

Cancer Genomics:

What Does It Mean for You?



The Connection Between Cancer and DNA

One person dies from cancer each minute in the United States. That's 1,500 deaths each day. As the population ages, this number is expected to increase. We need to understand cancer to control and ultimately conquer it. Many scientists are working hard to attack cancer where it starts — in our DNA.

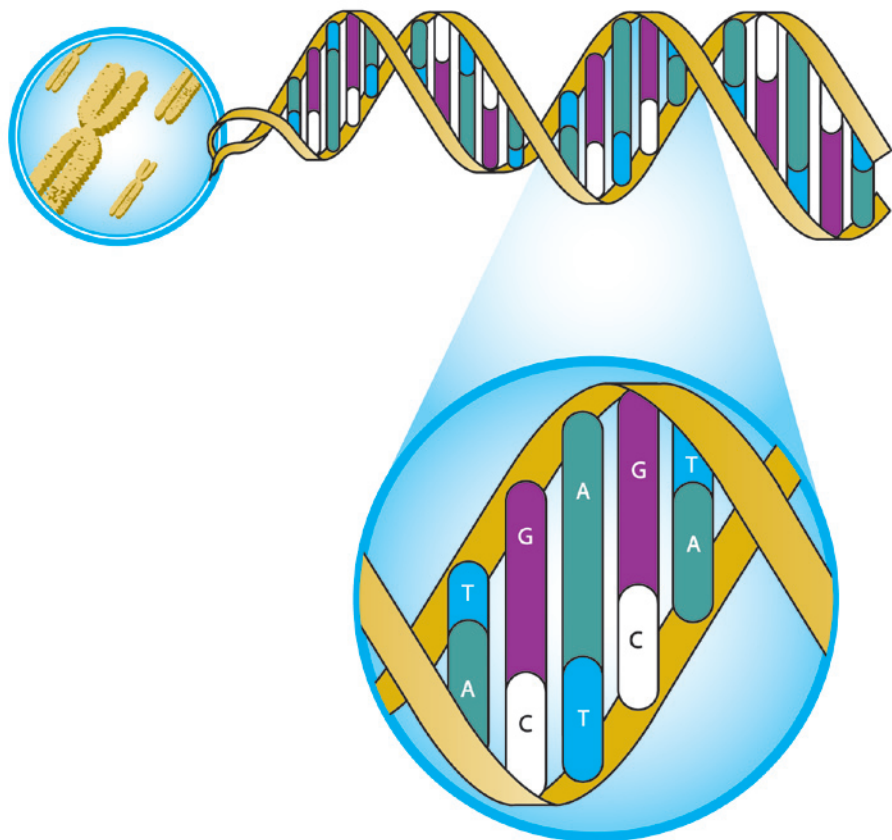
DNA, which stands for deoxyribonucleic acid, is the chemical carrying instructions that tell cells what to do. When those instructions have mistakes, cells may not function normally, including growing out of control to cause cancer.

These cancer-causing changes in DNA, called mutations, can be inherited, but most are acquired throughout life. They may be caused by environmental factors, such as chemicals, or from lifestyle choices, such as smoking. It generally takes the buildup of several different mutations to result in cancer. Several new research projects will look for and identify all the changes in cancer cells to better understand different forms of cancer and find new ways to control them. Why would researchers be interested in knowing all the changes in the DNA of cancer cells?

What Is a Genome & Why Does It Matter?

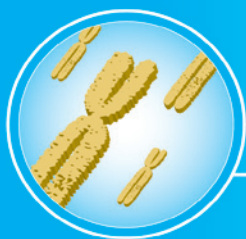
Think about all of the DNA in one of your cells. This complete set of DNA instructions is called your genome. In most cells, the genome is packaged into two sets of chromosomes, one set from your mother and one set from your father. These chromosomes are composed of 6 billion individual DNA letters.

In the English alphabet, there are 26 letters: A through Z. In the alphabet of your genome, there are 4 letters: A, C, G, and T. Just like the letters in a book make words to tell a story, so do the letters in our genomes. Small changes in the letters can change what a word or sentence means. It is the same way in your genome.



Genes are the parts of your genome that carry instructions to make the molecules, such as proteins, that do most of the work in our cells. Other parts of your genome act to switch genes on or off. This is important because, even though all of your cells carry the same genes, individual cells will use some genes but not others depending on what they do. For example, muscle cells use the genes needed to make muscle proteins but not the genes needed to make liver proteins.

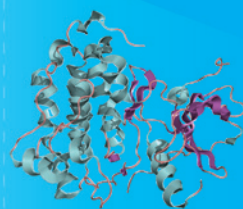
Changes in DNA can cause cells to produce the wrong amount of a certain protein or make a misshapen protein that doesn't work as it should. Since many proteins control how cells behave, these changes may lead to health problems. In cancer, these changes cause cells to survive and grow out of control, causing damage to surrounding tissues.



Chromosomes are single pieces of DNA that contain many genes.



DNA is a molecule that carries genetic information. Genes contain instructions for how to make proteins.



Proteins act alone or in groups to perform many functions.

What is The Cancer Genome Atlas?

The Cancer Genome Atlas (TCGA) is a landmark research program supported by the National Cancer Institute and National Human Genome Research Institute at the National Institutes of Health. TCGA researchers will identify the genomic changes in more than 20 different types of human cancer. By comparing the DNA in samples of normal tissue and cancer tissue taken from the same patient, researchers can identify changes specific to that particular cancer.

TCGA is analyzing hundreds of samples for each type of cancer. By looking at many samples from many different patients, researchers will gain a better understanding of what makes one cancer different from another cancer. This is important because even two patients with the same type of cancer may experience very different outcomes or respond very differently to treatments. By connecting specific genomic changes with specific outcomes, researchers will be able to develop more effective, individualized ways of helping each cancer patient.

What is TCGA Trying to Find?

TCGA will help us to understand what turns a normal cell into a cancer cell. By comparing DNA from normal and cancer tissue, we have already learned that:

- There are certain areas of the genome commonly affected in several types of cancers. Often, these changes affect genes that control pathways in cells that cause cells to divide and survive when they normally would die.
- Specific changes – also called signatures – allow us to tell one type of cancer from another. These signatures help doctors identify specific types of cancer, which may respond differently to various treatments or have a different prognosis.

What do these changes look like?

The four letters of the genome (A, C, G, and T) are in a specific order. By reading the order, or sequence, of the letters and using computers to compare the sequences, researchers can determine if just one of the billions of letters of our genome is different. We can also see if there are larger portions of our genome that have been duplicated, deleted, or rearranged.

Even a small change in a sequence could have a big impact. The following shows what might happen if the order of a gene's letters was changed.

Each word in a gene has three letters. If just one letter is changed, it can change the meaning of the sentence:

THE BIG **BOY** DID EAT ALL DAY
THE BIG **BAY** DID EAT ALL DAY

Because the letters are read in groups of three, additions or deletions of letters can cause the group of three to shift, losing the meaning of the sentence completely:

THE BIG **BYD IDE ATA LLD AY**
(The "O" in BOY has been deleted)

In some cases, the letters in the DNA are moved from one chromosome to another, or a chunk of DNA is flipped or rearranged. Any of these changes may alter the instructions found in the genome.

Information beyond the sequence

Sometimes, the changes are not in the actual sequence of the DNA. Some of the letters are marked by the addition of a special chemical. These marks change how a cell sees these sequences. They can even change whether a cell reads them at all. Therefore, these marks can change which proteins are made in which cells. The entire collection of chemical marks on your DNA are called the epigenome.

Scientists now have ways of finding the areas of the genome that have these marks. They can use these methods to find out when the DNA of a cancer cell has more or less of these marks, or has them in different places, than the DNA of a normal cell.

How Are We Doing It?

Teamwork: TCGA involves a large number of researchers around the world. From the doctors treating the patients who agree to donate tissue, to the groups that process samples and send materials to laboratories, to the individual researchers actively sequencing and analyzing the samples, the project has shown the power of teamwork in cancer research.



Creating an Atlas: TCGA is mapping all the mutations and other changes in more than 20 different types of cancer using remarkable new technologies. All of these changes are listed in a database for scientists around the world to use, enabling the next generation of cancer research. With this catalog of genomic changes, researchers can find new targets for medicines and discover clues to improve patient outcomes. TCGA is laying the foundation for personalized cancer care.

Computation: Finding the changes in the genome responsible for a cancer is like finding a needle in a haystack. Researchers write instructions for computers that tell the computers how to hunt through the huge amount of data. This field, called bioinformatics, is making the identification of these needles a possibility.

Laying the Foundation for Personalized Cancer Care

By cataloging all the changes in the genomes and epigenomes in many samples of many cancer types, we can begin to identify common changes. Some of these changes may reflect areas of the genome that can be targeted by specific drugs. Others will show a link between a specific change and how fast a disease will progress or how likely the tumor may come back after treatment.

We are studying genomics today in hopes of finding new clues for how to help patients tomorrow. While some early data are already bringing about changes in patient care, most of the data we are collecting will not immediately affect patients. There are many steps needed to translate genomic data to patient care, including determining which genomic changes are truly responsible for each cancer and identifying or developing therapies to correct the impact of those changes. This type of personalized medicine is not yet common, but studies like TCGA will make it a reality in the foreseeable future.

Learning More

If you are interested in learning more about cancer genomics, please visit our Web site at: <http://cancergenome.nih.gov>, contact us at tcga@mail.nih.gov or call **301-594-9831**.



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