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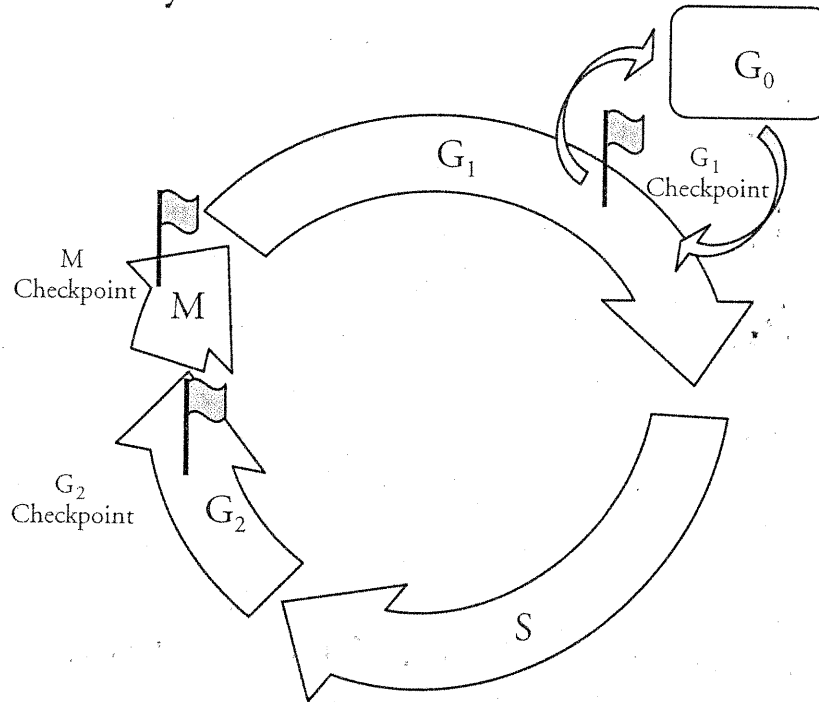
# Cell Cycle Regulation

How does a cell know it is time to divide?

## Why?

Quality control inspectors typically do not limit their product testing to the final product at the end of the assembly line. They monitor all aspects of production in hopes of preventing larger problems down the line. Likewise, when cells are progressing through the cell cycle there are processes in place that check on the cell's progress. Is everything happening according to plan? Are there sufficient resources to complete the task of cell division? Tightly regulating the cell cycle keeps a multicellular organism healthy by conserving materials. This ensures that new cells receive accurate genetic information, and also prevents uncontrolled growth that may lead to diseases like cancer.

## Model 1 – The Cell Cycle



1. Review the phases of the cell cycle in Model 1 by placing the abbreviated phase name (G<sub>1</sub>, S, G<sub>2</sub> or M) next to the proper description.

G<sub>1</sub>      The cell grows by producing more proteins and organelles.  
S         DNA replication occurs.  
G<sub>2</sub>      The cell prepares for cell division with the appearance of centrosomes.  
M         Mitosis and cytokinesis occurs.

2. Some cells, like mature nerve cells or muscle cells, do not divide. Other cells will divide only when the cellular environment signals that it is necessary. According to Model 1, what "phase" of the cell cycle are these cells said to be in when they are not dividing or planning to divide?

G<sub>0</sub>

\* Note: 50+ growth factors in animal cells  
PDGF = platelet derived growth factor  
- released by platelets at site of wound to trigger cell repair

3. There are three regulatory checkpoints built into the cell cycle.

a. Name the three checkpoints as shown on Model 1.

$G_1$  checkpoint,  $G_2$  checkpoint, M checkpoint

b. Indicate the phase of the cell cycle, and what part of the phase (early or later), where each checkpoint occurs.

$G_1$ -later,  $G_2$ -later, M-later

4. Progression through the cell cycle is dependent on both extra- and intracellular conditions. Consider the following conditions. Indicate which checkpoint(s) most likely responds to that condition.

a. The DNA has been completely replicated and checked for errors.

$G_2$

b. There is ample supply of energy and raw materials available.

$G_1, G_2$

c. All chromosomes are attached to the spindles.

M

d. There is adequate room in the environment for more cells.

$G_1$

5. Which checkpoint appears to regulate whether the cell is in  $G_0$  or not?

$G_1$

6. Predict the result of a mutation that allows a cell to move past checkpoint  $G_1$  even though the cell has not grown sufficiently.

-may get stopped at  $G_2$  or M      -apoptosis  
-may not form properly - too small to survive

7. Predict the result of a mutation that allows a cell to move past checkpoint  $G_2$  even though DNA replication has not been completed.

-may get stopped at M      -apoptosis  
-cell won't have proper DNA

8. Predict the result of a mutation that allows a cell to move past checkpoint M even though the chromosomes were not prepared for division.

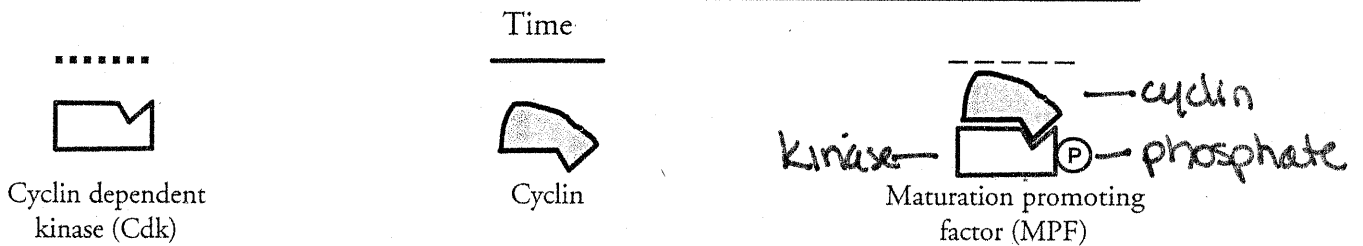
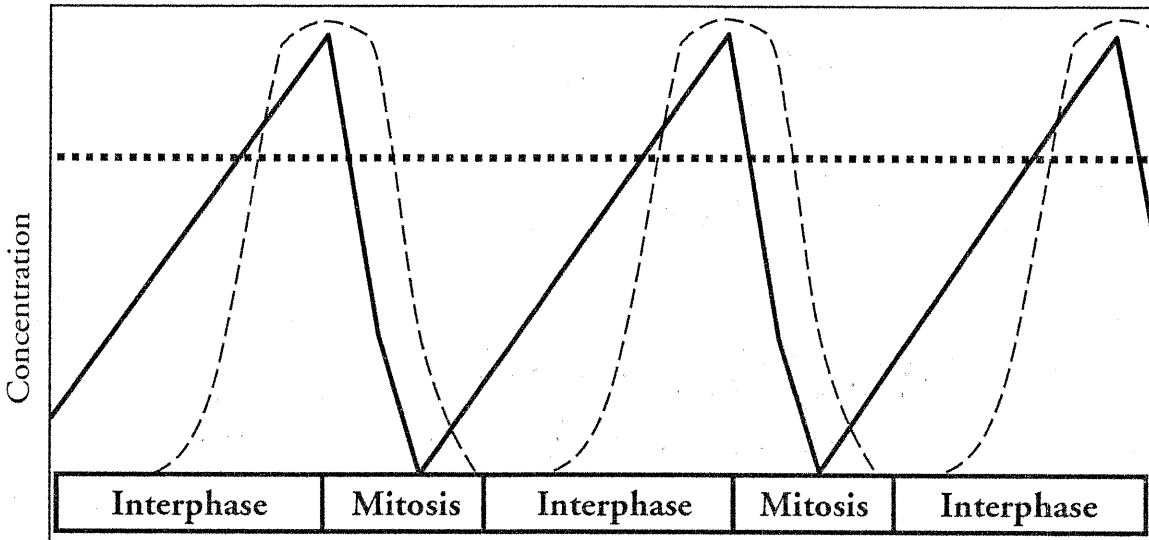
-dysfunctional cells      -apoptosis  
w/ wrong copies/#'s of  
chromosomes



## Read This!

What determines if a cell is in  $G^0$  or going through the cell cycle? What determines a “pass” at a check-point during the cell cycle? These questions are answered by both intracellular and extracellular chemical signals. **Growth factors** are one type of chemical signal. These proteins are released by specialized cells and trigger cell division. Surface proteins tell cells to stop dividing if the environment gets too crowded and cells are touching with too much pressure. Enzymes called **kinases** provide the energy (through phosphorylation) for many of the processes that must happen for successful mitosis to occur.

## Model 2 – Cyclin and Kinase



9. Draw the shape that represents the kinase in Model 2.



10. Draw the shape that represents cyclin in Model 2.



11. Recall that the purpose of the kinases is to phosphorylate other molecules, thus bringing them to a higher energy state. With this in mind, identify the three parts of the maturation promoting factor (MPF) shown in Model 2.

see Model

12. The graph in Model 2 divides the cell cycle into "interphase" and "mitosis." Which of the phases of the cell cycle in Model 1 fall into the "interphase" time frame?

G<sub>1</sub>, S, G<sub>2</sub>

13. Consider the graph in Model 2.

- a. Describe the changes in the concentration of cyclin dependent kinase (Cdk) as the cell moves through different phases of the cell cycle.

stays same

- b. Describe the changes in the concentration of cyclin as the cell moves through different phases of the cell cycle.

↑ interphase ↓ mitosis  
peak b/n interphase + mitosis

14. Propose an explanation for the change in the maturation promoting factor (MPF) concentration throughout the cell cycle based on your knowledge of the concentrations of Cdk and cyclin.

- when there is the most cyclin, there is the most MPF because the more substrate (cyclin) the more the MPF can help w/ rxns.

15. Can the change in cyclin concentration during mitosis be explained by the fact that the cell divides in two and thus divides the material in the cell into two smaller volumes? If no, propose an explanation for the change in concentration that is seen.

No, cyclin concentration goes down as it's used up.

16. Considering both Model 1 and Model 2, which checkpoint in the cell cycle is regulated by the concentration of MPF? Justify your reasoning.

G<sub>2</sub>-end of interphase has the highest concentration of MPF.

## Read This!

After MPF has done its job of phosphorylation, the cyclin portion of the complex is degraded. This means that the protein is broken up into parts that can be recycled by the cell. The kinase is not degraded, but instead used again as the cell goes through another cycle of division.

17. If cyclin was always available in the cell at high concentrations, what effect would this have on the cell cycle?

- cell cycle would continue unchecked through mitosis without using checkpoints.

18. How might a cell be affected by the development of a degradation-resistant cyclin mutant? Explain.

- If can't break down cyclin, MPF would always be active & might skip checkpoints

## Read This!

Cyclin proteins are encoded by a group of genes called **proto-oncogenes**. Besides cyclins, which function inside the cell, other proteins made by genes from this group are embedded in the cell membrane and receive extracellular signals that help to regulate the cell cycle and slow down the differentiation of new cells. **Tumor suppressor** genes make up another group of genes that regulate cell division. Genes from this group produce proteins that signal cells when they are getting too crowded, proteins whose function is to repair DNA, and still other proteins that regulate apoptosis (pre-programmed cell death). A tumor suppressor gene called p53 causes apoptosis when the cell is worn out or when defects are detected.

19. At which checkpoint in the cell cycle would a tumor suppressor gene

a. repair DNA function?

G<sub>2</sub>

b. check for adequate room for more cells?

G<sub>1</sub>

20. Create an analogy for the function of proto-oncogenes and tumor suppressor genes by assigning the role of a car's accelerator and brake pedals to each group. Using your previous knowledge, the information given above, and information in Model 2, complete the table below.

Regulatory Genes	Pedal	Justification
Proto-oncogenes	accelerator	- regulate cell cycle - allow passing G <sub>2</sub> → division
Tumor suppressor genes	brake	- slows down if too crowded



## Extension Questions

21. Cancer, which can be considered as unregulated cell division, often results from mutations in proto-oncogenes and tumor suppressor genes. Usually mutation in more than one gene from each group is involved. Suggest two or more combinations of mutations that would tend to allow the cell cycle to become unregulated.

- ① keep cyclin (mitosis keeps going) + mutation in tumor suppressor gene (mitosis keeps going)
- ② mutation in proto-oncogene (change in cell regulation) + mutation in tumor-suppressor gene (keeps going)
- ③ mutation in either above gene + p53 gene (no apoptosis)
- ④ change in DNA repair mechanisms + mutation in either above gene

22. Paclitaxel is a chemotherapy drug used to treat a variety of cancers. Paclitaxel inhibits both assembly and disassembly of microtubules.

- a. Which checkpoint in the cell cycle is affected by Paclitaxel?

M - microtubules are centrosomes + spindle fibers in metaphase + anaphase

- b. How does this drug inhibit the growth of cancer?

cell division does not finish

- c. Paclitaxel affects not only cancer cells, but normal cells as well. Would the effects of Paclitaxel be seen first in organs that have quickly dividing cells (like the intestine and hair follicles) or in organs that have slow or nondividing cells (like muscles and the nervous system). Justify your reasoning.

- Quick dividing cells won't divide (cancer cells are quick dividing)
- nondividing cells no impact
- slow dividing cells (probably in G<sub>0</sub>) so not much impact in time