

Cancer and the Cell Cycle

Directions:

In this activity, you will be reading some information about cancer and cell division. Read through the information below and then read the two corresponding articles. As you read the material, **highlight** key ideas and points of interest. **Underline** words for which you are unsure of the meaning. **Write** any questions or thoughts or ideas you have in the margins as you read and highlight. In other words, you must annotate the articles as you read them. When you are done, use the space provided at the end of the last article to write a two paragraph **summary** of the information from both readings.

Key Terms and Ideas:

Cancer: Cancer is essentially a **disease of the cell cycle** - the normal 'checkpoints' regulating mitosis are ignored or overridden by the cancer cell. Cancer begins when a single cell is **transformed**, or converted from a normal cell to a cancer cell.

Tumors: Good Cells gone Bad - The cancer cells proliferate to form mass of cancer cells called a tumor. As the tumor grows larger, it begins to release proteins from the cell to attract new blood vessel growth (this is called angiogenesis).

- **Benign:** tumor cells remain at original site. Can be removed surgically or killed by radiation, usually eliminating any further cancer development at that site.
- **Malignant:** some tumor cells send out signals that tell the body to produce a new blood vessel at the tumor site. These cells not only have their own food and oxygen supply, they also have an avenue for escape to a new part of the body - through the new blood vessel and into bloodstream. Cells that break away from the tumor begin to spread to surrounding tissues (via the bloodstream or lymph) and start new tumors = metastasis. Usually surgery is performed to remove the tumor, followed by radiation and chemotherapy.

1. Cell Division and Cancer

(www.nature.com)

Cancer cells are cells gone wrong — in other words, they no longer respond to many of the signals that control cellular growth and death. Cancer cells originate within tissues and, as they grow and divide, they diverge ever further from normalcy. Over time, these cells become increasingly resistant to the controls that maintain normal tissue — and as a result, they divide more rapidly than their progenitors and become less dependent on signals from other cells. Cancer cells even evade programmed cell death, despite the fact that their multiple abnormalities would normally make them prime targets for apoptosis. In the late stages of cancer, cells break through normal tissue boundaries and metastasize (spread) to new sites in the body.

How Do Cancer Cells Differ from Normal Cells?

In normal cells, hundreds of genes intricately control the process of cell division. Normal growth requires a balance between the activity of those genes that promote cell proliferation and those that suppress it. It also relies on the activities of genes that signal when damaged cells should undergo apoptosis.

Cells become cancerous after mutations accumulate in the various genes that control cell proliferation. According to research findings from the Cancer Genome Project, most cancer cells possess 60 or more mutations. The challenge for medical researchers is to identify which of these mutations are responsible for particular kinds of cancer. This process is akin to searching for the proverbial needle in a haystack, because many of the mutations present in these cells have little to nothing to do with cancer growth.

Different kinds of cancers have different mutational signatures. However, scientific comparison of multiple tumor types has revealed that certain genes are mutated in cancer cells more often than others. For instance, growth-promoting genes, such as the gene for the signaling protein Ras, are among those most commonly mutated in cancer cells, becoming super-active and producing cells that are too strongly stimulated by growth receptors. Some chemotherapy drugs work to counteract these mutations by blocking the action of growth-signaling proteins. The breast cancer drug Herceptin, for example, blocks overactive receptor tyrosine kinases (RTKs), and the drug Gleevec blocks a mutant signaling kinase associated with chronic myelogenous leukemia.

Other cancer-related mutations inactivate the genes that suppress cell proliferation or those that signal the need for apoptosis. These genes, known as tumor suppressor genes, normally function like brakes on proliferation, and both copies within a cell must be mutated in order for uncontrolled division to occur. For example, many cancer cells carry two mutant copies of the gene that codes for p53, a multifunctional protein that normally senses DNA damage and acts as a transcription factor for checkpoint control genes.

How Do Cancerous Changes Arise?

Gene mutations accumulate over time as a result of independent events. Consequently, the path to cancer involves multiple steps. In fact, many scientists view the progression of cancer as a microevolutionary process.

A series of mutations in a cell causes it to proliferate more than its immediate neighbors. As the cluster of dividing cells grows over time, further mutations turn atypical hyperplasia into a cancer (carcinoma). The spreading of cancer cells to other tissues and organs (metastasis) occurs when the adhesion of these cancerous cells breaks down, and they are able to travel easily to new locations.

To understand what this means, consider the following: When a mutation gives a cancer cell a growth advantage, it can make more copies of itself than a normal cell can — and its offspring can outperform their noncancerous counterparts in the competition for resources. Later, a second mutation might provide the cancer cell with yet another reproductive advantage, which in turn intensifies its competitive advantage even more. And, if key checkpoints are missed or repair genes are damaged, then the rate of damage accumulation increases still further. This process continues with every new mutation that offers such benefits, and it is a driving force in the evolution of living things — not just cancer cells.

How Do Cancer Cells Spread to Other Tissues?

During the early stages of cancer, tumors are typically benign and remain confined within the normal boundaries of a tissue. As tumors grow and become malignant, however, they gain the ability to break through these boundaries and invade adjoining tissues.

Invasive cancer cells often secrete proteases that enable them to degrade the extracellular matrix at a tissue's boundary. Proteases also give cancer cells the ability to create new passageways in tissues. For example, they can break down the junctions that join cells together, thereby gaining access to new territories.

Metastasis — literally meaning "new place" — is one of the terminal stages of cancer. In this stage, cancerous cells enter the bloodstream or the lymphatic system and travel to a new location in the body, where they begin to divide and lay the foundation for secondary tumors. Not all cancer cells can metastasize. In order to spread in this way, the cells must have the ability to penetrate the normal barriers of the body so that they can both enter and exit the blood or lymph vessels. Even traveling metastatic cancer cells face challenges when trying to grow in new areas.

Conclusion

Cancer is unchecked cell growth. Mutations in genes can cause cancer by accelerating cell division rates or inhibiting normal controls on the system, such as cell cycle arrest or programmed cell death. As a mass of cancerous cells grows, it can develop into a tumor. Cancer cells can also invade neighboring tissues and sometimes even break off and travel to other parts of the body, leading to the formation of new tumors at those sites.

2. Cell division study resolves 50-year-old-debate, may aid cancer research

A new study at Oregon State University has finally resolved a controversy that cellular biologists have been arguing over for nearly 50 years, with findings that may aid research on everything from birth defects and genetic diseases to the most classic "cell division" issue of them all – cancer. The results are being published in *PLoS Biology*, a professional journal. The studies were supported by the National Science Foundation and the American Heart Association.

The exact mechanism that controls how chromosomes in a cell replicate and then divide into two cells, a process fundamental to life, has never been completely pinned down, researchers say. You can find the basics in any high school biology textbook, but the devil is in the details.

"Researchers have been debating cell cleavage ever since the cell was discovered, with two basic models proposed around 1960 of how a contractile ring pulls together and allows a single cell to split into two," said Dahong Zhang, an OSU associate professor of zoology. "Part of the problem is that until now there was no decisive way to manipulate the cytoskeleton, such as the microtubules and filaments that are involved, and see what was happening as it occurred."

To address that, Zhang developed some new instrumentation that uses "microneedles" and state-of-the-art imaging techniques which allow direct manipulation of the cytoskeleton, while capturing the results of contractile ring formation. The system has not only solved this decades-old riddle, but "the technology is a very powerful new approach," Zhang said, that should find applications in other cell biology research issues.

