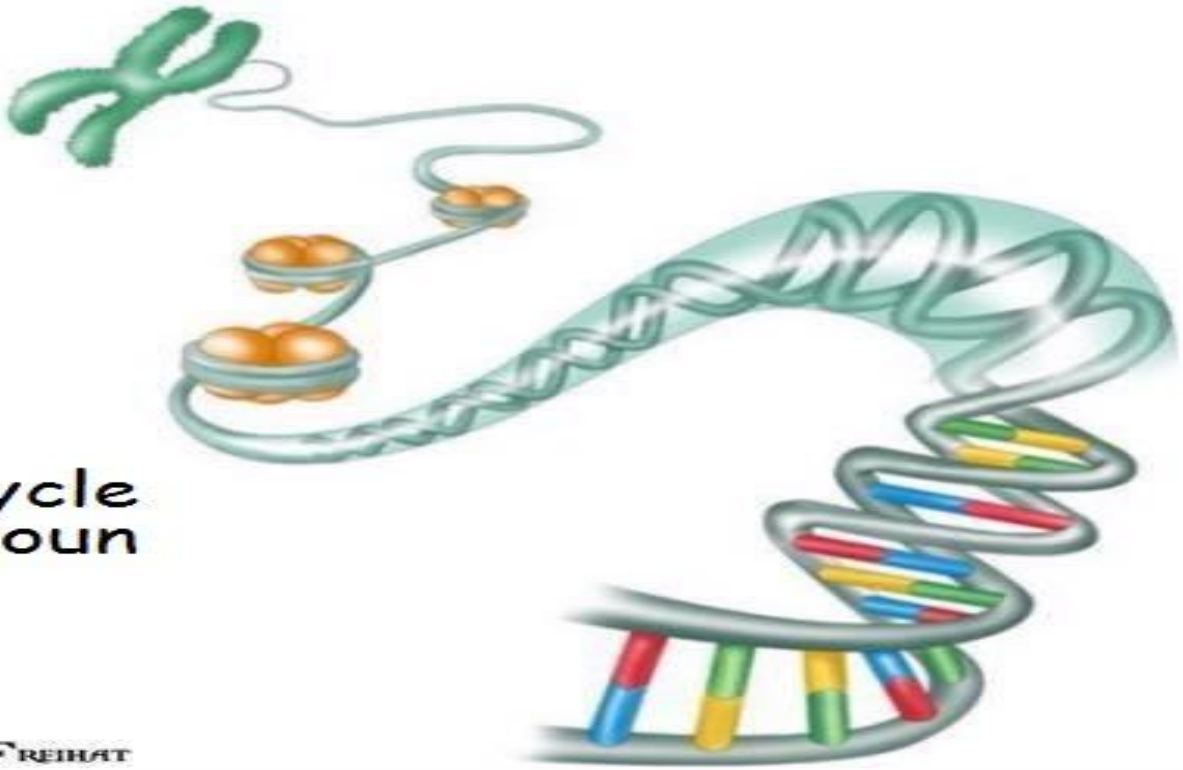
University of Jordan
Faculty of Medicine
Batch 2013-2019

Medical Committee
The University of Jordan

# Genetics & Molecular Biology

● Slides ○ Sheet ○ Handout ○ other.....



Number # 10

**Title:** Cell cycle

**Dr.** Dr. Mamoun

**Done By:**

**Date:**

**Price:**

Designed by Nadeen Al-Freihat

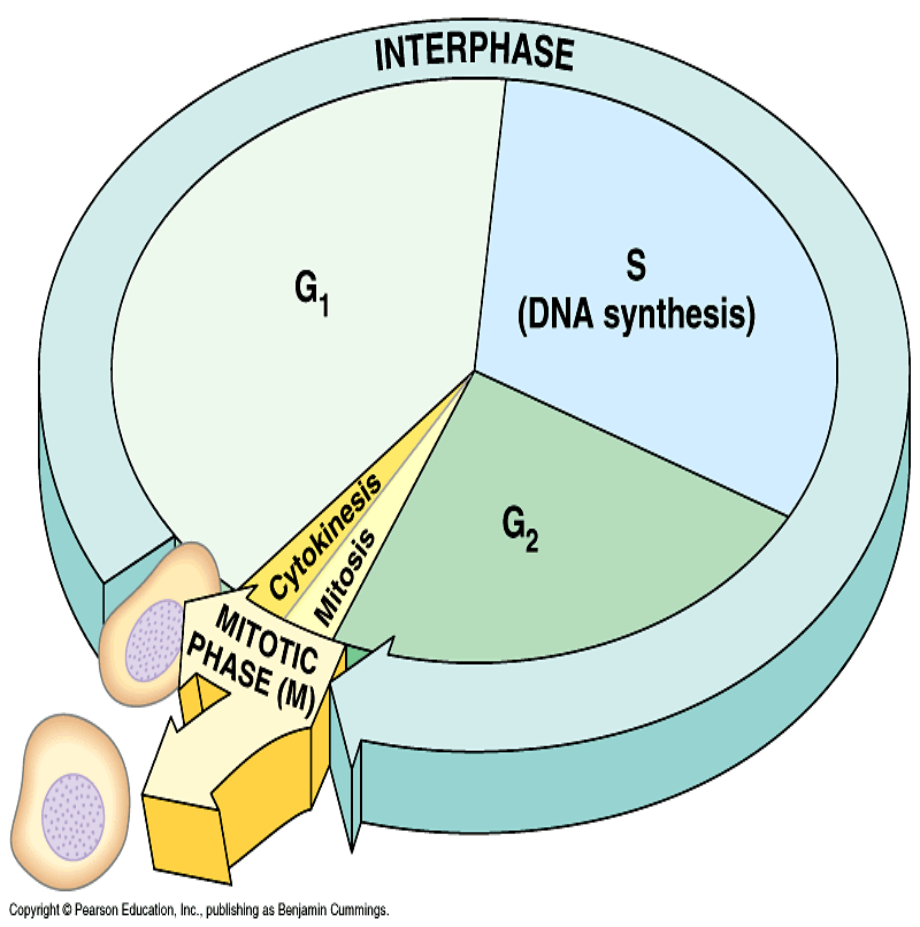

# Lecture 10: Cell cycle

**Dr. Mamoun Ahram**
**Faculty of Medicine**
**Second year, Second semester, 2014-2014**

***Principles of Genetics and Molecular Biology***

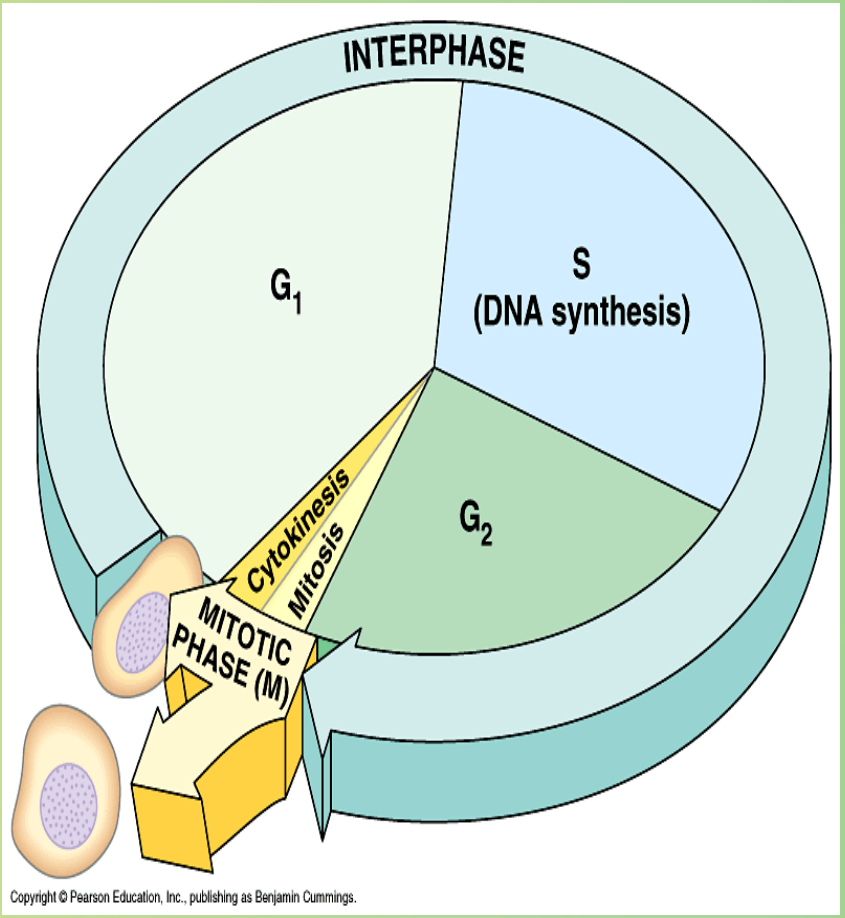
# The cell cycle

- A typical eukaryotic cell cycle divides ~every 24 hours.
  - Mitosis and cytokinesis = ~1 hour
- Interphase: cell growth and DNA replication occur in an orderly manner in preparation for cell division.
- Yeast cells: 90 minutes
- Zygote: no G1 or G2, but rapid S and M phases
- Some cells (neve cells) enter a quiescent stage ($G_0$ phase)



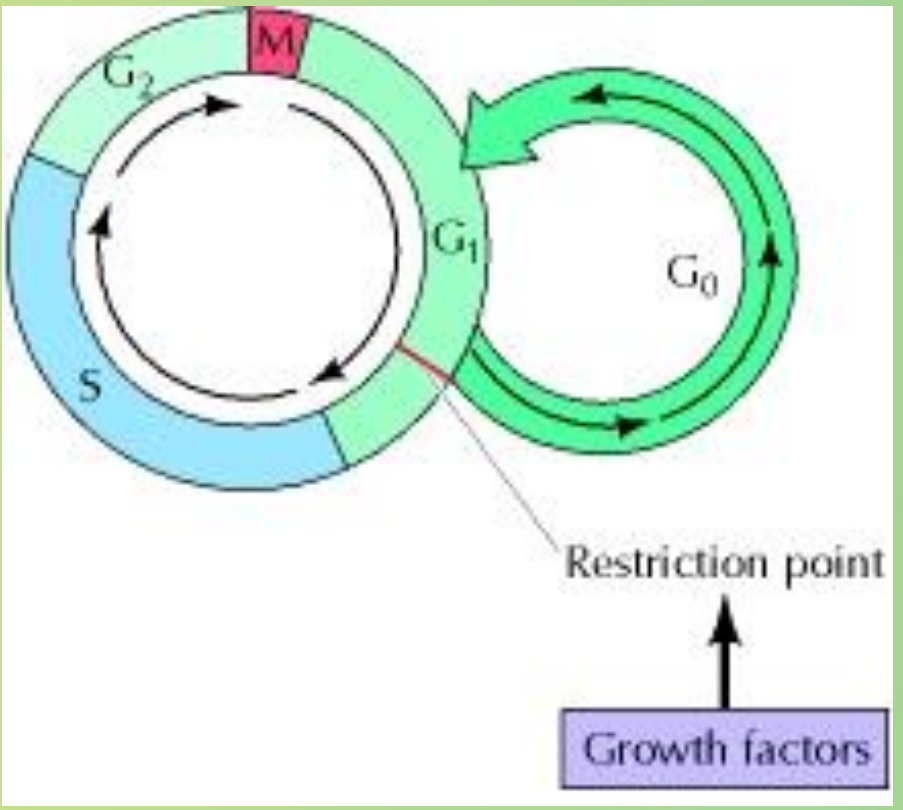
# Phases of cell cycle

- G1: increased metabolism and cell growth; cells are dipoloid (2n)
- S: DNA replication; cells are 2-4n
- G2: metabolism and cell growth; cells are 4n
- M: chromosomal segregation, nuclear and cell division (4n)



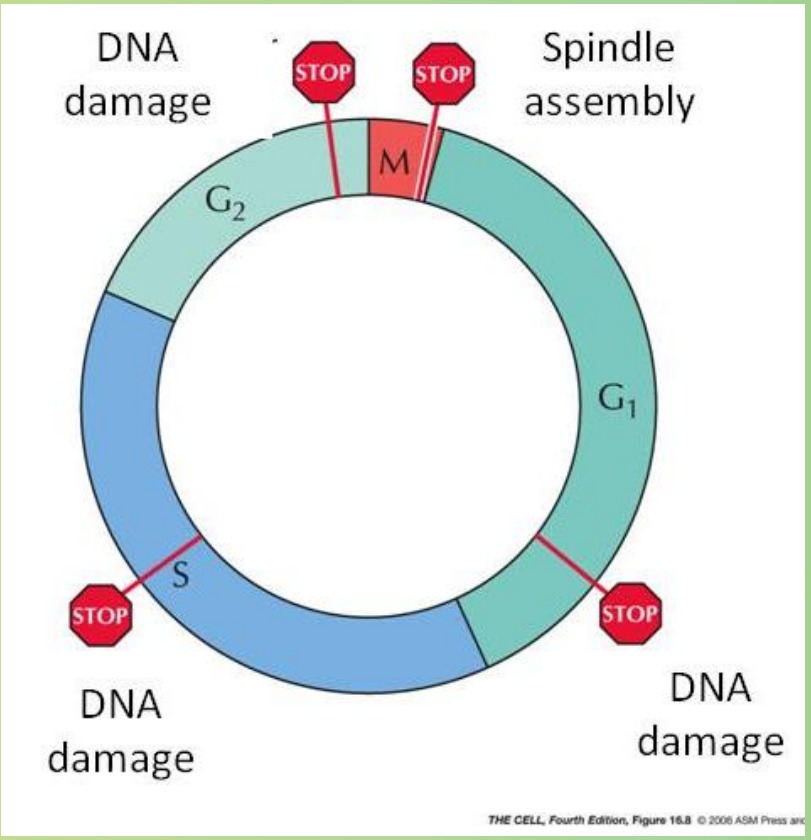
# Regulation of cell cycle

- Restriction point: a decision point in late $G_1$ regulated by the extracellular growth factors
- If not there, cells enter $G_0$ phase where they are metabolically active without growth.



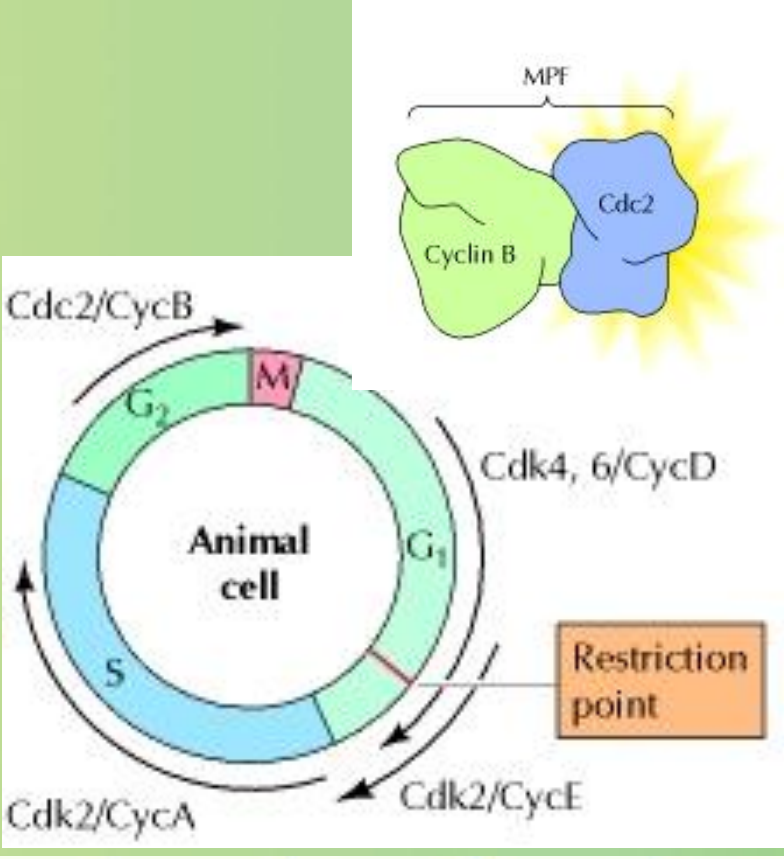
# Checkpoints

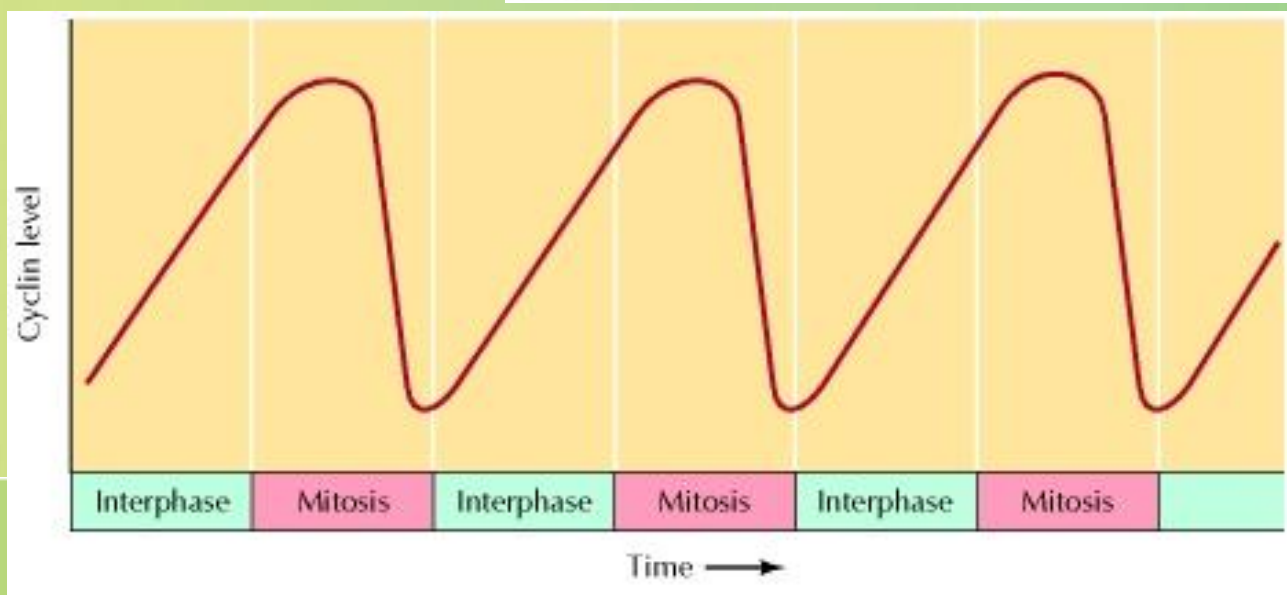
- **DNA damage checkpoints: to ensure that incomplete or damaged DNA is not replicated and passed on to daughter cells.**
- **Spindle assembly checkpoints monitor the alignment of chromosomes on the mitotic spindle.**



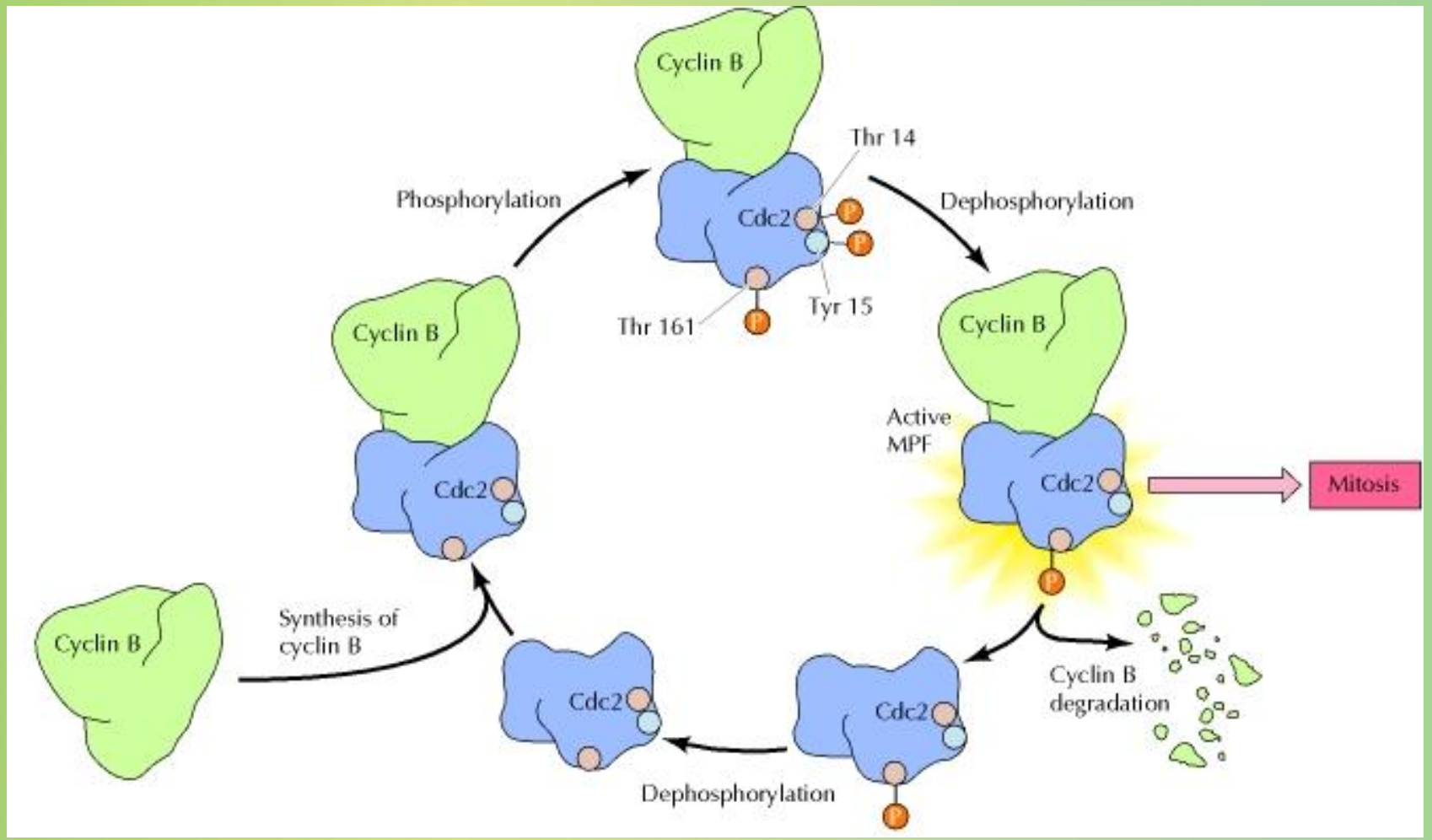
# Regulators of cell cycle

- **Cyclins: proteins that accumulate throughout interphase and are rapidly degraded toward the end of mitosis.**
- **Cyclin-dependent kinases (Cdk's): bind to cyclins and get activated.**
- **Cdk inhibitors: inhibit Cdk activity**

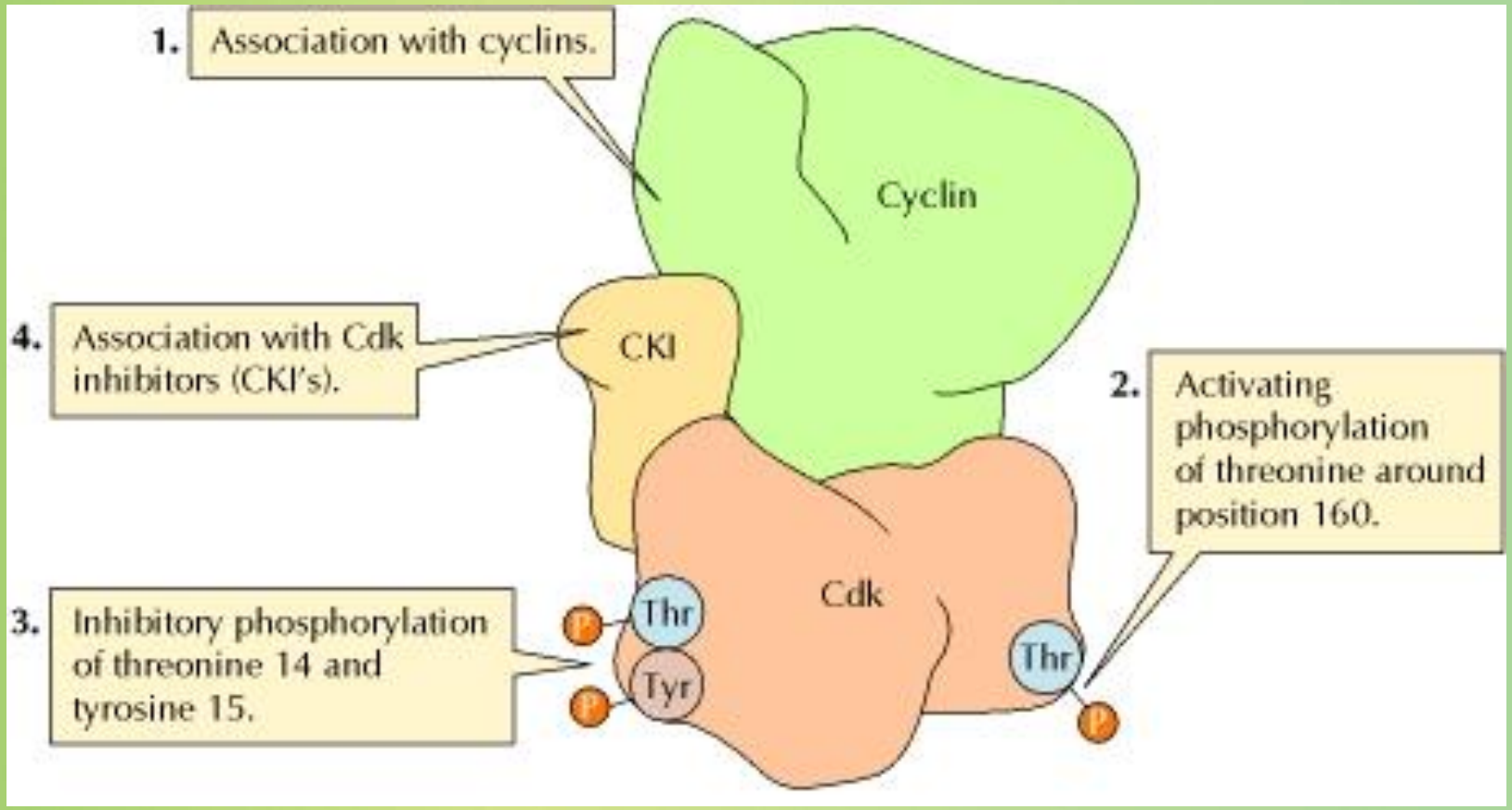


# Example of regulation of cell cycle progression

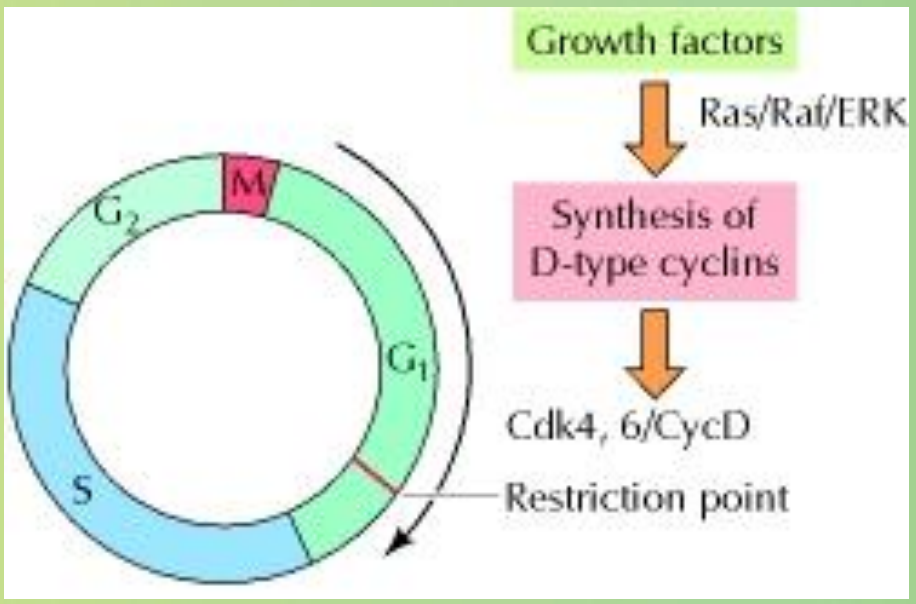


# Mechanisms of Cdk regulation



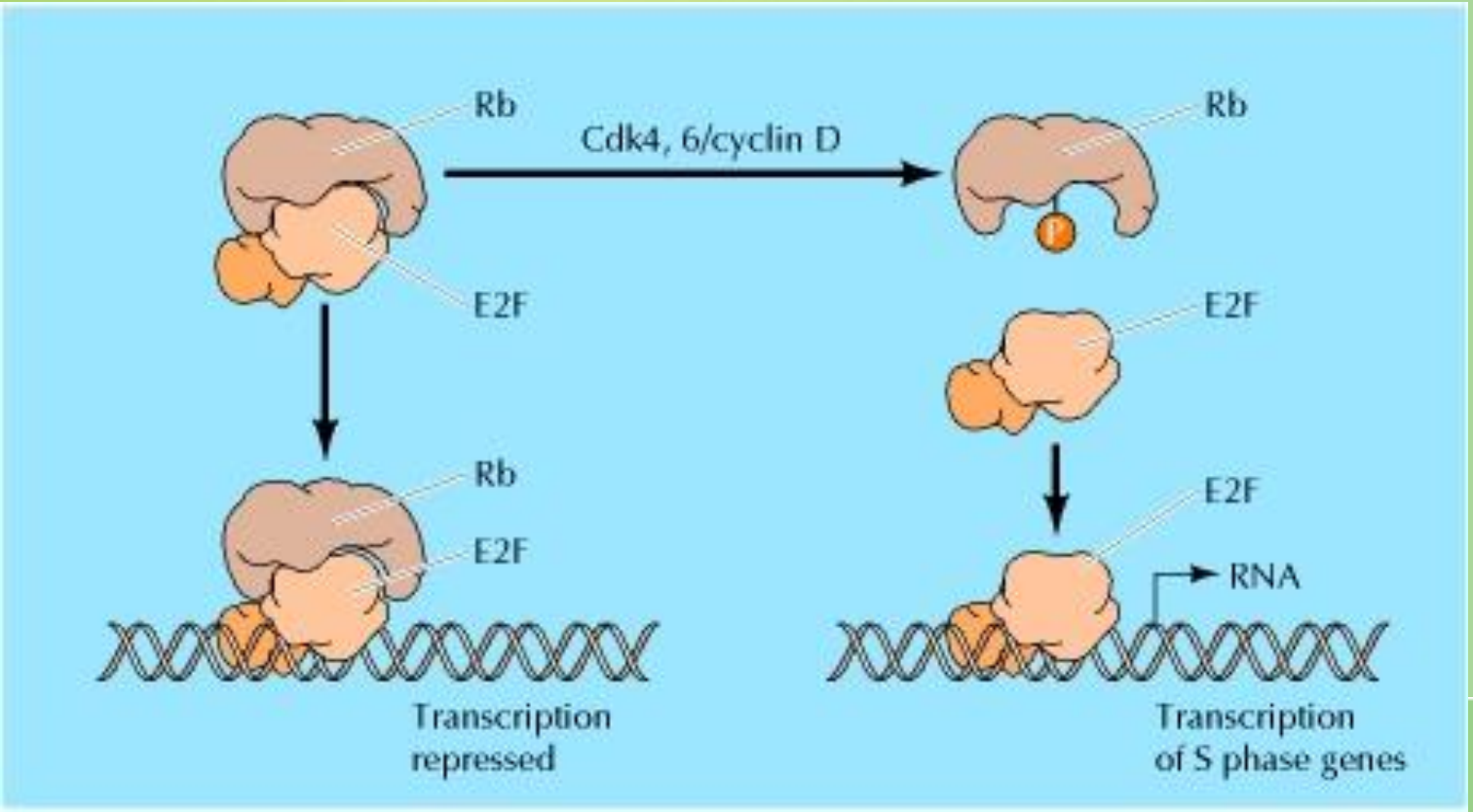
# Cells signaling and cell cycle

- Growth factors regulate cell cycle progression through the $G_1$ restriction point by inducing synthesis of D-type cyclins via the Ras/Raf/ERK signaling pathway.
- Defects in cyclin D regulation lead to the loss of growth regulation characteristic of cancer cells.



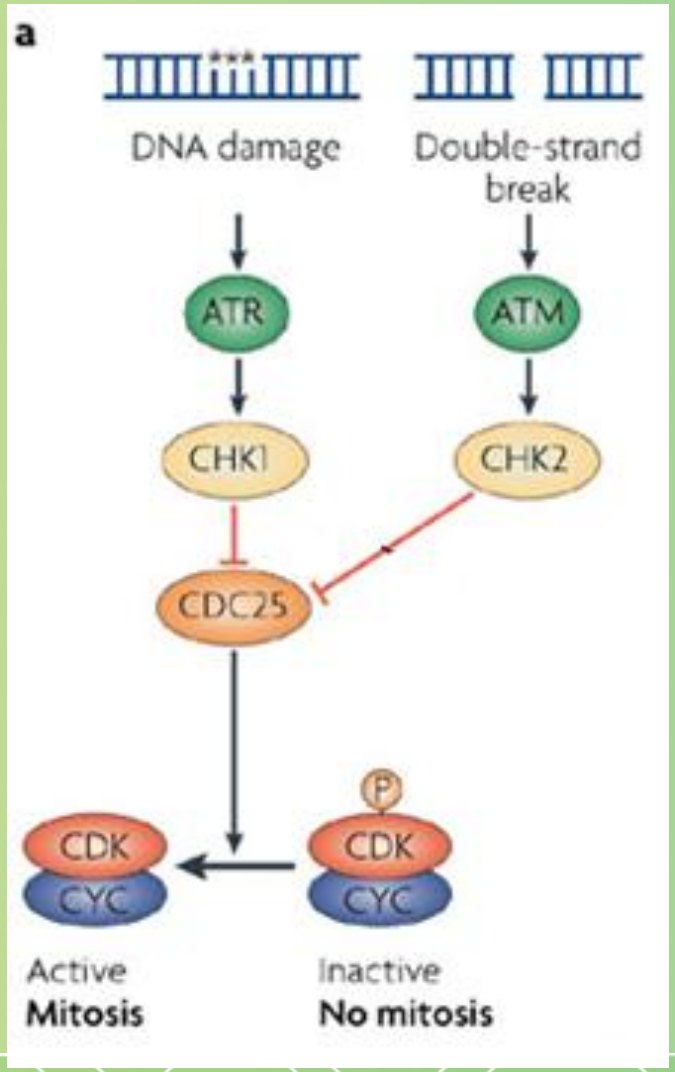
# Retinoblastoma

- When unphosphorylated, Rb binds to E2F proteins and represses transcription.
- E2F is freed when Rb is phosphorylated by Cdk4, 6/cyclin D stimulating cell cycle progression through restriction point.



# Cell cycle arrest by DNA damage

- ATM and ATR are protein kinases
  - ATR is activated by single-stranded DNA damage.
  - ATM is activated by double-strand DNA damage.
- ATR and ATM activate the checkpoint kinases, Chk1 and Chk2, respectively, which inhibit Cdc25 phosphatase.
- Phosphatases cannot activate Cdk's causing cell arrest.



# Role of p53 in cell cycle arrest

- DNA damage results in phosphorylation of p53 protein stabilizing it.
- Activated p53 activates expression of p21, which is a protein that inhibits a Cdk/cyclin complex.