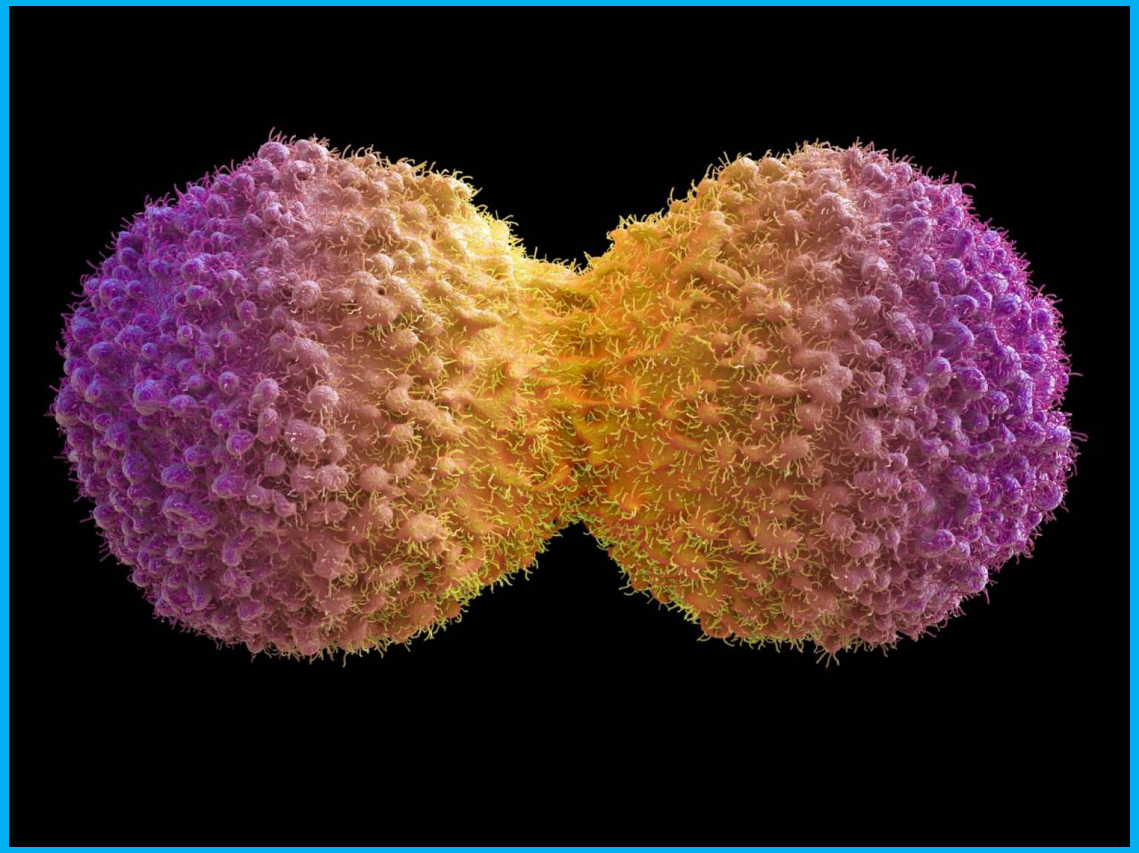


Cell Division

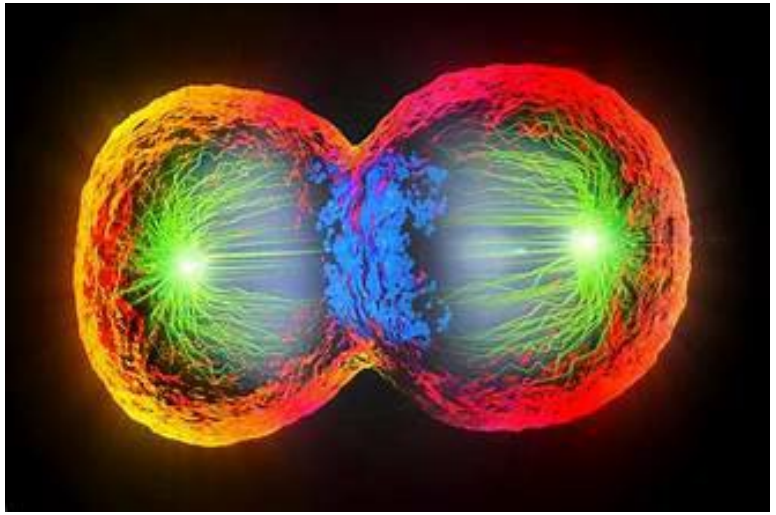
Marjorie D. Shaw, Ph.D.

OLLI Fall 2023

Study Group : 426

Life Comes From Life

Every cell comes from a previous cell, going back to the very first cell 3 billion years ago. An unbroken line of cells dividing.



Cells must
1) duplicate their contents
2) partition the duplicated contents and break into two
3) coordinate all these processes

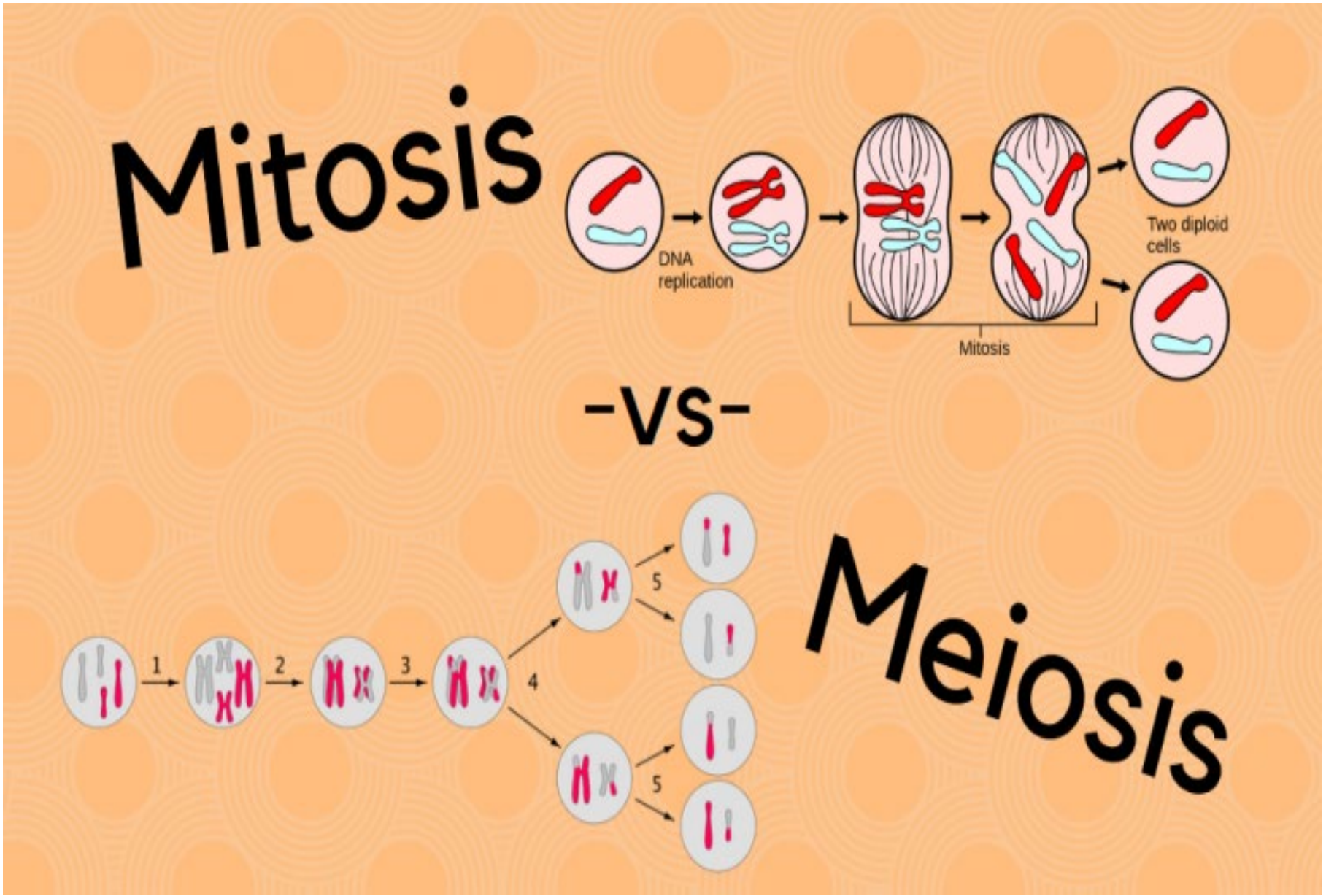
Cell Cycle : growth and division.

The enzymes needed for cell cycle in humans are essentially the same as those in yeast.

Two types of division

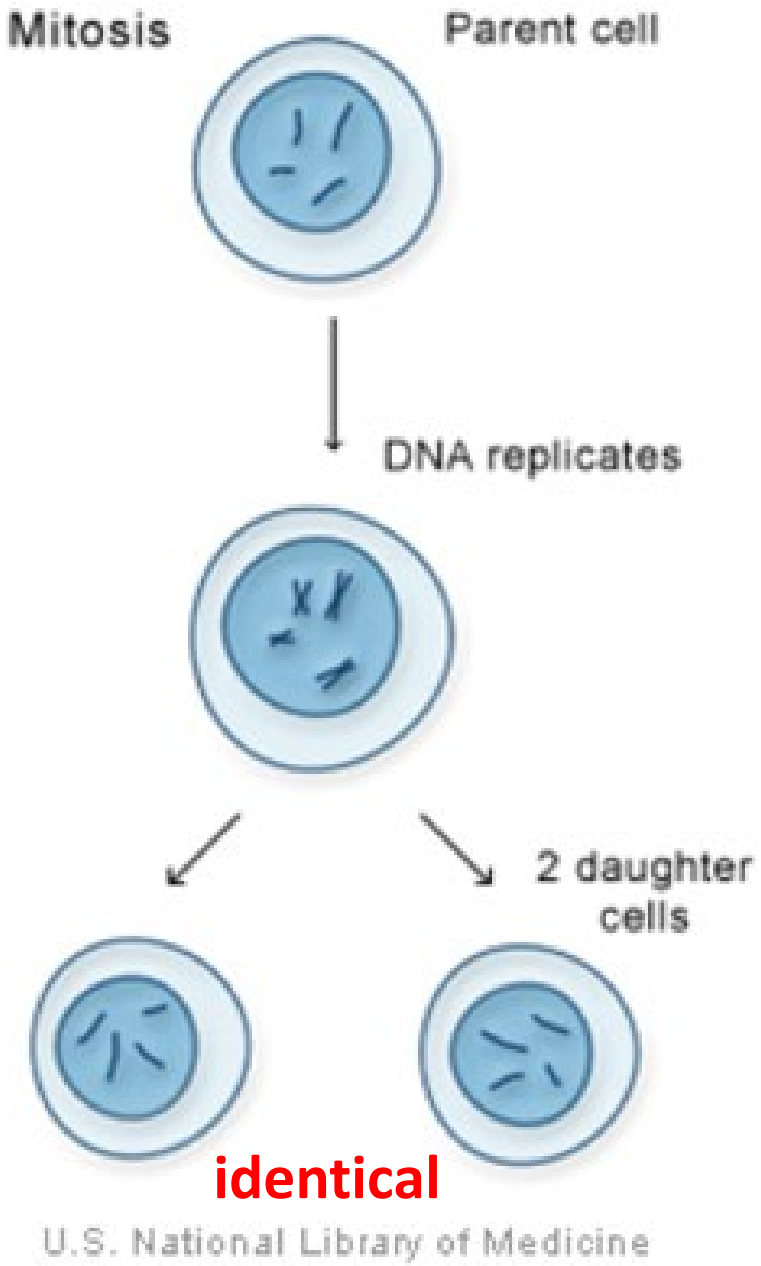
Mitosis: produces new somatic cells; identical to original. 23 **pairs** of chromosomes (diploid).

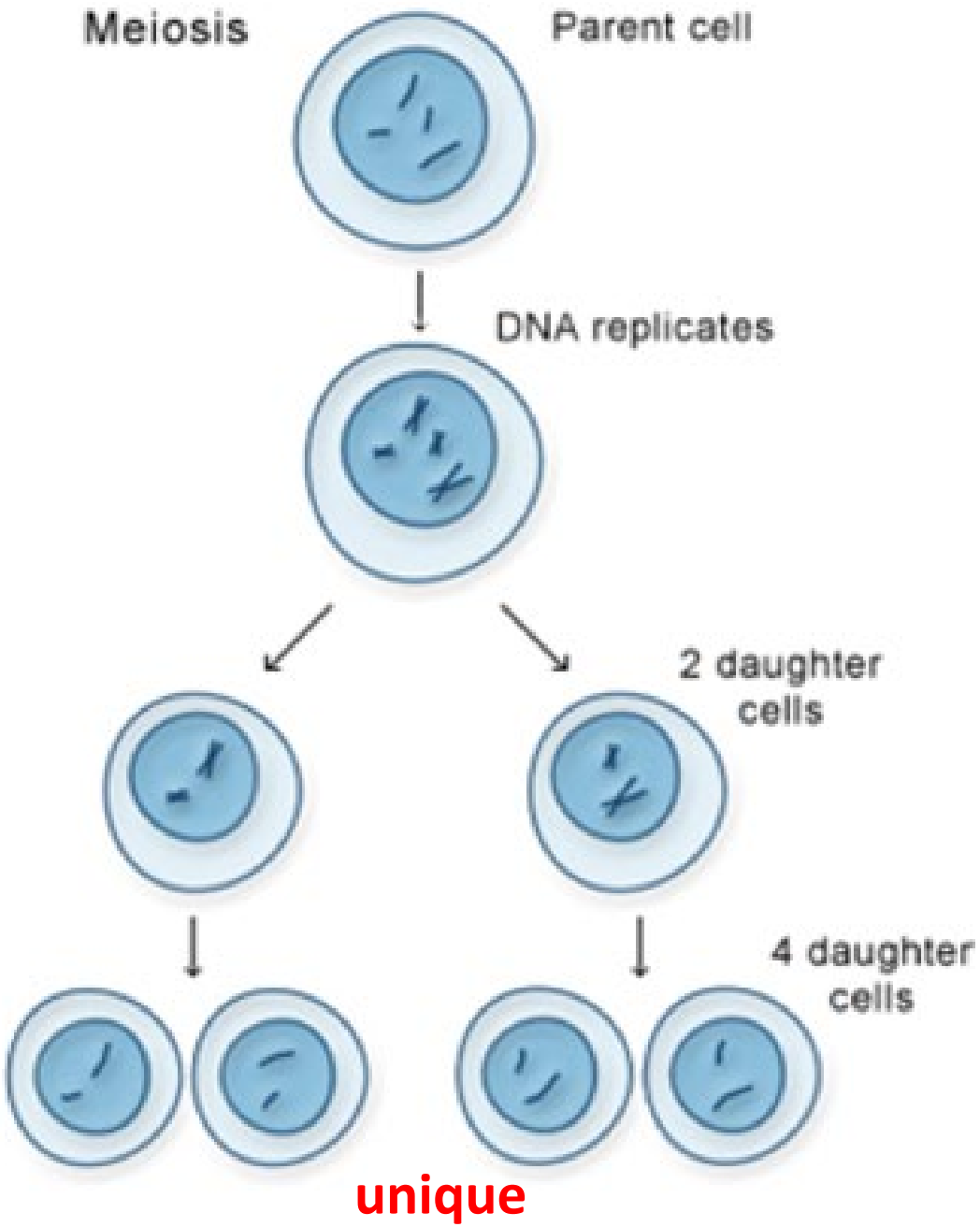
Meiosis: produces cells for sexual reproduction (sperm, ova); 23 **single** copies of chromosomes (haploid).



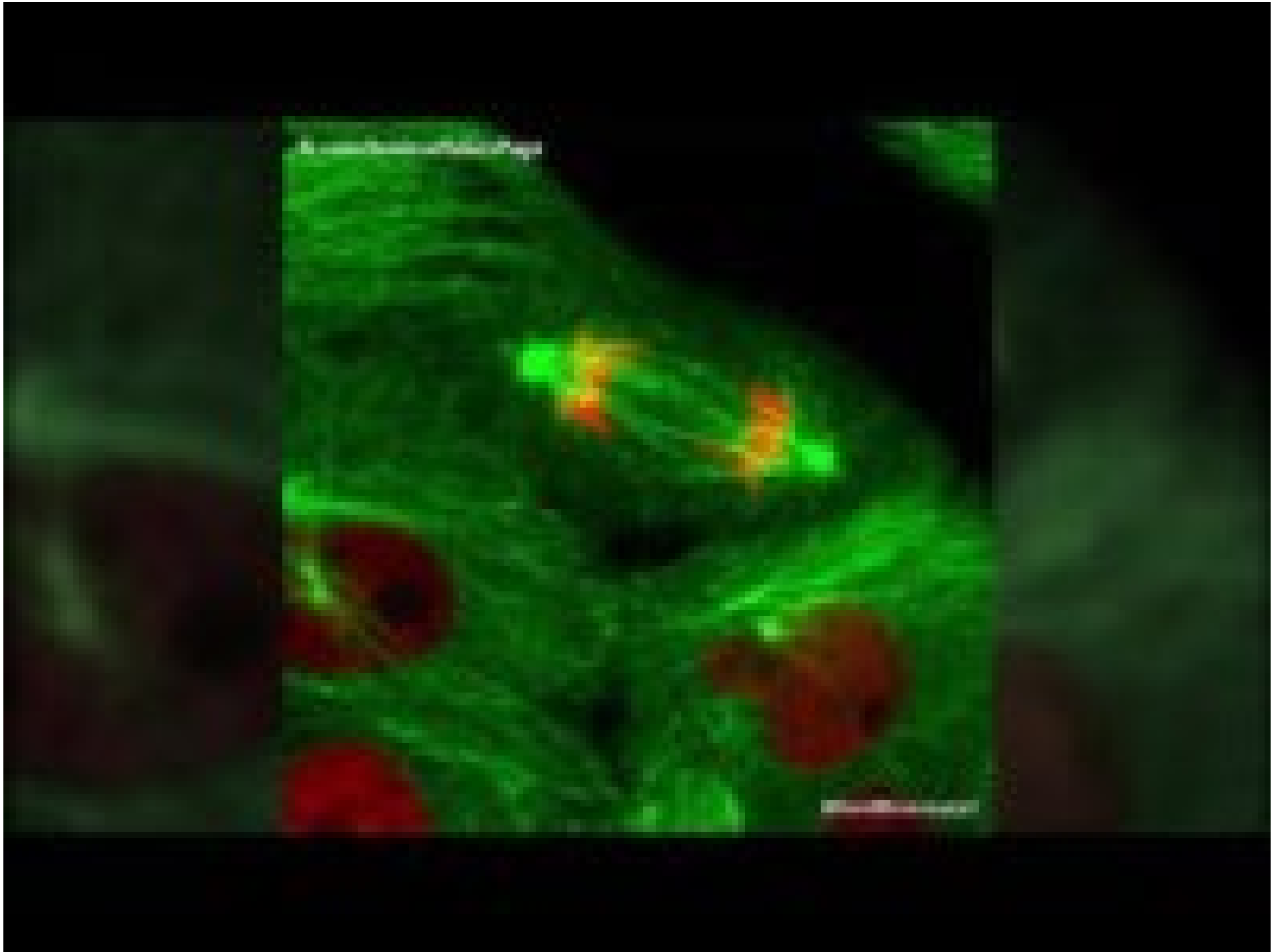
Mitosis vs Meiosis

2 identical daughter cells vs four unique gametes (sperm or ova).



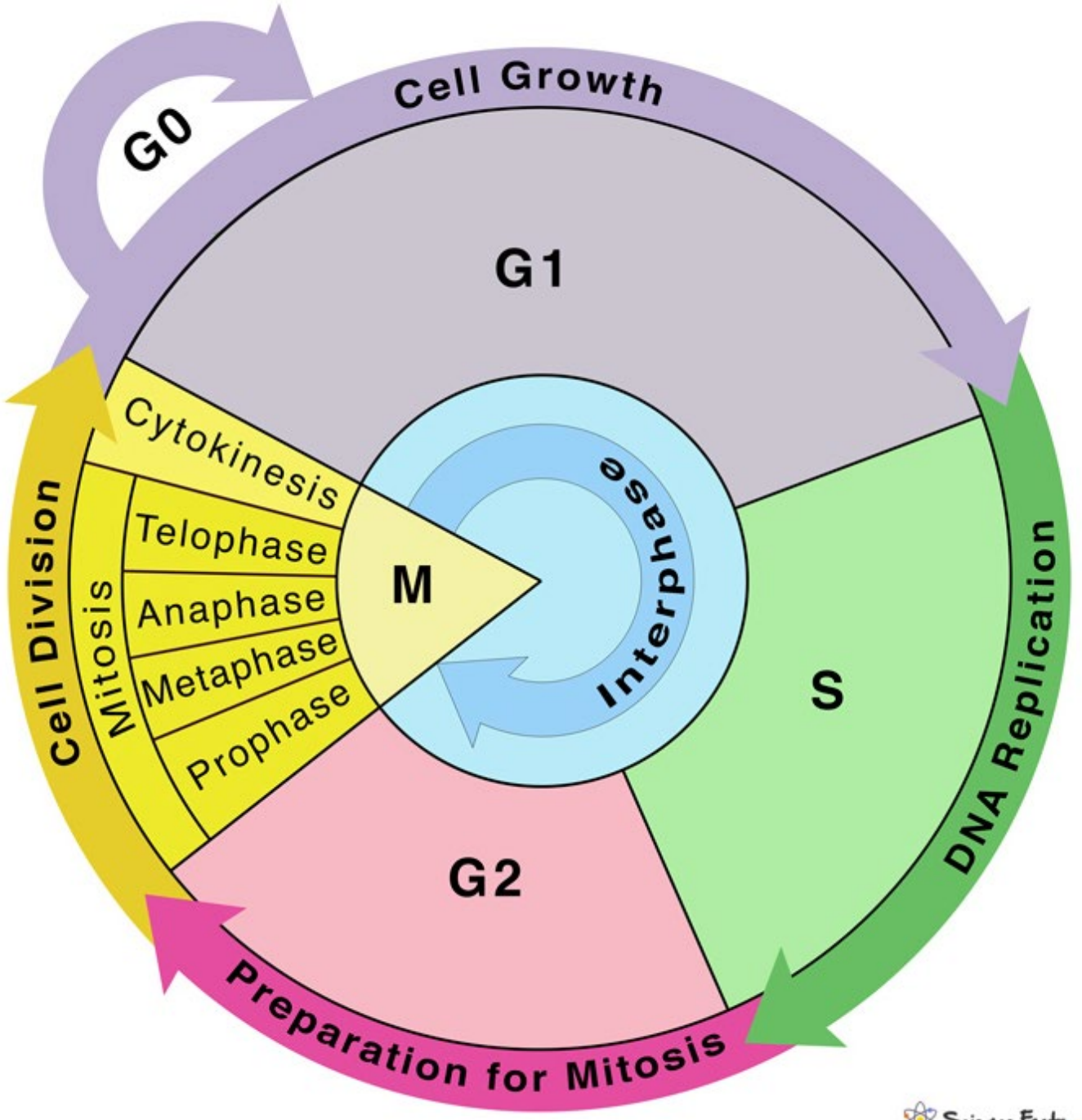


Live Action!



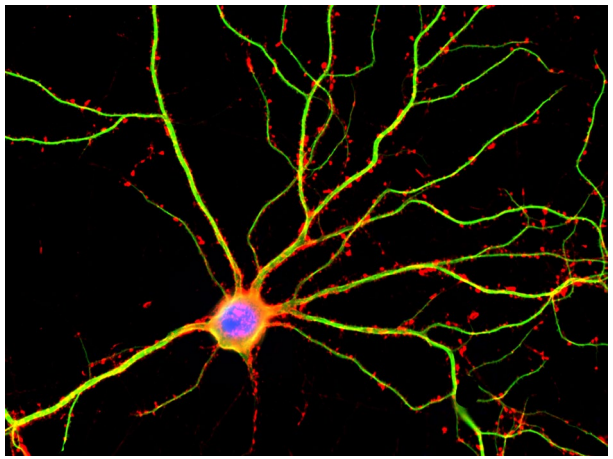
Mitosis: Part of Cell Cycle

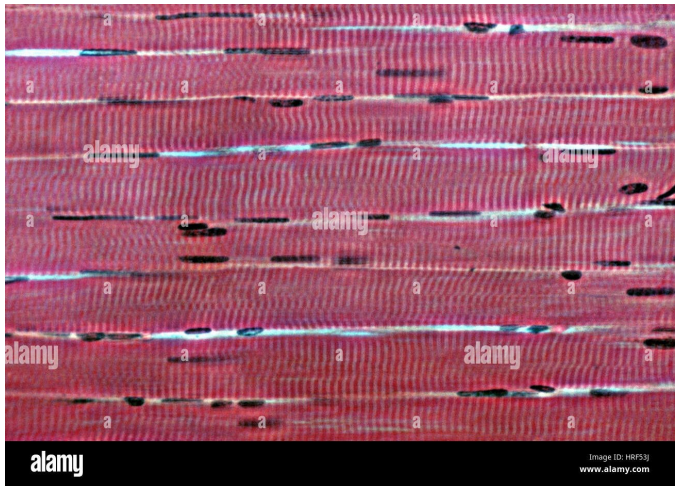
May occur daily or not for 100 years.
Mitosis vs **interphase**.
Mitosis is one part of the cell cycle ~ 1 hour

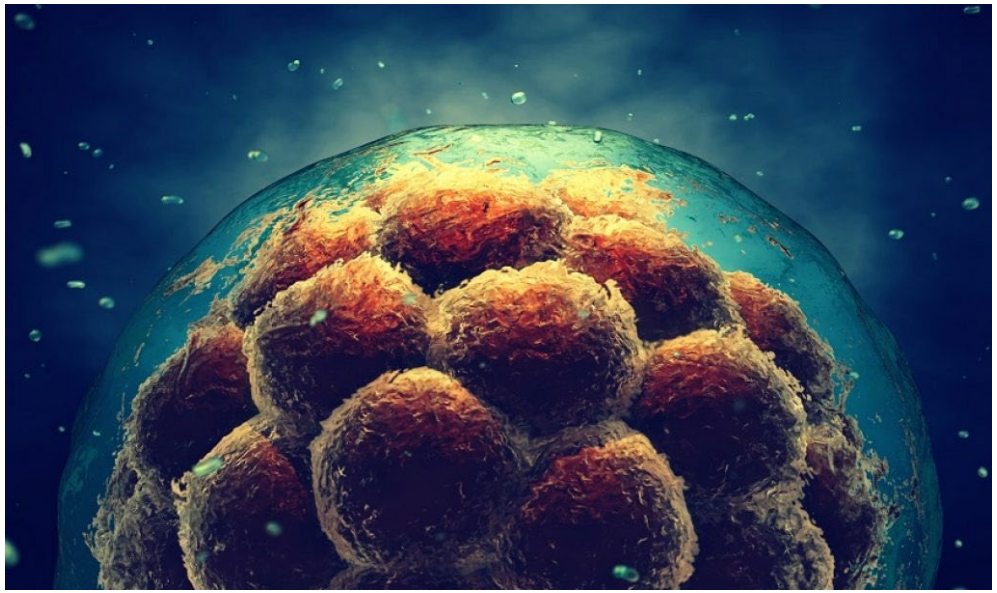


G_0: mature, functioning cells

Skeletal muscle, neurons, heart muscle remain in G_0 indefinitely (**terminal differentiation**). Stem cells of the embryo never enter G_0

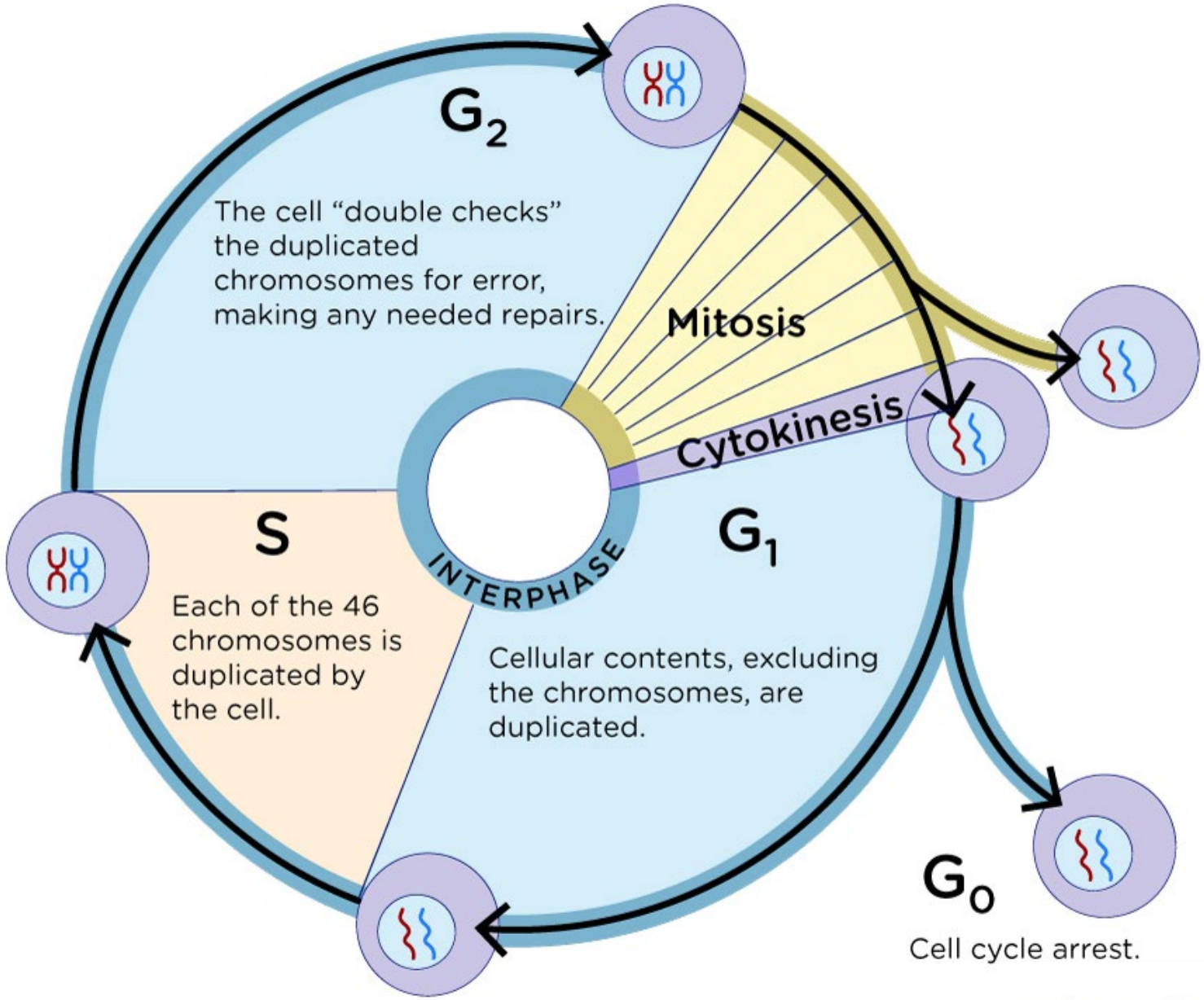






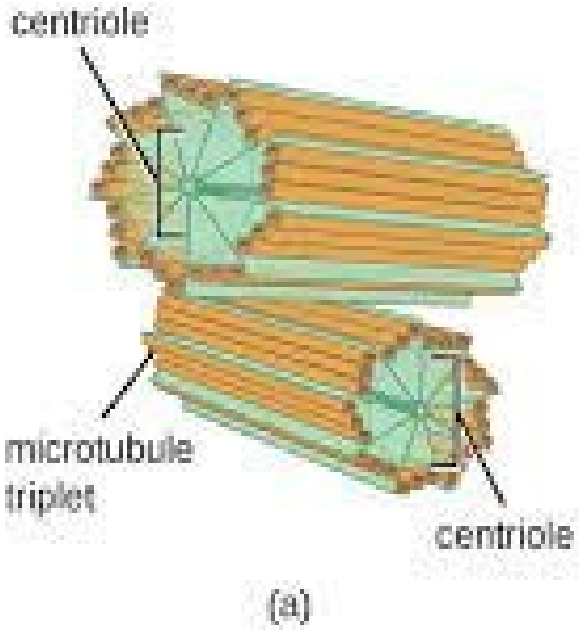
G1: growth

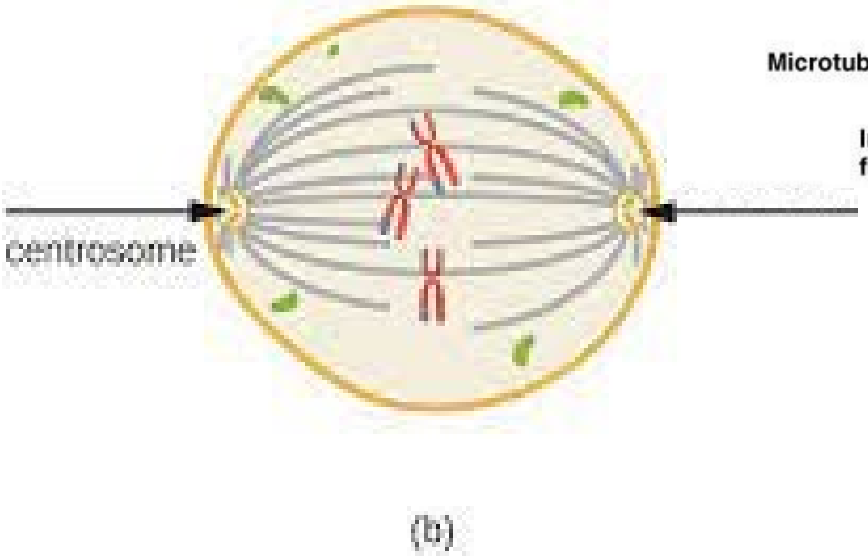
Not much to see, but the cell grows and most organelles are duplicated: mitochondria, ER, ribosomes, cytoskeleton, the enzymes needed for DNA transcription etc. but **not DNA**. Centriole replication begins.

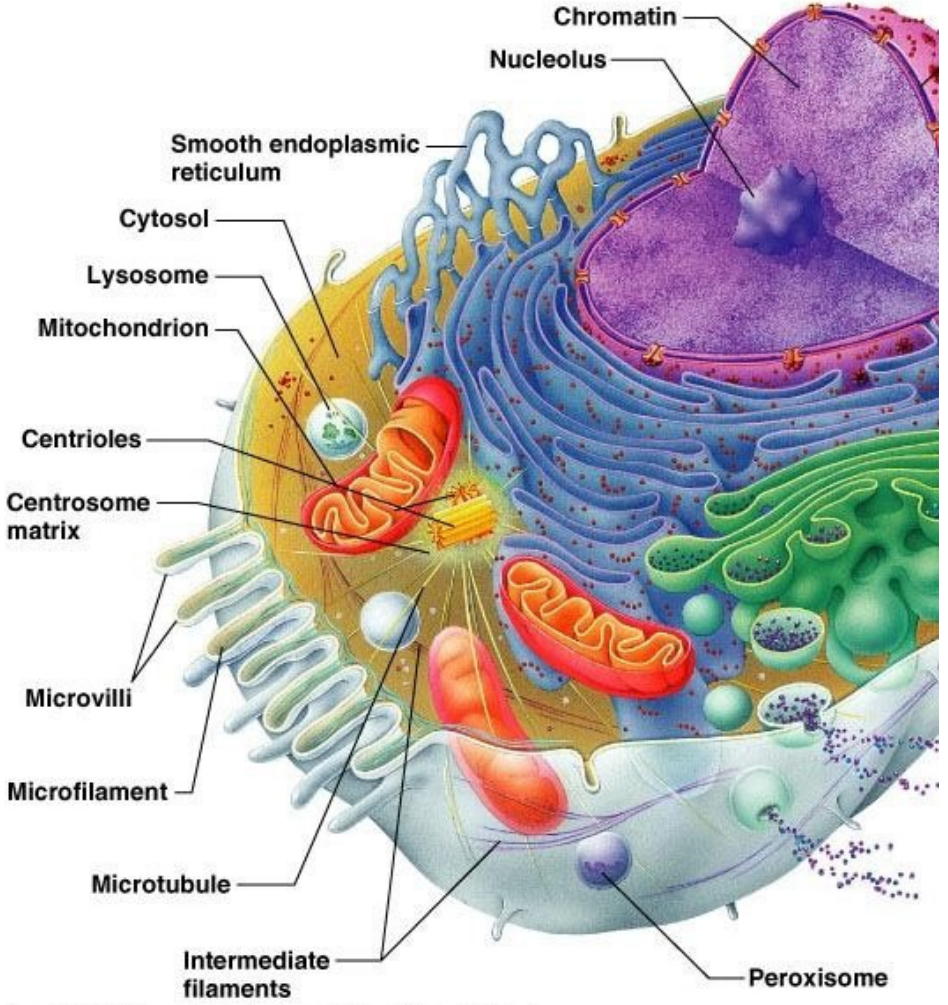


Centrosome

Has 2 centrioles. Organizing center for microtubules; makes the mitotic spindle to pull the chromatids apart. Must duplicate, so each new cell has copies of each of the pair.







G1 Checkpoint

Allows entry into S phase *only if* environmental and internal factors are favorable.

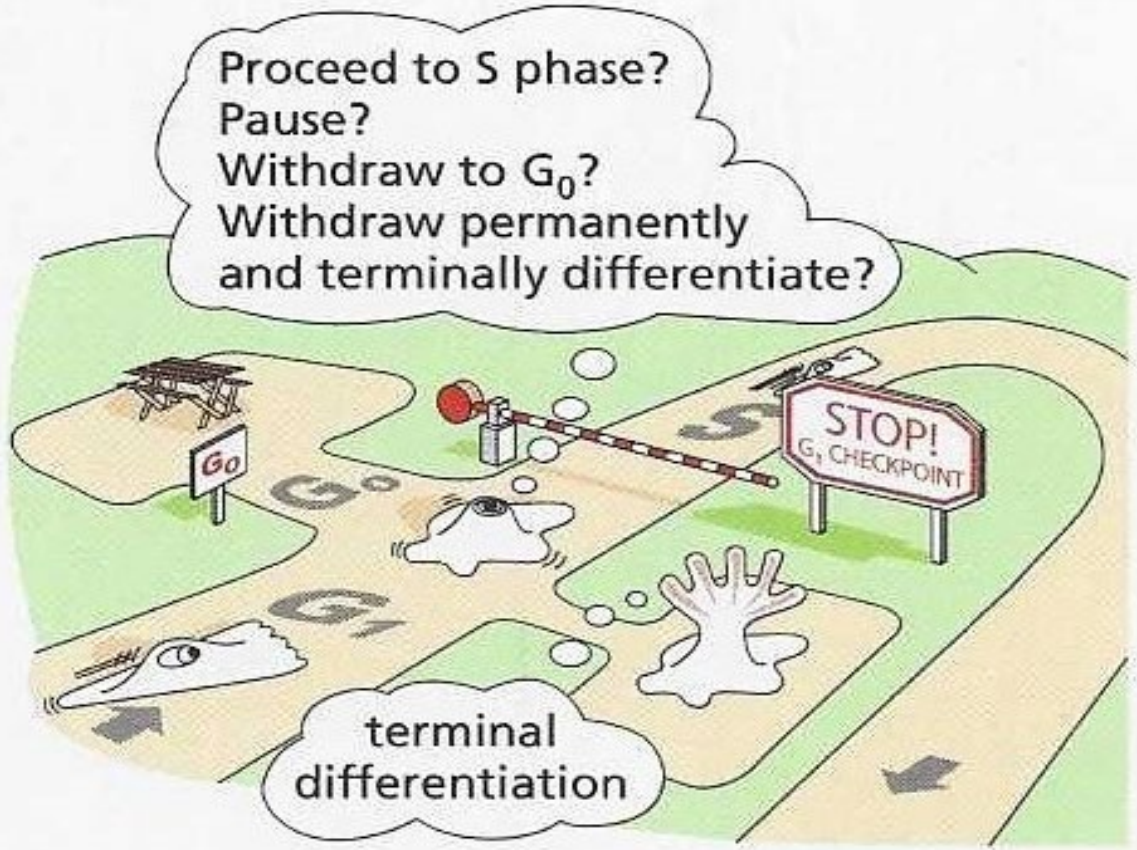


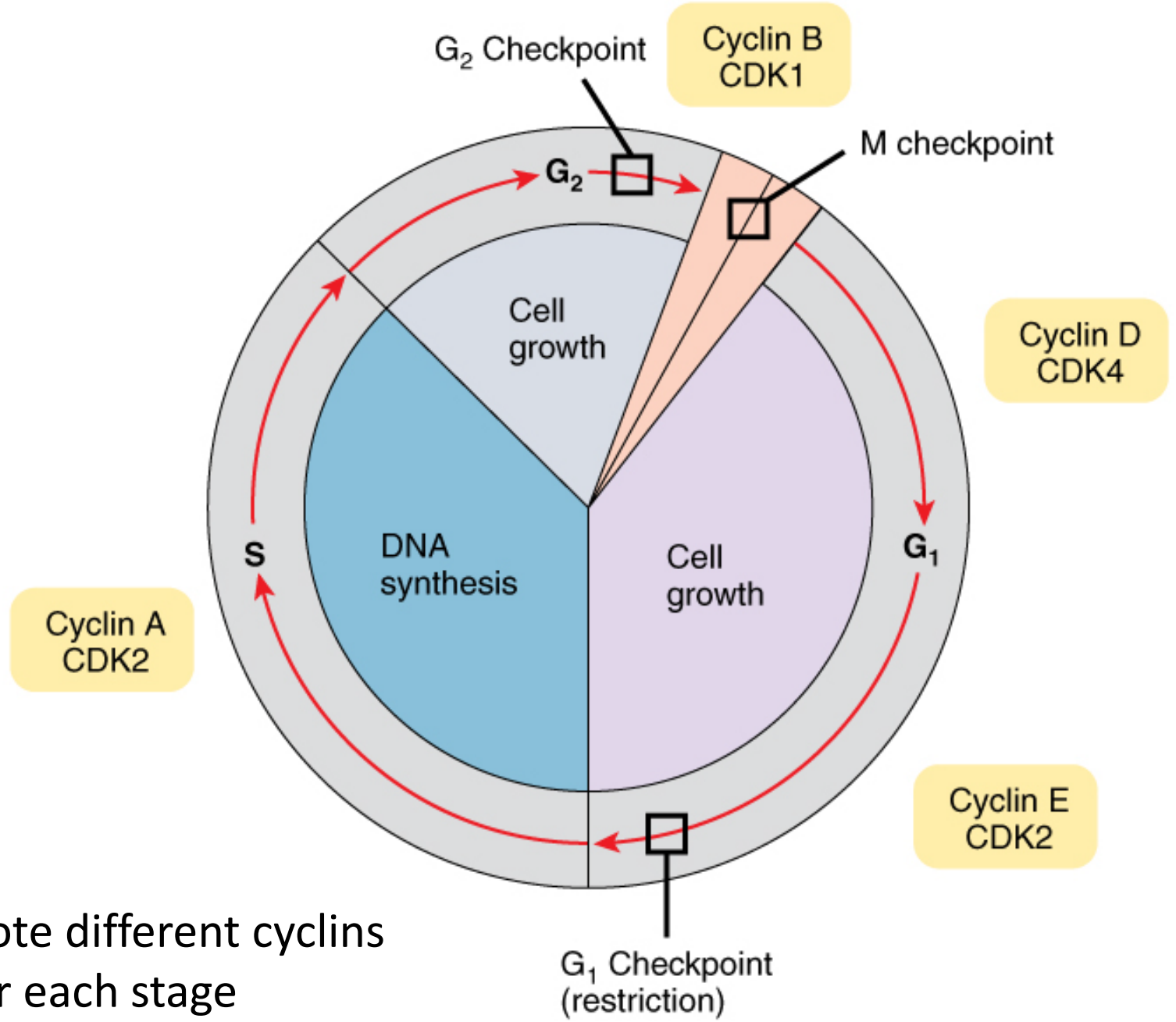
Figure 18–14 The Start transition offers the cell a crossroad. The cell can commit to completing another cell cycle, pause temporarily until conditions are right, or withdraw from the cell cycle altogether—either temporarily in G_0, or permanently in the case of terminally differentiated cells.

G1 checkpoint

Checks:
Growth factors
Nutrients
Cell size
DNA damage

If not ready, stays longer in G1 or goes back to G0.

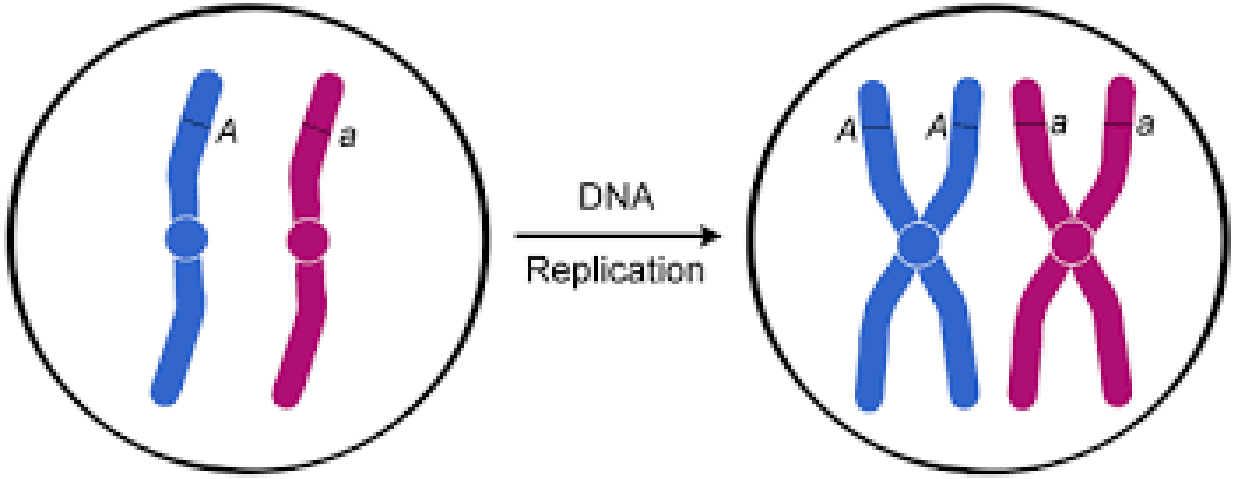
If enough Cyclin E protein has accumulated, it will cause transition to S phase by activating the enzymes needed.

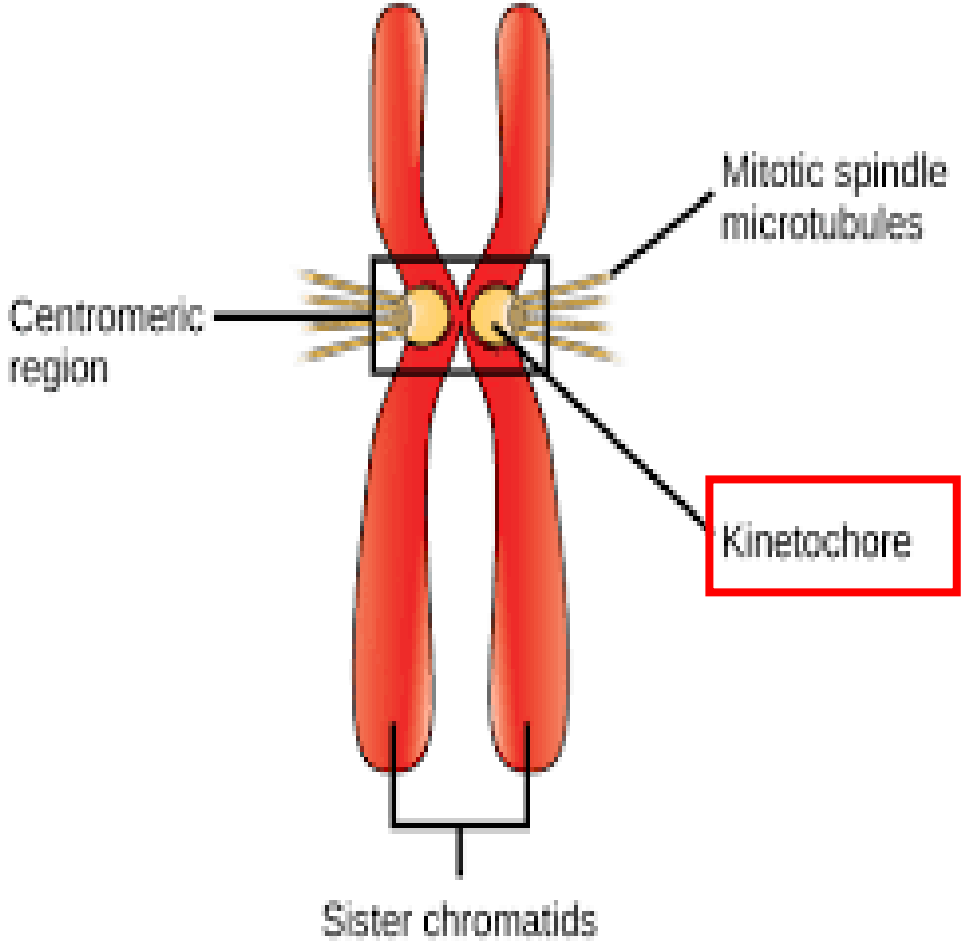


Note different cyclins for each stage

S phase: Transcription of DNA

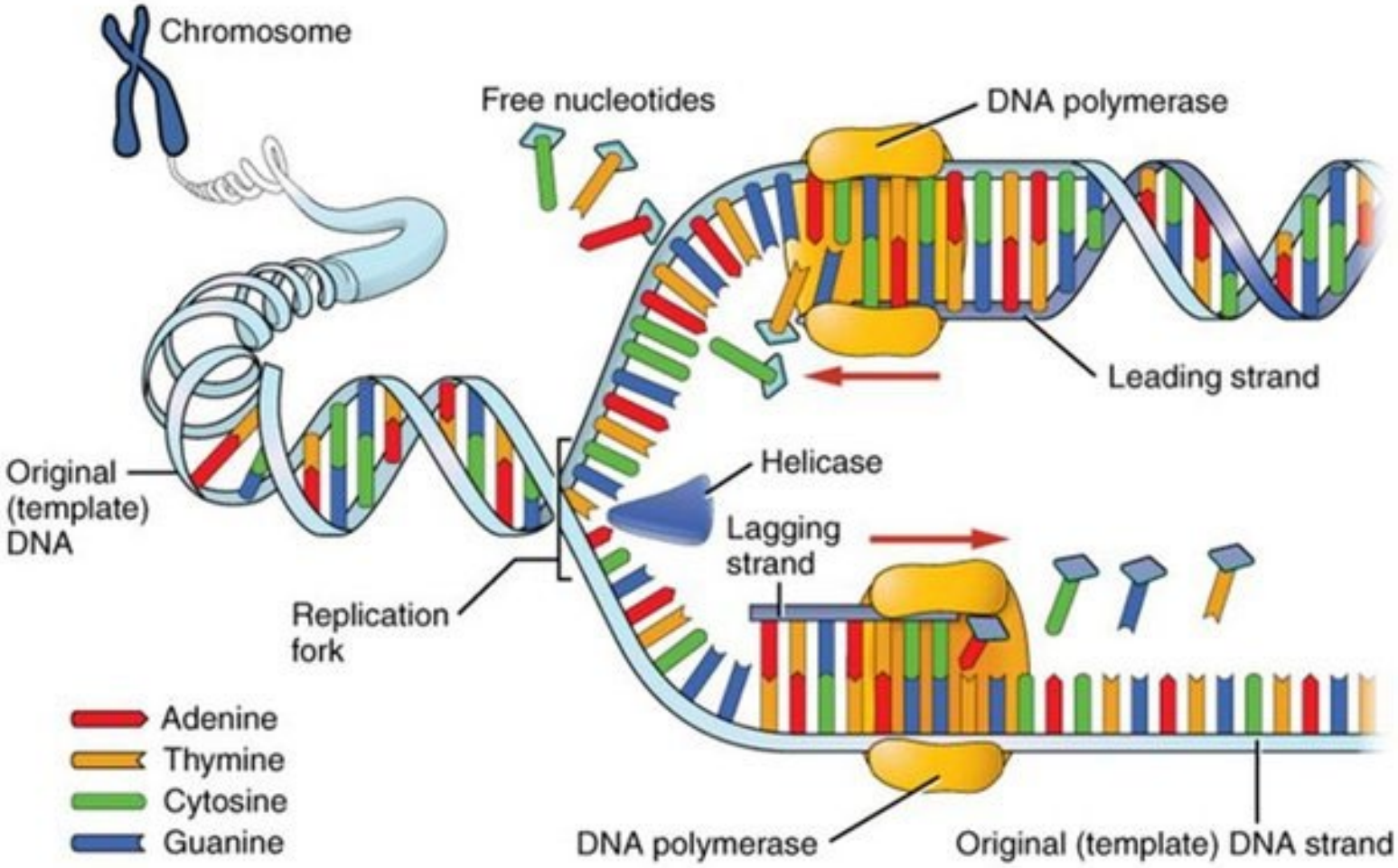
Same number of chromosomes, but each has two identical sister **chromatids**. The center region (centromere) has a protein (**kinetochore**) that will attach to microtubules of the spindle.





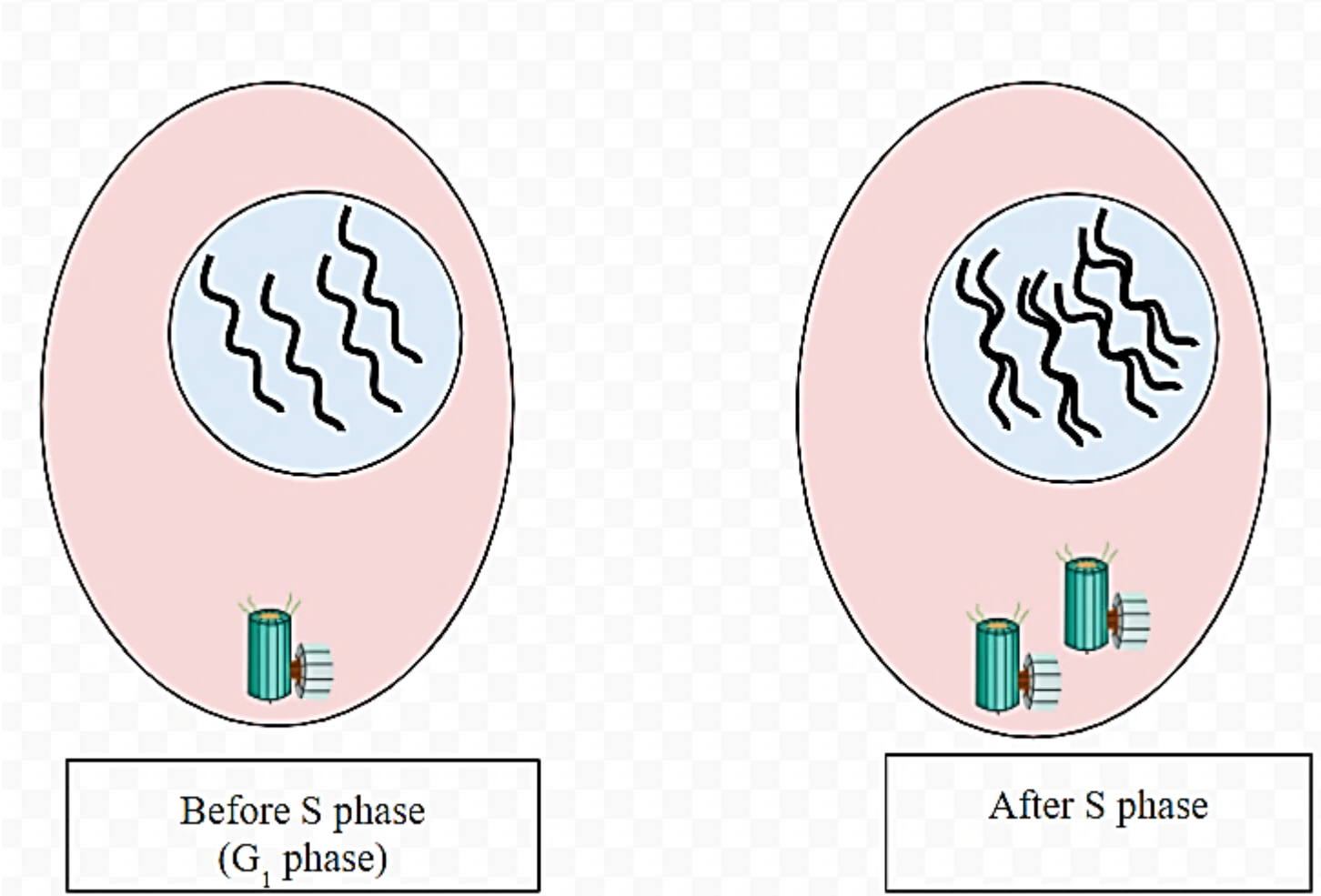
DNA Transcription

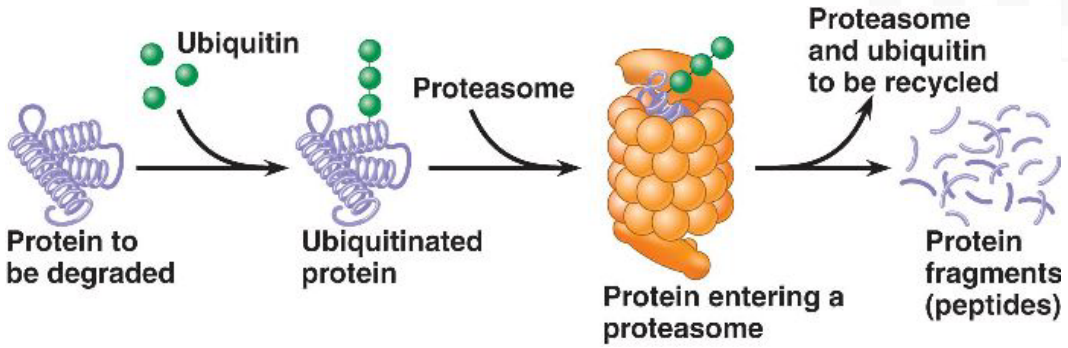
Helicase enzymes will unwind and separate the strands. ***DNA polymerase*** inserts complementary nucleotides, and links them together.



S phase

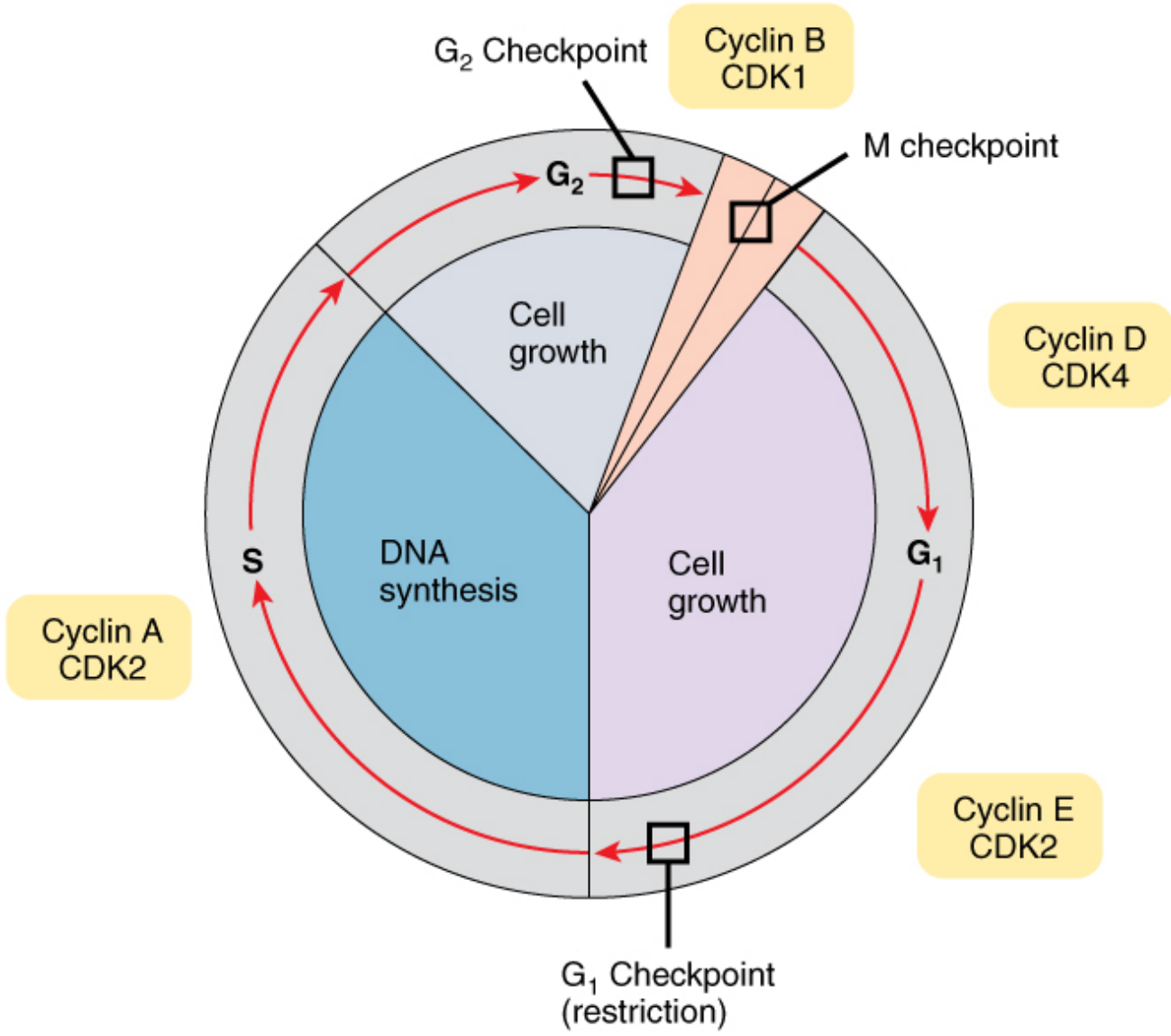
Centrioles finish duplicating, forming two centrosomes (microtubule-organizing centers). Sister chromatids are established. Cyclin E is sent to proteasomes and destroyed. **Cyclin A** increases to activate the enzymes for G2.





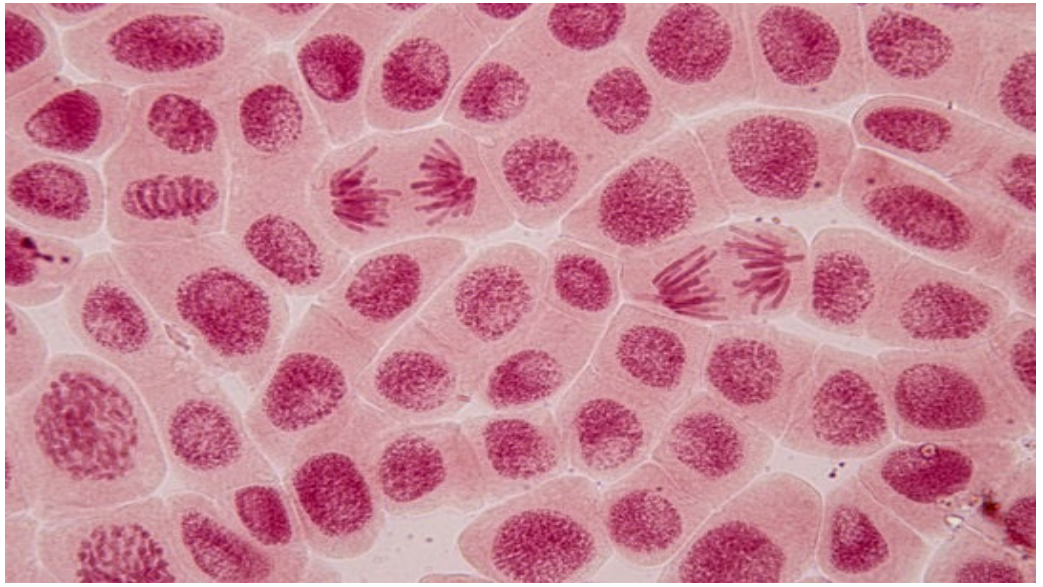
G2: final checkpoint

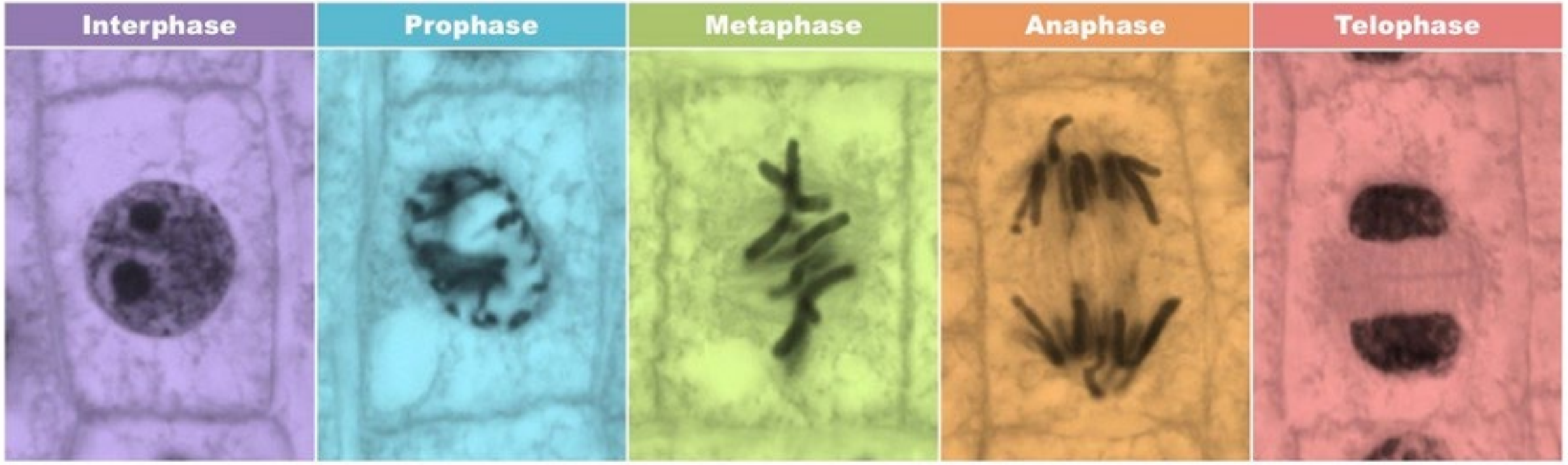
Double check : no broken, translocated, mutated, deleted DNA.
Cells subjected to radiation or chemotherapy will halt and die at this stage.
Tumor suppressing genes (eg p53) are activated; these genes monitor gene mutation; most frequent mutation in human cancer. If DNA cannot be repaired, initiates apoptosis (cell suicide).
Cyclin A gets destroyed and cyclin B increases.
Microtubules are assembled.



Mitosis

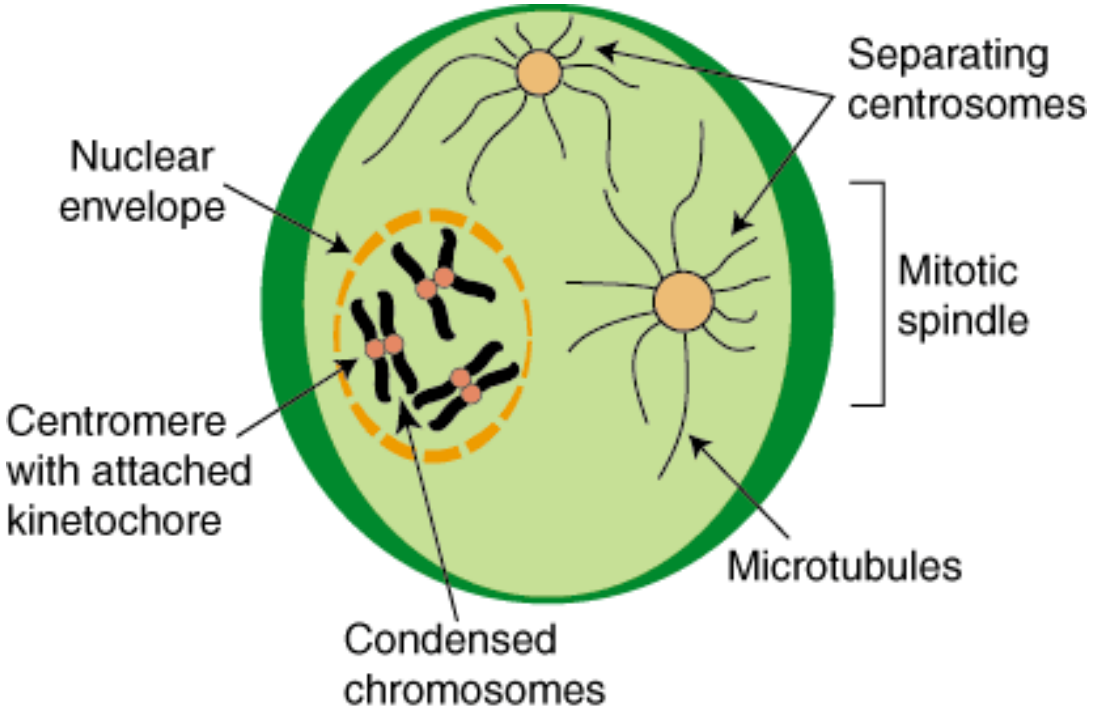
4 phases that result in division of cell into two identical daughter cells.

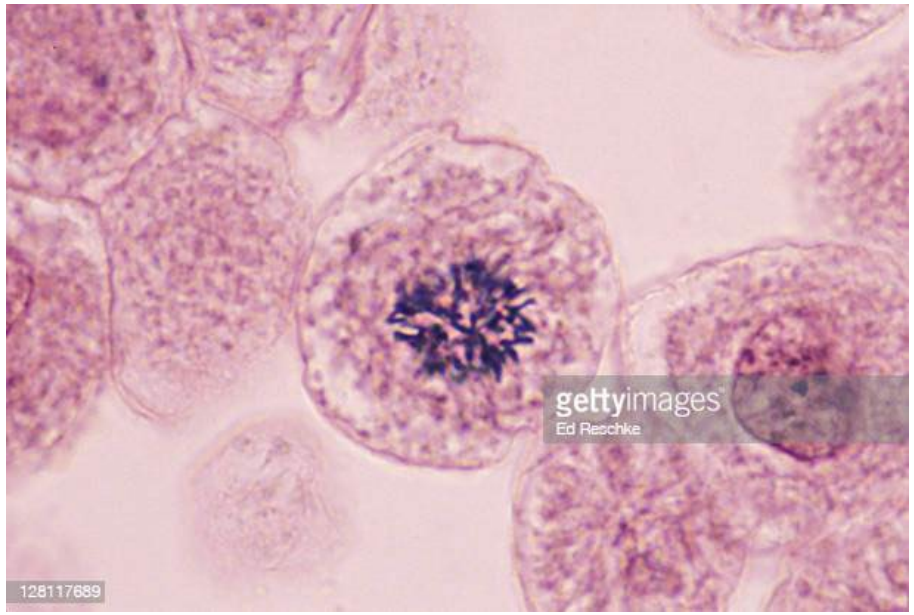




1. Prophase

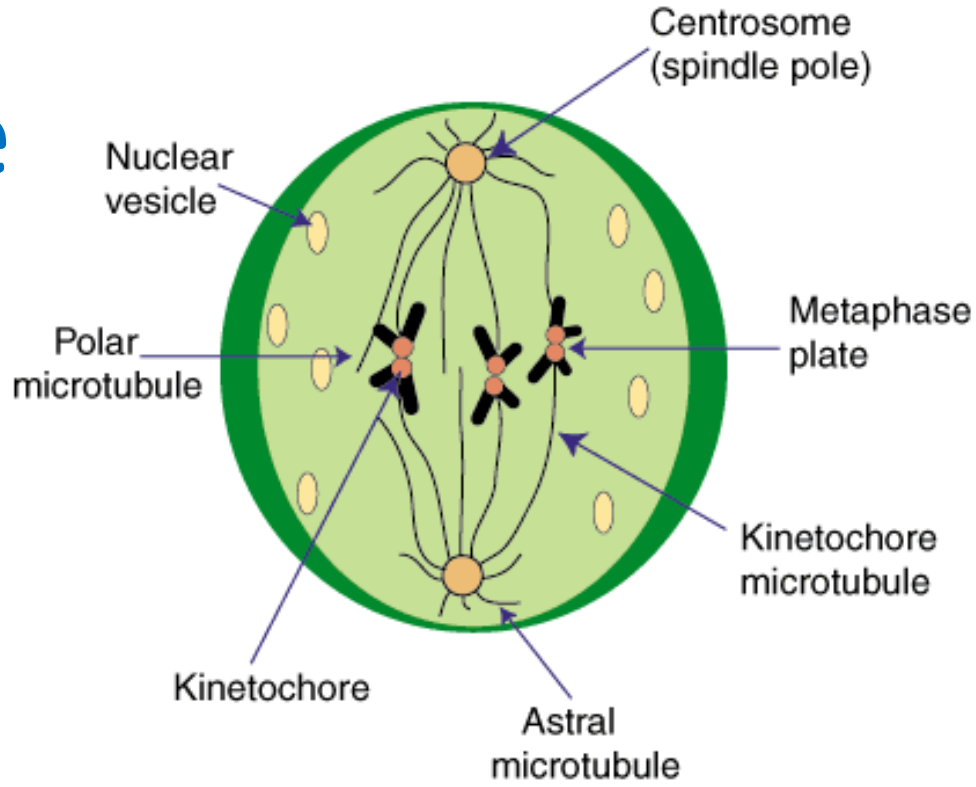
*Centrosomes migrate to opposing poles and begin organizing the spindle of microtubules.
*Nuclear membrane fragments and disappears.
*Chromosomes condense and become visible.

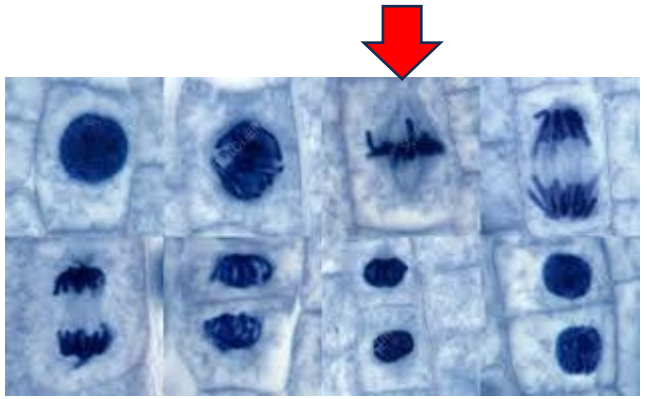


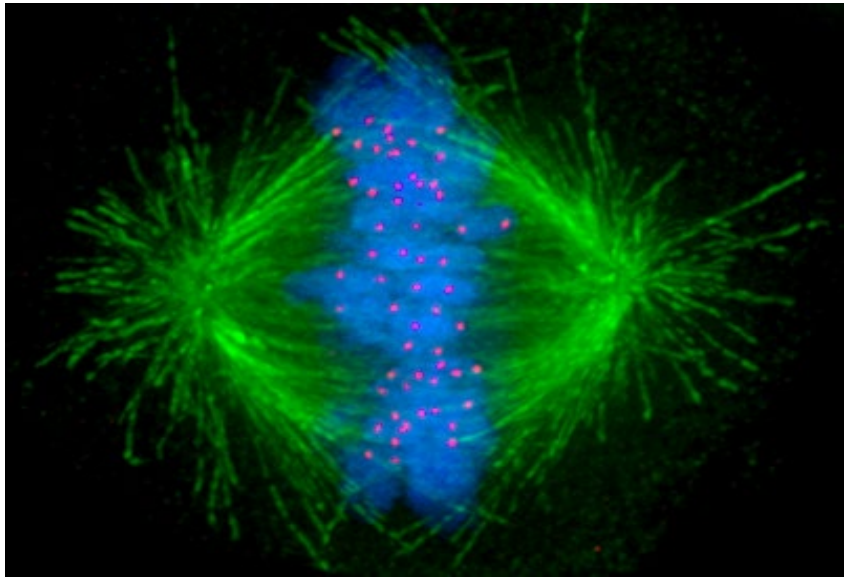


2. Metaphase

Chromosomes aligned at equatorial plate by mitotic spindle. Many cancer drugs work by inhibiting formation of microtubules.

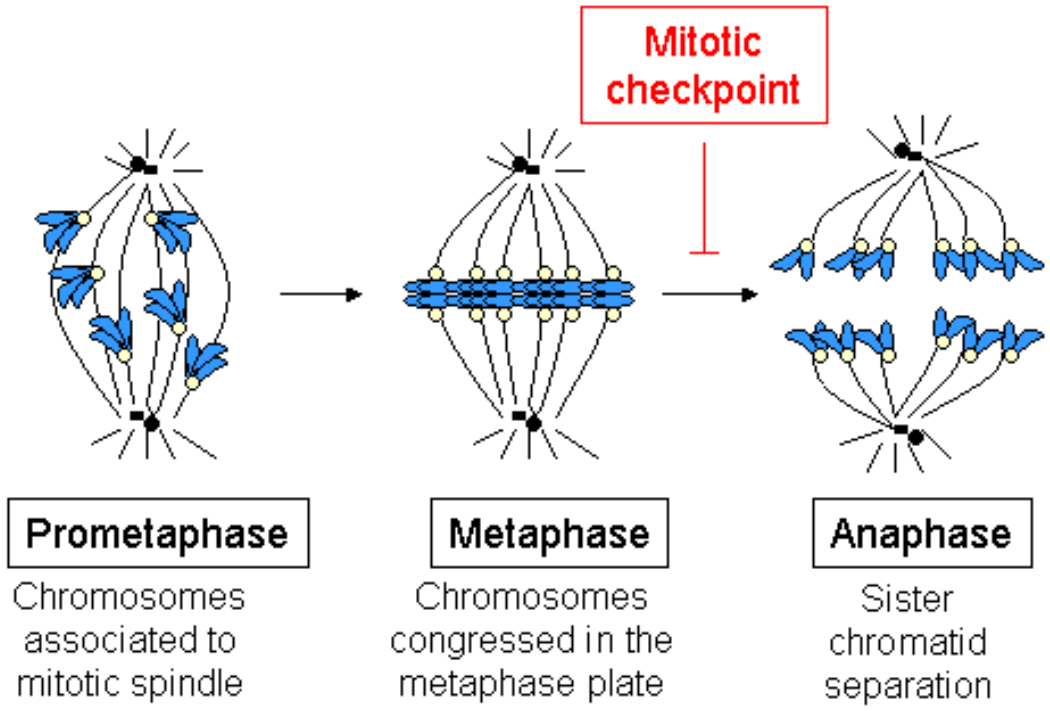


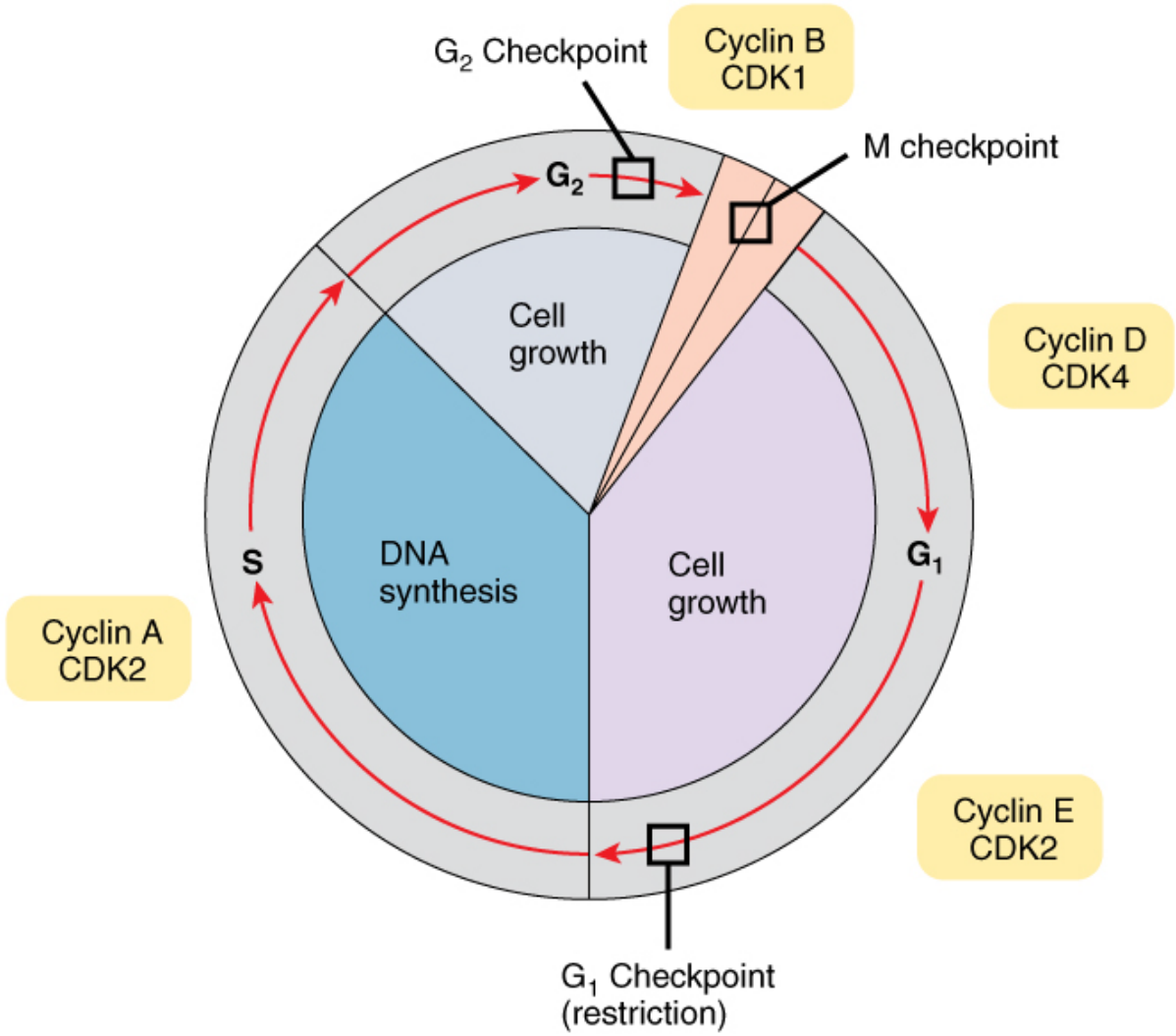




M Checkpoint

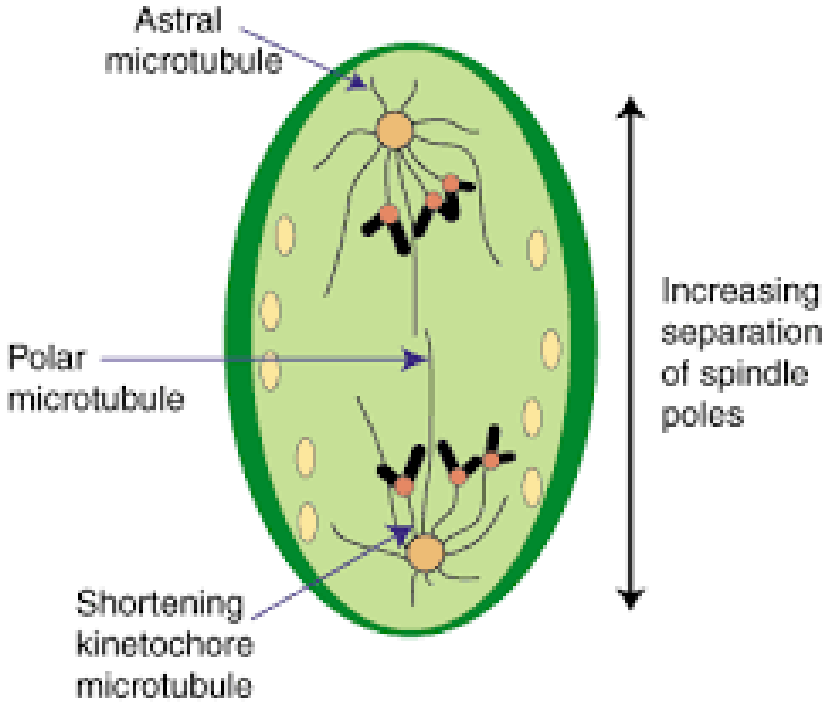
Checking that the chromosomes are properly lined up and able to separate cleanly.

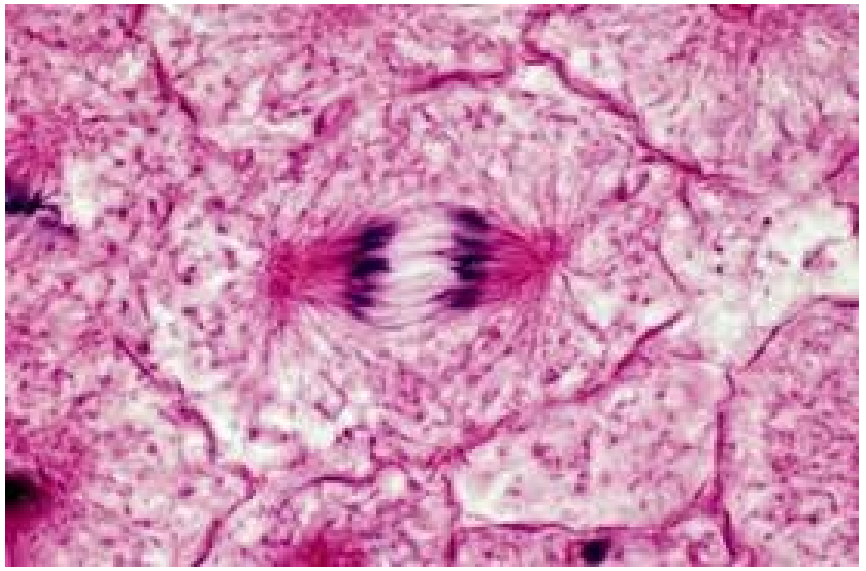


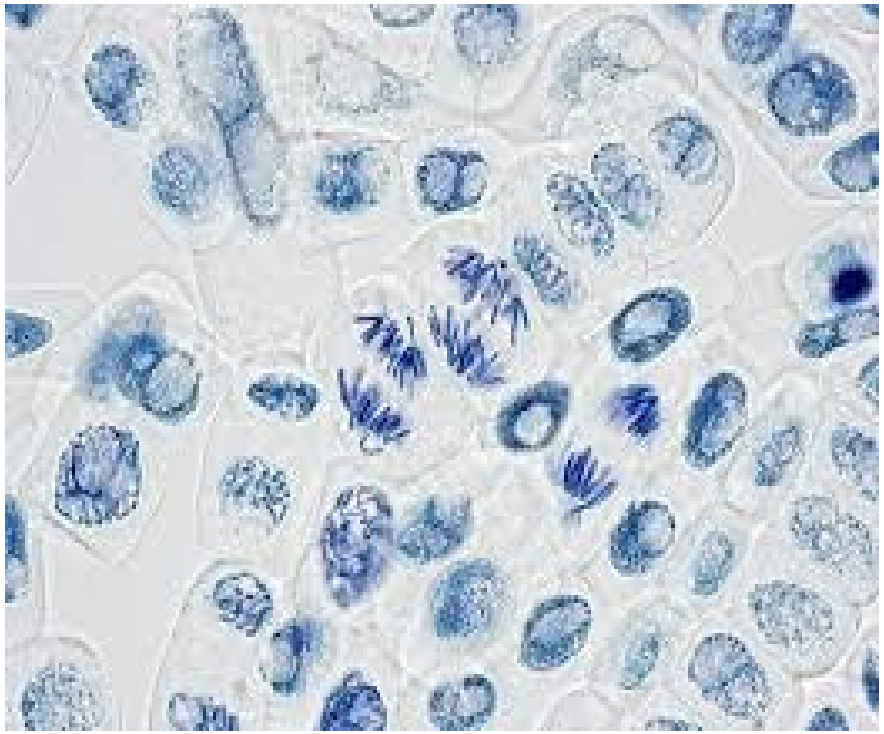


3. Anaphase

Kinetochores separate, dividing the sister chromatids into separate chromosomes. Microtubules pull kinetochores toward centrosomes.

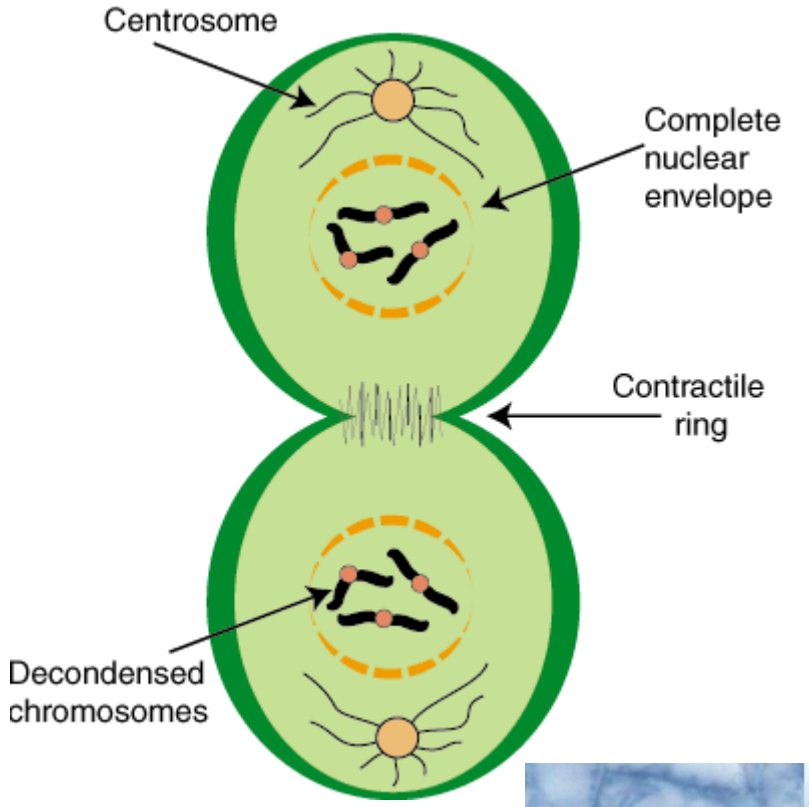


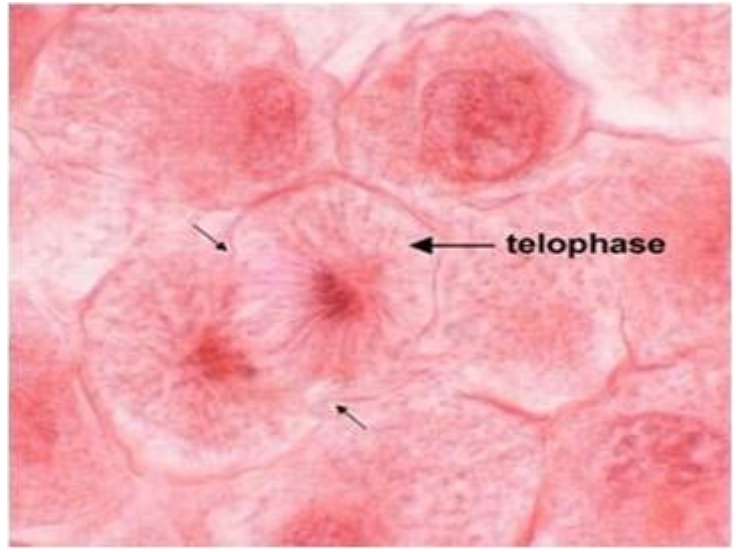


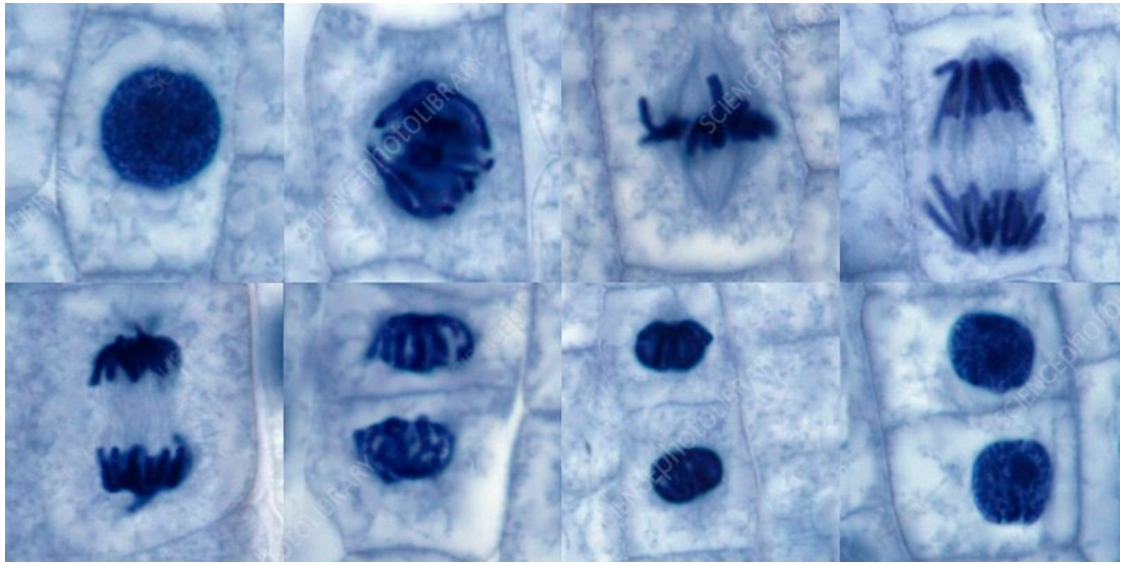


4. Telophase

Chromosomes at spindle poles decondense back to chromatin.
Microtubules disassemble.
Nuclear membrane reassembles. Nucleoli appear.
Cytokinesis occurs: contractile ring of actin filaments at cell equator constricts and divides cytoplasm into two.

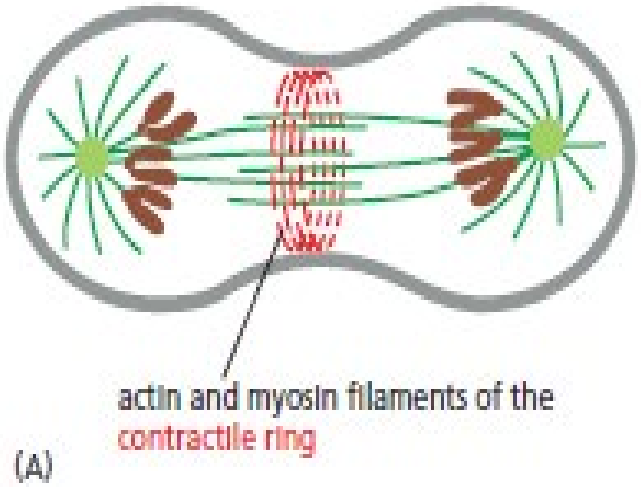


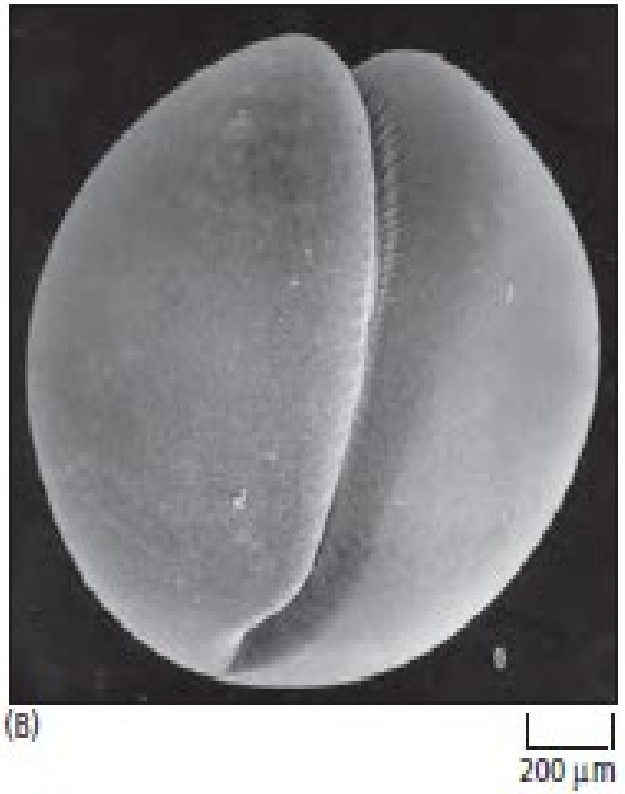




Contractile Ring

Actin and myosin cytoskeletal structures slide past each other: just like muscle.



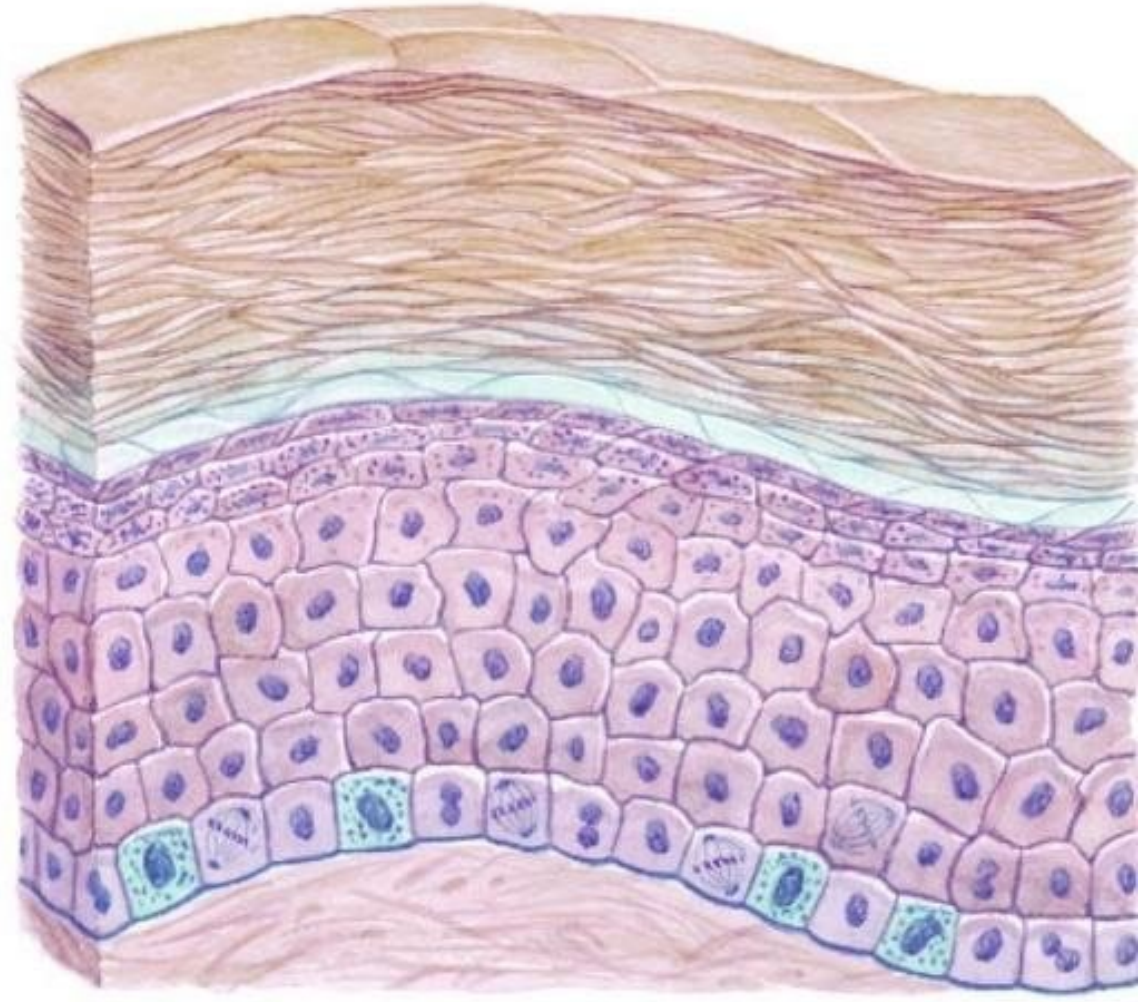


Cytokinesis. (A) The actin–myosin bundles of the contractile ring are oriented as shown, so that their contraction pulls the membrane inward. (B) In this low-magnification scanning electron micrograph of a cleaving frog egg, the cleavage furrow is especially prominent, as the cell is unusually large. The furrowing of the cell membrane is caused by the activity of the contractile ring underneath it. (C) The surface of a furrow at higher magnification.

Different Tissues Renewed at Different Rates

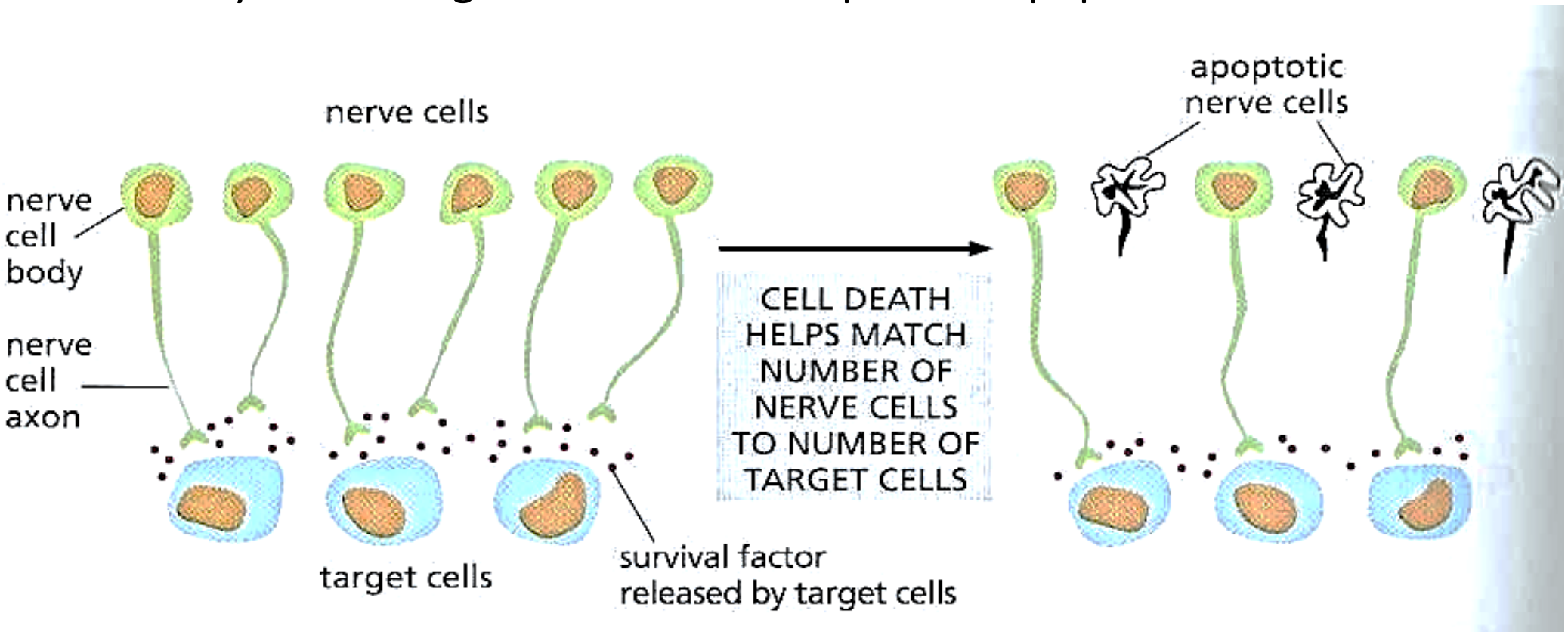
Turnover Times:
Intestinal lining: 3-6 days
Mouth lining: 14 days
Skin: 2 months
Bone: 10 years
Neurons: lifetime

Skin stem cells divide in basal layer and are pushed to the surface as they mature.



What Controls Division? Extracellular Signals

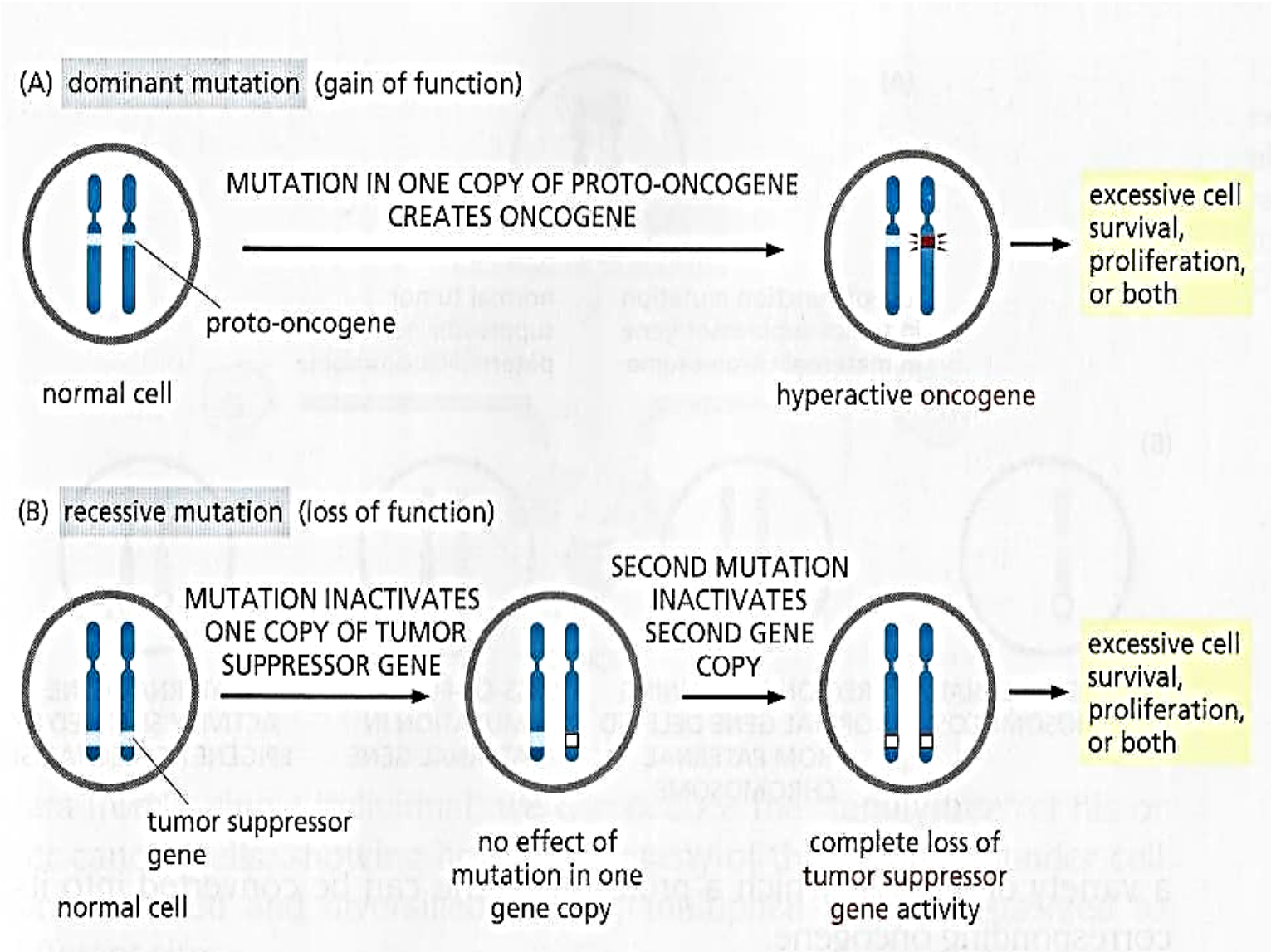
Mitogens: secreted by wounded tissues; stimulate cell division to replace damaged tissue.
Growth factors: secreted by neighboring tissues, often in embryos, to enlarge a tissue.
Apoptosis: during embryogenesis, often more cells are created than are needed. *Survival factors* secreted by interacting tissues needed to prevent apoptosis.



Cancer

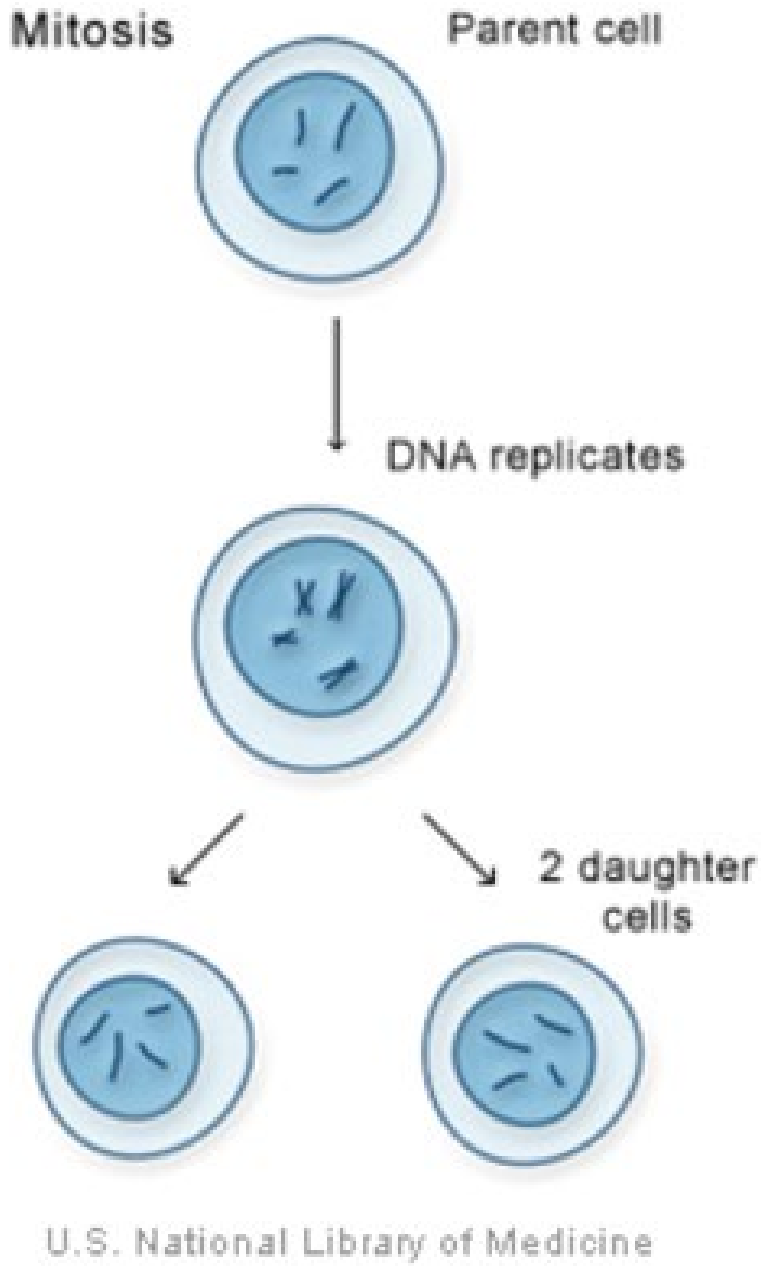
Other extracellular secretions act to inhibit growth in neighbors ("social" controls"). Cancers result when **multiple** mutations, occurring sequentially over many years, free a cell from outside control and it keeps dividing. Mutations allow the cells to avoid apoptosis, attract a blood supply, migrate inappropriately, invade new tissues.

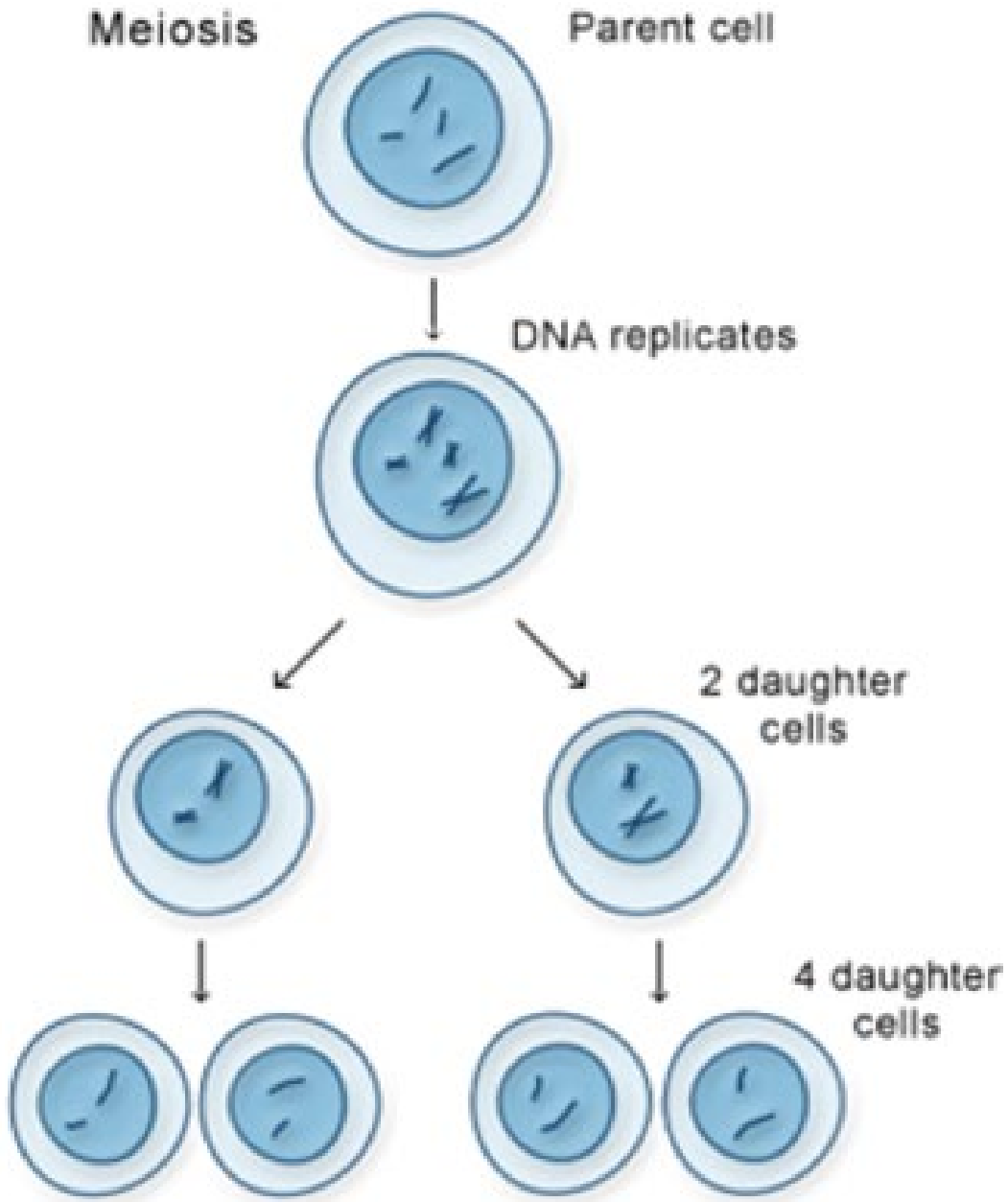
Certain genes that are critical to cancer progression are called **oncogenes** or **tumor-suppressor genes.**



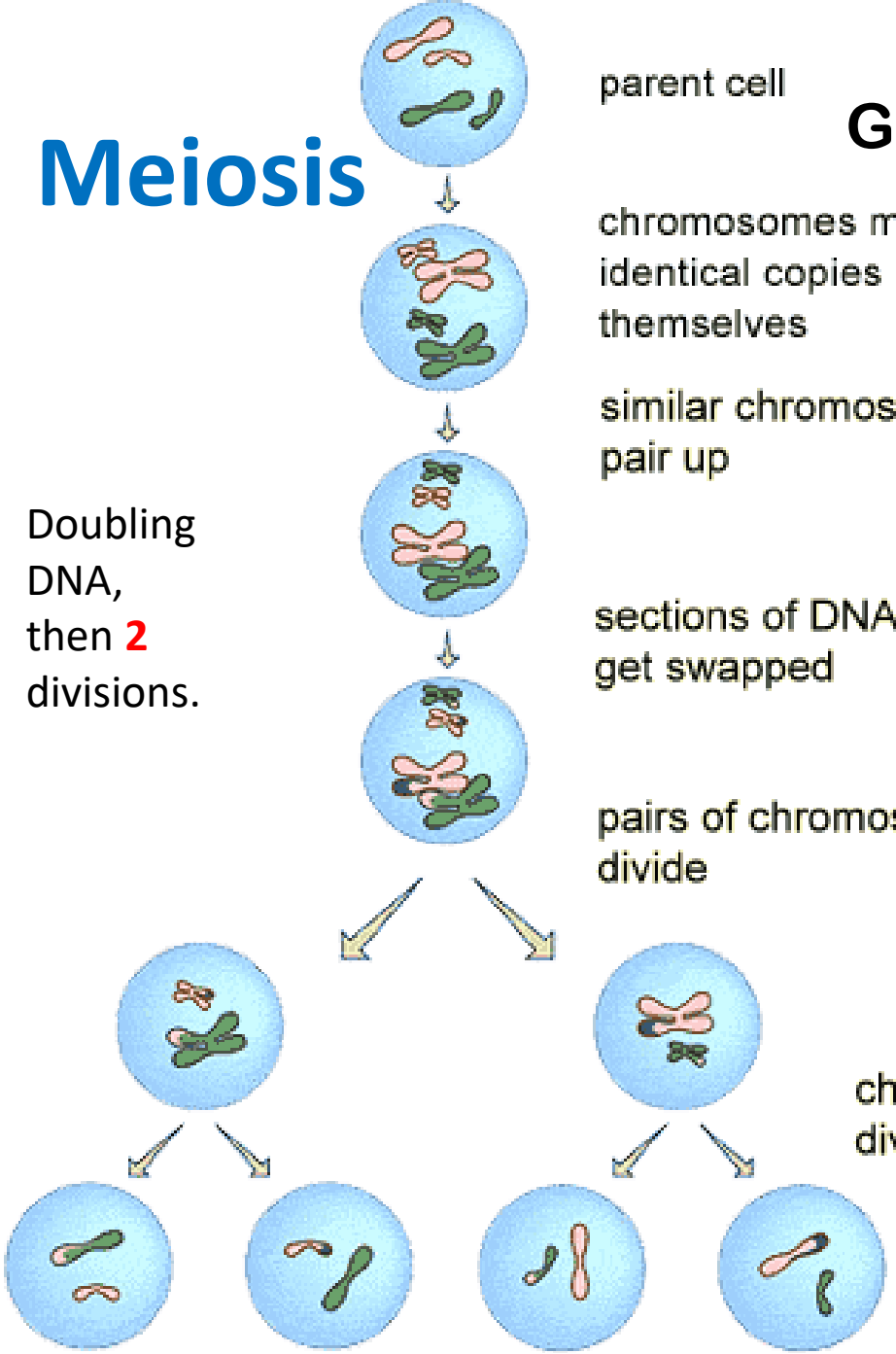
Mitosis vs Meiosis

2 identical daughter cells vs four unique gametes





Meiosis



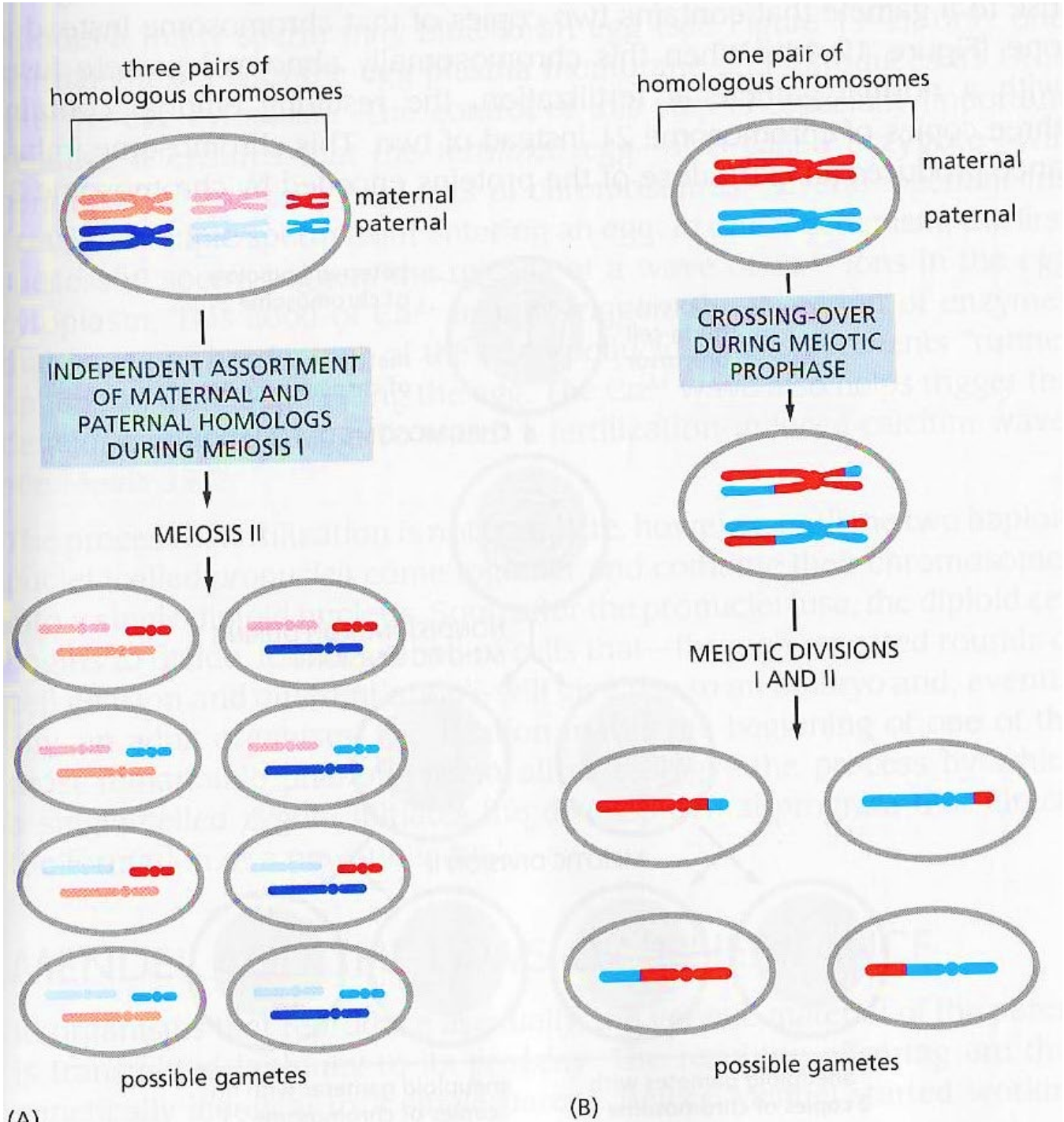
Germ cell in ovary or testes

Doubling DNA, then **2** divisions.

Increased genetic variability

71 splices/generation

Haploid gametes: unique



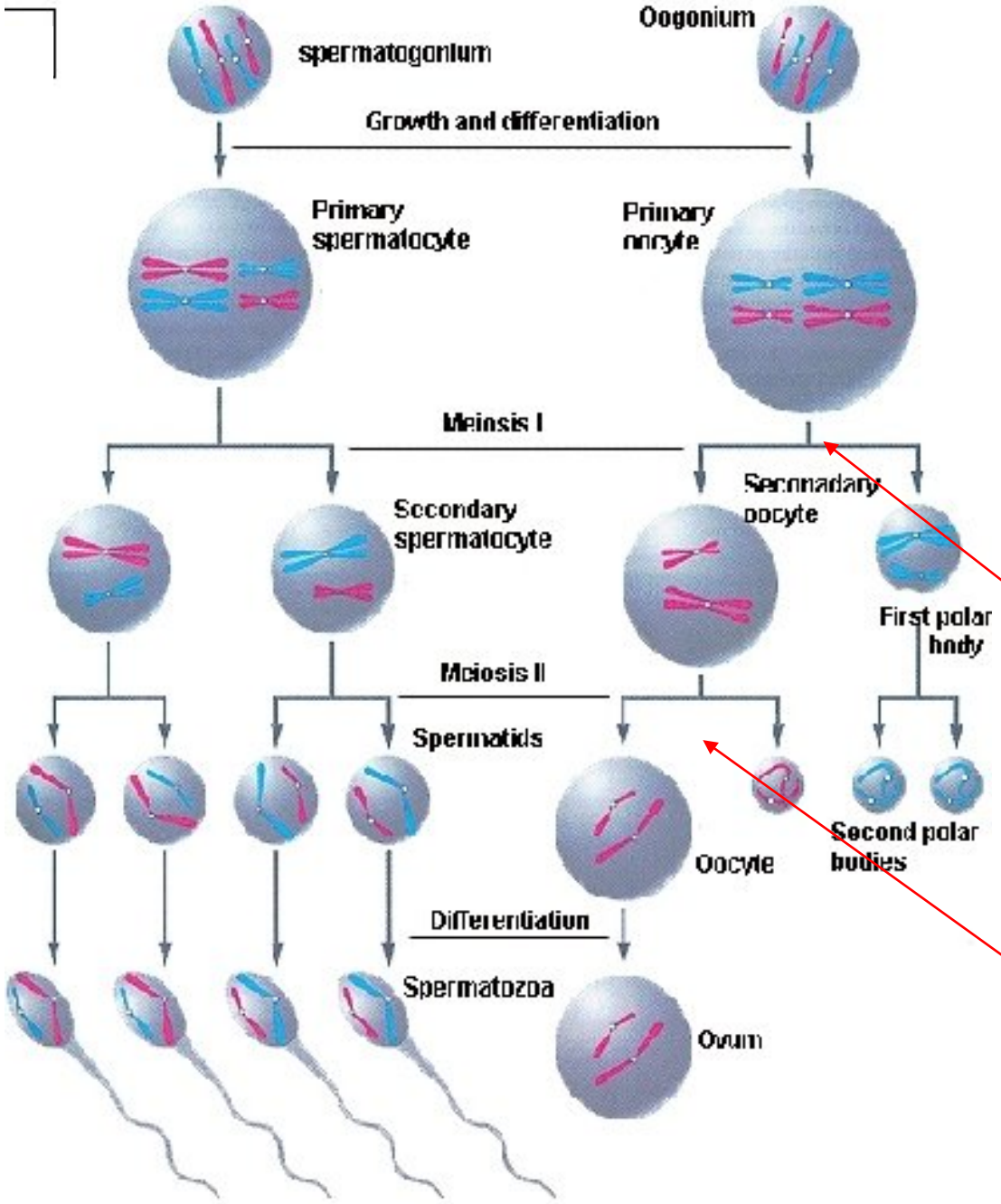
Unique Combinations

Independent assortment: at first division, maternal and paternal chromosomes are randomly assigned.

Crossing-over: Maternal and paternal chromosomes can trade segments.

Male

Male meiosis makes 4 sperm but female only one huge ovum. Male meiosis begins at puberty and continues a lifetime.



Female

Meiosis begins in utero

Paused in prophase I in ovary

Meiosis I completed only in ovulated oocyte

Meiosis II completed only at fertilization

Male vs Female timing

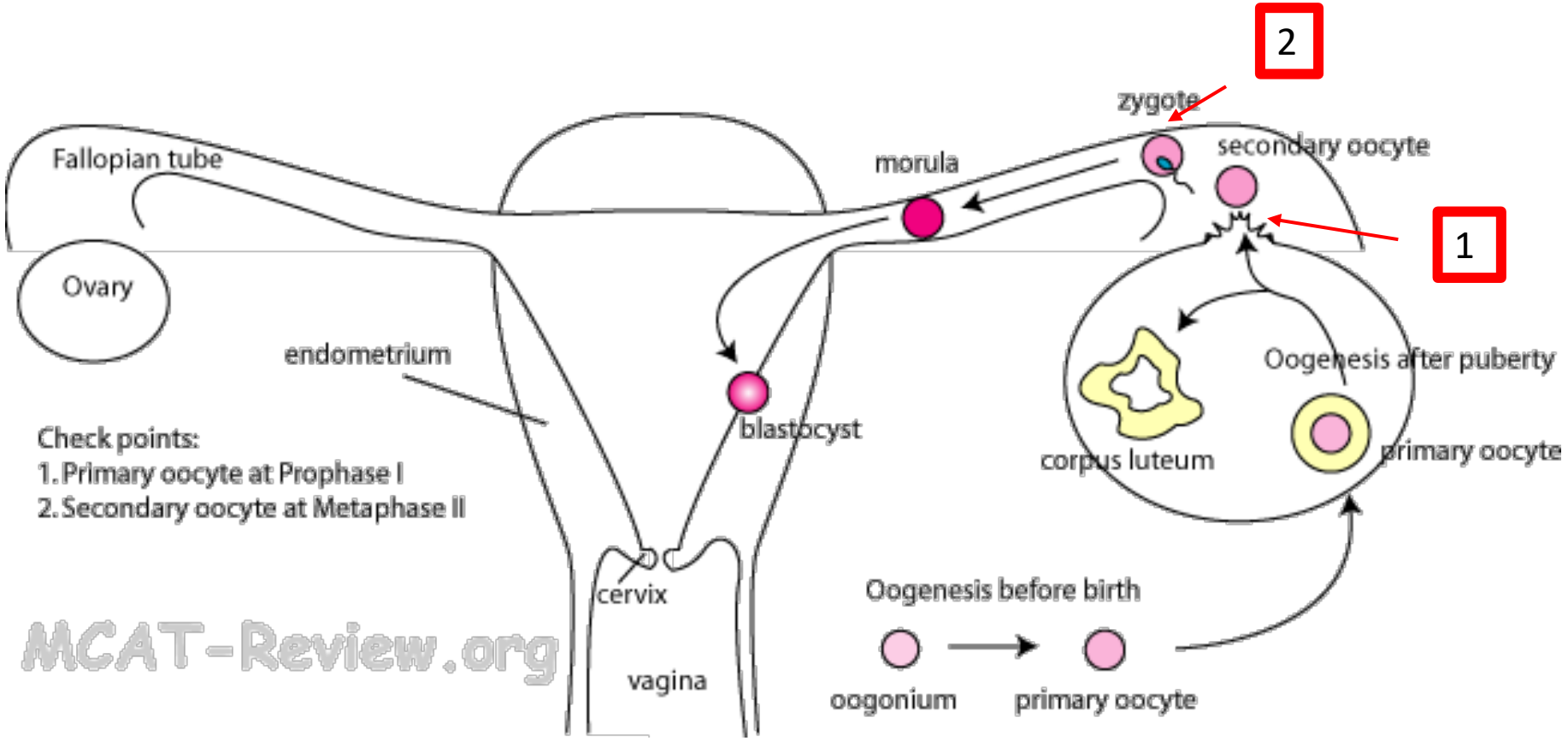
- **Males:**
- Meiosis and sperm production begins at puberty
- Continuous process that males will always undergo – takes 9 weeks

- **Females:**
- Meiosis and egg production begins before birth. Process stops abruptly, and does not begin again until puberty
- At puberty, one egg each month resumes meiosis and finishes its development
- Process stops when a women reaches menopause (around 50 years of age)
- Meiosis of a singe egg could take 50 years to complete!

Timing

1. Meiosis I completed at ovulation; stuck in prophase for 10-50 years.

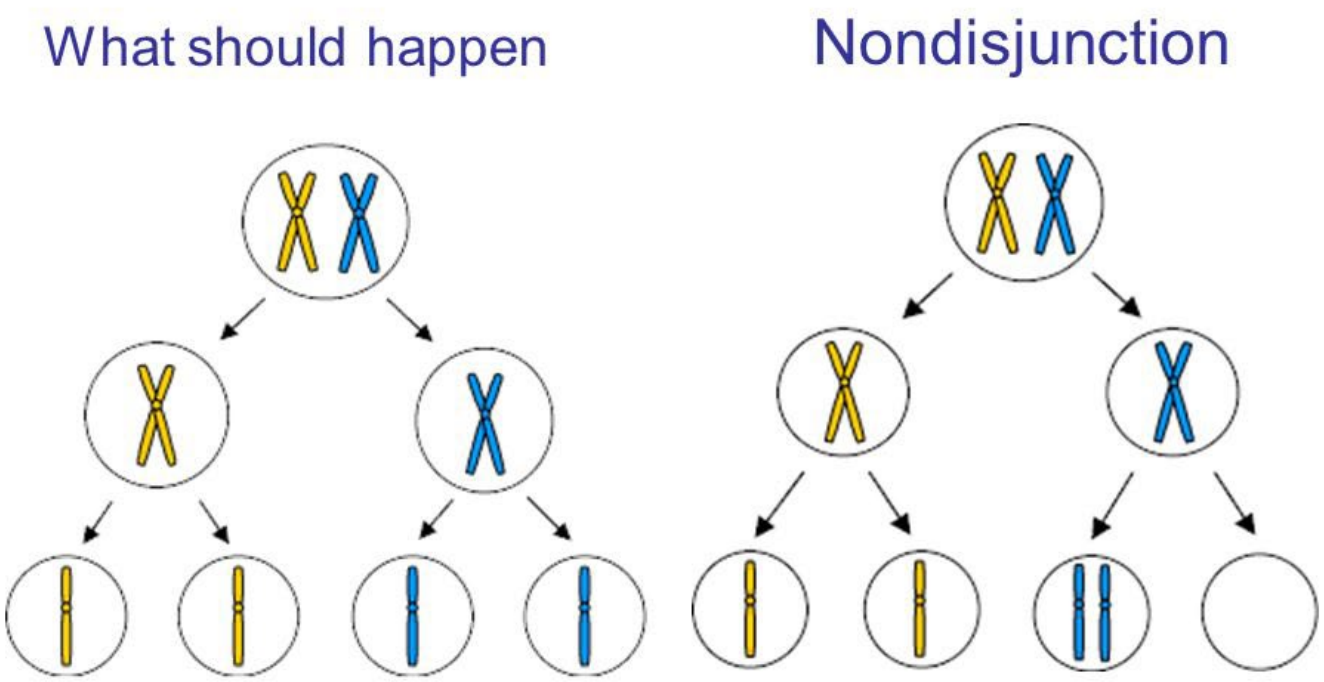
2. Meiosis II completed at fertilization.



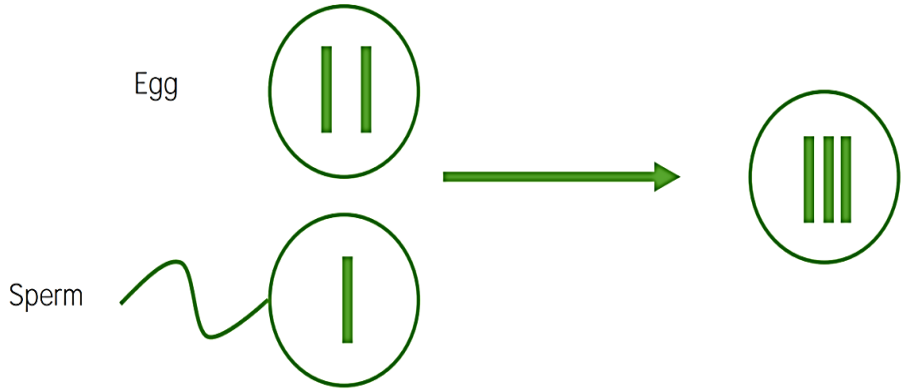
Problems

Nondisjunction

- The failure of homologous chromosomes to separate properly during meiosis.



Most **trisomies** are nonviable. Down syndrome results from trisomy 23.



Mutations

10 new mutations every time a cell divides.
Some harmless, some cause deformed proteins, but only in that cell.
If the mutation is in a germ cell, can be inherited.
Why older *fathers* more likely to pass on genetic mutations, while older *mothers* more likely to pass on chromosomal abnormalities.