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MCB II

Midterm 2

The Cell Cycle Game (On Python)

For my submission, I made a short video demonstrating a program that I created using the programming language, Python. This video was sent directly to Professor Carlos because I was unable to attach it to NYUClasses (sorry for the inconvenience!). The program is an interactive game where the user creates a cell and attempts to help the cell complete one full cell cycle. To begin this process, the user has to receive an extrinsic signal such as TGF-β, and then pass all the checkpoints of the cell cycle (G1, S, G2 and anaphase). If the cell fails any of the checkpoints, the user is prompted to repair the cell or to undergo apoptosis. As the cell progresses through the cell cycle, the fluctuations of the cyclin levels are printed to the screen.

The cell cycle is often described to be the life cycle of a cell and it is divided into many different stages: G1, S, G2 and M. G0 is another state that a cell can be in. It is often called the quiescent state because the cells are resting and typically do not leave this state to undergo mitosis. Notable examples of cells that are in this state are neurons and cardiac cells.

The stages of the cell cycle are regulated by both extrinsic factors, such as growth factor TGF-β, as well as intrinsic ones, namely cyclins. Cyclins are a class of proteins that accumulate at specific stages of the cell cycle. They come in many different forms and each type is associated with a distinct stage of the cycle. They attach to Cyclin Dependent Kinases (CDKs), forming a heterodimer. CDKs also come in many different versions and each version associates with a particular cyclin type. The combination of the different cyclins and the CDKs helps

determine the function of their heterodimer complex. These heterodimers initiate activities that cause a cell to enter into a specific cell cycle stage or to maintain in a distinct stage (high levels of nuclear D1 and CDK4/6 promote activities that keep a cell in the G1 phase). The CDKs will not initiate their cell cycle promoting activities unless they are binded by their accompanying cyclins. Therefore, cyclin levels are strictly regulated. Cyclin levels are increased by increasing transcription of the particular cyclin and they are decreased by ubiquitin-ligase based protein degradation.

In a typical cell cycle, the cell usually begins in the G1 phase, growing and waiting for an extrinsic signal to begin dividing. At this stage, there is a relatively high concentration of nuclear D1 cyclin, which interacts with CDK4/6. The extrinsic signal can come in the form of a growth factor such as TGF-β. Once the cell receives this signal, it begins to leave the G1 stage to prepare for entry into the S phase. In this process, the cell has to pass the G1 checkpoint, which checks that the cell is large enough for division and that it does not have DNA damage. If the cell fails the checkpoint, the cell will remain in the G1 stage until the DNA damage is repaired and/or the cell grows large enough to undergo division. As the cell enters the S phase, nuclear D1 cyclin decreases and cyclin E increases, which forms a heterodimer with CDK2.

In the S phase, the cell replicates their DNA in preparation for division. During this stage, the cell will reach the intra-S checkpoint, which checks that the cell has replicated its DNA properly and that there were no errors during the replication process. If DNA damage is found, the cell has to correct it before progressing. If the damage is irreparable, the cell will undergo apoptosis. Cyclin E begins to decline as the cell progresses in the S-phase. Meanwhile, cyclin A levels increase and complexes with CDK2. However, in the latter portion of the S-phase, cyclin

A begins to interact with CDC2 instead of CDK2. The cyclin A and CDC2 heterodimer helps the cell transition into the G2 phase.

In the G2 stage, the cell continues to prepare for mitosis. Here, the cell meets another checkpoint that checks the DNA to verify that DNA replication occurred properly. As with the prior checkpoints, if there is DNA damage, the cell cycle will halt and the cell will attempt to correct the damage. If the damage is irreparable, the cell will undergo apoptosis. As G2 progresses, cyclin A decreases and cyclin B increases and begins to complex with CDC2. A peak in the cyclin B level marks the transition of the cell from the G2 phase to the M phase.

During the M phase, the cell undergoes mitosis. The steps of mitosis are prophase, metaphase, anaphase and telophase followed by cytokinesis. At the anaphase step, the cell pulls apart the sister chromatids of the double stranded chromosomes to opposite ends of the cell. Here, an anaphase checkpoint verifies that the spindle fibers were properly attached to the chromatids before the chromatids are separated. Without this crucial checkpoint, the cell would be more susceptible to nondisjunction, which could lead to polyploidy in the daughter cells.

Once the cell finishes dividing, they will re-enter the G1 stage. This transition is marked by a decrease of the cyclin B/CDC2 complex and a rapid increase of nuclear D1. The level of the nuclear D1 and CDK4/6 heterodimer will remain relatively high, keeping the cell in the G1 stage until another growth factor prompts it to divide again.