kinetochore.

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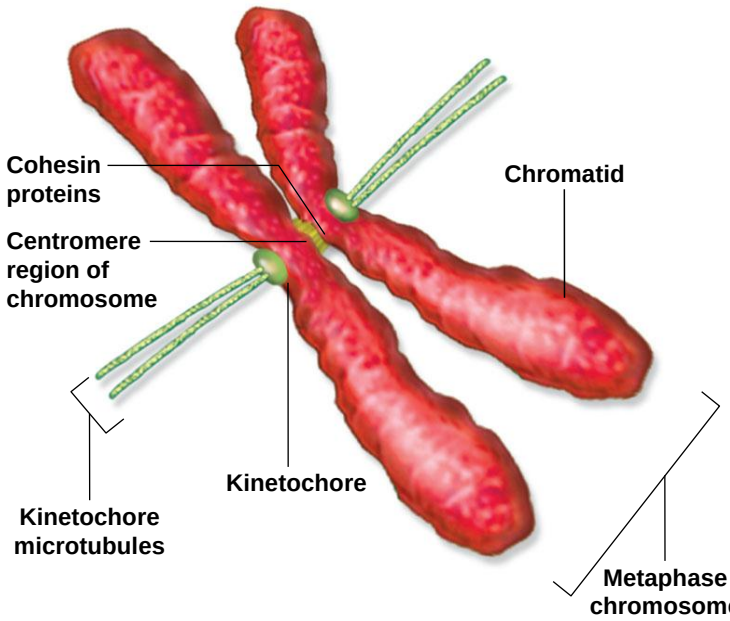

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Interphase

During G_2 chromosomes undergo **condensation**, becoming tightly coiled.

Centrioles (microtubule-organizing centers) replicate & one centriole moves to each pole.

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Mitosis

Mitosis is divided into 5 phases:

1. prophase
2. prometaphase
3. metaphase
4. anaphase
5. telophase

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Mitosis

Prophase:

-chromosomes continue to condense

-centrioles move to each pole of cell

-spindle apparatus assembled

-nuclear envelope dissolves

-longest of 4 mitotic phases

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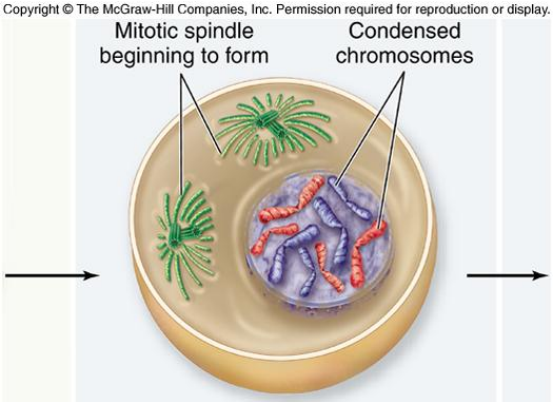

- Chromosomes condense and become visible
- Chromosomes appear as two sister chromatids held together at the centromere
- Cytoskeleton is disassembled: spindle begins to form
- Golgi and ER are dispersed
- Nuclear envelope breaks down

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Mitosis

Prometaphase:

-chromosomes become attached to spindle apparatus by their kinetochores

-a second set of microtubules formed from poles to each kinetochore

-microtubules begin to pull each chromosome toward center of cell

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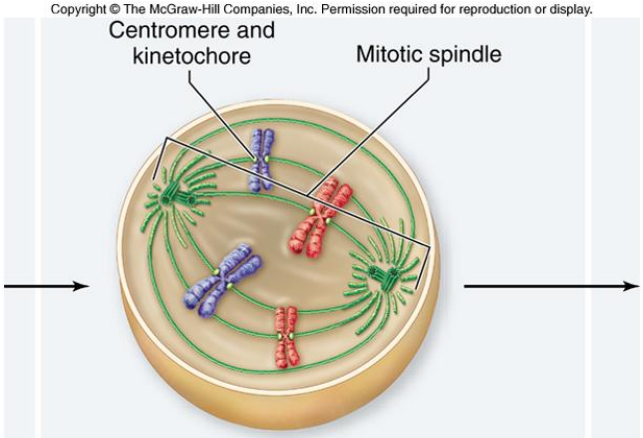

- Chromosomes become attached to microtubules at the kinetochores
- Each chromosome is oriented such that the kinetochores of sister chromatids are attached to microtubules from opposite poles.
- Chromosomes move to equator of the cell

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Mitosis

Metaphase:

-microtubules pull chromosomes to align them at the center of cell

-**metaphase plate**: imaginary plane through the center of cell where chromosomes align

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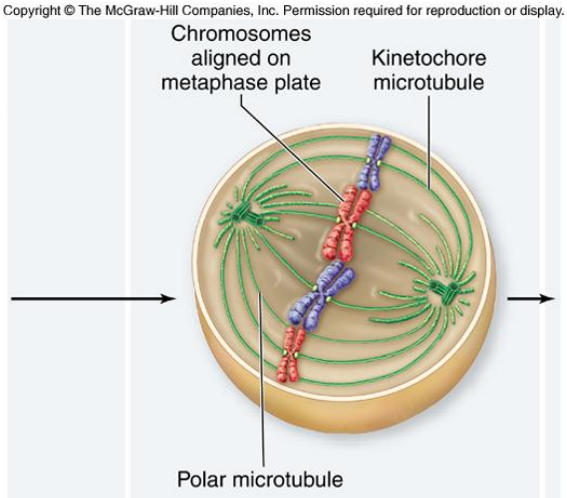

- All chromosomes are aligned at equator of the cell, called the metaphase plate
- Chromosomes are attached to opposite poles and are under tension

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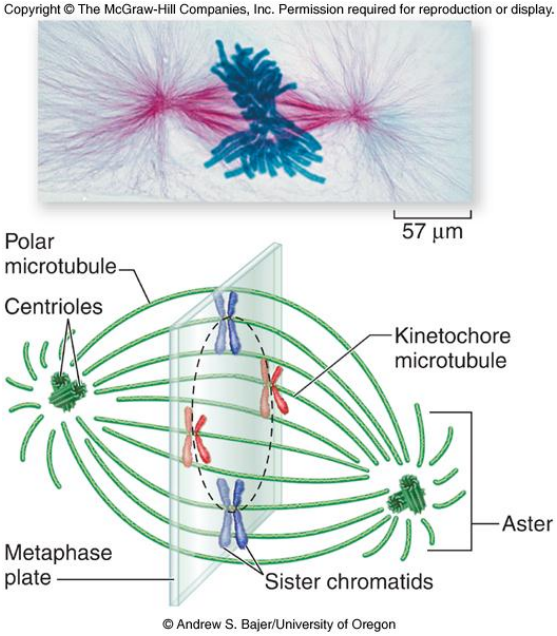

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Mitosis

Anaphase:

-removal of cohesin proteins causes centromeres to separate

-microtubules pull sister chromatids toward poles

-in anaphase A kinetochores pulled apart

-in anaphase B the poles move apart

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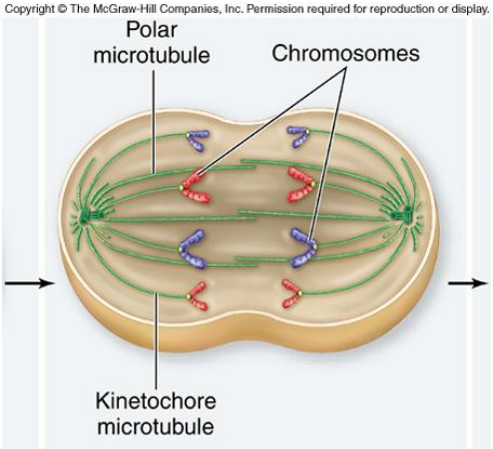

- Proteins holding centromeres of sister chromatids are degraded, freeing individual chromosomes
- Chromosomes are pulled to opposite poles (anaphase A)
- Spindle poles move apart (anaphase B)

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Mitosis

Telophase:

-spindle apparatus disassembles

-nuclear envelope forms around each set of sister chromatids

-chromosomes begin to uncoil

-nucleolus reappears in each new nucleus

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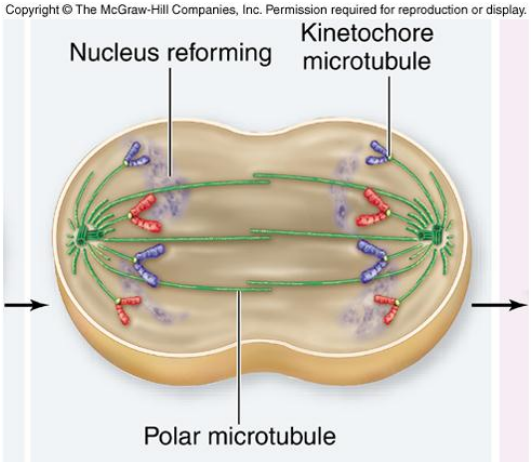

- Chromosomes are clustered at opposite poles and decondense
- Nuclear envelopes re-form around chromosomes
- Golgi complex and ER re-form

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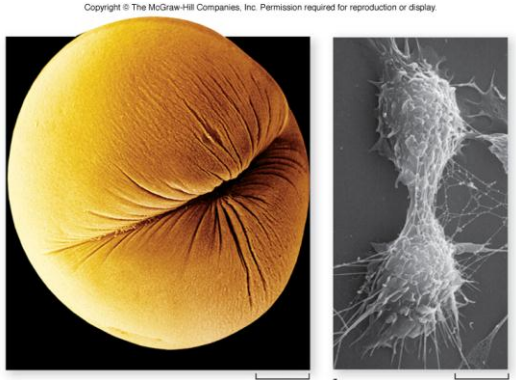
Cytokinesis
(cytoplasmic division)

Cytokinesis – cleavage of cell into equal halves

-animal cells – constriction of **actin filaments** produces a **cleavage furrow**



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Control of Cell Cycle

Cell cycle controlled at 3 checkpoints:

1. G_1/S checkpoint
   -cell "decides" to divide
2. G_2/M checkpoint
   -cell makes commitment to mitosis
3. late metaphase (spindle) checkpoint
   -cell ensures all chromosomes attached to spindle

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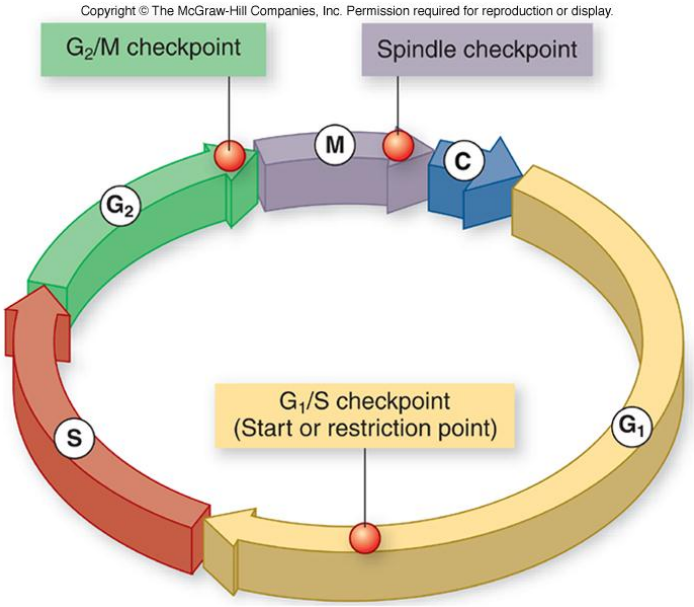
Cell Cycle



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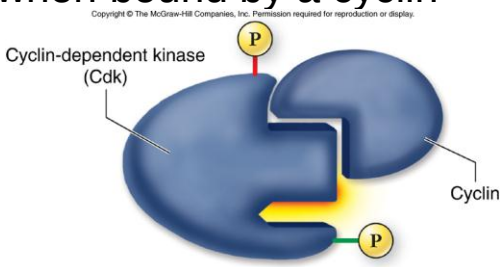
Control of Cell Cycle

cyclins – proteins produced in synchrony with cell cycle

-regulate passage of cell through cell cycle checkpoints

cyclin-dependent kinases (Cdks) – enzymes drive cell cycle

-activated only when bound by a cyclin



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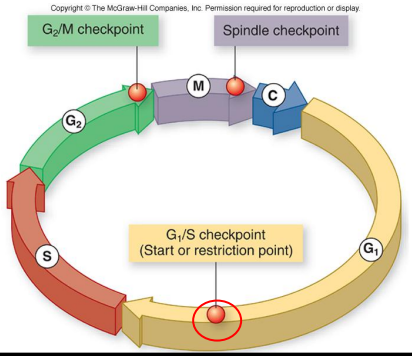
Control of Cell Cycle

At G_1/S checkpoint:

-G_1 cyclins accumulate

-G_1 cyclins bind with Cdc2: create active G_1/S Cdk

-G_1/S Cdk phosphorylates # of molecules that ultimately increase enzymes required for DNA replication



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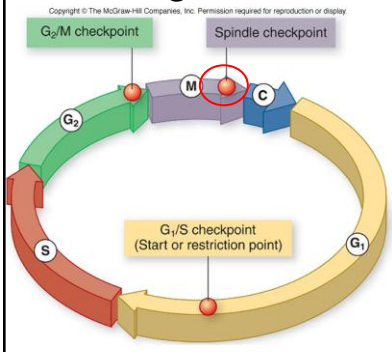
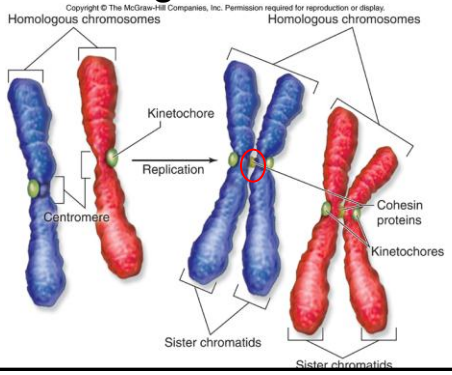
Control of Cell Cycle

At spindle checkpoint:

-signal for anaphase to proceed transmitted through **anaphase-promoting complex (APC)**

-APC activates proteins removing **cohesin** holding sister chromatids together





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Control of Cell Cycle

Growth factors:

-can influence cell cycle

-trigger intracellular signaling systems

-can override cellular controls that otherwise inhibit cell division

platelet-derived growth factor (PDGF) triggers cells to divide during wound healing

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Control of Cell Cycle

Cancer: failure of cell cycle control

2 kinds of genes when mutated disturb cell cycle:

1. **tumor-suppressor genes**
2. **proto-oncogenes**

Mutations:

- **UV/X ray radiation**
- **Chemical**
- **Bacterial/Virus/Fungal**
- **EMF (electromagnetic fields)**
- **Stress**
- **Air pollution**

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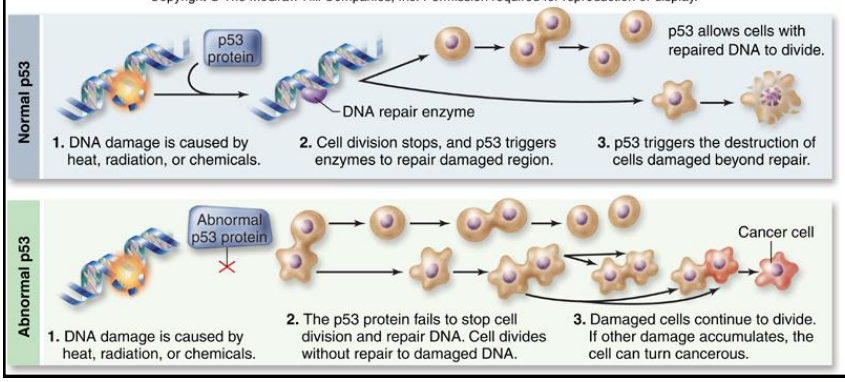
Control of Cell Cycle

Tumor-suppressor genes:

-prevent development of cells with mutations

-*p53* halts cell division if damaged DNA detected

-*p53* absent or damaged in many cancerous cells



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Control of Cell Cycle

Proto-oncogenes:

-some encode receptors for growth factors

-some encode signal transduction proteins

- proto-oncogenes —mutations→ **oncogenes**

-oncogenes: → cancer when introduced into cells

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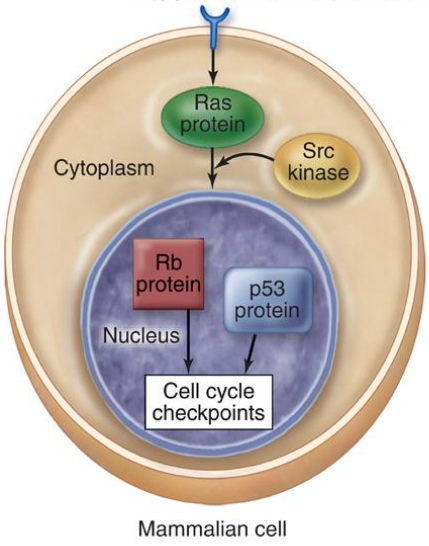

Proto-oncogenes

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.

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