Cells and Cancer

CONTENT PRIMER

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The Cell Cycle

There are five main divisions of the cell cycle: G0, G1, S, G2, and M (Figure 1). Each division has a different purpose in the cell cycle. The longest phase in terms of duration, the G0 phase acts as a resting phase for a cell. During the G1 phase, the cell begins to prepare for cell division by growing and synthesizing proteins and enzymes, integrating mitogenic and growth inhibitory signals, and increasing the amount of cytoplasm in the cell. Then, the cell undergoes DNA replication and synthesis during the S phase. In the G2 phase, the cell finishes preparing for cell division: growth and synthesis of proteins and enzymes continue, organelles are reproduced, and the cytoskeleton breaks down. The M phase, also known as mitotic phase, is the division of the nucleus, and occurs in various stages - prophase, prometaphase, metaphase, anaphase and telophase. The last stage of the M phase is cytokinesis, which is the division of the cytoplasm. During mitosis, chromosomes segregate, and a cell divides to form two daughter cells.

Triggers and Checkpoints

Before a cell can go through the cell cycle, it must pass several “checkpoints” to prevent mistakes and ensure it can properly divide. Before the cell cycle begins, there is a “trigger” that initiates the cell cycle. For example, at the end of the G1 phase, the cell must pass the G1 checkpoint where it is checked that it is big enough and that it has the correct proteins needed to begin the S phase. If the cell does not meet the requirements at the G1 checkpoint, then it will either return to the G0 phase, or the cycle is stopped altogether. The G2 checkpoint occurs during the S phase, and it checks cell size and protein reserves and whether DNA has been replicated correctly. This helps prevent cells from initiating mitosis while experiencing DNA damage. If the cell does not pass the G2 checkpoint, it will either abort the cycle or delay mitosis so DNA repair can occur. The M checkpoint occurs at the end of the metaphase to see if sister chromatids and microtubules are attached correctly to each other. The cycle will not continue until the kinetochores of each pair of sister chromatids are firmly anchored to at least

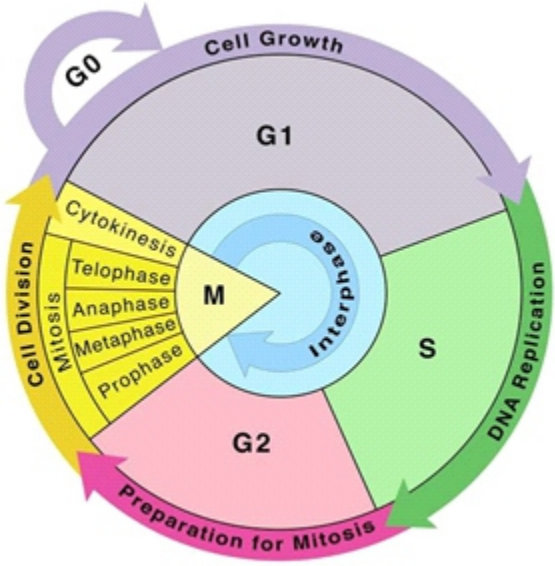

Figure 1. *A diagram of the cell cycle that illustrates the order of each phase in relation to the other phases (Image from Mukherjee, 2021).*

two spindle fibers. If this check fails, it results in uneven distribution of chromatids which is referred to as nondisjunction of chromatids.

Proto Oncogenes & Tumor Suppressor Genes

Proto-oncogenes (e.g., Her2) are genes that code for proteins that promote normal cell division and differentiation in response to appropriate signals. Proto-oncogenes are considered accelerators or the “gas pedals” of the cell cycle, while their counterpart, the tumor suppressor genes, are considered the “brakes.” If a proto-oncogene is mutated, it becomes an oncogene, which is always turned on. When an oncogene is turned on, the cell divides uncontrollably leading to tumors, eventually becoming cancerous. Tumor suppressor genes (e.g., p21, p53, and Rb) code for proteins that repair DNA, initiate cell death, or stop the advancement of the cell cycle when needed. When this gene becomes mutated, it loses normal brake functions leading to relentless cell growth without control and also loses its repairing ability, leading to tumors, which can eventually become cancerous.

Cancer

Cancer is the uncontrolled growth and cell division of abnormal cells that spread to the surrounding tissues. Cancer forms when a mutation in a gene produces faulty proteins that affect the regulation of the cell cycle. When a mutated cell cannot control its growth, a surplus of the cells is created. When a mass of mutated cells clumps together, it creates a benign or malignant tumor. Benign tumors are contained in the original site and have a clean boundary between the tissue and tumor. They also have a few genetic changes. Malignant tumors on the other hand migrate to surrounding tissues becoming metastatic and accumulate several genetic changes. It takes more than one single mutation to cause cancer. In most cases, a cell becomes cancerous only after it has acquired several mutations in several genes that regulate the cell cycle or repair DNA. Cancer affects people with age as their cells accumulate more mutations over time. Individuals who have inherited high risk mutations require fewer additional mutations to get cancer. Substances in the environment can also lead to damaged and cancerous cells. For instance, exposing the body to ultraviolet rays from the sun damages DNA. The earlier the cancer is detected, the easier it is to treat. Cancer treatments include surgery, radiotherapy and chemotherapy.

Smoking and Vaping

Tobacco use is known to cause cancer. Smoke from cigarettes causes tar to accumulate in the lungs; this clogs cilia and makes it more difficult for the tar to be transported out of the lungs, leading to more buildup. Other chemicals in cigarettes act as carcinogens that can damage or change cell's DNA causing mutations, which overtime can accumulate and potentially cause cancer.

The nicotine used in vaporizers, or vape pens, is not a carcinogen but has been shown to promote cell division and inhibit apoptosis—the controlled death of cells. Some vaporizers contain other cancer-causing substances such as formaldehyde and toluene. Vaping can also deliver heavy metals to the lungs, and the vaping fluid contains carcinogens such as formaldehyde, which can cause cancer.

References

Mukherjee, S. (2021, January 18). *Cell Cycle*. ScienceFacts. https://www.sciencefacts.net/cell-cycle.html