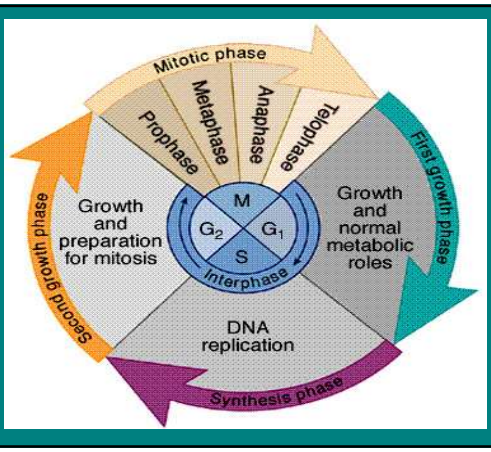
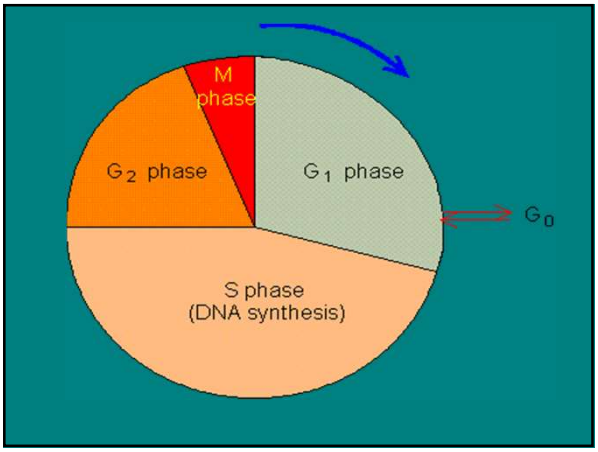
Ch 12

Regulation of the Cell Cycle





The Cell Cycle

1. What is it and why does it exist?

-The timing and rate of cell division is crucial to normal growth and maintenance.

-The cell cycle regulates these timings.

CONTROL OF CELL CYCLE

- Continuous replacement of cells, ex. skin.
- Muscle / nerve arrested in G1.

  If a cell from an arrested G1 is transplanted into a cell in S, the cell will finish cycle

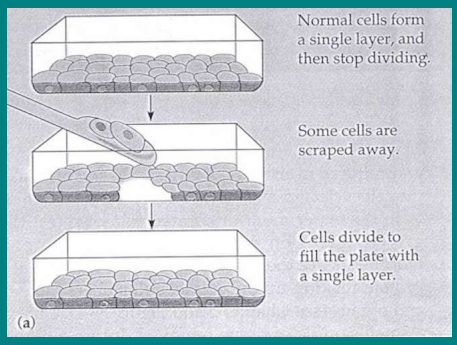
• Cardiac cells arrested in G2. It too, if fused will undergo mitosis

Stimulatory substances cause cells to proceed through critical checkpoints G1 ---- S ----- G2 ----- M

Platelets

- Hormones called growth factors stimulate certain cells to divide.
- Platelets release PDGF (platelet derived growth factor) which triggers fibroblasts to help wound heal.

CROWDING



Its Control…

- The cell cycle is controlled by an operating set of molecules in the cell that will trigger and coordinate key events.
- **KINASES-** These are enzymes that activate or inactivate other proteins by phosphorylating them.
- Some kinases drive the cell cycle. They're always around in fairly constant concentration but the problem is…they can only be activated when they are attached to **CYCLIN**.

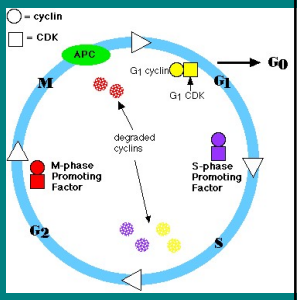
- **CYCLIN- Regulatory protein. Named cyclin because their concentration (produced at constant rate) change cyclically during cell cycle. Cyclin is like the cell clock.**
- **-CYCLIN-DEPENDENT kinase** or **Cdks depend on cyclin to be active**. Its concentration stays the same but activity in response to cyclin changes.
- So the **Cdk** activity will be rising and falling with changes in concentration of cyclin.
- **MPF** (maturation promoting factor) is one of the first cyclin-Cdk complexes discovered.

CYCLINS

CYCLINS: rise and fall w/ the stages of cell cycle

CDK: cyclin-dependent kinases concentration remains fairly stable,

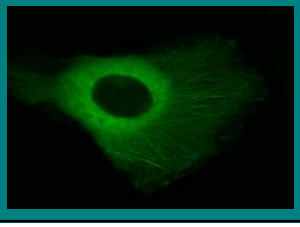
but each must bind to appropriate cyclin to be activated

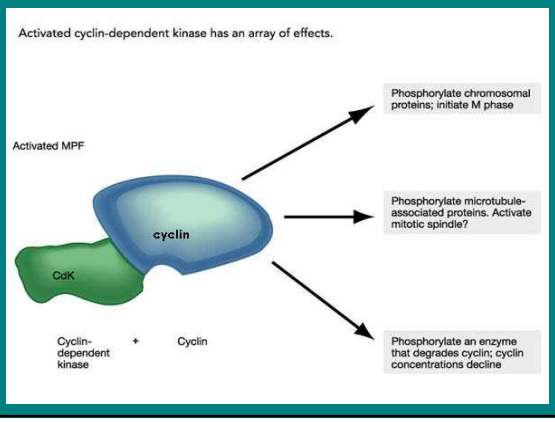


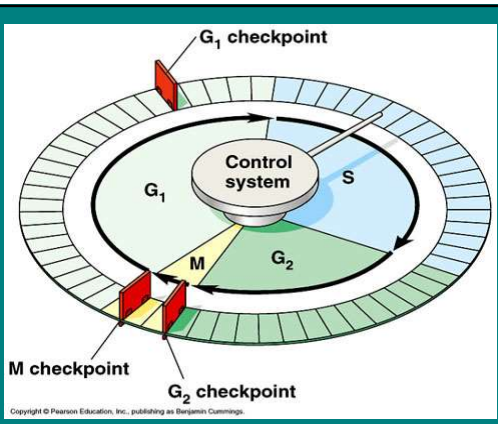
To Summarize…

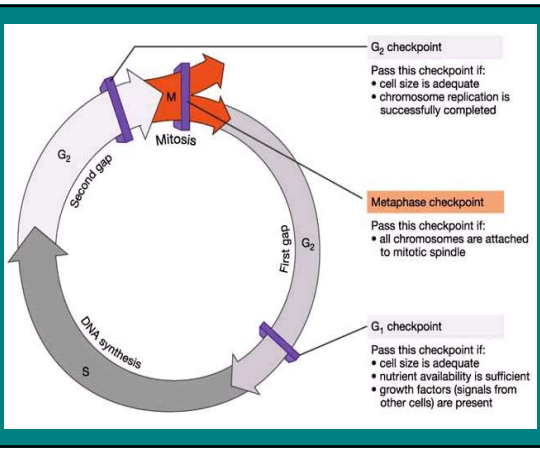
Kinase= enzymes that catalyze transfer of phosphate group from ATP to a target protein

- Kinases involved in Cell Cycle= Cdks
- Cdks + Cyclin= active!= MPF

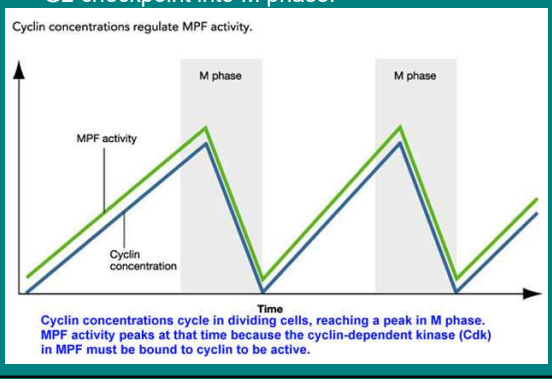








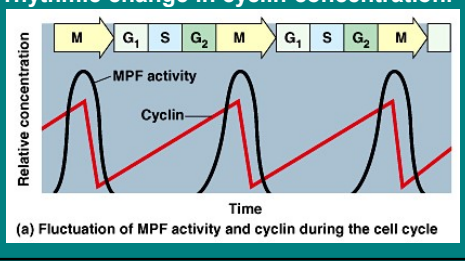
- MPF will trigger the cell's passage past the G2 checkpoint into M phase.

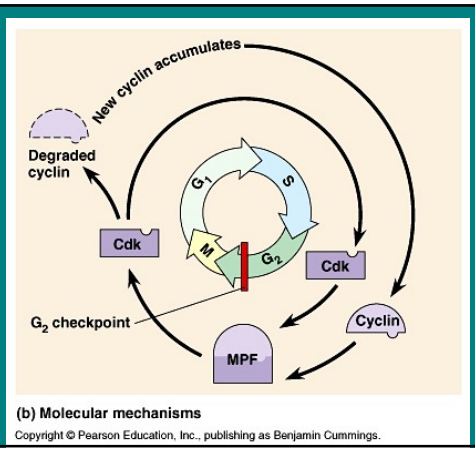


- Not only does MPF activate mitosis, but it also will switch itself off all by itself too!
- It does this by initiating a process that will lead to destruction of its cyclin.
- Destruction is important! This actually will keep driving the cycle past the M phase checkpoint which controls the onset of anaphase

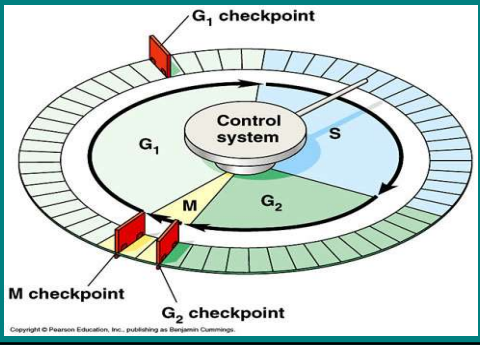
The Mitotic clock.

- **The activity of Mitosis Promoting Factor (MPF), which triggers mitosis, fluctuates with a rhythmic change in cyclin concentration.**





- So what about the G1 checkpoint? The cell must be big enough with the right amount of DNA.



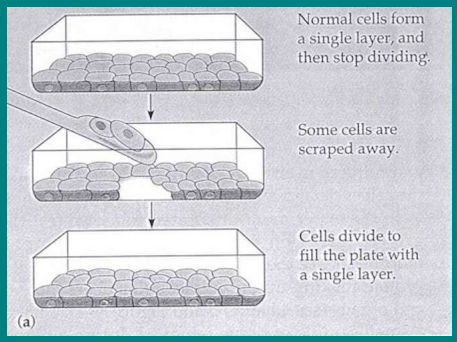
Cancer Cells

- Cancer Cells have escaped from all control…
- 1. They do not follow density-dependent inhibition

2. They do not have anchorage dependence.

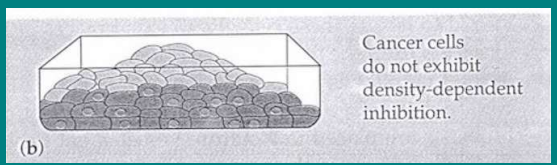
- 3. Some do not seem to require a growth factor.
- 4. They escape checkpoints. (Should a cancer cell stop dividing, it is not at a checkpoint)

CROWDING

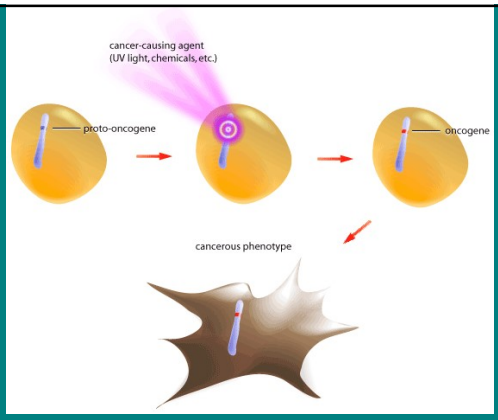


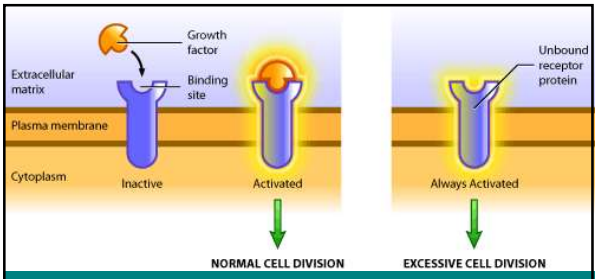
Density-Dependent Inhibition

This type of inhibition may be due to shortage of nutrients, increase in waste or inability for proper anchoring.



- Enzymes regulate the passage of cells through these checkpoints.
- ***Oncogenes*** (cancer causing genes) may code for enzymes that no longer function, thus the cell moves quickly through the cell cycle.

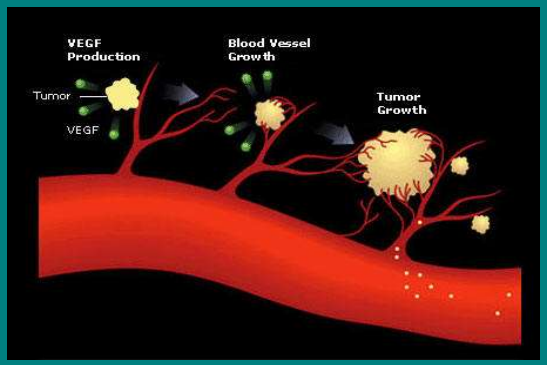




A modified receptor. Under normal circumstances membrane-bound receptors require the binding of their ligand to be in an activated state. In contrast, receptors encoded by oncogenes do not require the regulatory step of ligand binding to be active.

Some More Twisted Ways Of Cancer…

- They have an unusual number of chromosomes
- They have an irregular metabolism
- They can secrete their own growth hormones which allow them to grow AND they can stimulate blood vessel growth to "feed them"



Immune Cells Normally Destroy These Abnormal Cells Unless…

- They evade destruction, and then proliferate to form a tumor (unregulated growing mass of cells)
- If they remain at this original site, the mass is BENIGN and can be removed
- But…because cancer cells don't have much anchorage, they may spread to other parts of the body where they become MALIGNANT