Genes and Cancer

Cancer begins when some of the genes in a cell become abnormal, causing the cell to grow and divide out of control. Here you can learn more about how changes in a cell’s genes can lead to cancer.

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Gene Changes and Cancer

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The human body is made up of trillions of cells - the basic building blocks of any complex animal.

These cells normally work together to form organs, such as the heart, liver, and skin. In order for cells to work together, they have to have certain traits or characteristics. For example, they need to be able to divide to make new cells at the right time, stay where they’re needed, and not crowd out nearby cells.

Cancer begins when cells in the body become abnormal and start to grow out of control. This is caused by certain changes in a cell’s genes.
What are genes?

Genes are pieces of DNA inside each cell. They tell the cell how to make the proteins it needs to function. Each gene contains the code (instructions) to make a certain protein, and each protein has a specific job. For example, some genes code for proteins that help the cell grow and divide to make new cells. Other genes code for proteins that help keep cell growth under control.

Genes are contained in chromosomes, which are long strands of DNA in each cell. Each chromosome has many different genes.

Most human cells have 23 pairs of chromosomes. One chromosome of each pair is inherited from a person’s mother, and the other comes from their father. This is why children tend to look like their parents, and why they may have a tendency to develop certain diseases that run in their families.

All the cells in the body have the same genes, but each cell uses only the genes it needs. That is, it turns on (activates) the genes it needs at the right time and turns off other genes that it doesn’t need. Turning on some genes and turning off others is how a cell becomes specialized, such as becoming a muscle cell or a bone cell, for example. Some genes stay active all the time to make proteins needed for basic cell functions. Other genes are shut down when their job is finished and can be turned on again later if needed.

Changes in genes

While we all have basically the same set of genes, we also have differences in our genes that make each of us unique.

The ‘code’ or ‘blueprint’ for each gene is contained in chemicals called nucleotides. DNA is made up of 4 nucleotides (A, T, G, and C), which act like the letters of an alphabet. Each gene is made up of a long chain of nucleotides, the order of which tells the cell how to make a specific protein.

Gene variants and mutations

Some people have changes in the nucleotides of a gene, which are known as variants (or mutations). For example, one nucleotide ‘letter’ might be switched for another, or one or more letters might be missing, when compared to most other people’s genes.

Gene variants can have different effects on the proteins they code for. For example:
Some gene variants might not have any noticeable effect on the protein.
Some variants might lead to very minor changes in the protein. For example, a variant might result in a protein that’s shaped a little differently and is therefore a bit less effective than the ‘normal’ version of the protein.
Some variants might have larger effects. For example, a variant might result in a protein that doesn’t work at all.

Gene variants that lead to changes in proteins can affect all of the cells with that variant, which might even affect the whole body.

The overall effects of some gene variants might not necessarily be ‘good’ or ‘bad.’ For example, gene variants account for differences in people’s hair or eye color. On the other hand, some variants can lead to a disease (such as cancer) or increase the risk of a disease. These are referred to as pathogenic variants. (These are also what many people think of when they hear the term mutation.)

Inherited versus acquired gene mutations

Gene variants, including mutations, can be either inherited or acquired.

An inherited gene mutation, as the name implies, is inherited from a parent, so it’s present in the very first cell (once the egg cell is fertilized by a sperm cell) that eventually becomes a person. Since all the cells in the body came from this first cell, this mutation is in every cell in the body, and can also be passed on to the next generation. This type of mutation is also called a germline mutation (because the cells that develop into eggs and sperm are called germ cells) or a hereditary mutation.

It typically takes more than one gene mutation for a cell to become a cancer cell. But when someone inherits an abnormal copy of a gene, their cells already start out with one mutation. This makes it easier (and quicker) for other mutations to happen, which can lead to a cell becoming a cancer cell. This is why cancers related to inherited mutations tend to occur earlier in life than cancers of the same type that are not inherited.

Inherited gene mutations are not the main cause of most cancers. To learn about some of the more common inherited gene mutations that can lead to cancer, see Family Cancer Syndromes.

An acquired gene mutation is not inherited from a parent. Instead, it develops at some point during a person’s life. Acquired mutations occur in one cell, and then are passed on to any new cells that come from that cell. This mutation cannot be passed on to a
person’s children, because it doesn’t affect their sperm or egg cells. This type of mutation is also called a sporadic mutation or a somatic mutation.

Acquired mutations can happen for different reasons. Sometimes they happen when a cell’s DNA is damaged, such as after being exposed to radiation or certain chemicals. But often these mutations occur randomly, without having an outside cause. For example, during the complex process when a cell divides to make 2 new cells, the cell must make another copy of all of its DNA, and sometimes mistakes (mutations) occur while this is happening. Every time a cell divides is another chance for gene mutations to occur. The number of mutations in our cells can build up over time, which is why we have a higher risk of cancer as we get older.

Acquired gene mutations are a much more common cause of cancer than inherited mutations.

Other ways gene activity can be changed

Some of the changes inside cells that can lead to cancer don’t involve gene variants or mutations. Cells can turn some of their genes on and off in other ways, and some of these might also affect how a cell grows and divides.

As mentioned earlier, different genes are more active in some cells than in others. Even within a certain cell, some genes are active at some times and inactive at others. Turning these genes on and off isn’t done by changing the DNA sequence (as is the case with variants and mutations). Instead, the changes in gene activity occur by other means known as epigenetic changes. There are several types of these changes:

- **DNA methylation:** In this type of change, a small chemical group called a methyl group is attached to the DNA so that the gene can’t start the process of making the protein it codes for. This basically turns off the gene. On the other hand, removing the methyl group (in a process called demethylation) can turn a gene on.

- **Histone acetylation/histone modification:** Chromosomes are made up of strands of DNA wrapped around proteins called histones. Histone proteins can be changed by adding (or subtracting) a small chemical group called an acetyl group. Adding acetyl groups (acetylation) can activate (turn on) that part of the chromosome, while taking them away (deacetylation) can deactivate it (turn it off). Drugs called histone deacetylase (HDAC) inhibitors can help in the treatment of some types of cancer by turning on genes that help control cell growth and division.

- **RNA interference:** Inside each cell, DNA acts as long-term storage for our genes. But DNA isn’t in the same part of the cell where proteins are made. For a protein to
be made, a copy of its genetic code (in the form of messenger RNA, or mRNA), needs to be made from the DNA first. This piece of mRNA can then bring the instructions to the part of the cell where proteins are made. mRNA is only used for a short time to make the protein, and then it’s broken down. If the cell needs more of that protein, it makes more mRNA. RNA interference is another way cells can turn off genes. A cell can make other forms of RNA that stick to mRNA. This can cause the mRNA to break down or stop it from delivering its code. Drugs are being developed to target the forms of RNA involved in RNA interference. This might help turn off specific genes that cause cancer.

How changes in genes can affect cancer risk

Some genes normally help control when our cells grow, divide to make new cells, repair mistakes in DNA, or cause cells to die when they’re supposed to. If these genes aren’t working properly, it can affect cancer risk. For example:

- Changes in genes that normally help cells grow, divide, or stay alive can lead to these genes being more active than they should be, causing them to become **oncogenes**. These genes can result in cells growing out of control.
- Genes that normally help keep cell division under control or cause cells to die at the right time are known as **tumor suppressor genes**. Changes that turn off these genes can result in cells growing out of control.
- Some genes normally help repair mistakes in a cell’s DNA. Changes that turn off these **DNA repair genes** can result in the buildup of DNA changes within a cell, which might lead to them growing out of control.

DNA changes that create oncogenes or that turn off tumor suppressor genes or DNA repair genes might lead to cancer, although typically it takes several gene changes before a cell becomes a cancer cell. To learn more, see [Oncogenes, Tumor Suppressor Genes, and DNA Repair Genes](https://www.cancer.org/).  

Changes in some other genes don’t lead to cancer directly, but they might still make someone more likely to get cancer. For example, some gene changes can limit how well the body breaks down some of the toxins in tobacco smoke. Among people who smoke, people with these kinds of gene changes might be more likely to get lung and other smoking-related cancers.

Gene changes can also play a role in other conditions that might impact cancer risk.
example, some gene variants can affect body weight. People with extra body weight are more likely to get some types of cancer, so these variants might also indirectly affect cancer risk.

Gene variants and other changes are common. We all have them, and their effects can add up to influence our cancer risk.

**Hyperlinks**


**References**


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Oncogenes, Tumor Suppressor Genes, and DNA Repair Genes

- Oncogenes
- Tumor suppressor genes
- DNA repair genes

Our bodies are made up of trillions of cells, which must work together to keep us healthy. Our cells need to be able to divide to make new cells to help the body grow, or to replace cells that have died. At the same time, cell growth and division need to be controlled, so the cells don’t grow too much and crowd out the cells around them.

It may be helpful to think of a cell as a car. For it to work properly, there need to be ways to control how fast it goes – that is, ways to speed up cell growth and division if it’s needed (like a gas pedal), and ways to keep this growth under control or slow it down (like a brake pedal). There also need to be ways to fix parts of the car if they break down.

Cell growth is normally controlled by the actions of certain genes inside each cell. Cancer begins when cells in the body become abnormal and start to grow out of control. This happens where there are changes in genes that affect cell growth.

The main types of genes that play a role in cancer are:

- Oncogenes
- Tumor suppressor genes
- DNA repair genes

Cancer is often the result of changes in more than one of these types of genes within a cell.

**Oncogenes**

Proto-oncogenes are genes that normally help cells grow and divide to make new cells, or to help cells stay alive. When a proto-oncogene mutates (changes) or there are too many copies of it, it can become turned on (activated) when it is not supposed to be, at which point it’s now called an oncogene. When this happens, the cell can start to grow out of control, which might lead to cancer.
A proto-oncogene normally functions in a way much like the gas pedal on a car. It helps the cell grow and divide. An oncogene is like a gas pedal that is stuck down, which causes the cell to divide out of control.

Oncogenes can be turned on (activated) in cells in different ways. For example:

- **Gene variants/mutations:** Some people have differences in the ‘code’ of their genes that can cause an oncogene to be turned on all the time. These types of gene changes can be inherited from a parent, or they can occur during a person’s life, when a mistake is made when copying the gene during cell division.

- **Epigenetic changes:** Cells normally have ways of turning genes on or off that don’t involve changes in the genes themselves. Instead, different chemical groups can be attached to genetic material (DNA or RNA) that affect whether a gene is turned on. These types of epigenetic changes can sometimes lead to an oncogene being turned on. For more on epigenetic changes, see Gene Changes and Cancer.

- **Chromosome rearrangements:** Chromosomes are long strands of DNA in each cell that contain its genes. Sometimes when a cell is dividing, the sequence of the DNA in a chromosome can be changed. This might put a gene that functions as a type of ‘on’ switch next to a proto-oncogene, keeping this gene turned on even when it shouldn’t be. This new oncogene can result in the cell growing out of control.

- **Gene duplication:** Some cells have extra copies of a gene, which might lead to them making too much of a certain protein.

A small number of family cancer syndromes are linked to an inherited change in an oncogene. These types of changes can sometimes be the first step in a cell becoming a cancer cell. But most changes involving oncogenes are acquired during a person’s lifetime, rather than being inherited.

**Tumor suppressor genes**

Tumor suppressor genes are normal genes that slow down cell division or tell cells to die at the right time (a process known as apoptosis or programmed cell death). When tumor suppressor genes don’t work properly, cells can grow out of control, which can lead to cancer.

A tumor suppressor gene is like the brake pedal on a car. It normally helps keep the cell from dividing too quickly, just as a brake keeps a car from going too fast. When something goes wrong with a tumor suppressor gene, such as a pathogenic variant
(mutation) that stops it from working, cell division can get out of control.

Inherited changes in tumor suppressor genes have been found in some family cancer syndromes. They cause certain types of cancer to run in families. But most tumor suppressor gene mutations are acquired during a person’s lifetime, not inherited.

For example, TP53 is an important tumor suppressor gene. It codes for the p53 protein, which helps keep cell division under control. Inherited changes in the TP53 gene can lead to Li-Fraumeni syndrome. Family members with this syndrome have an increased risk of several types of cancer, because all of their cells have this TP53 gene change.

Changes in the TP53 gene are also very common in cancer cells in people without an inherited cancer syndrome. These TP53 changes are acquired during the person’s life. These changes can help the cancer cells grow, but they are found only in the cancer cells, not in other cells in the body, so they can’t be passed on to a person’s children.

**DNA repair genes**

When a cell divides to make new cells, it needs to make a new copy of all of its DNA. This is a complex process, and sometimes it results in mistakes in the DNA.

Genes known as DNA repair genes act like a person who repairs a car. They help fix mistakes in the DNA, or if they can’t fix them, they trigger the cell to die so the mistakes can’t cause any further problems.

When something goes wrong with one of these DNA repair genes, it can allow more mistakes to build up inside the cell. Some of these might affect other genes, which could lead to the cell growing out of control.

As with other types of gene changes, changes in DNA repair genes can either be inherited from a parent or acquired during a person’s lifetime.

Examples of DNA repair genes include the BRCA1 and BRCA2 genes. People who inherit a pathogenic variant (mutation) in one of these genes have a higher risk of some types of cancer, particularly breast and ovarian cancer among women. (For more information, see Family Cancer Syndromes.) But changes in these genes are also sometimes seen in tumor cells in people who did not inherit one of these mutations.
Hyperlinks


References


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