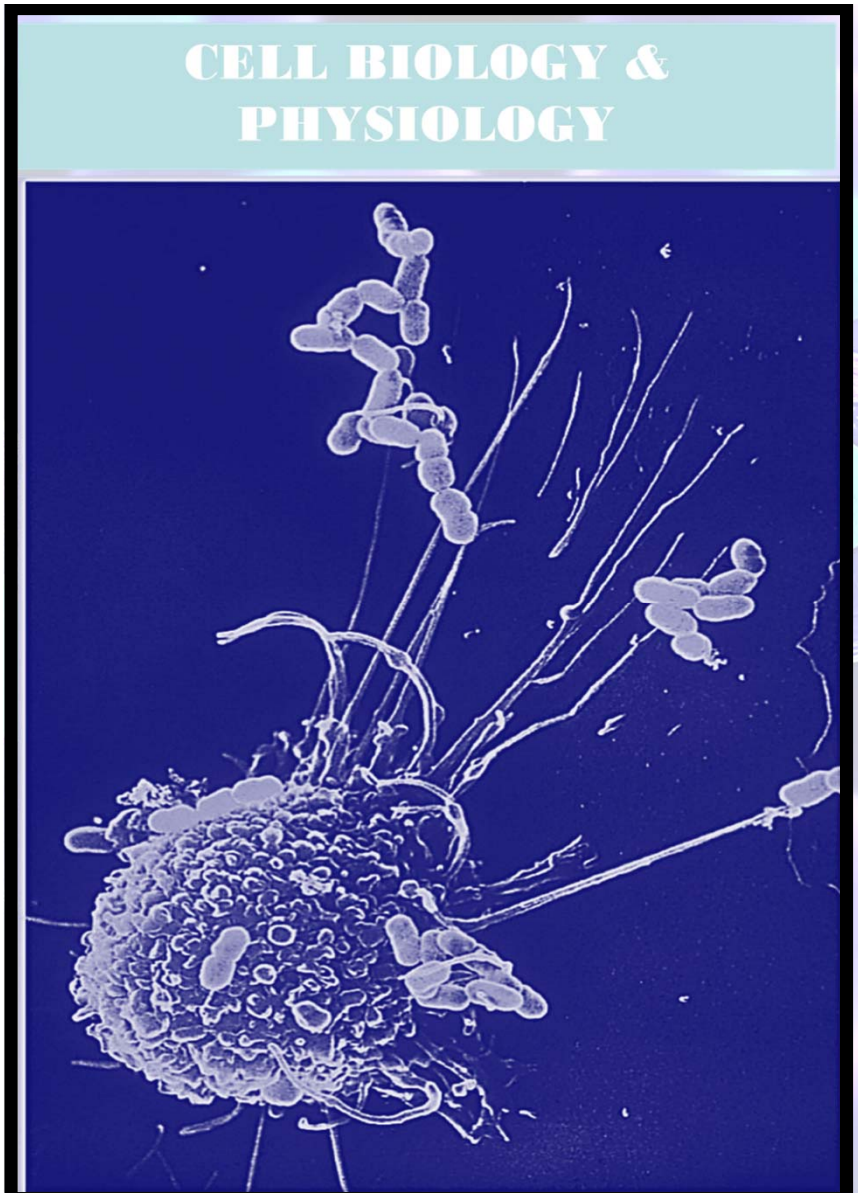

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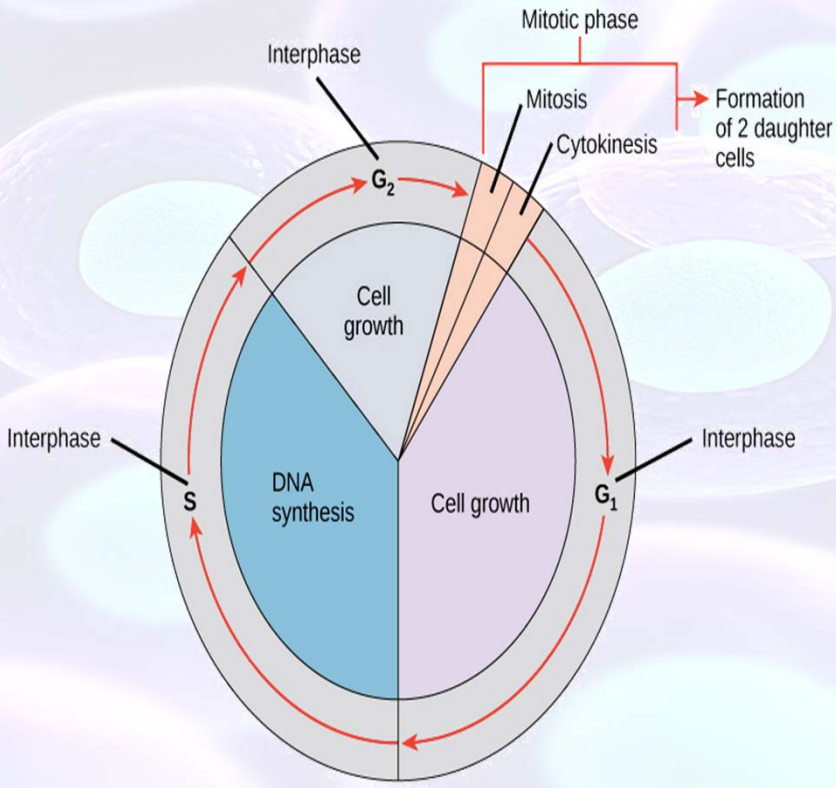
ZOO (242)

The eukaryotic cell cycle is regulated by a molecular control system

- The timing and rate of cell division in different parts of a plant or animal are crucial to normal growth, development, and maintenance.
- The frequency of cell division varies with the type of cell. For example,
  - Some human cells divide frequently throughout life (skin cells).
  - Others human cells have the ability to divide but keep it in reserve (liver cells).
  - Mature nerve and muscle cells do not appear to divide at all after maturity.
- Investigation of the molecular mechanisms regulating these differences provides important insights into the operation of normal cells and may also explain how cancer cells escape controls.

The cell cycle:

- The continuity of life depends on cells growing, replicating their genetic material, and then dividing.
- The cell cycle consists of two major stages:
- Interphase: cells grow and make a copy of its genetics material.
- M (mitosis) phase: Cells divide its genetics material and produce a new daughter cells.



Inter phase is the longest part of cell cycle

- Interphase can be subdivided into three phases: G1 (Gap 1), S (DNA synthesis) and G2 (Gap 2).
- G1 and G2 are gaps between two obvious landmarks (DNA synthesis and cell division (mitosis)).
- In the G1 phase, the cell is growing and also preparing for the process of DNA replication.
- S phase is defined as the stage where the DNA replication occurs.
- G2 phase: the cell grows more, makes proteins and organelles, and begins to reorganize its contents in preparation for mitosis.

- G0: cells exist the cycle and stop dividing. This either a temporary resting period and re-enter the cell cycle or more permanent.
- For instance:
- Cells reach an end phase of development and no longer divide (e.g. neuron), these cells leave the cell cycle and enter the G0 phase, where they remain metabolically active and viable.
- Occasionally, cells either fail to enter G0 phase or do not remain in the G0 phase, which results in their continual proliferation (growth and division). This uncontrolled cell proliferation can lead to cancerous growth.

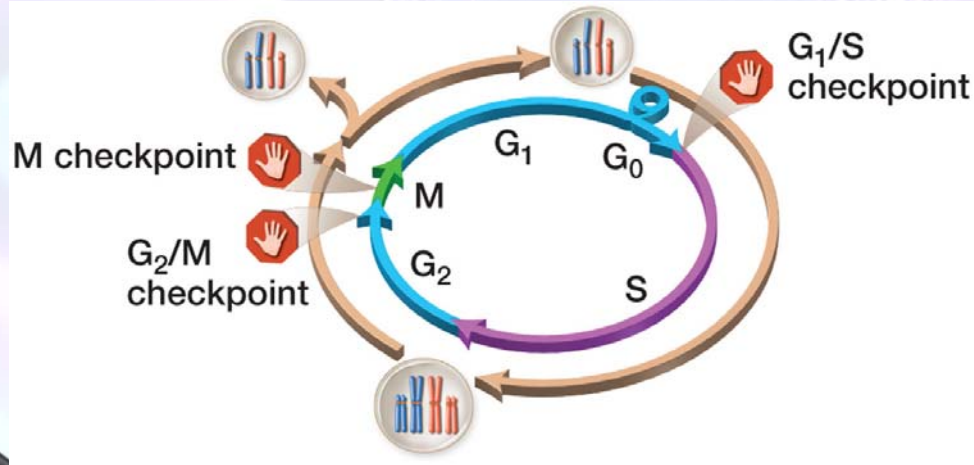
Mitosis (M phase) is usually the shortest period.

- Mitosis or the M phase has four stages:
  1. Prophase
  2. Metaphase
  3. Anaphase
  4. telophase.

The length of time required for a complete life cycle varies with cell type.

Cell cycle checkpoints:

- These checkpoints allow the cell to make sure that various events have been properly completed before it moves to the next phase of the cell cycle.
- Such as the initiation of mitosis can be delayed until all necessary conditions are in place, such as the repair of the damaged DNA.
- There are three major checkpoints in the cell cycle



1. The G1/S checkpoint:

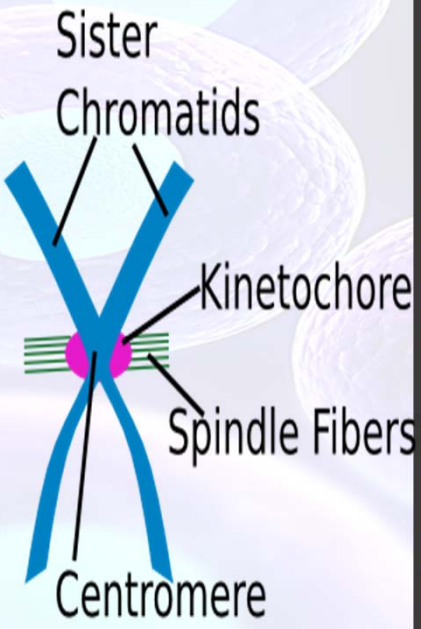
- Determines whether the cell has reached the proper size and determines if the DNA is damaged. For example, if the cell attempts to replicate damaged DNA, breaks will occur in the DNA or replication will be blocked.

2. The G2/M checkpoint:

- Evaluates whether DNA replication is completed and if any damaged DNA still needs to be repaired.

3. The M checkpoint (spindle checkpoint):

- Evaluates whether spindle fibers are properly assembled and attached to the kinetochores.
- If either of these two events is not completed, the chromosomes cannot faithfully be separated into the daughter cells.

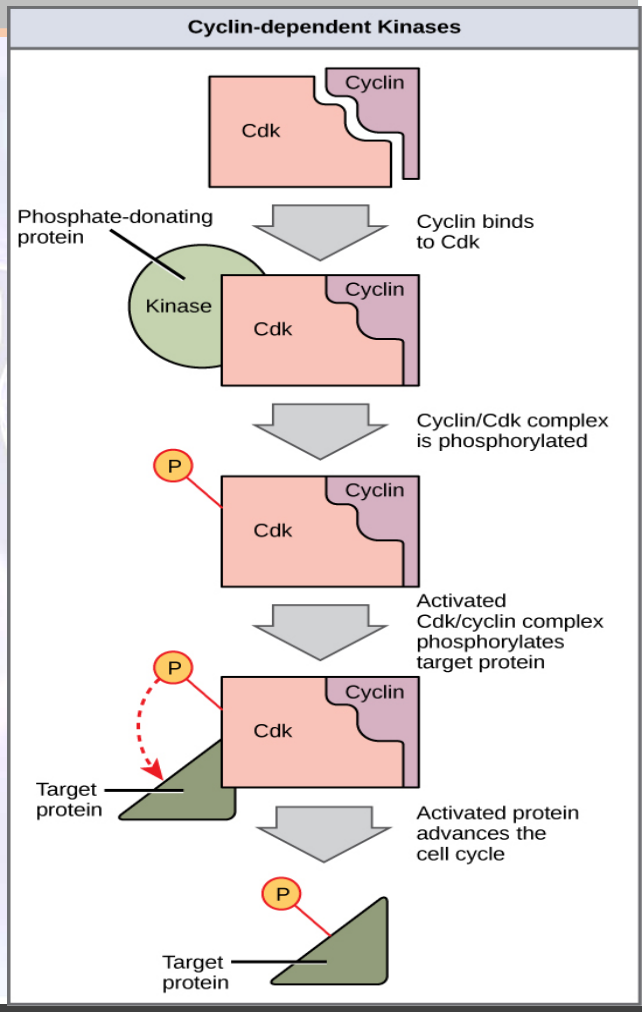


Positive Regulation of the Cell Cycle:

2 groups of proteins, called cyclins and cyclin-dependent kinases (Cdks), are responsible for the progress of the cell through the various checkpoints. Once the cell moves to the next phase of the cell cycle, the cyclins that were active in the previous phase are degraded.

Cyclins control the cell cycle only when they are tightly bound to Cdks.
the Cdk/cyclin complex must also be phosphorylated in specific locations.

Like all kinases, Cdks are enzymes (kinases) that phosphorylate other proteins by changing its shape. The proteins phosphorylated by Cdks are involved in letting the cell to process to next phase



Negative regulation of cell cycle

Negative regulators stop the cell cycle for example: group of tumor suppressor genes, retinoblastoma protein (Rb), P53 and P21.

Any damage of these genes result in initiation of cancer cells.

Rb, p53, and p21 function mainly at the G1/S checkpoint.

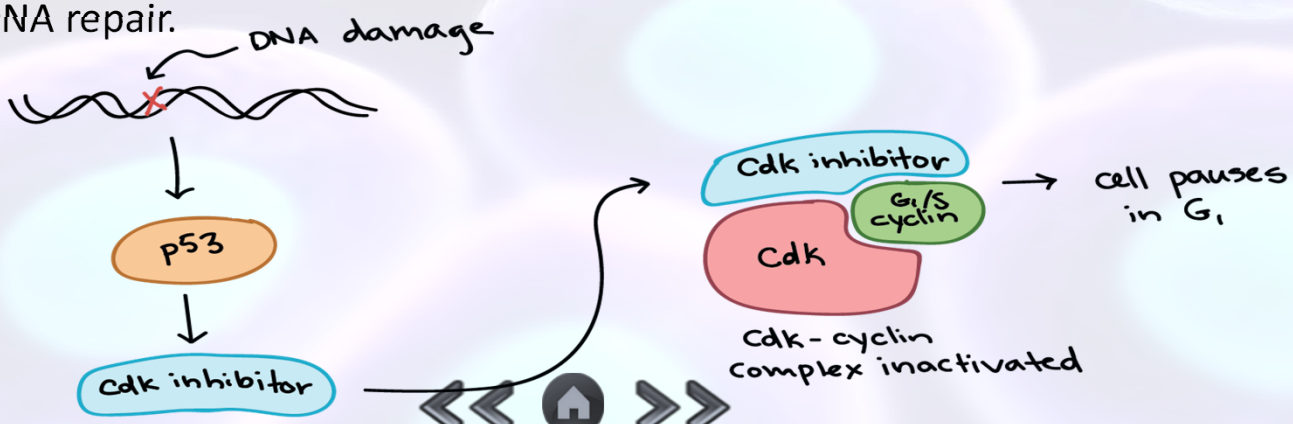
p53

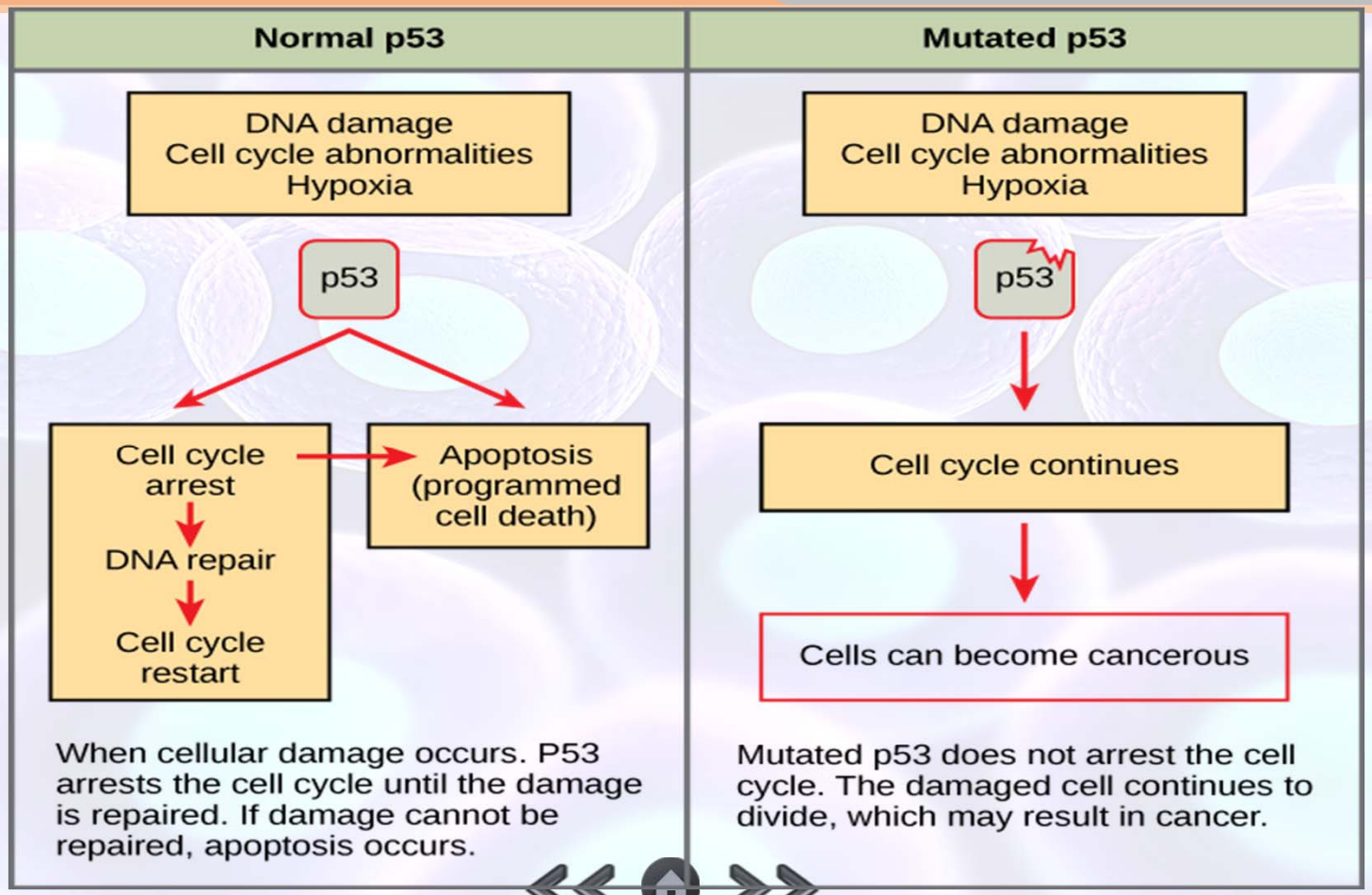
p53 functions on several levels to make sure that cells do not pass on their damaged DNA through cell division.

1- p53 stops the cell cycle at the G1/S check point by triggering production of **Cdk inhibitor** (**CKI**) proteins. The CKI proteins bind to Cdk-cyclin complexes and block their activity, letting time for DNA repair.

2- p53 activates DNA repair enzymes.

3- If DNA damage is not fixed, p53 will trigger a programmed cell death (apoptosis). so damaged DNA is not passed on.




Normal p53
DNA damage
Cell cycle abnormalities
Hypoxia
p53
Cell cycle arrest
DNA repair
Cell cycle restart
Apoptosis (programmed cell death)
When cellular damage occurs. P53 arrests the cell cycle until the damage is repaired. If damage cannot be repaired, apoptosis occurs.
Mutated p53
DNA damage
Cell cycle abnormalities
Hypoxia
p53
Cell cycle continues
Cells can become cancerous
Mutated p53 does not arrest the cell cycle. The damaged cell continues to divide, which may result in cancer.

Summary

- **The eukaryotic cell cycle is regulated by a molecular control system.**
- Signaling molecules present in the cytoplasm regulate progress through the cell cycle. • The **cell cycle control system** is molecularly based. Cyclic changes in regulatory proteins work as a cell cycle clock. The key molecules are **cyclins** and **cyclin-dependent kinases (Cdks)**.
- The clock has specific **checkpoints** where the cell cycle stops until a go-ahead signal is received.
- Cell culture has enabled researchers to study the molecular details of cell division. Both internal signals and external signals control the cell cycle checkpoints via signal transduction pathways.

Summary

- Most cells exhibit **density-dependent inhibition** of cell division as well as **anchorage dependence**.
- Cancer cells elude normal cell cycle regulation and divide out of control, forming tumors. **Malignant tumors** invade surrounding tissues and can undergo **metastasis**, exporting cancer cells to other parts of the body, where they may form secondary tumors. Recent advances in understanding the cell cycle and cell signaling, as well as techniques for sequencing DNA, have allowed improvements in cancer treatment

References

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- Chapter 12 "The Cell Cycle" Biology By Campbell and Reece 9th Ed.