CONCEPT: G₁ PHASE AND S PHASE ENTRY

- G₁ phase is a ______ phase that occurs after interphase but before DNA replication and cell division
 - □ The G₁ to S phase transition is critical because once it enters S phase the cell has to divide or die
 - Initiated by **START**
 - □ Mitogens are extracellular signals that the cell receives during interphase to signal for growth and division
 - Stimulate G₁ phase cylins and cyclin-dependent kinases
 - Also inhibits S and M phase cyclins to prevent a rapid re-division before the cell is ready

EXAMPLE: Mitogens stimulating the cell cycle

Regulation of cell cycle - Schematic

Extracellular growth signal

Cyclin D CDK4

Activation of E2F responsive genes via phosphorylation and deactivation of RB

Cyclin E CDK2 complex

Cyclin A-CDK2 complex

Cyclin A-CDK2 complex

Cyclin A-CDK2 complex

Cyclin CDK2

Cyclin CDK4

Cyclin CDK4

Cyclin CDK4

Cyclin CDK4

Cyclin CDK4

Cyclin CDK5

Cyclin CDK5

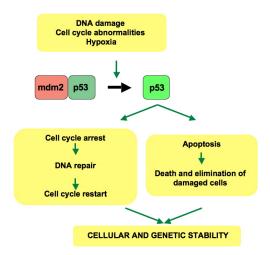
Cyclin CDK6

Cyclin CDK6

Cyclin CDK7

- $\ \square$ If the DNA is ______ the cell will halt in G_1
 - p53 is a transcription regulator that halts entrance into S phase if the DNA is damaged
 - p53 is mutated in a large amount of cancers
- □ If the cell is determined to not be ready for division it can enter into **G**_o which is a non-dividing state
 - The cell can remain here for prolonged periods of time
 - Terminally differentiates cells (like nerve cells) can stay in Go for forever

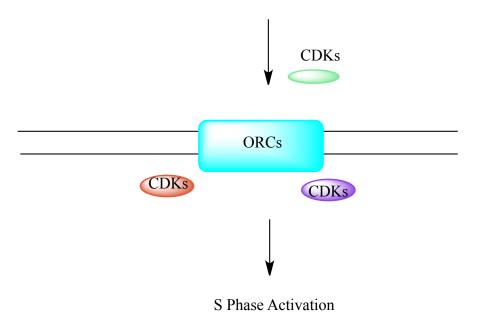
EXAMPLE: p53 and the Cell Cycle



S Phase Entry

- S-Cdks are the main driving proteins responsible for the cell ______ S phase
 - □ **S-Cdk** triggers S phase by:
 - Activating DNA helicases
 - Promoting replication fork formation
 - □ The **pre-replicative complex** is recruiting to *origins of replication* by S-Cdk
 - Concentration gradients: Concentrations of molecules differ on either side of a membrane

EXAMPLE: S-Cdks activation S phase



PRACTICE:

- 1. What protein halts entry into S phase when DNA is damaged?
 - a. Mitogen
 - b. p53
 - c. S-Cdk
 - d. M-Cdk

- 2. Which of the following is NOT a function of S-Cdks?
 - a. Causing the entrance of the cell into S phase
 b. Recruiting DNA helicases

 - c. Activating mitogens
 - d. Promoting the formation of the replication fork