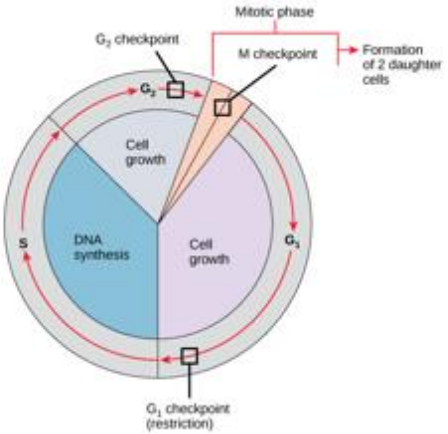
WEEK 4

UNIT 1_7: CELL CYCLE REGULATION	**Where ? How long?**	***Explanations /Questions***
Learning outcomes By the end of this section, you will be able to: • Identify major checkpoints in the cell cycle. • Explain how errors in cell division can lead to cancer.	5 minutes	

ACTIVITY AHEAD OF LESSON: CELL CYCLE REGULATION		25 minutes	
Purpose:	The cell cycle has to be controlled in order to be accurate and avoid errors complicated process. Therefore, there are checkpoints in the cycle that can stop the process in case of any mistake. This activity is intended to understand the how the checkpoints regulated the process of cell division.		
Over to you:	Watch this short this video on cell cycle regulation. Then watch it again, attempt MCQ suggested in the activity. ***Be certain to note anything that you don't understand.***		
Activity:	Make a summary of 200 words about consequences of failure of cell cycle regulation and submit it in the LMS by end of week 4		

CELL DIVISION REGULATION		
The cell cycle is regulated by a molecular control system The timing and rates of cell division in different parts of an animal or plant are crucial for normal growth, development, and maintenance. The frequency of cell division varies with cell type. Some human cells divide frequently throughout life (skin cells). Others 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. **Regulation of the Cell Cycle at Internal Checkpoints** Cell cycle checkpoints are **regulatory pathways** in eukaryotic cell that control the timing and order of cell cycle progression through various phase. To ensure that critical conditions such as DNA replication, and chromosome segregation are completed in proper way in order there are internal control mechanisms that stop a damaged cell from continuing to divide. Three major checkpoints are found in the G1, G2, and M phases.	10 minutes	**External events can regulate the cell cycle** **E.g.:** A lack of Human Growth Hormon (HGH) can inhibit cell division, leading to Dwarfism, whereas too much HGH can result in gigantism.

The G1 checkpoint The G1 point also known as the "**restriction point**" in animal cells, is the most important. If the cell receives a go-ahead signal at the G1 checkpoint, the S phase is initiated. The cell will only pass the checkpoint if it is an appropriate size, enough energy reserves and if the DNAis not damage. **The G_2 Checkpoint** The G_2 checkpoint has to ensure proper conditions for entry into the mitotic phase are met. As in the G_1 checkpoint, cell size and protein reserves are assessed. However, the most important role of the G_2 checkpoint is to ensure that all of the chromosomes have been replicated and experiences a DNA damage checkpoint.  **Figure 1.11: The cell cycle is controlled at three checkpoints**. Integrity of the DNA is assessed at the G_1 checkpoint. Proper chromosome duplication is assessed at the G_2 checkpoint. Attachment of each kinetochore to a spindle fiber is assessed at the M checkpoint. By OpenStax on Nov 27, 2018 OpenStaX.[image], accessed on February 14,2019 , https://cnx.org/contents/s8Hh0oOc@10.1:Vbi92lHB@10/The-Cell-Cycle. **The M Checkpoint** The M checkpoint also known as the spindle checkpoint happens near the end of the metaphase stage of mitosis. The M phase checkpoint ensures that all the chromosomes are properly attached to the spindle at the metaphase plate before anaphase. This ensures that daughter cells do not end up with missing or extra chromosomes. A signal to delay anaphase originates at kinetochores that have not yet attached to spindle microtubules.	10 minutes	If the cell does not receive a go-ahead signal, it exits the cycle and switches to a no dividing state, the G0 phase. Most cells in the human body are in this phase. **E.g.:** neurons and red blood cells.

IN CLASS ACTIVITY: REGLATORY MOLECULES IN CELL CYCLE		20 minutes	
Purpose:	To identify the main regulatory molecules involved in cell cycle regulations		
Over to you:	Using your laptop, click on this link for open resources and read the paragraph regulatory molecules of the cell cycle.		
Activity:	Draw a simple diagram of the cell cycle and place on it the three checkpoints for cell cycle regulation. Then answer following questions: - What is positive regulation? - What is negative regulation? - Describe the association of cyclins and cyclin-dependent kinases (Cdks). - Name the three regulatory molecules and explain the function of each. - Describe how the positive and negative controls differ.		

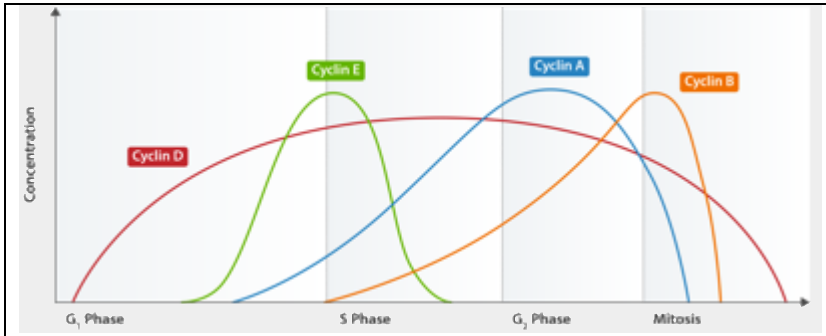


Figure 1. 12: The concentration of cyclin proteins change throughout the cell. By Benutzer, January 22, 2007. Accessed on February 20,2019. https://en.wikipedia.org/wiki/Cyclin#/media/File:Cyclin_Expression.svg/

Regulator Molecules of the Cell Cycle

Positive regulation

2 Types of Regulatory Molecules, together act as a checkpoint:

- Kinases are enzymes in which phosphorylate molecules are present in constant level. Cyclin dependent kinases (Cdk) are inactive (G1 and G2) until cyclin are present.
- Cyclins are with Kinases and serve as a checkpoint, their level fluctuates cyclically.
- Cyclin-Cdk complex also known as MPF (M-phase promoting factor) promotes certain activities that eventually lead to the next stage of the cell cycle. Having the minimum concentration of these complexes help the cell cycle proceed through the checkpoints.

Negative regulation

These regulatory molecules stop the cell cycle. The best known are **Retinoblastoma proteins (Rb), p53 and p21**. P53 tumor suppressor protein is essential for stopping cells with damaged DNA from entering S phase while Rb binds to transcription factor and inhibits synthesis of essential proteins required for cell cycle. P21 represents a major target of p53 activity and thus is associated with linking DNA damage to cell cycle arrest.

20 minutes

Project this video and this , then Ask the students to feed back to the class what they learned in the In-Class activity.

Then re-explain how regulator molecules control cell cycle through positive and negative regulation , being certain to address any identified gaps in understanding.

IN CLASS ACTIVITY: CANCER AND CELL CYCLE			
Purpose:	To establish how the cell cycle relates to cancer	20 minutes	
Over to you:	Read through the click (go to the animation) and the open resource about the cell cycle and go to paragraph cancer and cell cycle. Answer the questions below.		
Activity:	Answer the following questions: - Cancer is the result of an improperly regulated cell cycle. Describe two reasons why cells can form tumors? - Normally, proto-oncogenes stimulate the cell cycle. What are oncogenes and how do they affect the cell cycle? - Normally, tumor suppressor genes inhibit the cell cycle. How do mutated tumor suppressor genes affect the cell cycle? ***Submit answers in the LMS by end of week 4***		

CANCER AND CELL CYCLE

Cancer is partly a disease of uncontrolled cell growth.
Cell cycle and check point genes are found misregulated or mutated in cancer.
Two class of genes provide important signals that regulate the cell cycle :

- Proto-oncogenes
- Tumor Suppressor Gene

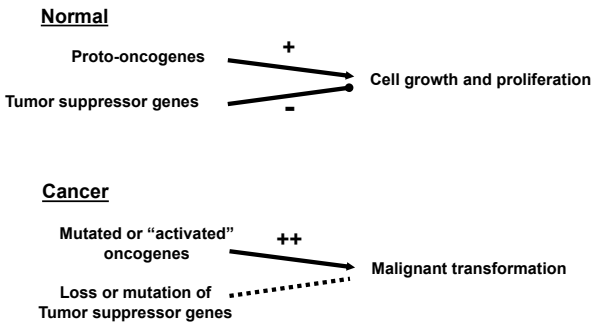
Proto-oncogenes

A proto-oncogene is a normal gene that is responsible for cell growth, cell differentiation, cell division, and apoptosis. Mutations in proto-oncogene can cause it to turn into an oncogene. An oncogene is a gene that causes a cell to become cancerous.
E.g.: the *RAS* gene

Tumor Suppressor Gene

A tumor suppressor gene or anti-oncogene is a gene that codes for negative regulator protein that functions to suppress the formation of cancer.
E.g. : p53

What are the genes responsible for tumorigenic cell growth?



10 minutes

Animation of Tumor Suppressor Gene Mutation example: p53.

Remind students that everyone has tumor suppressor genes and proto-oncogenes.

Anticipated time required for Unit 1.7 activities :

Theory : 2h all activities + 2h self-learning