CHAPTER 2: UNDERSTANDING CANCER

INTRODUCTION

We are witnessing an era of great discovery in the field of cancer research. New insights into the causes and development of cancer are emerging. These discoveries have brought a sense of optimism to scientists, health care providers, and people affected by cancer. There is hope that we will soon be able to more effectively prevent and treat cancer.

Learning about cancer will help you better understand the disease and how it is treated. Becoming familiar with cancer-related terms can help you communicate more effectively with your health care team. This knowledge can also help you keep abreast of new discoveries and promising new therapies.

WHAT IS CANCER?

Cancer is a condition caused by the uncontrolled growth of cells. Different kinds of cancer are named according to the type of cell that is growing in an uncontrolled way. Cancer can arise from nearly any part of the body. There are more than 125 different types of cancer.

Normal cells grow, divide, and die in a controlled way and with a predictable lifespan. In adults, most cells divide only to replace old cells or to repair damage. Cancer cells have been damaged in such a way that they have lost their normal control mechanisms. They grow and divide at a rapid rate, and outlive their normal lifespan.

Most types of cancer lead to the formation of tumors, abnormal clusters of cells. However, not all tumors are cancerous. Tumors that cannot invade neighboring tissues or spread to other parts of the body are called benign tumors. With rare exceptions, benign tumors do not cause serious disease and are not life threatening. Malignant tumors are cancerous tumors.
Malignant tumors can invade and destroy neighboring tissues and organs, and spread to other parts of the body. This spread of cancer cells from one part of the body to another distant site is called metastasis. In short, malignant tumors are capable of invasion and metastasis, but benign tumors do not have these capabilities.

HOW COMMON IS CANCER?

The National Cancer Institute estimates that approximately 8.9 million Americans alive today have been diagnosed with cancer at some time in their lives. According to the 2003 Cancer Facts & Figures report issued by the American Cancer Society, men in the United States have approximately a one in two chance of developing cancer in their lifetime. For women, the lifetime risk of developing cancer is just over one in three. In 2003, approximately 1,285,000 people in the United States were newly diagnosed with non-skin cancers. Cancer is the second leading cause of death in the United States killing over half a million people each year. Approximately 16 million new cancer cases have been diagnosed since 1990.

WHAT CAUSES CANCER?

Cancer cells are abnormal because they contain damaged genetic material. The genetic material of human cells is contained in 23 pairs of chromosomes (see Figure 1). Chromosomes are tiny structures inside cells that are made up of a substance called deoxyribonucleic acid or DNA. The DNA inside each cell of your body contains your unique genetic blueprint. Every cell of a person’s body contains an identical copy of his or her unique DNA.

Specific segments of DNA are called genes. Every chromosome contains thousands of genes, each containing the message or genetic code for a specific feature or function of the body.

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Genes control every aspect of the body’s structure and function. They control physical features such as height, hair color, eye color, and bone structure. Characteristics such as natural athletic or musical capability, tolerance for pain, and susceptibility to certain diseases are also controlled by genes. Cellular functions such as the ability to repair damage, divide when new cells are needed, and even to die in a specific timeframe are all genetically controlled.

Throughout our lifetime, we are exposed to many things that can damage our DNA. Chemicals in the environment such as asbestos, tobacco smoke, radon, air pollution, radiation from the sun and other sources, viruses, and even chemicals from our own bodies can cause genetic damage. Our bodies have mechanisms to repair genetic damage. Cancer occurs when genetic damage either overwhelms or slips past the body’s normal repair mechanisms. Generally, it takes several different genetic flaws accumulated over a long period of time for a cell to become cancerous.

The abnormalities that lead to cancer are in the genes that control a cell’s life cycle. These genes control when a cell divides and dies. Normally, a cell divides only when it gets a genetic message triggering it to do so. Similarly, cells normally die according to a genetically programmed timeframe. When the genes that control cell division and death are damaged, cells divide uncontrollably and do not die in the normal timeframe. As a result, cancerous cells accumulate in the body forming tumors that eventually crowd out normal cells. Cancer cells do not perform the necessary jobs that normal cells do. Therefore, as cancer cells crowd out normal cells, body functions begin to fail.

**Oncogenes and Tumor Suppressor Genes**

Scientists have identified two major categories of genes that are damaged in cancer cells, tumor suppressor genes and oncogenes. Cancer cells usually have mutations or changes in several of these genes. The damage in these genes leads to the uncontrolled cell growth (also known as cell proliferation) that distinguishes cancer cells from normal cells. Tumor suppressor genes and oncogenes have opposite functions. In normal cells, these genes work together to control cell proliferation.
Proto-oncogenes are the normal predecessors of oncogenes. All normal cells have proto-oncogenes. They trigger controlled cell growth and division in normal cells. When proto-oncogenes are damaged, they become oncogenes and promote uncontrolled cell proliferation. Therefore, oncogenes are abnormal genes that promote the development of cancers. Some examples of oncogenes common in lung cancer include \textit{ras}, \textit{myc}, \textit{bcl-2}, and \textit{c-erbB-2}.

Unlike oncogenes, tumor suppressor genes help prevent cancer by keeping cell growth under control. Everyone has tumor suppressor genes. The products of these genes act like brakes on a car, stopping the cell growth and division cycle. Because tumor suppressor genes have the opposite effect of oncogenes, they are sometimes called antioncogenes. If normal tumor suppressor genes are damaged or even lost as is sometimes the case with severe genetic damage, cell growth may become uncontrolled resulting in cancer. Tumor suppressor genes can be damaged by exposure to chemicals or radiation. It is also possible to inherit abnormal tumor suppressor genes, which increases the risk of developing cancer. RB (the retinoblastoma gene) and p53 are two common examples of tumor suppressor genes. P53 mutations are seen in more than 50\% of non-small cell lung cancers (NSCLC) and over 80\% of small cell lung cancers (SCLC).\textsuperscript{1,3} P53 acts to regulate cell proliferation and has a role in programmed cell death, which is known as \textit{apoptosis}.

Researchers are working to develop new therapies and drugs that target the genetic damage present in cancer cells. However, it can take years to perform the work needed to find therapies that are safe and effective for patients. \textit{Chapters 6} and 7 review current and potential new therapies for lung cancer.

\textbf{WHAT IS CELL DIFFERENTIATION?}

You may have heard the term \textit{cell differentiation} in discussions about cancer. When a cell grows and develops normally, it undergoes a maturation process in which it becomes specialized to perform specific functions. This maturation process is called cell
differentiation. Differentiation causes cells to take on specific characteristics that reflect the function of the tissue the cell came from through cell division. Therefore, a new, differentiated lung cell looks and functions like all other lung cells. As cells become more differentiated, they become more restricted in what they can do. Differentiation is the reason a kidney cell cannot behave as a muscle cell, and a lung cell cannot function as a brain cell.

Abnormal cell proliferation can begin at any point during a cell’s differentiation process. When a single cell divides, it results in two daughter cells. The daughter cells typically have the same cellular characteristics of their parent cell. If an immature or undifferentiated cell begins proliferating, all the cells produced from the original cell will also be undifferentiated. Differentiation is a process. Therefore, cells that begin proliferating abnormally can reflect varying degrees of differentiation.

As cancer cells rapidly grow and divide, the new cells being produced tend to become progressively less differentiated. As cells become less differentiated, they lose their capability to perform the functions of the tissue where they originated. Highly undifferentiated cells are often incapable of performing any tissue-specific functions. Undifferentiated cells do not have the same appearance as mature cells (see Figure 2).

Their size, shape, and internal characteristic differ from that of normal cells. Highly undifferentiated cells may have such an abnormal appearance that it is difficult to determine from what type of tissue the cells came.

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The term differentiation is also used to describe how the cells of a tumor appear compared to normal cells from the tissue in which the tumor arose. Tumors classified as well differentiated contain cells that bear some degree of resemblance to the normal cells of the original tissue. Undifferentiated tumors have cells that no longer look like normal cells. Some researchers have found an association between poor cell differentiation and decreased survival among patients with NSCLC, especially those with stage I tumors.

**HOW DOES CANCER SPREAD?**

One of the defining characteristics of cancer cells is their ability to invade neighboring tissues and to metastasize or spread to sites of the body distant from the tissue of origin. Metastasis occurs when cancer cells break away from the original tumor. The cells travel through the body via the blood or lymphatic system to another part of the body where they grow and proliferate forming a new tumor (see Figure 3).

![Figure 3: The Metastatic Process*](image)

Cancers are named according to the tissue from which they originate. When cancer cells metastasize and a new tumor grows in a different tissue, it is still the same cancer. For example, lung cancer often metastasizes and causes tumors in the brain, bones, and liver. Therefore, someone with lung cancer may have tumors in several different places, but all of the tumors are the result of the lung cancer, which has metastasized to other locations.

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SUMMARY

All cancer cells share the same fundamental characteristics of uncontrolled growth and the ability to invade neighboring tissues and/or spread to distant sites. The transformation of normal cells into cancer cells is the result of genetic damage. Environmental chemicals, radiation, and a person’s genetic makeup can all contribute to the genetic damage that leads to the development of cancer. Tumor suppressor genes and oncogenes are the two major categories of genes involved in development of cancer.

Approximately nine million Americans alive today have been diagnosed with cancer at some point in their lives. Cancer is the second leading cause of death in the United States. Currently, one out of every four Americans dies of cancer.