

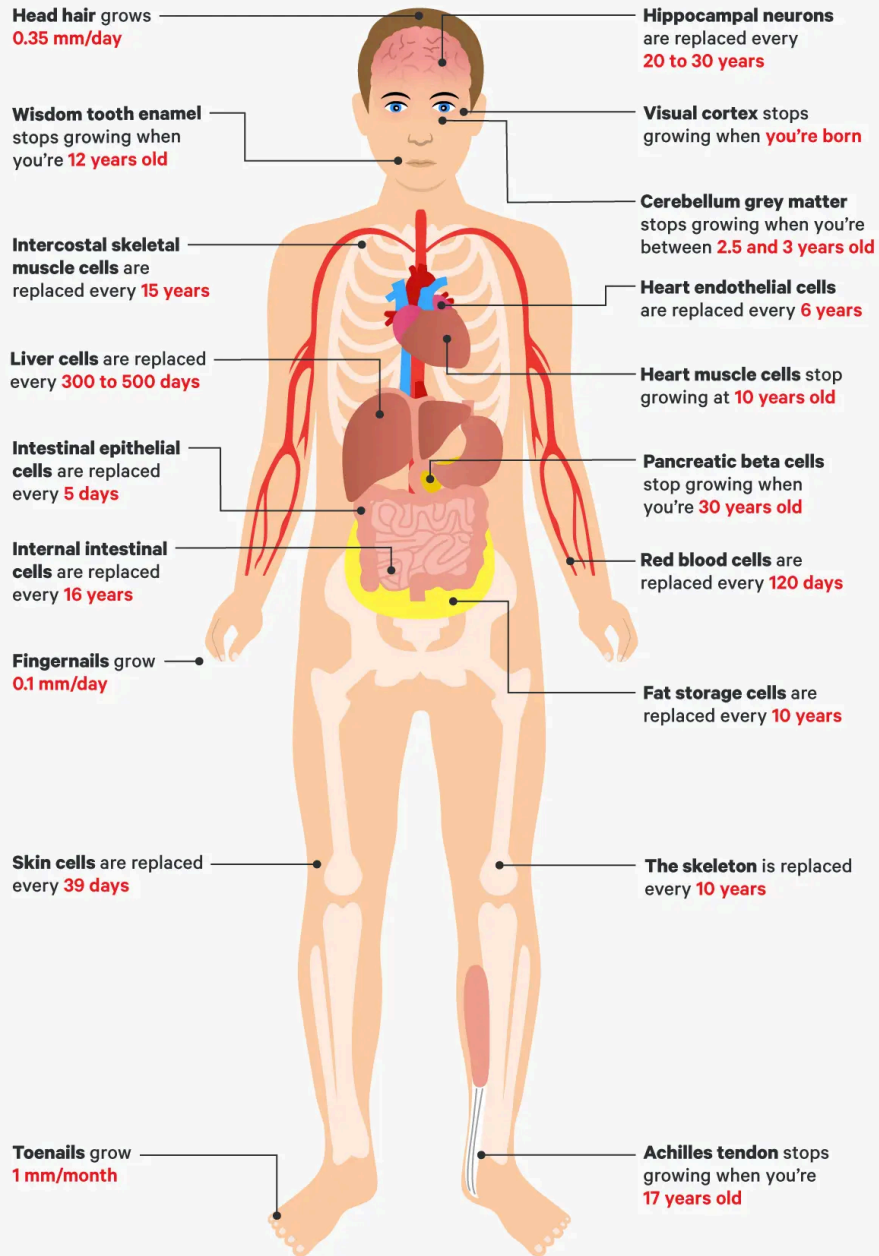
Chapter 9: The Cell Cycle

What you must know:

- ▶ The structure of the replicated chromosome.
- ▶ The events that occur in interphase of the cell cycle (G1, S, G2).
- ▶ The role of cyclins and cyclin-dependent kinases in the regulation of the cell cycle.
- ▶ Ways in which the normal cell cycle is disrupted to cause cancer or halted in certain specialized cells.
- ▶ The features of mitosis that result in the production of genetically identical daughter cells including replication, alignment of chromosomes (metaphase), and separation of chromosomes (anaphase).



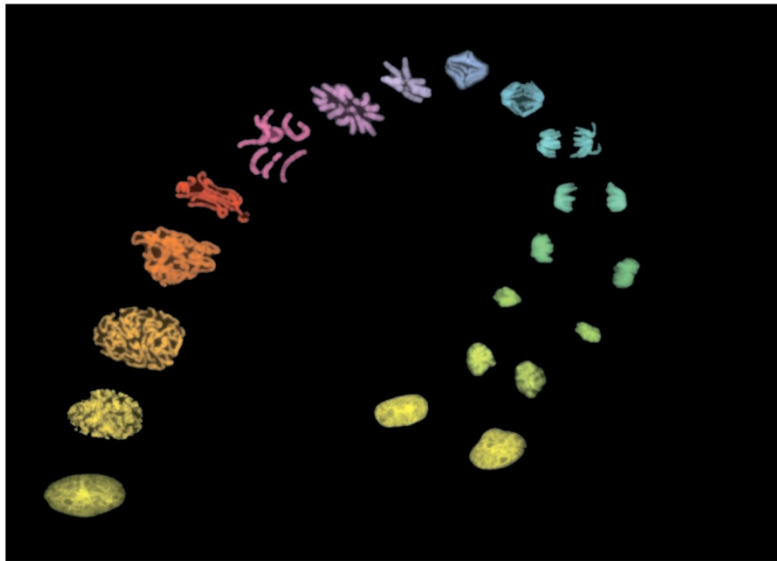
THE AVERAGE LIFE OF YOUR CELLS



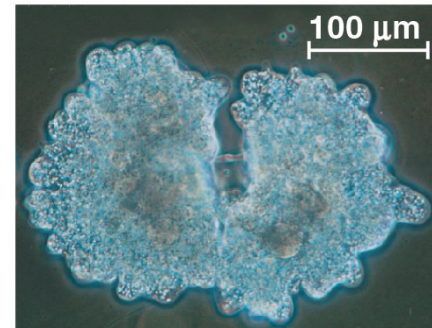
Cell Cycle: life of a cell from its formation until it divides into two cells

Functions of Cell

Division: Reproduction, Growth and Tissue Repair

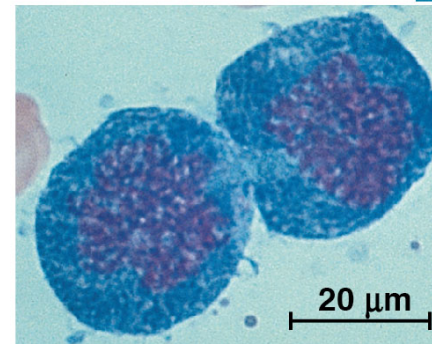
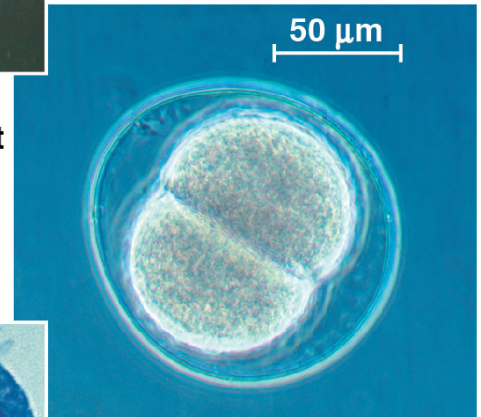


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◀ (a) Reproduction

▶ (b) Growth and development

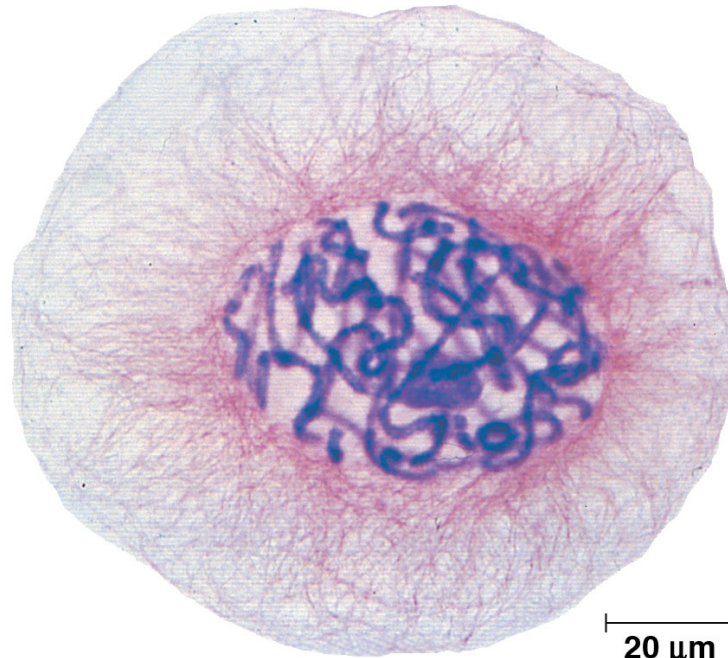


◀ (c) Tissue renewal

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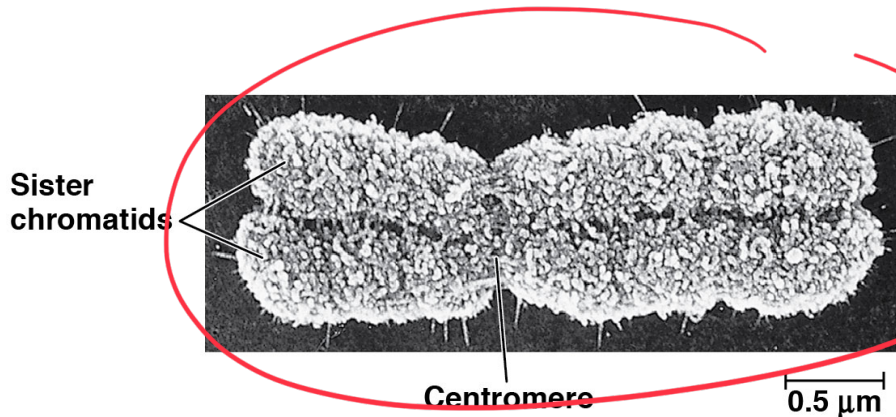
Genome = all of a cell's genetic info (DNA)

- ▶ Prokaryote: single, circular chromosome
- ▶ Eukaryote: more than one linear chromosomes
 - ▶ Eg. Human: 46 chromosomes, mouse: 40, fruit fly: 8

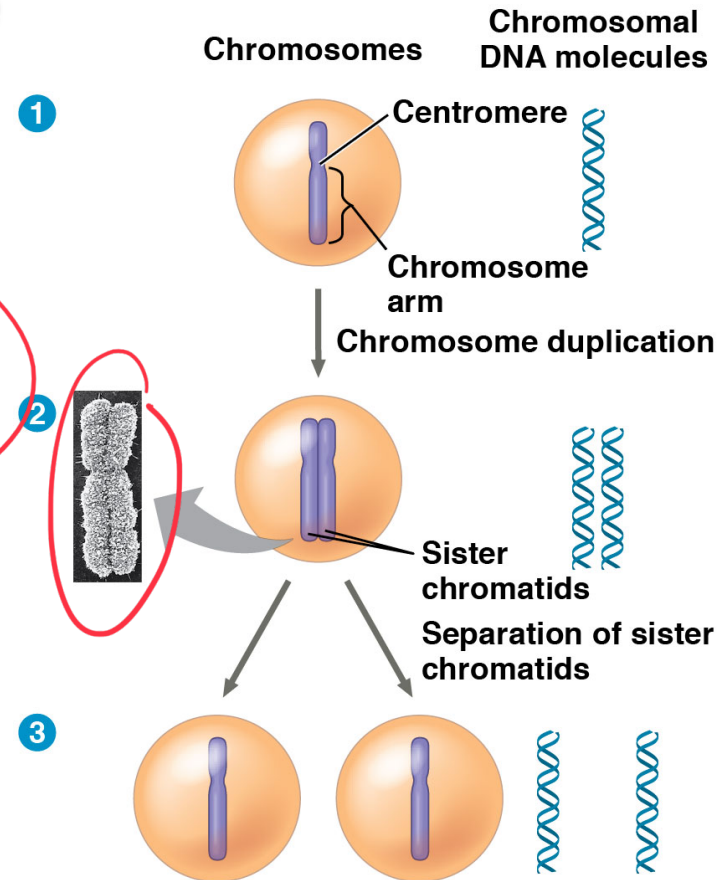


Each chromosome must be duplicated (replicated) before cell division *S-Phase*

- ▶ Duplicated chromosome = 2 sister chromatids attached by a centromere



sister { } sister



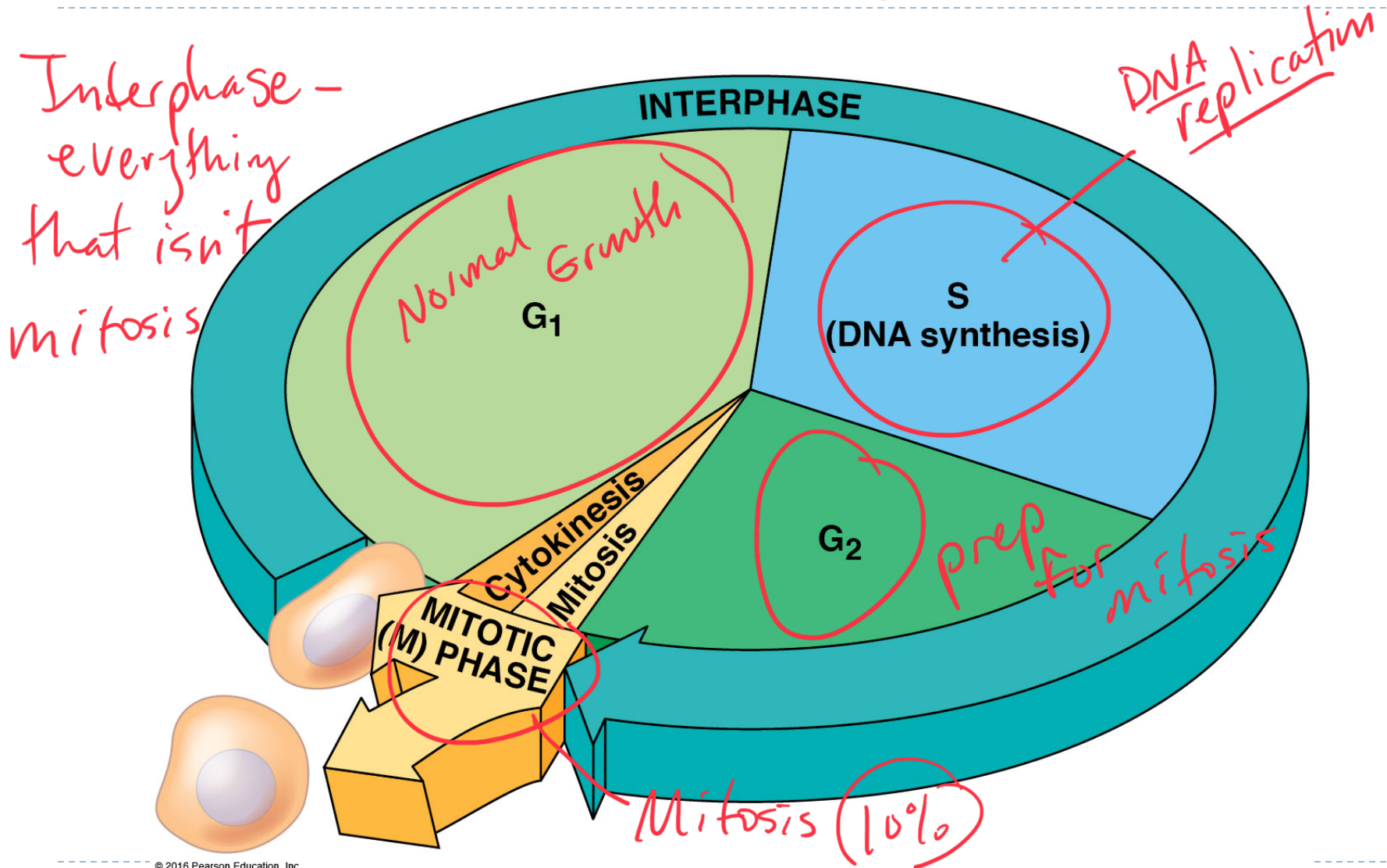
Somatic Cells

- ▶ Body cells
- ▶ Diploid ($2n$): 2 of each type of chromosome
- ▶ Divide by mitosis
- ▶ Humans: $2n = \underline{46}$

Gametes

- ▶ Sex cells (sperm/egg)
- ▶ Haploid (n): 1 of each type of chromosome
- ▶ Divide by meiosis
- ▶ Humans: $n = \underline{23}$

Phases of the Cell Cycle



Phases of the Cell Cycle

- ▶ The *mitotic* phase alternates with *interphase*:

$\{ G_1 \rightarrow S \rightarrow G_2 \rightarrow \text{mitosis} \rightarrow \text{cytokinesis}$

- ▶ Interphase (90% of cell cycle)

- ▶ G₁ Phase: cell grows and carries out normal functions

- ▶ S Phase: duplicates chromosomes (DNA replication)

- ▶ G₂ Phase: prepares for cell division

- ▶ M Phase (mitotic)

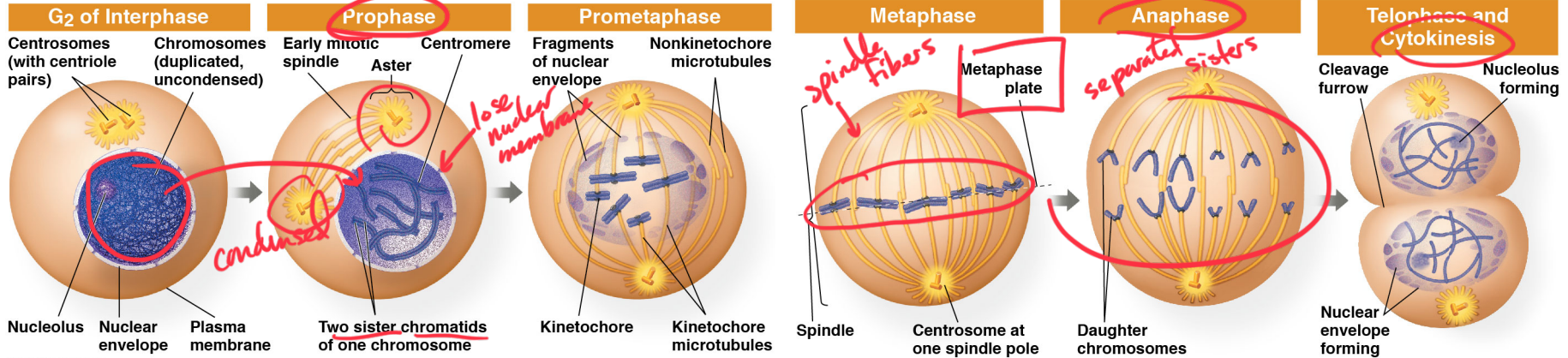
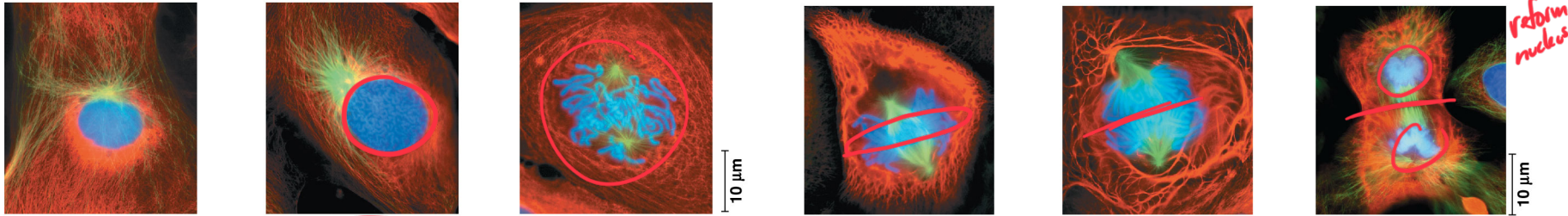
- ▶ Mitosis: nucleus divides

- ▶ Cytokinesis: cytoplasm divides
-



Mitosis: Prophase → Metaphase → Anaphase → Telophase

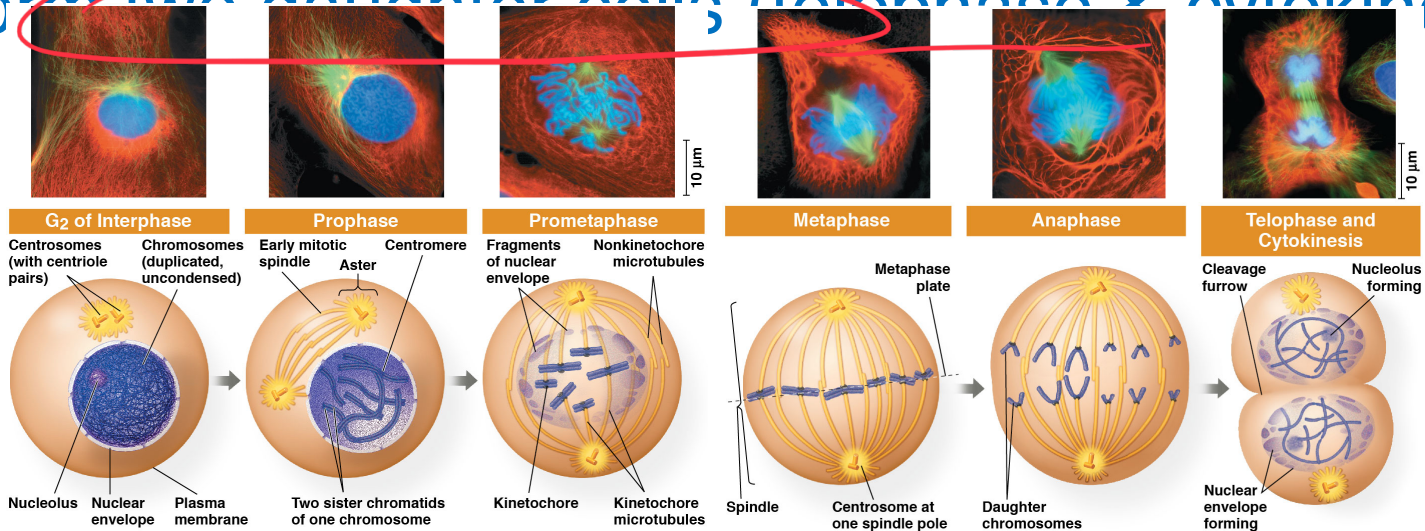
PMAT



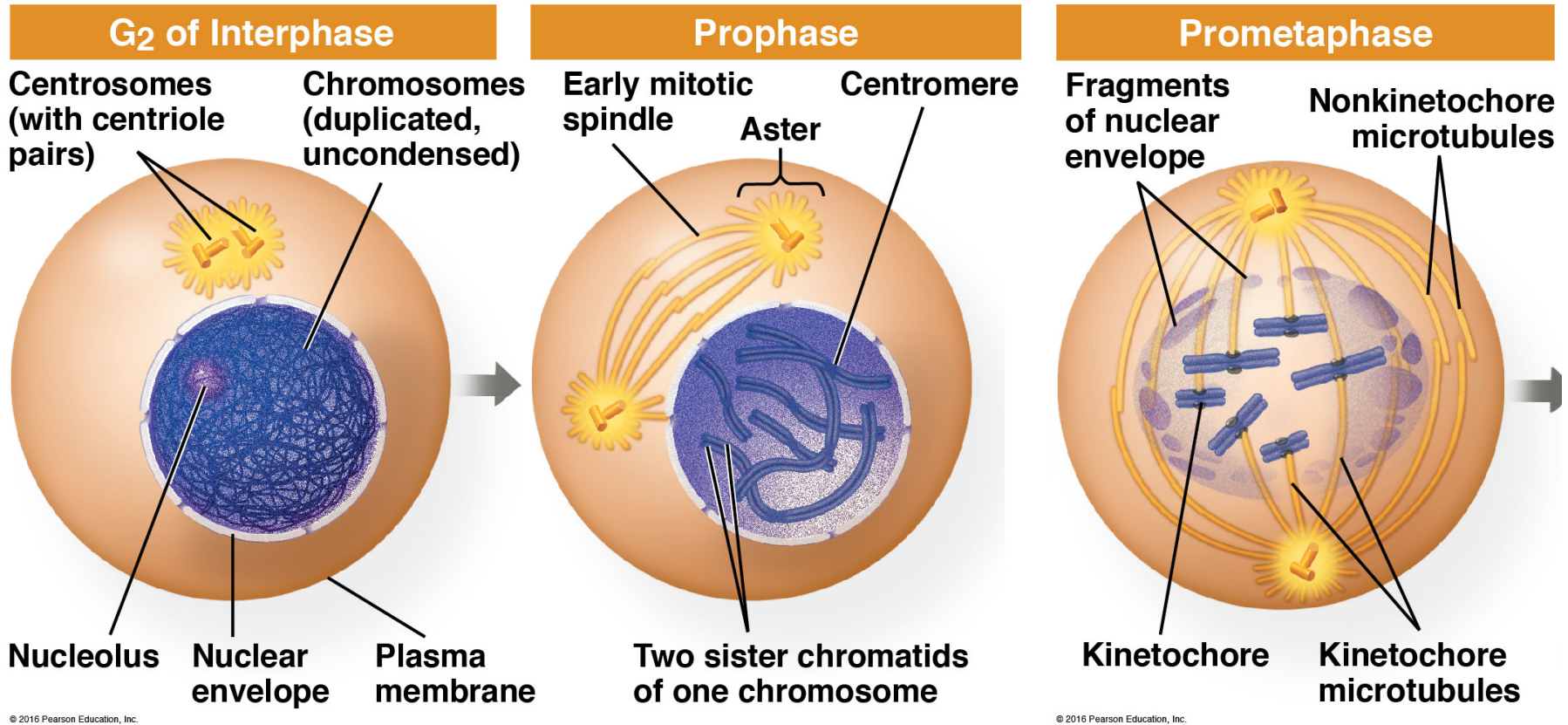
Mitosis

▶ Continuous process with observable structural features:

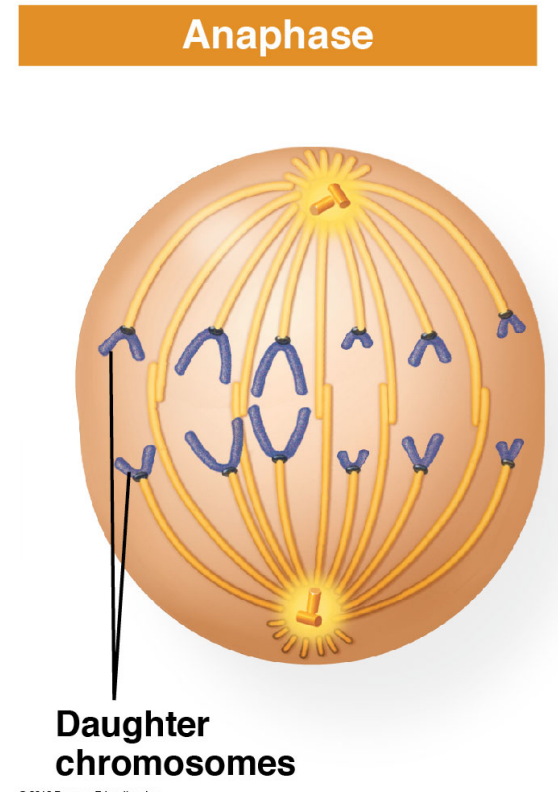
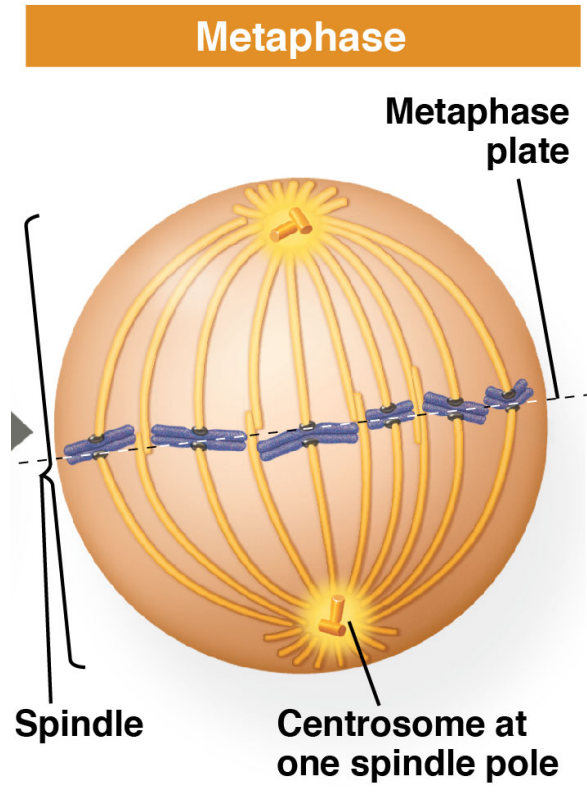
- ▶ Chromosomes become visible (prophase)
- ▶ Alignment at the equator (metaphase)
- ▶ Separation of sister chromatids (anaphase)
- ▶ Form two daughter cells (telophase & cytokinesis)



Prophase & Prometaphase



Metaphase & Anaphase

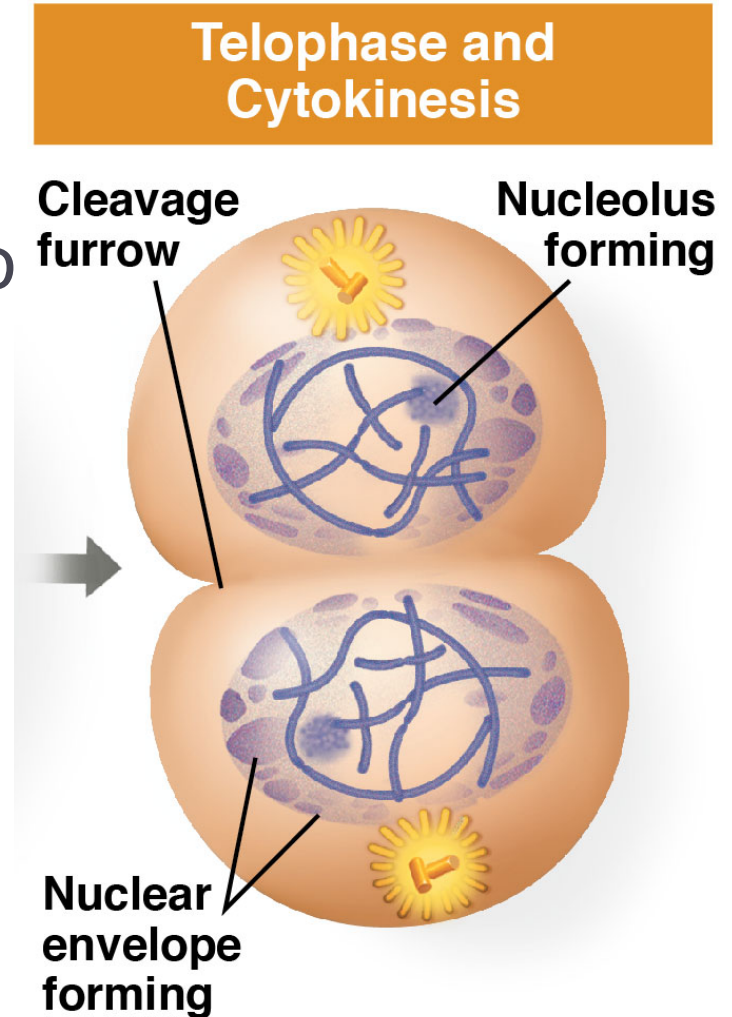


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Telophase & Cytokinesis

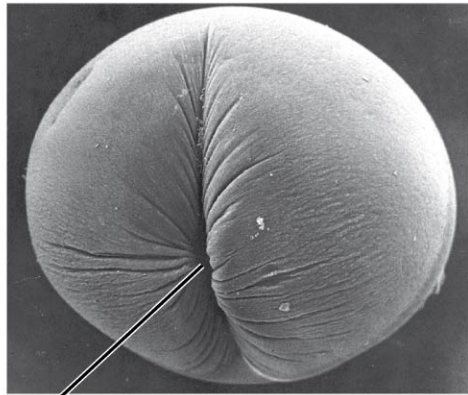
Cytokinesis

- ▶ Cytoplasm of cell divided
- ▶ **Animal Cells:** cleavage furro
- ▶ **Plant Cells:** cell plate forms



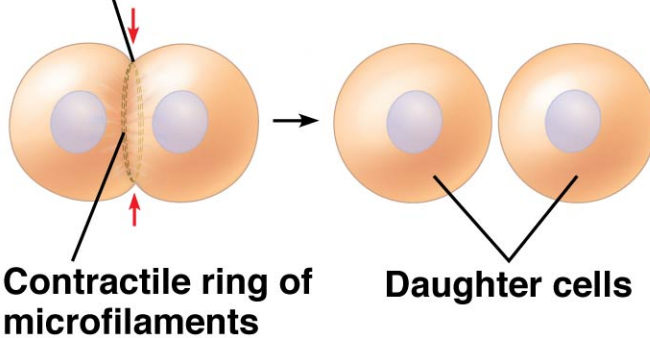
Cytokinesis in Animal vs. Plant Cells

(a) Cleavage of an animal cell (SEM)



100 μm

Cleavage furrow

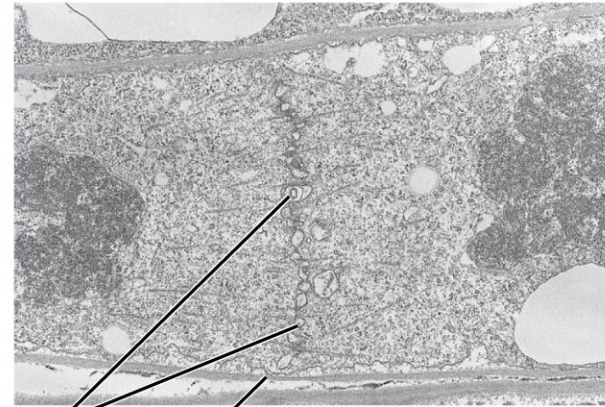


Contractile ring of microfilaments

Daughter cells

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(b) Cell plate formation in a plant cell (TEM)



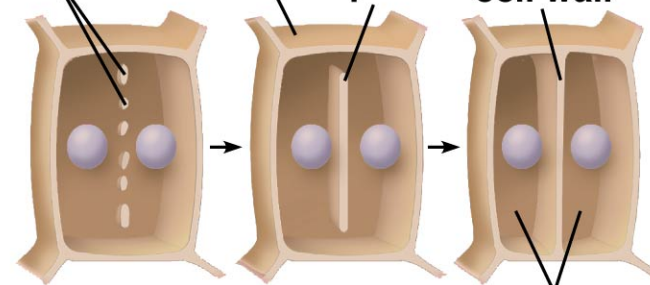
1 μm

Vesicles forming cell plate

Wall of parent cell

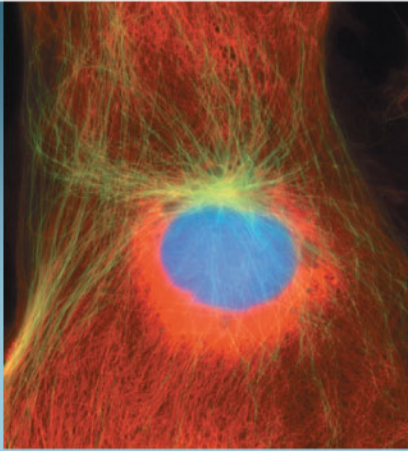
Cell plate

New cell wall

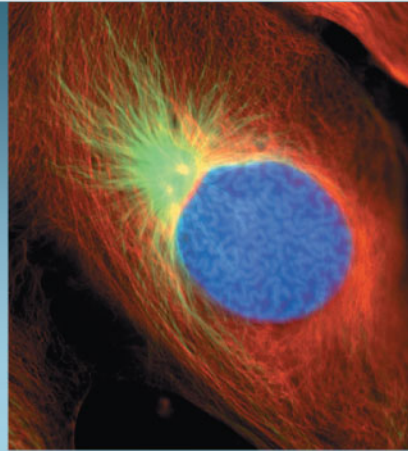


Daughter cells

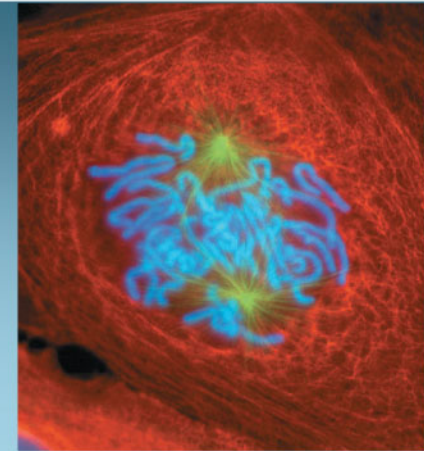
Animal Cell Division



G₂ of Interphase

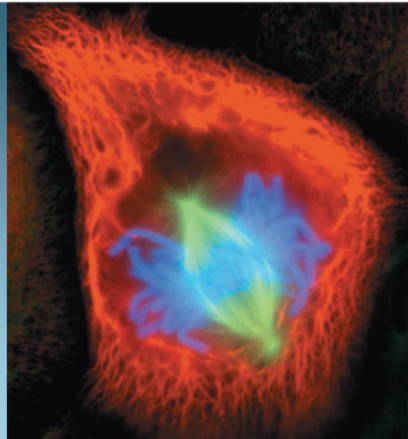


Prophase

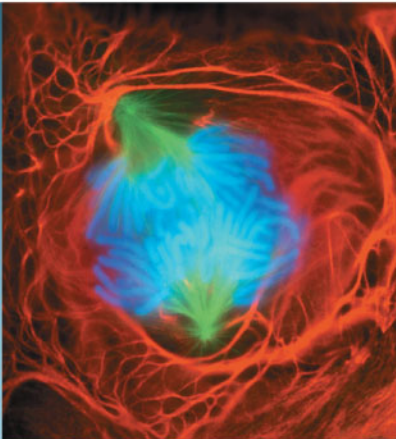


Prometaphase

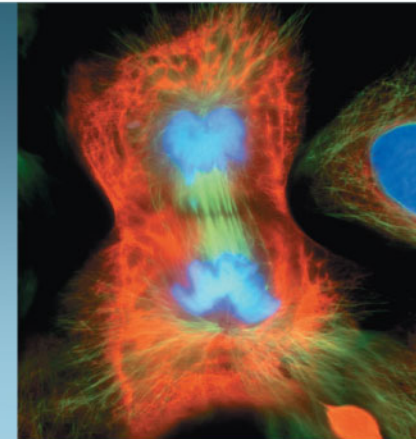
10 μ m



Metaphase



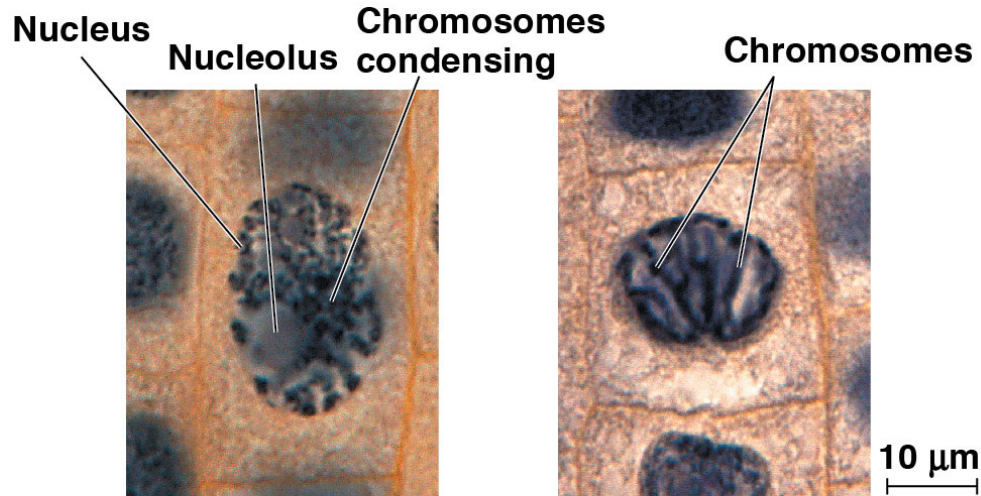
Anaphase



Telophase and Cytokinesis

10 μ m

Plant Cell Division



1 Prophase

2 Prometaphase

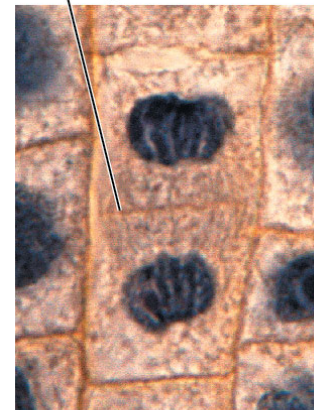
Cell plate



3 Metaphase

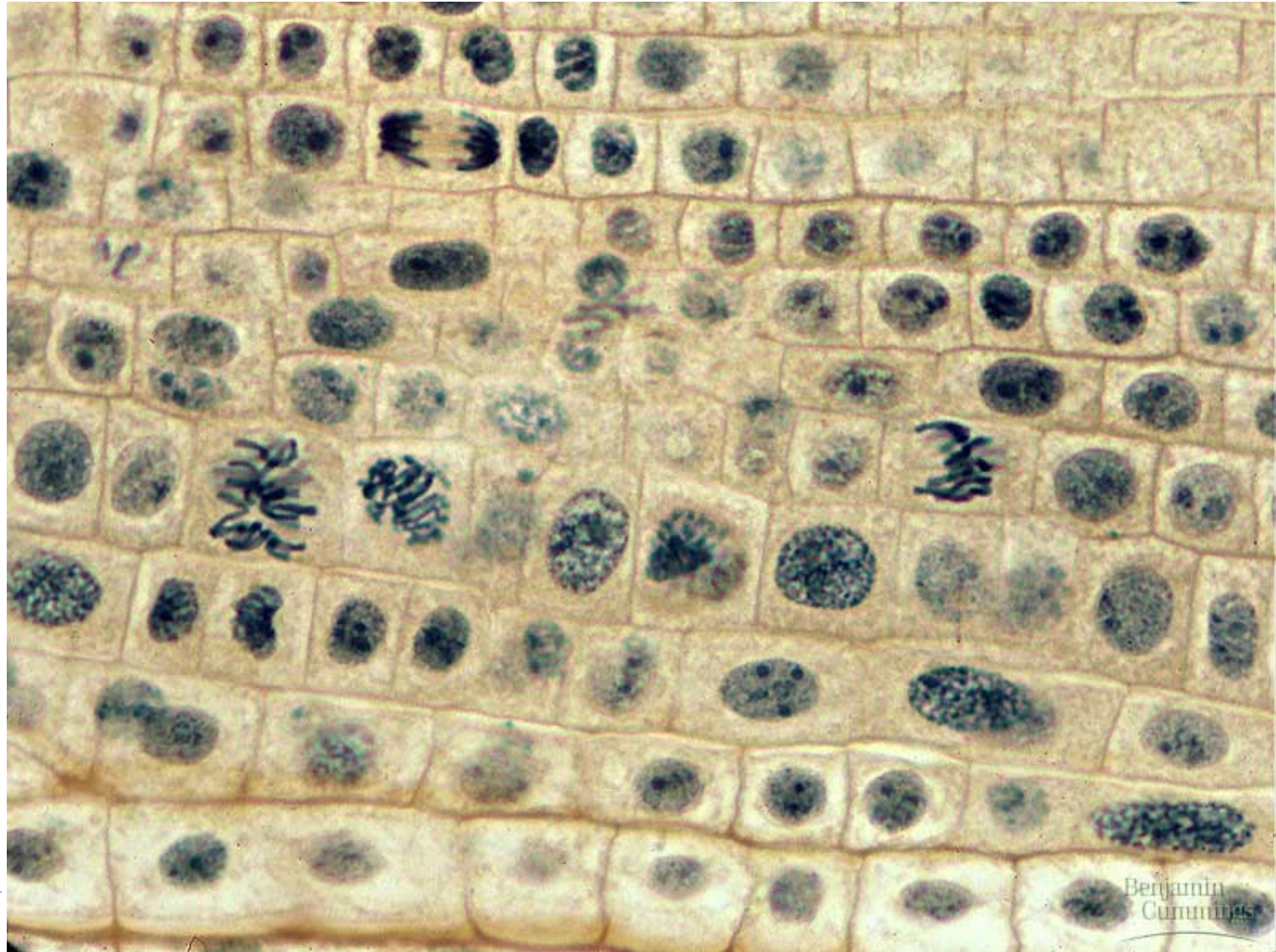


4 Anaphase

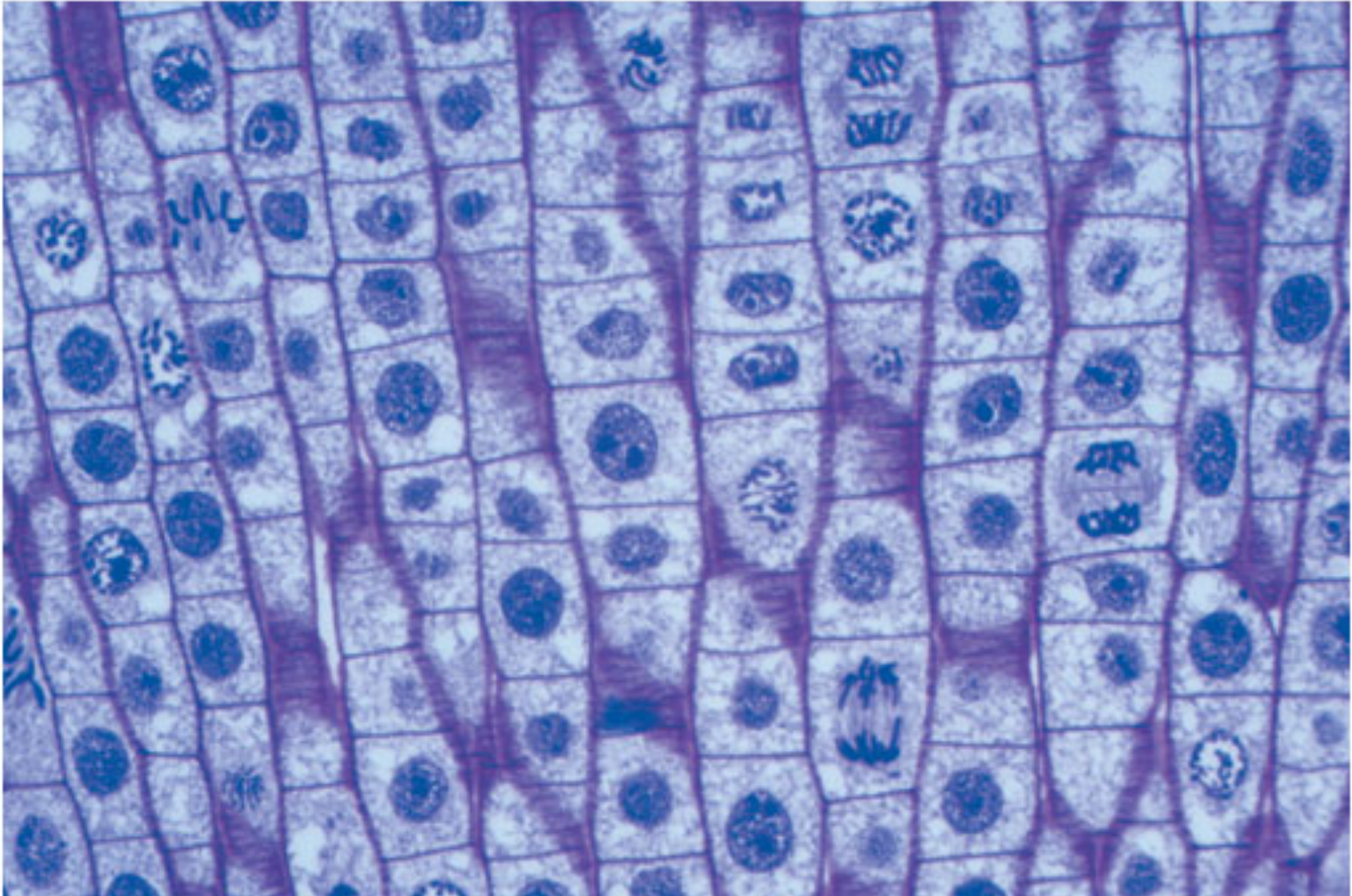


5 Telophase

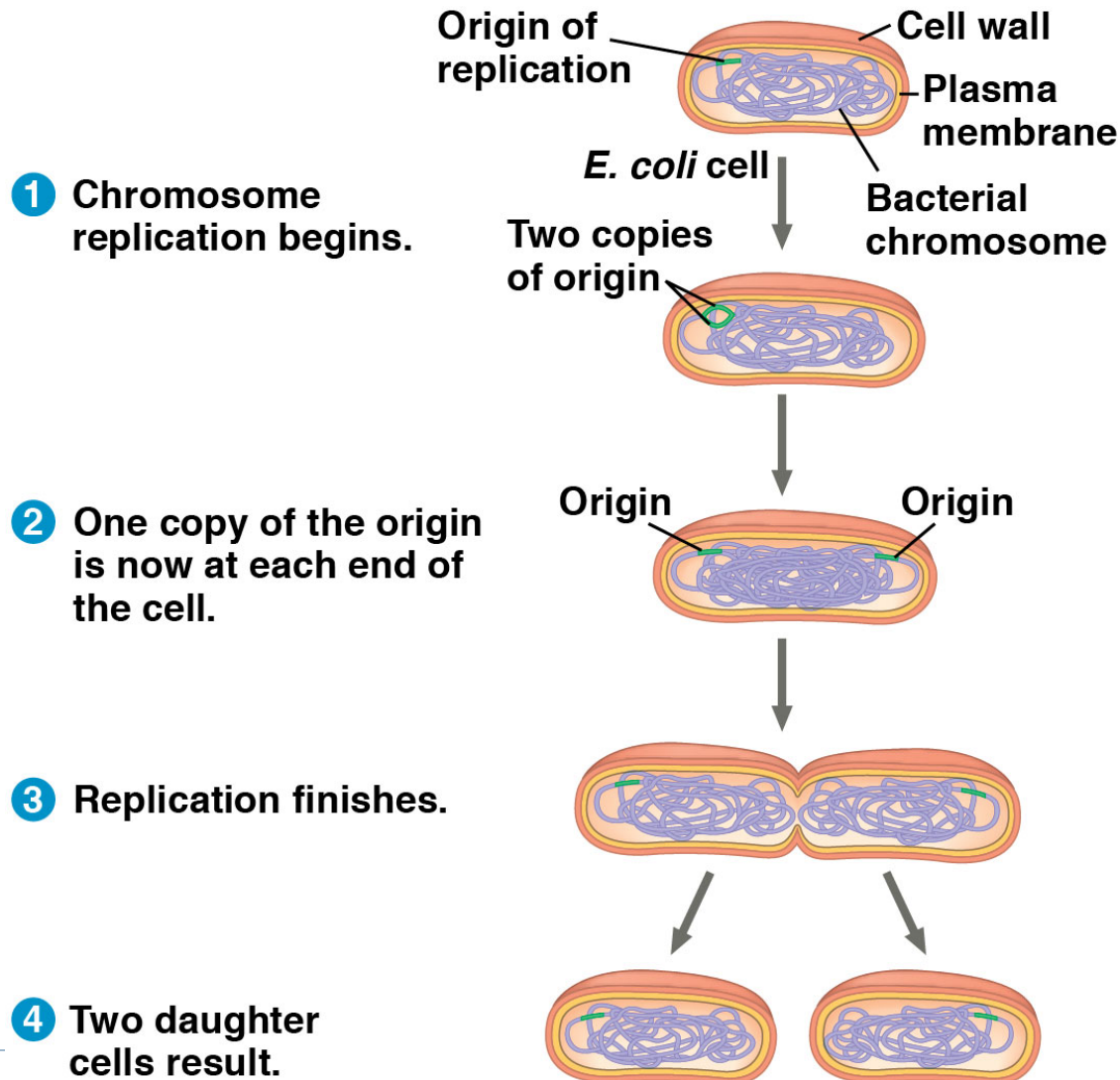
Which phases of the cell cycle can you identify?



Which phases of the cell cycle can you identify?

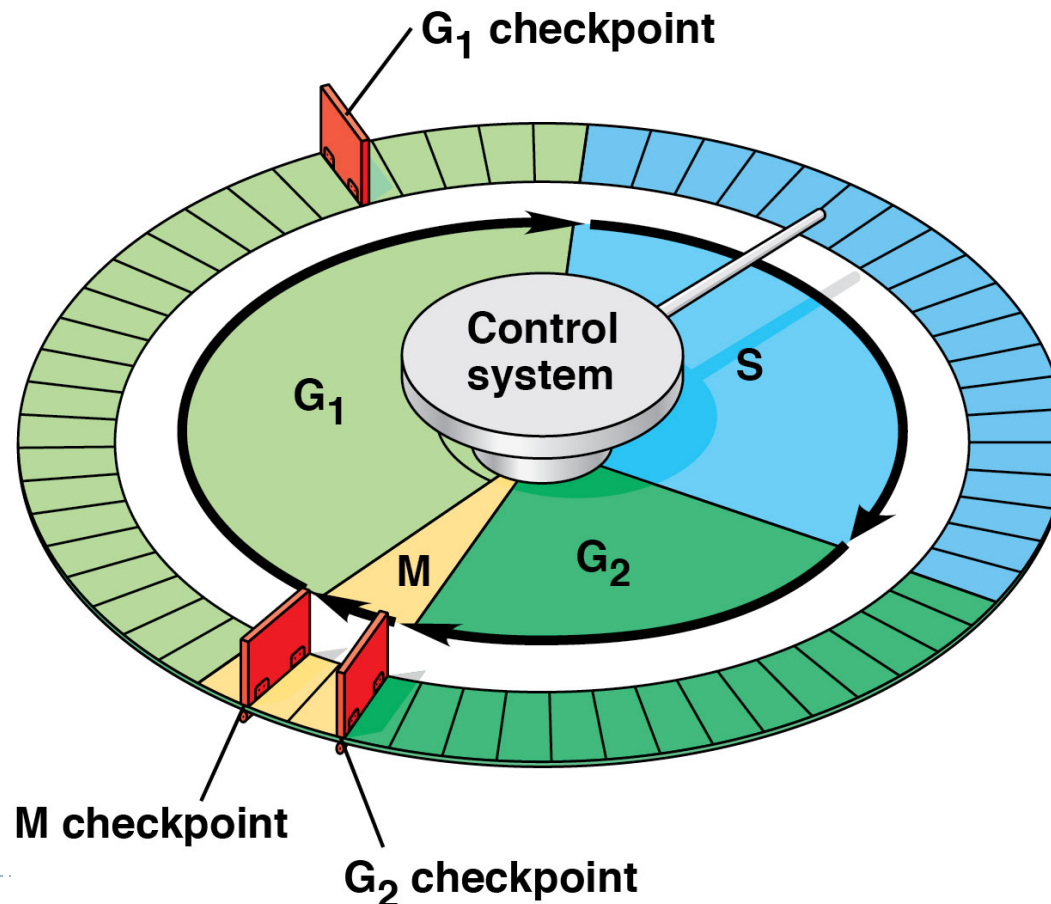


Bacterial cells divide by **Binary Fission**



Cell Cycle Control System

- ▶ **Checkpoint** = control point where **stop/go** signals regulate the cell cycle



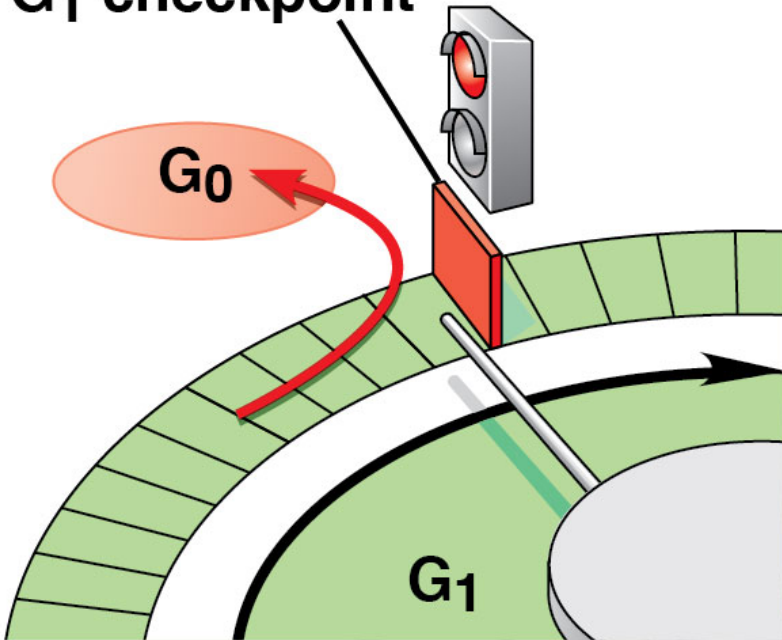
Major Checkpoints

1. **G₁ checkpoint** (Most important!)
 - ▶ Controlled by cell size, growth factors, environment
 - ▶ “Go” → completes whole cell cycle
 - ▶ “Stop” → cell enters nondividing state (G₀ Phase)
 - ▶ Nerve, muscle cells stay at G₀; liver cells called back from G₀
2. **G₂ checkpoint**
 - ▶ Controlled by DNA replication completion, DNA mutations, cell size
3. **M-spindle (Metaphase) checkpoint**
 - ▶ Check spindle fiber (microtubule) attachment to chromosomes at kinetochores (anchor sites)



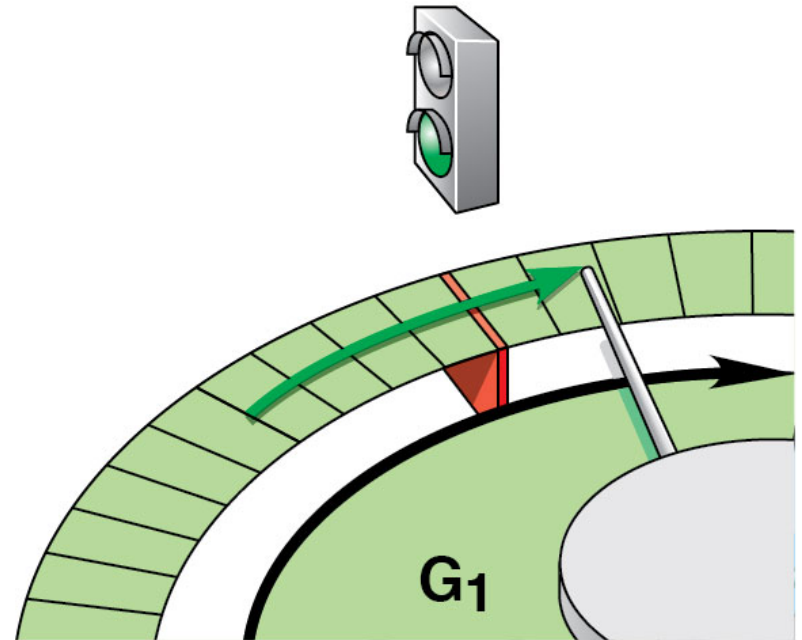
G₁ Checkpoint

G₁ checkpoint



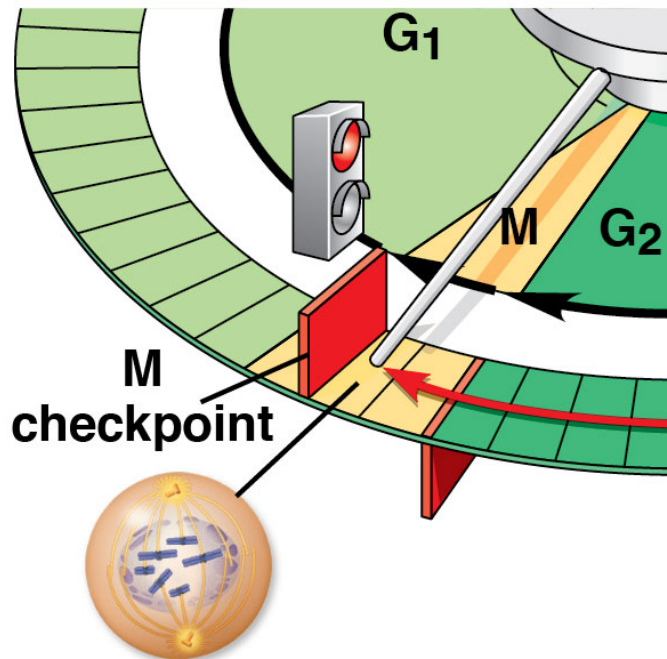
Without go-ahead signal, cell enters G₀.

(a) G₁ checkpoint



With go-ahead signal, cell continues cell cycle.

M Checkpoint

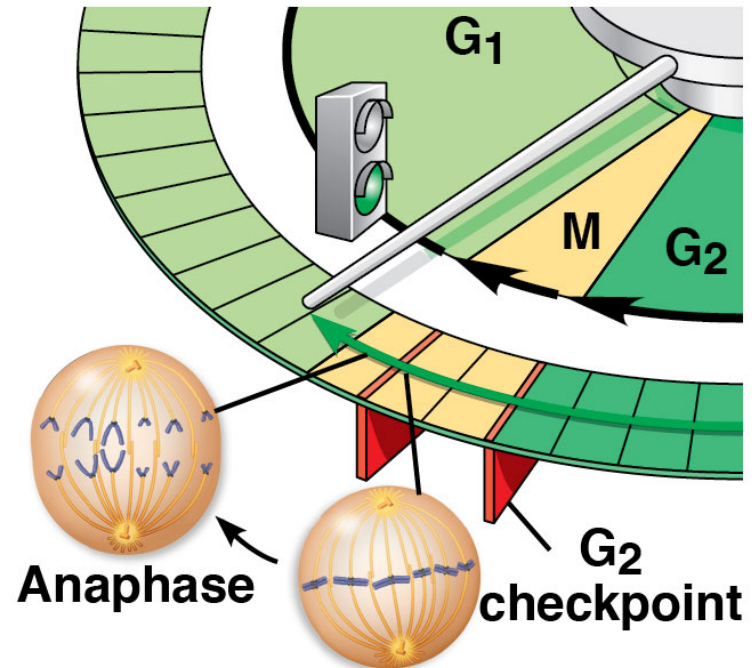


Prometaphase

Without full chromosome attachment, stop signal is received.

(b) M checkpoint

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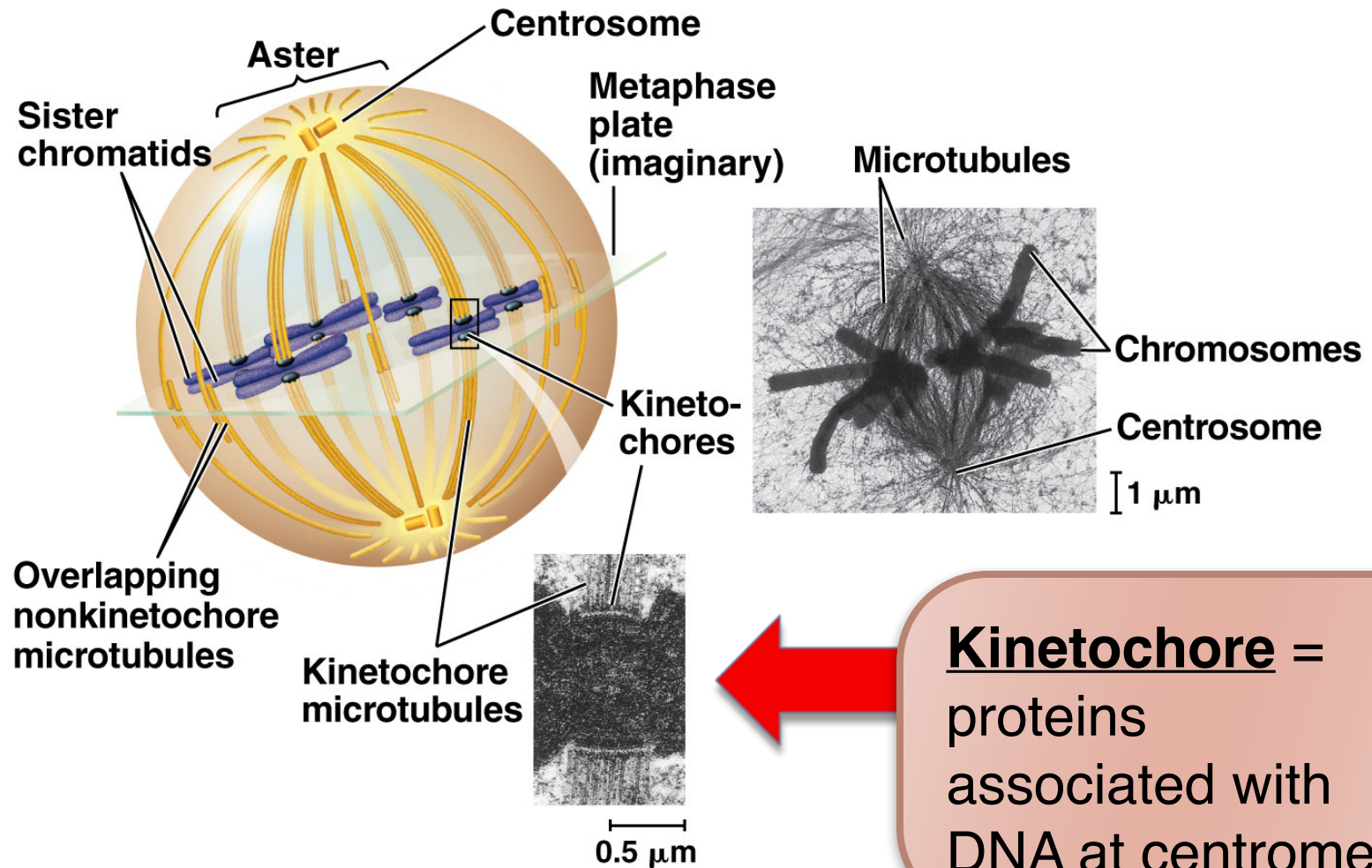


Metaphase

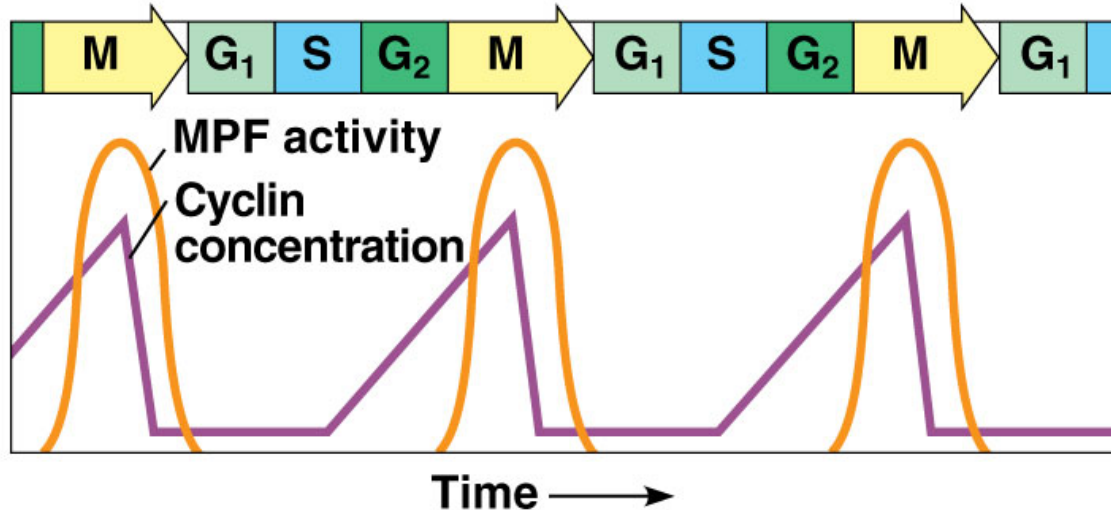
With full chromosome attachment, go-ahead signal is received.



M-spindle Checkpoint: Mitotic spindle at metaphase



Internal Regulatory Molecules



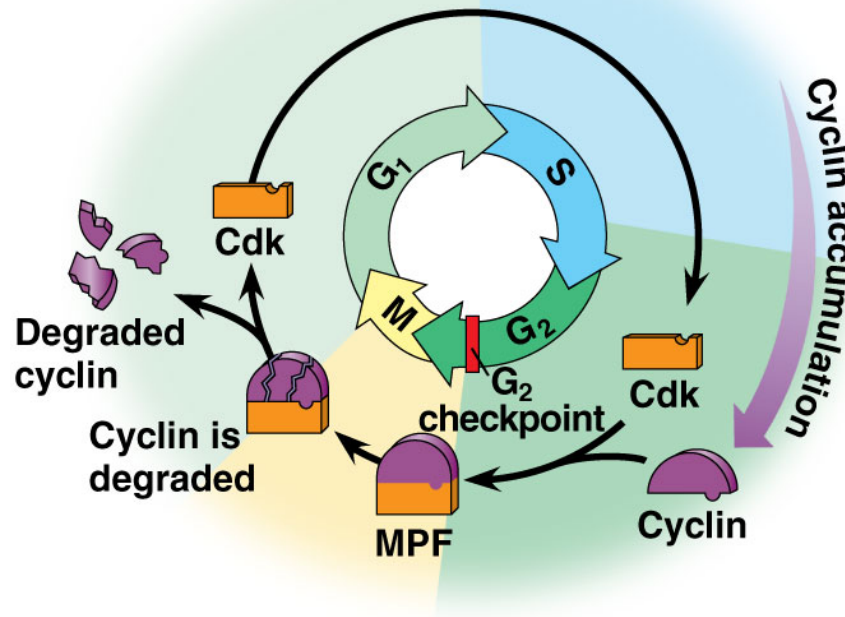
(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle

- **Kinases** (cyclin-dependent kinase, **Cdk**): protein enzyme controls cell cycle; active when connected to **cyclin**
- **Cyclins**: proteins which attach to kinases to activate them; levels fluctuate in the cell cycle

Internal Regulatory Molecules

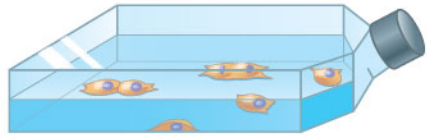
MPF = maturation-promoting factor

- specific **cyclin-Cdk complex** which allows cells to pass G_2 and go to M phase

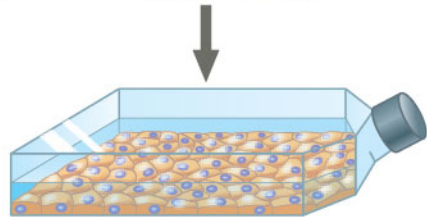


(b) Molecular mechanisms that help regulate the cell cycle

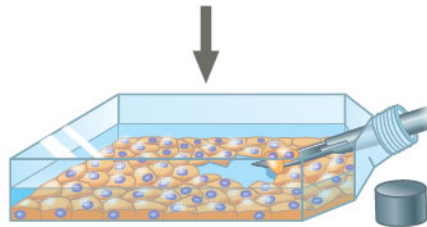
External Regulatory Factors



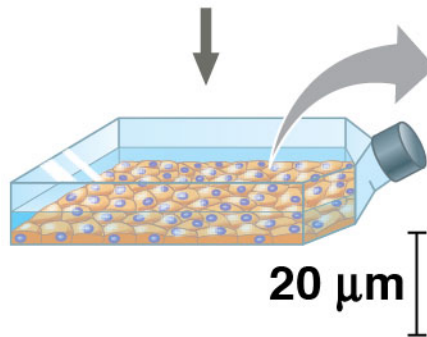
Anchorage dependence: cells require a surface for division



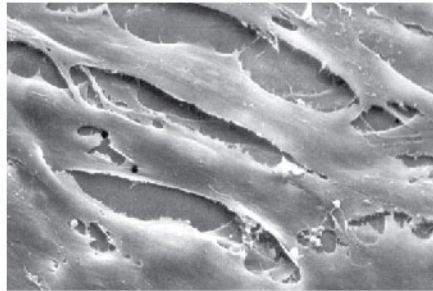
Density-dependent inhibition: cells form a single layer



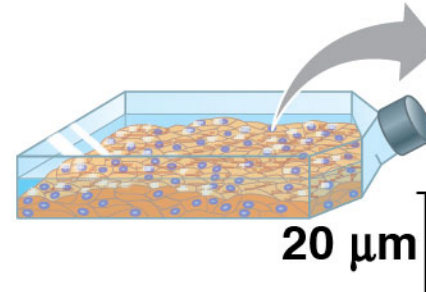
Density-dependent inhibition: cells divide to fill a gap and then stop



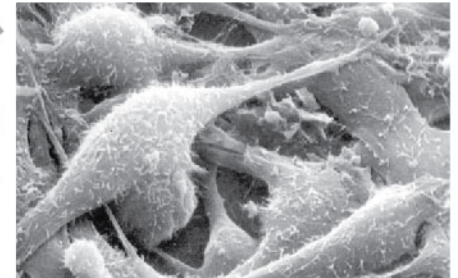
20 µm



(a) Normal mammalian cells



20 µm



(b) Cancer cells

External Regulatory Factors

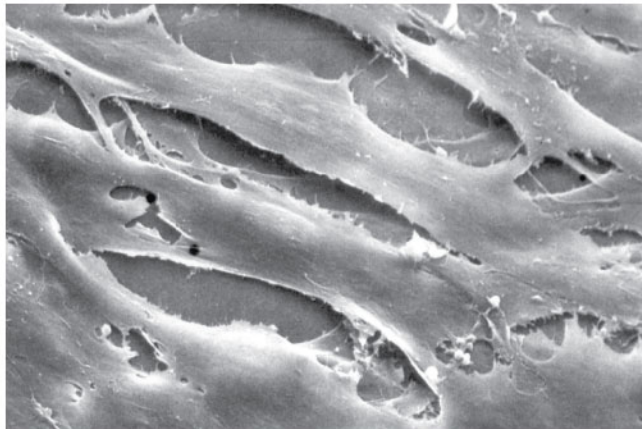
- ▶ Growth Factor: proteins released by other cells to stimulate cell division
- ▶ Density-Dependent Inhibition: crowded cells normally stop dividing; cell-surface protein binds to adjoining cell to inhibit growth
- ▶ Anchorage Dependence: cells must be attached to another cell or ECM (extracellular matrix) to divide



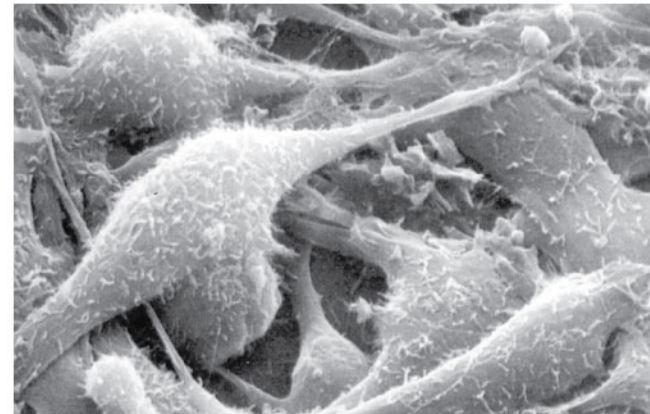
Cancer Cells

Cancer: Disorder in which cells lose the ability to control growth by not responding to regulation.

- ▶ multistep process of about 5-7 genetic changes (for a human) for a cell to transform
- ▶ loses anchorage dependency and density-dependency regulation



(a) Normal mammalian cells

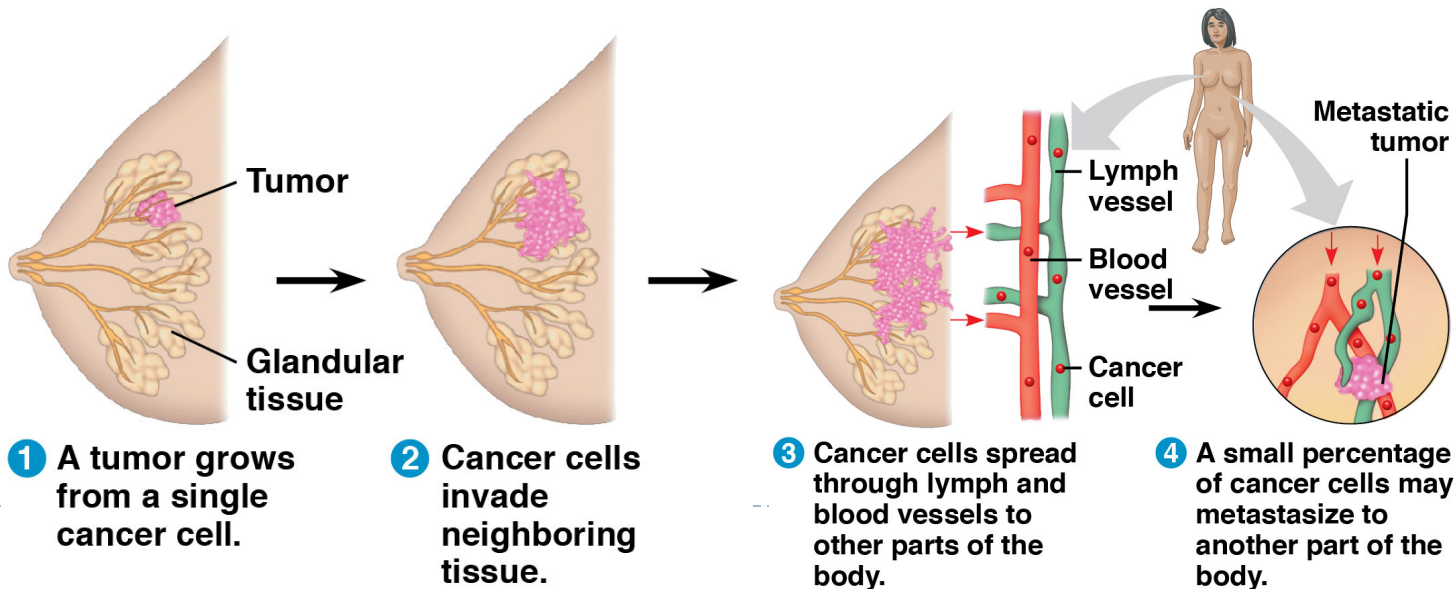


(b) Cancer cells

Transformation: Process that converts a normal cell to a cancer cell

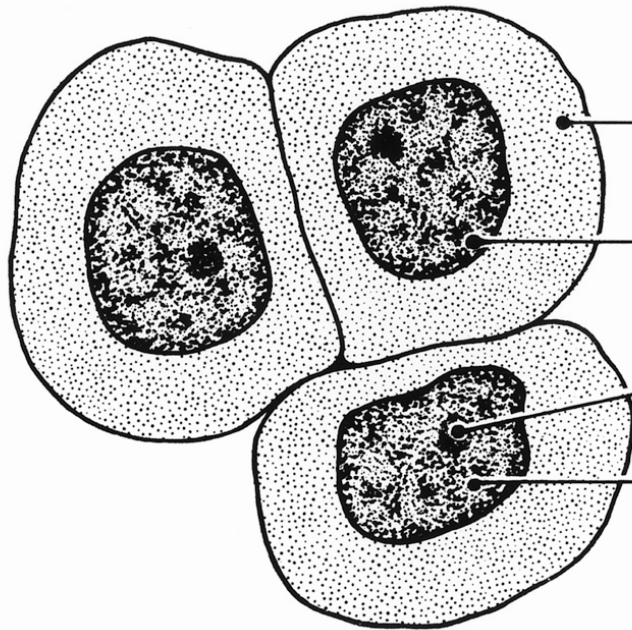
Tumors = mass of abnormal cells

- ▶ **Benign tumor:** lump of cells remain at original site
- ▶ **Malignant tumor:** invasive - impairs functions of 1+ organs (called cancer)
- ▶ **Metastasis:** cells separate from tumor and travel to other parts of body



Normal and Cancer Cells Structure

Normal



Cytoplasm

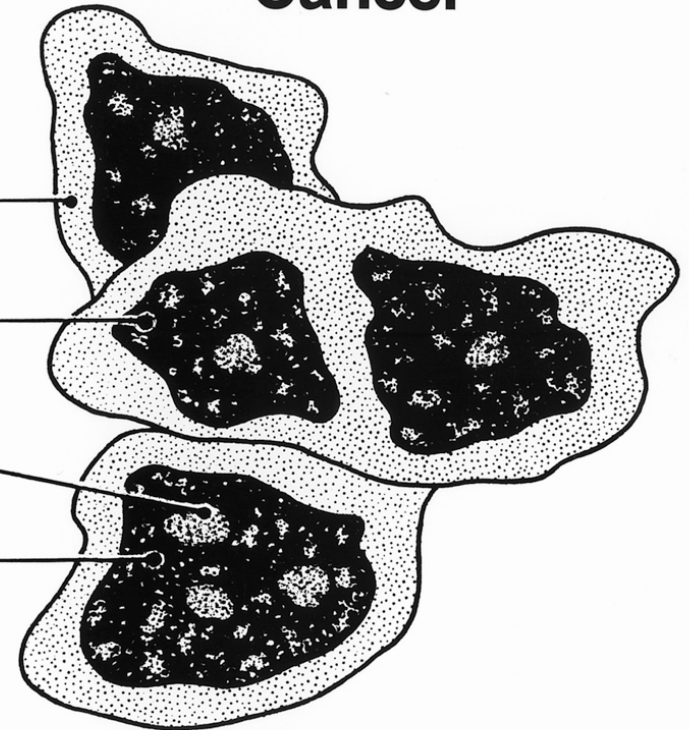
Nucleus

Nucleolus

Chromatin

- Large cytoplasm
- Single nucleus
- Single nucleolus
- Fine chromatin

Cancer



- Small cytoplasm
- Multiple nuclei
- Multiple and large nucleoli
- Coarse chromatin

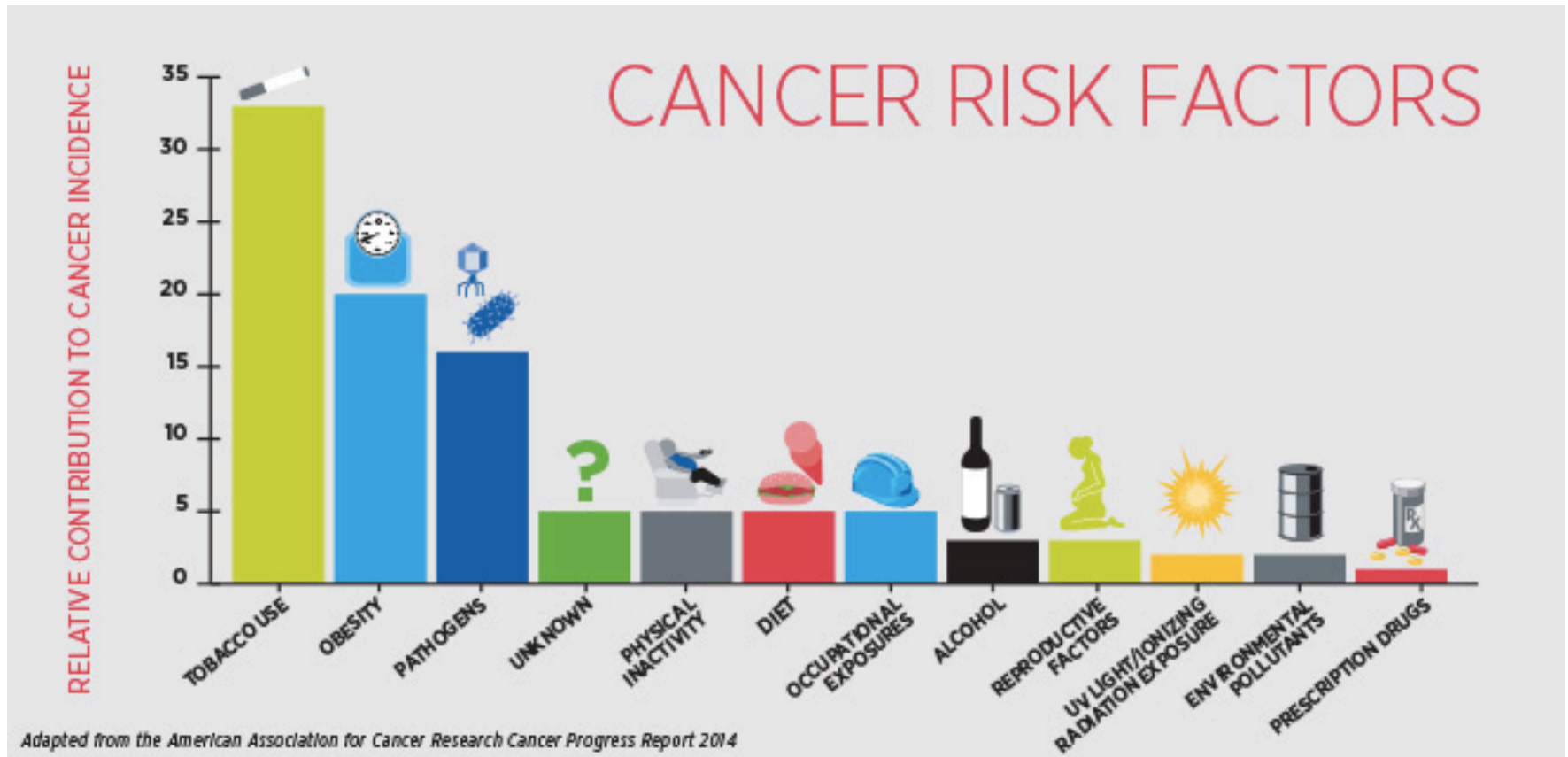
Cancer Cells

- ▶ Some have abnormal #'s of chromosomes
- ▶ Metabolism disabled
- ▶ Lose attachment to ECM → spread to other tissues
- ▶ Signaling molecules cause blood vessels to grow toward tumor

Treatment:

- ▶ Surgery, radiation, chemotherapy
- ▶ Personalized Medicine:
 - ▶ Breast Cancer: 20-25% tumors show high HER2 receptors → use Herceptin to block HER2 protein

Cancer Risk Factors



Anyone can get cancer but there are ways to **minimize** risk:

- ▶ Don't smoke, legal or illegal (includes hookahs, chew, 2nd-hand smoke)
- ▶ Use sun protection
- ▶ Exercise and keep weight at ideal level
- ▶ Eat 5-7 servings of fruit and veggies **a day**
- ▶ Use screening/preventative measures-breast/testicle/mole checks
- ▶ Practice abstinence or use condoms
- ▶ Vaccines (eg. HPV)





 American Institute for Cancer Research

10 CANCER PREVENTION RECOMMENDATIONS

- MAINTAIN A HEALTHY WEIGHT** (Icon: scale)
- MOVE MORE** (Icon: person running)
- EAT WELL** (Icon: apple)
- ENJOY A PLANT BASED DIET** (Icon: leafy vegetable)
- REDUCE RED MEAT, AVOID PROCESSED MEAT** (Icon: steak)
- CUT DOWN ON ALCOHOL** (Icon: wine glass)
- EAT LESS SALT** (Icon: salt shaker)
- AFTER TREATMENT, CANCER SURVIVORS SHOULD FOLLOW THE CANCER PREVENTION RECOMMENDATIONS** (Icon: person with bandage)
- IF YOU CAN, BREASTFEED YOUR BABY** (Icon: person holding baby)
- FOR CANCER PREVENTION DON'T USE SUPPLEMENTS** (Icon: pills)

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CANCER PREVENTION
Together We Can®

And always remember – do not smoke or chew tobacco.

Summary of the Cell Cycle

