Zoo-352 Principles of genetics
Lecture 3

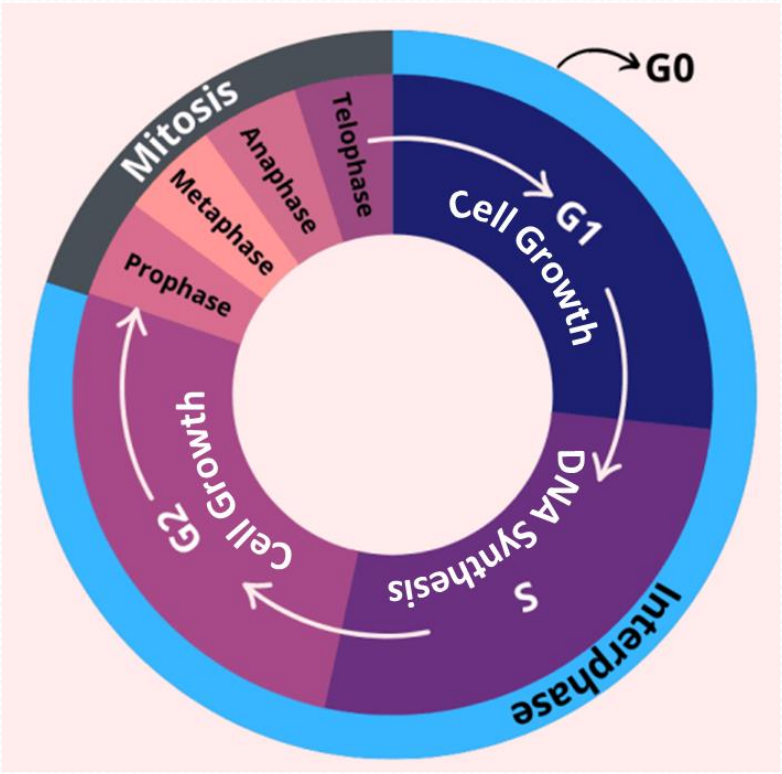
The cell cycle and its checkpoints

Outlines:

- The cell cycle definition.
- The phases of the cell cycle.
- The interphase of the cell cycle
- The Mitotic phase of the cell cycle.
- The cell cycle checkpoints.
- Regulatory molecules of the cell cycle.

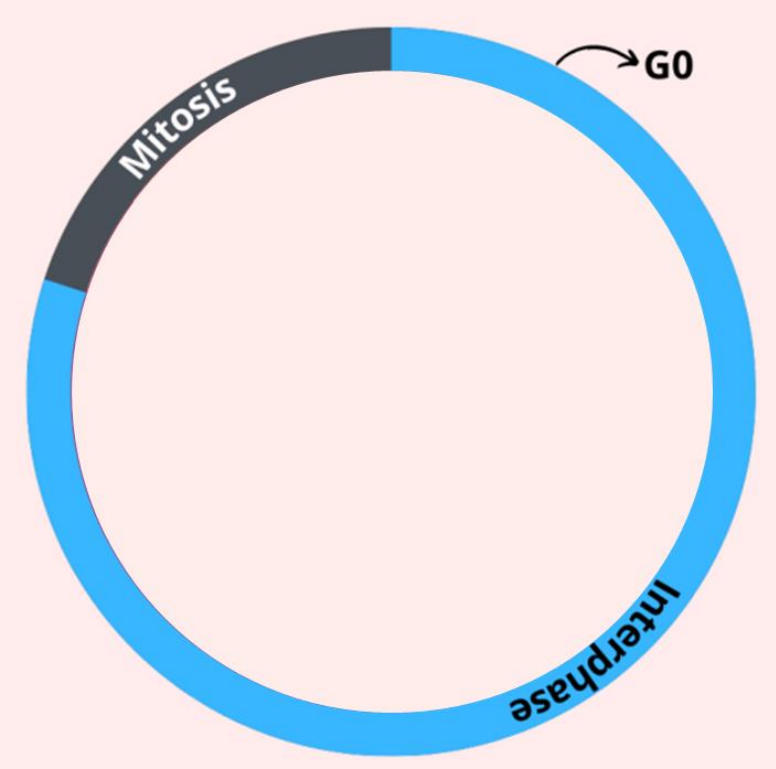
The definition of the cell cycle:

- The continuity of life depends on cells growing, replicating their genetic material, and then dividing- a process called the cell cycle.
- The interval time between each mitotic cell division is termed a cell cycle.
- A cell cycle is a series of events that takes place in a cell as it grows and divides.



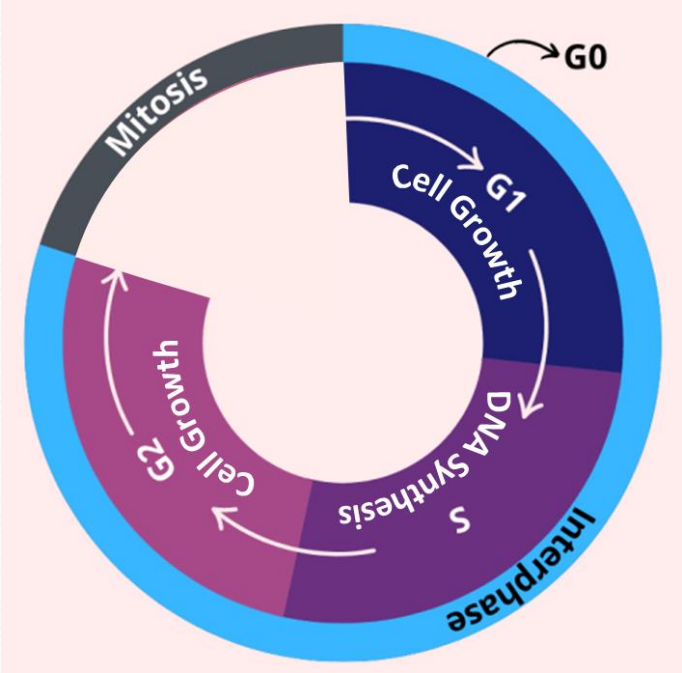
The phases of the cell cycle:

- The cell cycle consists of two basic phases (stages): interphase and M phase.
- Interphase: Cells grow and make a copy of the genetics materials.
- Mitotic (M) phase: Cells divide the genetics materials and produce a new daughter cells.



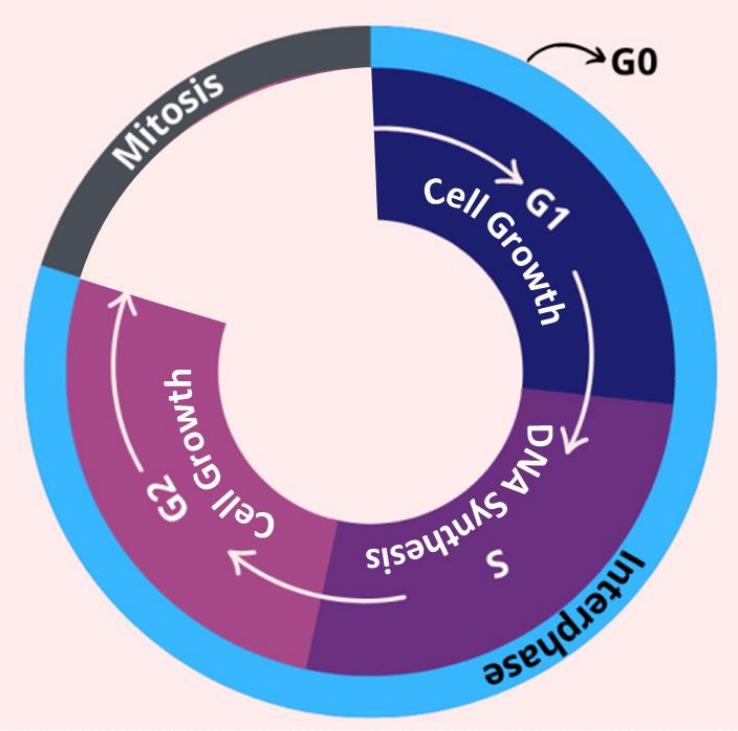
The interphase of the cell cycle:

- Interphase is subdivided into three ordered stages:
  1. G1 (Gap 1),
  2. S (DNA synthesis) and
  3. G2 (Gap 2).
- G1 and G2 are gaps between two obvious landmarks: DNA synthesis (S phase) and mitosis (M phase).
- Interphase is the longest part of cell cycle.



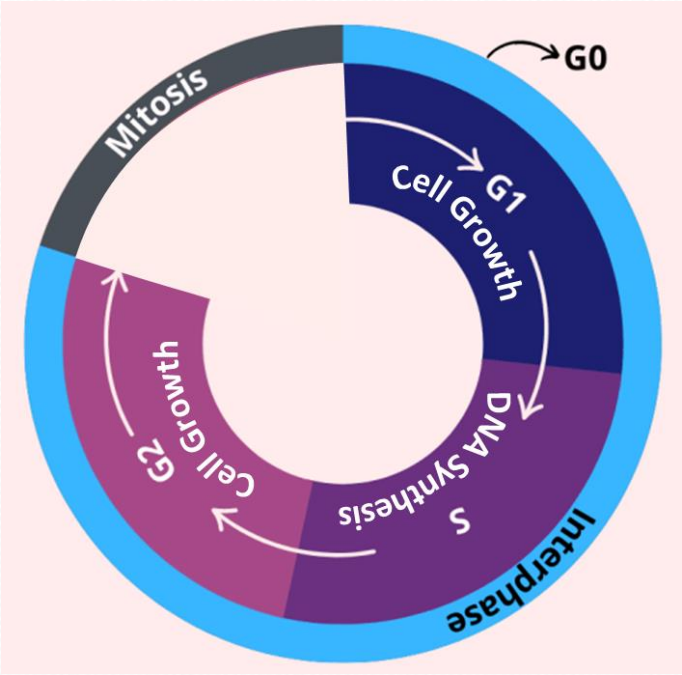
The interphase of the cell cycle:

- In the G1 phase, the cell is growing also preparing for the process of DNA replication.
- S phase is defined as the stage where the DNA replication occurs.
- G2 phase is where the cell grows more, makes proteins and organelles, and begins to reorganize its contents in a preparation for mitosis.



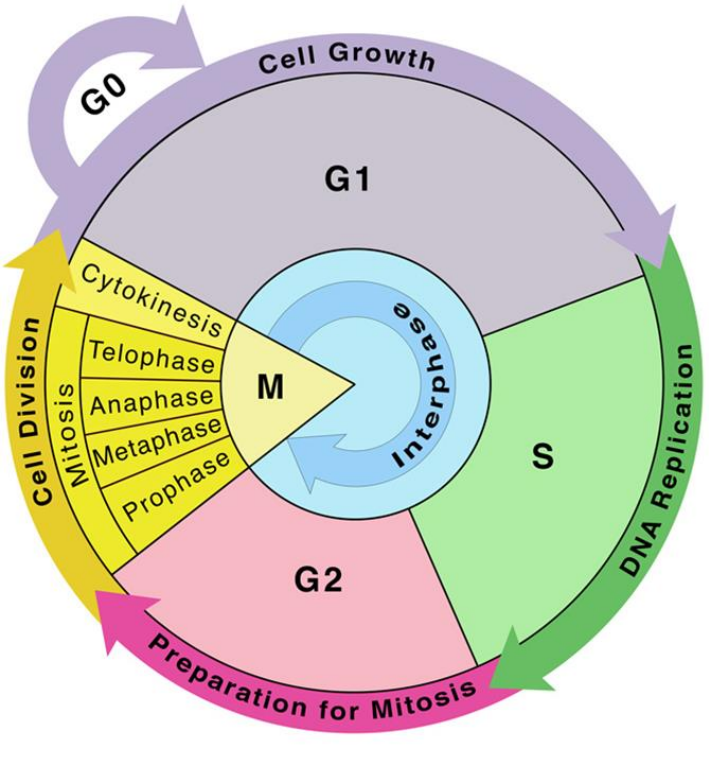
What is the stage of G0 phase of the cell cycle?

- The cell cycle can continue for the life of some cells.
- Neuron (nerve cell), do not continue to grow and divide after they completely differentiate.
- G0 is the stage where cells exist the continuous cycle of growth & division and stop dividing.
- This either a temporary resting period and re-enter the cell cycle, or more permanent.
- Neurons leave the cell cycle to enter the G0 phase, where these cells remain metabolically active and viable.



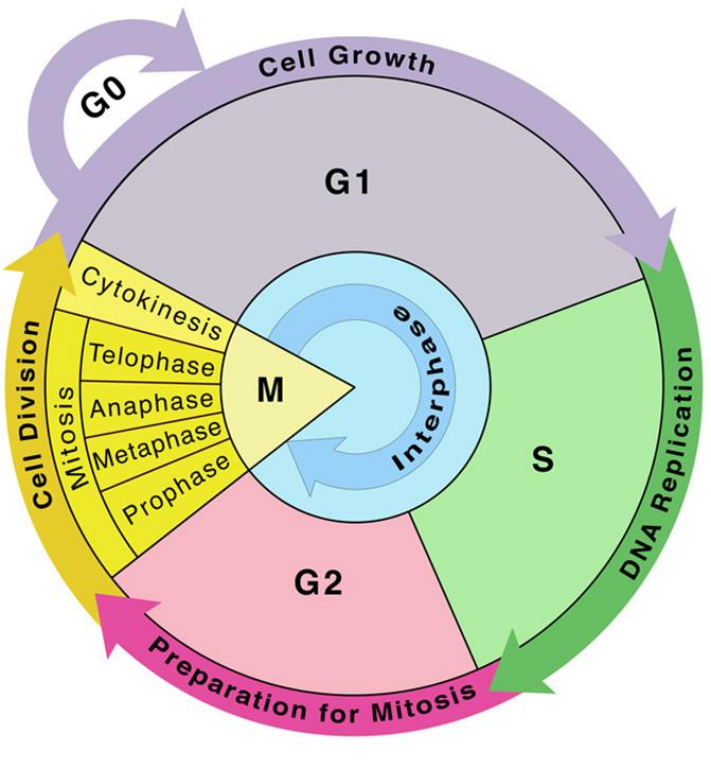
The exit to the G0 phase:

- Occasionally, cells either fail to enter G0 phase or do not remain in the G0 phase, which results in re-enter the cell cycle for continual proliferation (growth and division).
- The uncontrolled cell proliferation leads to cancerous growth.



The M Phases of the cell cycle (Mitotic phase):

- The M phase consists of two parts:
  A. Mitosis: Has four stages.
     1. Prophase
     2. Metaphase
     3. Anaphase
     4. Telophase
  B. Cytokinesis: The cytoplasmic division of a cell at the end of mitosis or meiosis, bringing about the separation into two daughter cells.



The duration of the cell cycle phases:

- The time required for a complete life cycle varies depending on the cell type.
- M phase (Mitosis) is usually the shortest period.

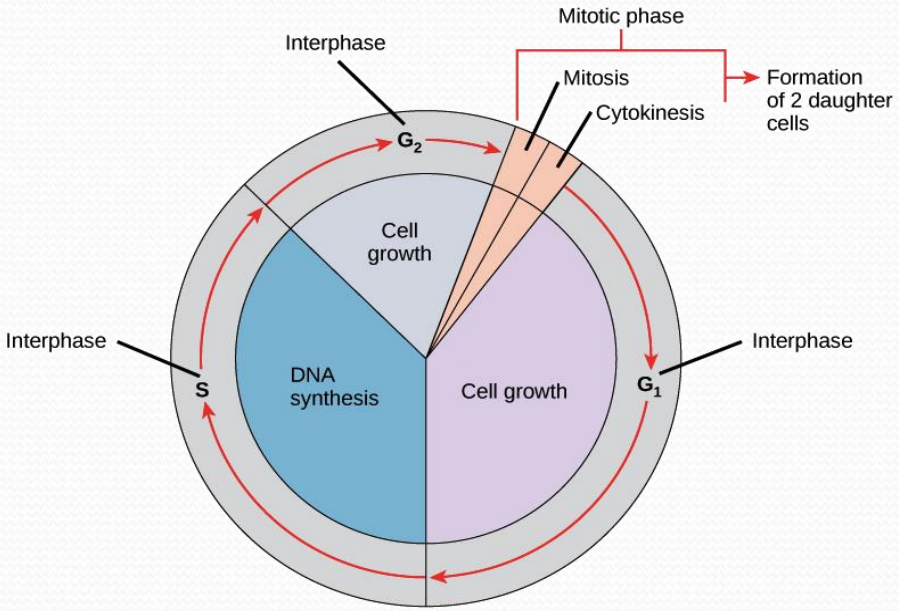


Figure 1: A presentation for the proportions of the duration of each cell cycle phase in a eukaryotic cell

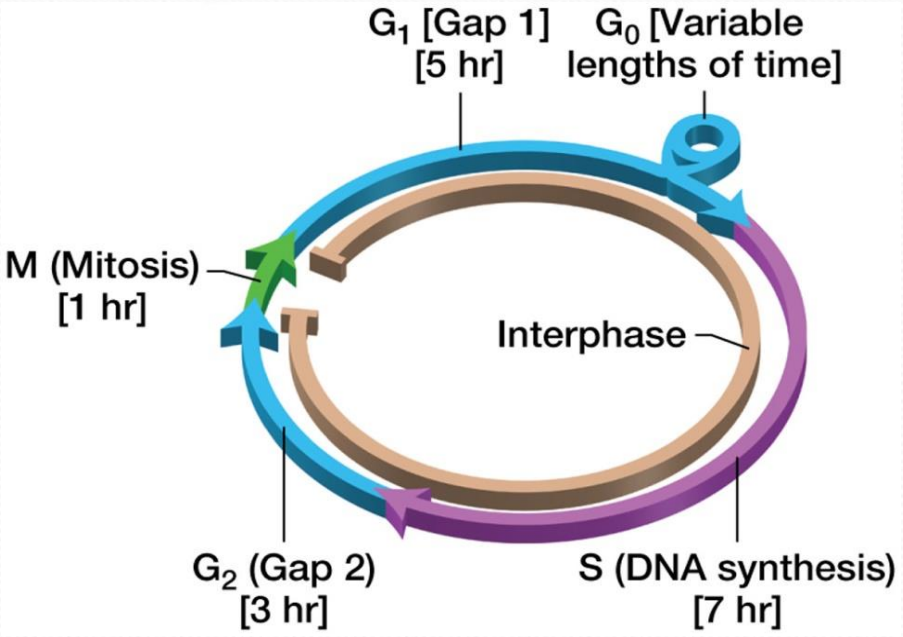
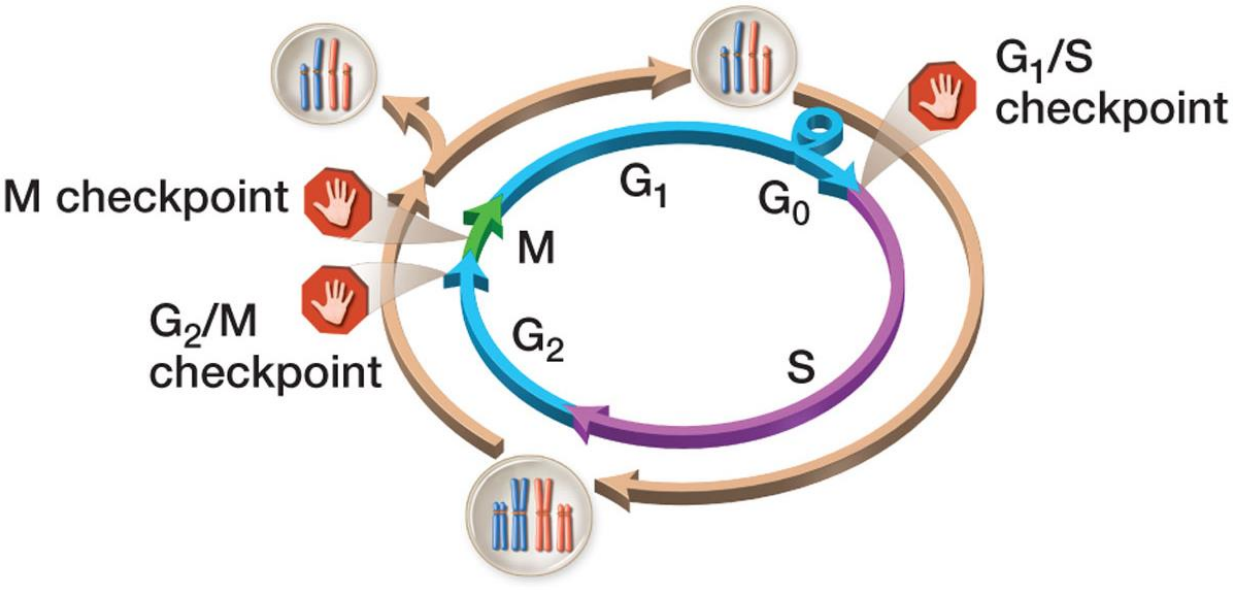


Figure 2: Typical cell cycle of a human cell

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.
- Some points in 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 (Figure 2):



1. The G1/S checkpoint:

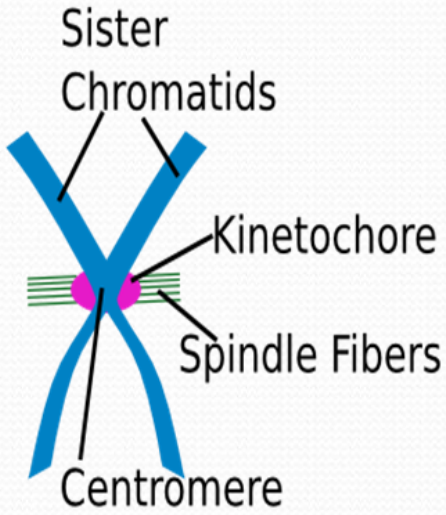
- Determines whether the cell has reached the proper size and determines if the DNA is damaged.
- For example, if the cell attempts to replicate damaged DNA, breaks will occur in the DNA or replication will be blocked.

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.

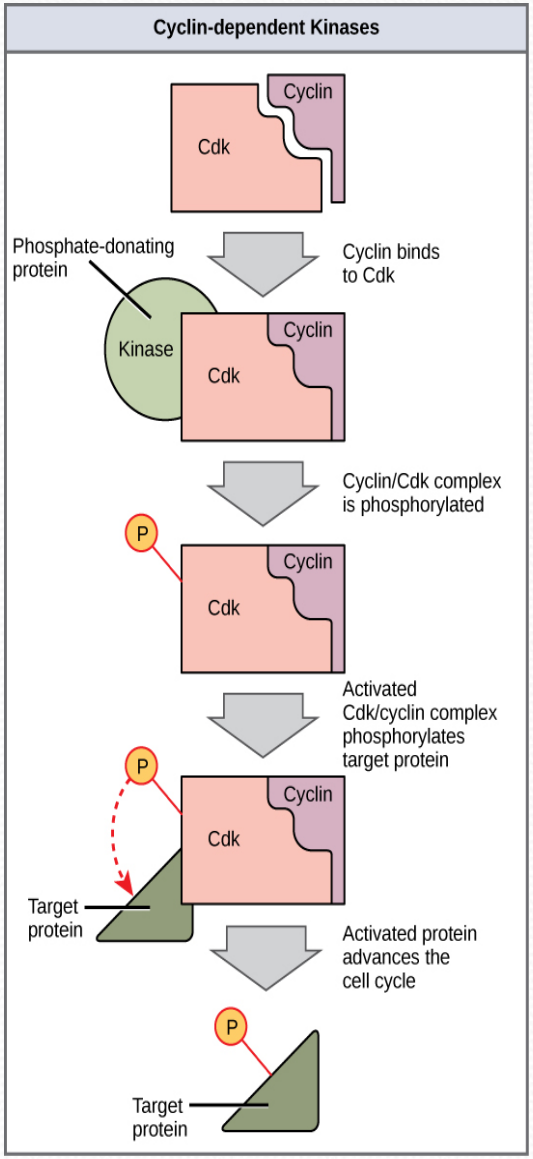


Regulation of the cell cycle checkpoints:

- The cell cycle routinely arrests when genetic damaged is present, giving the cell a chance to repair the damage before committing to cell division.
- If the damaged is too extreme, the cell can enter a programmed cell death (apoptosis).
- If the G1/S checkpoint detects DNA damage, the p53 protein targets the cells for regulated death.
- If the p53 gene is defective, then the controlled death of the damaged cells would not take place, and the possible uncontrolled cell growth would result in cancer.
- In fact, a number of human cancers, including colon, breast, and lung cancers, have been shown to be associated with mutations in the p53 gene.

Regulatory molecules of the cell cycle (Positive Regulation):

- Positive regulators helps in the progression of cell cycle.
- Two 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 that phosphorylate other proteins by changing its shape. The phosphorylated proteins by Cdks are involved in passing the cell to next phase.



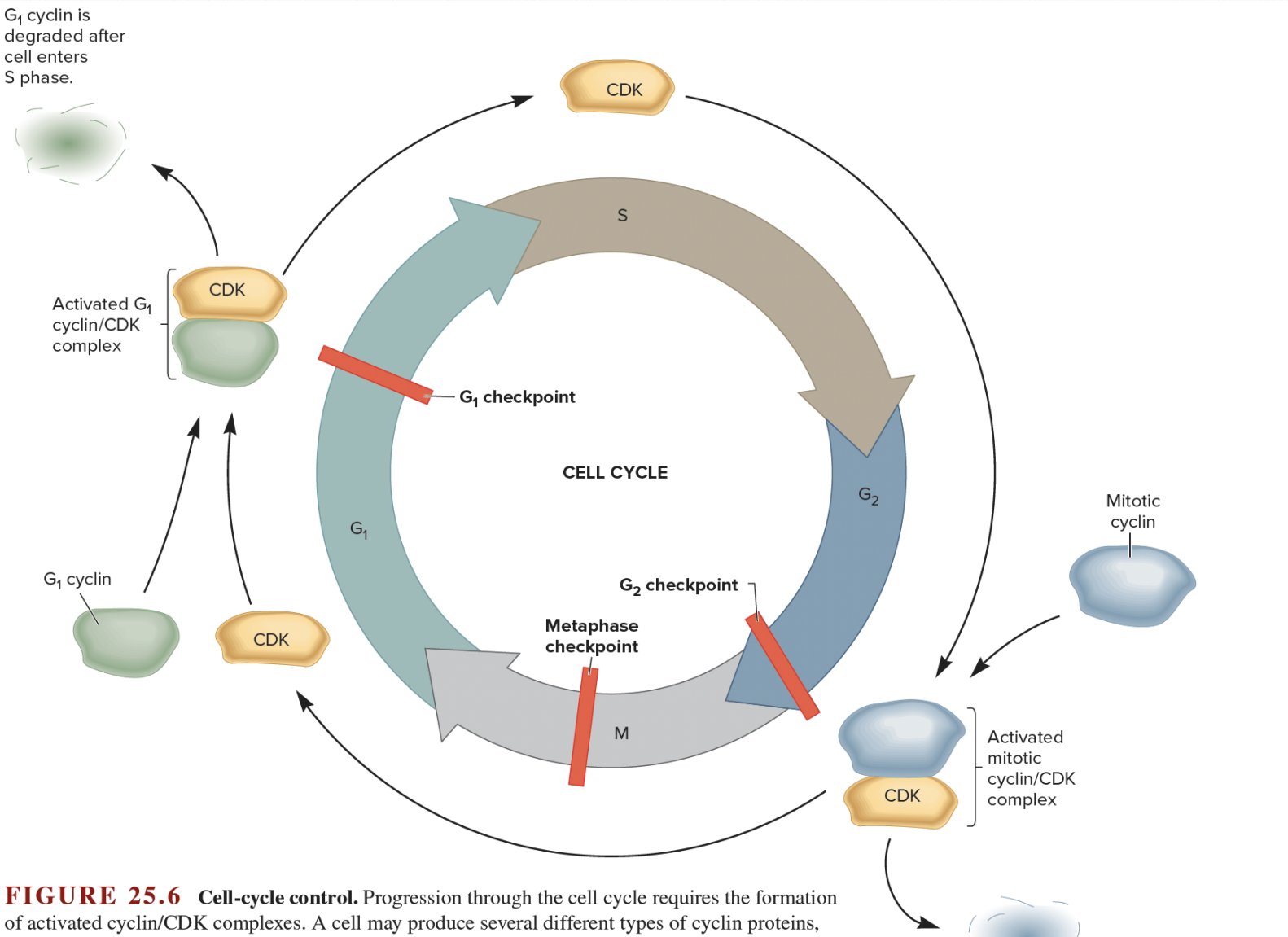
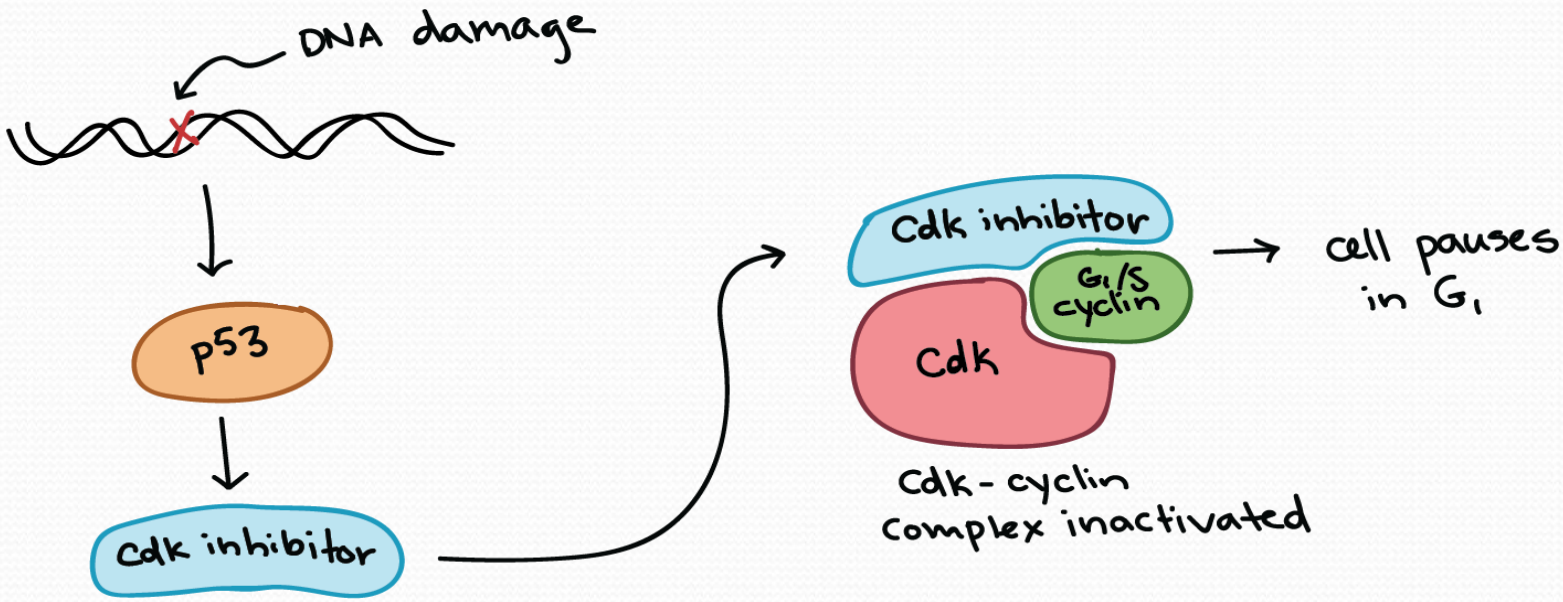


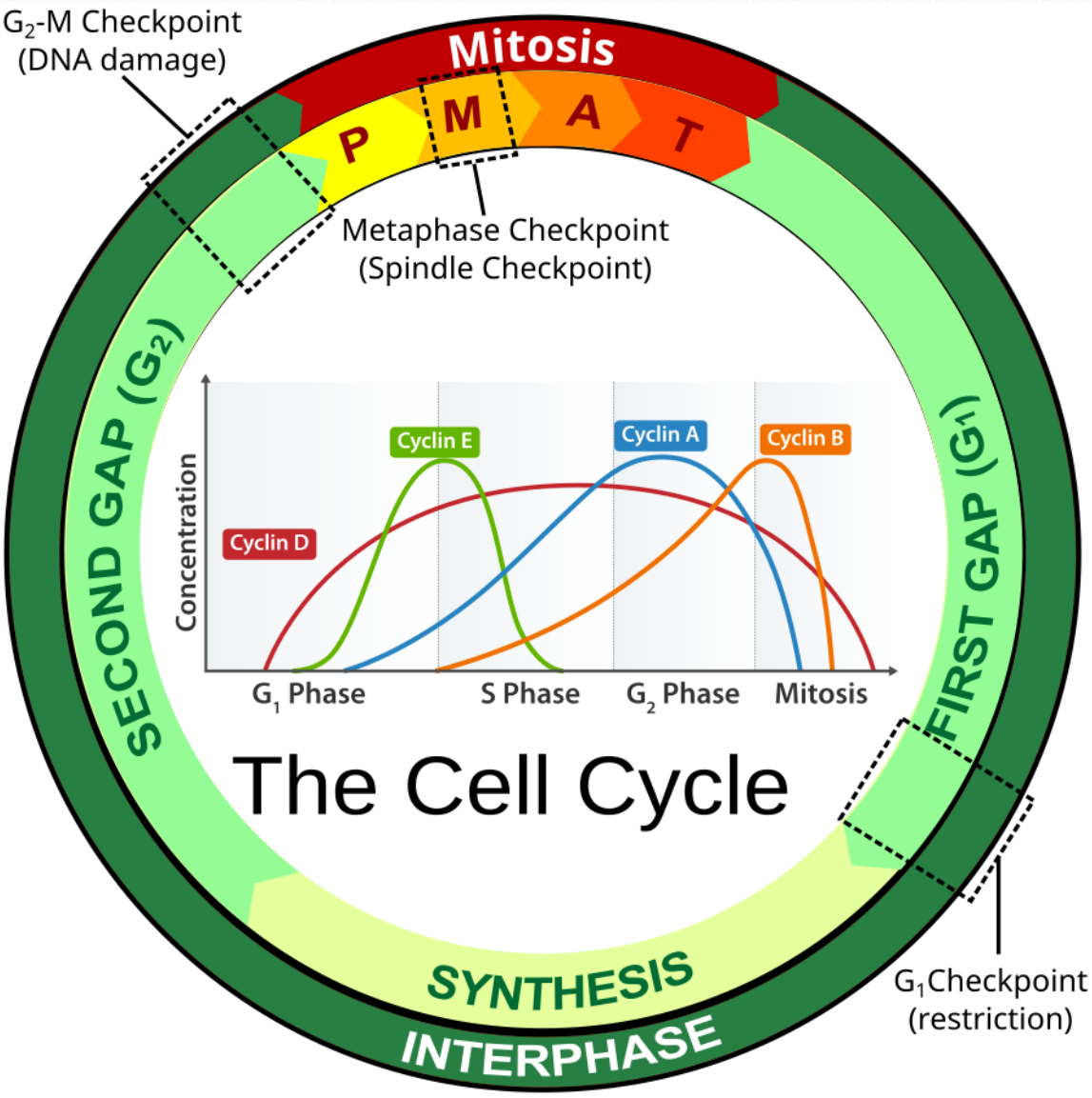
FIGURE 25.6 **Cell-cycle control.** Progression through the cell cycle requires the formation of activated cyclin/CDK complexes. A cell may produce several different types of cyclin proteins, which are typically degraded after the cell has advanced to the next phase. The formation of activated cyclin/CDK complexes is regulated by checkpoint proteins. If these proteins detect DNA damage, they will prevent the formation of activated cyclin/CDK complexes. In addition, other checkpoint proteins can detect chromosomes that are incorrectly attached to the spindle apparatus and prevent further progression through metaphase. Note that this is a simplified diagram of the cell cycle of humans.

Regulatory molecules of the cell cycle (Negative Regulation):

- Negative regulators stop (inhibit) the processes of the cell cycle.
- For example: a group of tumor suppressor genes: retinoblastoma protein (Rb), p53 and p21. These proteins (Rb, p53, and p21) function mainly at the **G1/S checkpoint**.
- Any damage to these genes results in the initiation of cancer cells.



Summary


G2-M Checkpoint
(DNA damage)
Mitosis
P
M
A
T
Metaphase Checkpoint
(Spindle Checkpoint)
SECOND GAP (G2)
FIRST GAP (G1)
Concentration
Cyclin D
Cyclin E
Cyclin A
Cyclin B
G1 Phase
S Phase
G2 Phase
Mitosis
The Cell Cycle
SYNTHESIS
INTERPHASE
G1Checkpoint
(restriction)

Quiz: The cell cycle and its checkpoints

1. The two major phases of the cell cycle are ____ and ___ .
   - interphase, M
   - G1, G2
   - G1, M
   - G0, G1

2. Once the cell is fully differentiated, it enters to ____ phase.
   - G0
   - G1
   - G2
   - M

3. In a typical cell cycle of a human cell, the M phase take about ___ .
   - 1h
   - 3h
   - 5h
   - 7h

4. ____ is a negative regulatory molecule of the cell cycle.
   - cyclins
   - p53
   - chromatin
   - bases