What is DNA?

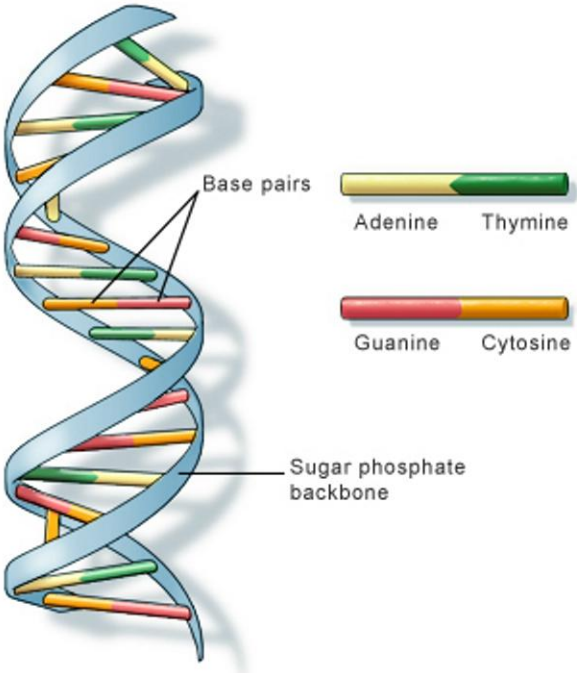
DNA, or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms. Nearly every cell in a person's body has the same DNA. Most DNA is located in the cell nucleus (where it is called nuclear DNA), but a small amount of DNA can also be found in the mitochondria (where it is called mitochondrial DNA or mtDNA).

The information in DNA is stored as a code made up of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T). Human DNA consists of about 3 billion bases, and more than 99 percent of those bases are the same in all people. The order, or sequence, of these bases determines the information available for building and maintaining an organism, similar to the way in which letters of the alphabet appear in a certain order to form words and sentences.

DNA bases pair up with each other, A with T and C with G, to form units called base pairs. Each base is also attached to a sugar molecule and a phosphate molecule. Together, a base, sugar, and phosphate are called a nucleotide. Nucleotides are arranged in two long strands that form a spiral called a double helix. The structure of the double helix is somewhat like a ladder, with the base pairs forming the ladder's rungs and the sugar and phosphate molecules forming the vertical sidepieces of the ladder.

An important property of DNA is that it can replicate, or make copies of itself. Each strand of DNA in the double helix can serve as a pattern for duplicating the sequence of bases. This is critical when cells divide because each new cell needs to have an exact copy of the DNA present in the old cell.

DNA is a double helix formed by base pairs attached to a sugar-phosphate backbone.



Chromosomal aberrations:

Any change in normal chromosome of the cell, referred as chromosomal aberration. This may be due to structural or numerical change.

Structural change: Following structural changes can lead to diseases.

1. **Deletion:** This is due to loss of a part of a chromosome.
2. **Duplication:** This is due to addition or duplication of a part of chromosome.
3. **Translocation:** This is due to movement of a part of chromosome to other chromosome. Leukemia (acute myelogenous leukemia & chronic myelogenous leukemia).
4. **Inversion:** This is due to reverse orientation of a part of chromosome.

Sickle cell anaemia (SCD):

It is an autosomal recessive disorder of hemoglobin gene characterized by a sickle shape of RBC with hard and sticky structure. SCD occurs due to a point mutation which leads to conversion of seventh amino acid of Hb protein i.e. glutamic acid to valine.

Hemophilia:

It is an X linked recessive disorders mainly affecting males because of presence of single copy of X chromosome in males. It is a group of hereditary genetic disorder that impairs the blood clotting ability. Hemophilia A is caused due to factor VIII deficiency and hemophilia is caused by factor IX deficiency. Hemophilia lowers blood plasma clotting factor levels needed for a normal clotting process. Thus when a blood vessel gets injured, a temporary scab does form, but the missing coagulation factors prevent fibrin formation, which is necessary to maintain the blood clot. A hemophiliac does not bleed more intensely but it bleeds for longer time than a normal person.

Cancer by Loss of Function of Genes:

Another category is tumor suppressor genes or anti-oncogenes which encodes protein for inhibiting cell proliferation. Inactivation of these genes results excessive proliferation of cells. The protype of this gene is retinoblastoma (Rb) gene which inactivation leads to tumor develop in neural precursor cells of retina. The other gene is Guardian of genome p53 gene which encodes a nuclear phosphoprotein that inhibits formation of small cell lung cancer and colon cancer.

Courtesy of Professor Bevin P. Engelward. Used with permission.

What Are Oncogenic Infections?

Cancer often is linked to lifestyle choices (such as smoking), a person's genetic * makeup, and environmental influences. Researchers now have begun to make connections between the development of certain types of cancer and specific viral, bacterial, and parasitic infections. These infections are referred to as oncogenic, or tumor-producing, infections.

Oncogenic viruses transfer their genetic material to other cells and then remain in the body for a long time as a latent infection (meaning that they are dormant, or inactive, but not dead).

* **Genetic** refers to heredity and the ways in which genes control the development and maintenance of organisms.

* **Carcinogens** are substances or agents that can cause cancer.

* **Warts** are small, hard growths on the skin or inner linings of the body that are caused by a type of virus.

* **strains** are various subtypes of organisms, such as viruses or bacteria.

There are several **infections that have been linked to the development of cancer...**

*Human papillomavirus or HPV

*Epstein-Barr virus (EBV) is commonly known as the virus that causes infectious mononucleosis...

EBV is associated primarily with the development of Hodgkin's disease and non-Hodgkin's lymphoma * (both cancers of the lymphatic system *).

*Hepatitis B and C virus (HBV and HCV) infections primarily affect the liver.

Helicobacter pylori (H. pylori) * bacterium causes most cases of gastric (stomach) and duodenal * ulcers *. The infection can be treated with antibiotics. People infected with *H. pylori* are at higher risk of stomach cancers, such as gastric lymphoma and adenocarcinoma.

Oncogenic Infections	Associated Cancers
Human papilloma virus (HPV) infection	Cervical and penile cancers
Epstein-Barr virus (EBV) infection	Lymphomas and nasopharyngeal cancer
Hepatitis B and C virus (HBV or HCV) infection	Liver cancer
Helicobacter pylori infection	Stomach cancer
Human lymphotrophic virus type 1 (HLTV-1) infection	Lymphomas

Oncogenes and tumor suppressor genes (here after referred to as ‘‘cancer genes’’) result in cancer when they experience substitutions that prevent or distort their normal function.

What are genes?

Genes are pieces of DNA (deoxyribonucleic acid) inside each cell that tell the cell what to do and when to grow and divide. Each gene is made up of a specific DNA sequence that contains the code (the instructions) to make a certain protein, each of which has a specific job or function in the body. Each human cell has about 25,000 genes. Most genes are contained in *chromosomes*. A chromosome is a long strand of DNA wrapped around a special protein called histone. Most chromosomes contain many different genes. Most human cells contain 23 pairs of chromosomes – one pair of sex chromosomes (either XX in Females or XY in males) plus 22 pairs of non-sex chromosomes called autosomes. Sperm and egg cells only contain half as many chromosomes (23). Chromosomes are passed from parents to their children through sperm and egg cells. One chromosome of each pair is inherited from the mother, and the other comes from the father. This is why children look like their parents, and why they may have a tendency to develop certain diseases that run in their families.

A cell uses its genes selectively; that is, it can turn on (or activate) the genes it needs at the right Moment and turn off other genes that it doesn't need. All the cells in the body (except egg and Sperm) contain the same genes. Turning on some genes and turning off others is how a cell becomes specialized. That is how a cell becomes a muscle cell and not a bone cell, for example. Some genes stay active all the time to make proteins needed for basic cell functions. Others shut Down when their job is finished and start again later if needed.

Dominant vs. recessive genes

We have 2 versions (copies) of most genes – one from each parent. For some versions of a gene, only one copy is needed to see a certain quality or disease (in genetics this is called a trait). These genes are called *dominant*. If both copies have to be the same to see that trait, it is called *recessive*. For example, the gene for brown eyes is dominant while the gene for blue eyes is recessive, so if you get one copy of the brown eye gene from one parent and a copy of the blue eye gene from the other, you will have brown eyes. You will only get blue eyes if you get 2 copies of the blue eye gene (one from each parent). This classification applies to gene

mutations as well. If you only need to inherit one copy of a gene mutation to get a disease or syndrome, it is called dominant. If you need 2, it is called recessive.

Changes in genes

Gene mutations are abnormal changes in the DNA of a gene. The building blocks of DNA are called bases. The sequence of the bases determines the gene and its function. Mutations involve changes in the arrangement of the bases that make up a gene. Even a change in just one base among the thousands of bases that make up a gene can have a major effect.

A gene mutation can affect the cell in many ways. Some mutations stop a protein from being made at all. Others may change the protein that is made so that it no longer works the way it should or it may not even work at all. Some mutations may cause a gene to be turned on, and make more of the protein than usual. Some mutations don't have a noticeable effect, but others may lead to a disease. For example, a certain mutation in the gene for hemoglobin causes the disease sickle cell anemia.

Cells become cancer cells largely because of mutations in their genes. Often many mutations are needed before a cell becomes a cancer cell. The mutations may affect different genes that control cell growth and division. Some of these genes are called tumor suppressor genes. Mutations may also cause some normal genes to become cancer-causing genes known as oncogenes.

We have 2 copies of most genes, one from each chromosome in a pair. In order for a gene to stop working completely and potentially lead to cancer, both copies have to be "knocked out" with mutations. That means for most genes, it takes 2 mutations to make that gene stop working Completely. There are 2 major types of gene mutations, inherited and acquired:

Mutations and cancer

Experts agree that it takes more than one mutation in a cell for cancer to occur. When someone has inherited an abnormal copy of a gene, though, their cells already start out with one mutation. This makes it all the easier (and quicker) for enough mutations to build up for a cell to become cancer. That is why cancers that are inherited tend to occur earlier in life than cancers of the same type that are not inherited.

Even if you were born with healthy genes, some of them can become changed (mutated) over the course of your life. These acquired mutations cause most cases of cancer. Some acquired

Mutations can be caused by things that we are exposed to in our environment, including cigarette smoke, radiation, hormones, and diet. Other mutations have no clear cause, and seem to occur randomly as the cells divide. In order for a cell to divide to make 2 new cells, it has to copy all of its DNA. With so much DNA, sometimes mistakes are made in the new copy (like typos). This leads to DNA changes (mutations). Every time a cell divides, it is another opportunity for mutations to occur. The numbers of gene mutations build up over time, which is why we have a higher risk of cancer as we get older.

It is important to realize that gene mutations happen in our cells all the time. Usually, the cell detects the change and repairs it. If it can't be repaired, the cell will get a signal telling it to die in a process called *apoptosis*. But if the cell doesn't die and the mutation is not repaired, it may

lead to a person developing cancer. This is more likely if the mutation affects a gene involved with cell division or a gene that normally causes a defective cell to die. Some people have a high risk of developing cancer because they have inherited mutations in certain genes.

Gene variants

People can also have different versions of genes that are not mutations. Common differences in Genes are called *variants*. These versions are inherited and are present in every cell of the body. The most common type of gene variant involves a change in only one base (nucleotide) of a gene. These are called single nucleotide polymorphisms (SNPs, pronounced "snips"). There are Estimated to be millions of SNPs in each person's DNA.

Other types of variants are less common. Many genes contain sequences of bases that are repeated over and over. A common type of variant involves a change in the number of these repeats. Some variants have no apparent effect on the function of the gene. Others tend to influence the function of genes in a subtle way, such as making them slightly more or less active. These changes don't cause cancer directly, but can make someone more likely to get cancer by affecting things like hormone levels and metabolism. For example, some gene variants affect levels of estrogen and progesterone, which can affect the risk of breast and endometrial cancers. Others can affect the breakdown of toxins in cigarette smoke, making a person more likely to get lung and other cancers.

Gene variants can also play a role in diseases that impact cancer risk – like diabetes and obesity. Variants and low-penetrance mutations can be similar. The main difference between the two is How common they are. Mutations are rare, while gene variants are more common.

Still, since these variants are common and someone can have many of them, their effect can add Up. Studies have shown that these variants can influence cancer risk and, together with low penetrance mutations, they may account for a large part of the cancer risk that runs in families.

Other ways cells change genes and gene activity although all of the cells of your body contain the same genes (and DNA), different genes are Active in some cells than in others. Even within a certain cell, some genes are active at some times and inactive at others. Turning on and off of genes in this case isn't based on changes in the DNA sequence (like mutations), but by other means called *epigenetic* changes.

DNA methylation: In this type of epigenetic change, a molecule called a methyl group is attached to certain nucleotides. This changes the structure of the DNA so that the gene can't start the process of making the protein for which it codes (this process is called transcription

Histone modification: Chromosomes are made up of DNA wrapped around proteins called histones.

RNA interference: RNA (ribonucleic acid) is important inside cells as the middle step that allows genes to code for proteins. But some small forms of RNA can interfere with gene expression by attaching to other pieces of RNA, or even affecting histones or DNA itself. Drugs are being developed that affect abnormal genes in cancer cells through RNA interference.

Oncogenes and tumor suppressor genes

Two of the main types of genes that play a role in cancer are oncogenes and tumor suppressor Genes. Oncogenes Proto-oncogenes are genes that normally help cells grow. When a proto-oncogene mutates (changes) or there are too many copies of it, it becomes a "bad" gene that can become permanently turned on or activated when it is not supposed to be. When this happens, the cell grows out of control, which can lead to cancer. This bad gene is called an oncogene. 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. A proto-oncogene normally functions in a way that is much like a gas pedal. It helps the cell grow and divide. An oncogene could be compared with a gas pedal that is stuck down, which causes the cell to divide out of control.

A few cancer syndromes are caused by inherited mutations of proto-oncogenes that cause the oncogene to be turned on (activated). But most cancer-causing mutations involving oncogenes are acquired, not inherited. They generally activate oncogenes by:

• Chromosome rearrangements: Changes in chromosomes that put one gene next to another, Which allows one gene to activate the other?

• Gene duplication: Having extra copies of a gene, which can lead to it making too much of a Certain protein.

Tumor suppressor genes

Tumor suppressor genes are normal genes that slow down cell division, repair DNA mistakes, or tell cells when to die (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 keeps the cell from dividing too quickly, just as a brake keeps a car from going too fast. When something goes wrong with the gene, such as a mutation, cell division can get out of control.

An important difference between oncogenes and tumor suppressor genes is that oncogenes result from the *activation* (turning on) of proto-oncogenes, but tumor suppressor genes cause cancer when they are *inactivated* (turned off).

Inherited abnormalities of 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, not inherited. For example, abnormalities of the *TP53* gene (which codes for the p53 protein) have been found in more than half of human cancers. Acquired mutations of this gene appear in a wide range of cancers.

C**ancer diagnosis and monitoring treatment**

Certain mutations are commonly found in the cells of some types of cancers. Finding certain Mutations in cells can confirm the diagnosis of that cancer. Testing cells for the mutation can also be used after diagnosis to see how the cancer is responding to treatment.

For example, the leukemia cells of patients with chronic myeloid leukemia (CML) contain a Mutated gene called *BCR-ABL*. In order to be diagnosed with CML, this mutation must be present, so testing for this mutation is used to confirm the diagnosis. Very sensitive tests can tell how many copies of this mutation are present in a blood sample (which indicates how many CML cells are present). These tests can find even tiny amounts, representing small numbers of CML cells among millions of normal cells. The number of copies is determined when treatment

is started, and then again sometime later to see how well the treatment is working. If treatment has put the leukemia into remission, this test can be used to see if it is coming back and new treatment is needed.

Drugs targeting genes or gene mutations

Drugs have been developed that target some of the gene changes in certain cancers. Actually these drugs often target the protein made by the abnormal gene (and not the gene itself).

For example, *HER2/neu* is a proto-oncogene in normal cells that helps them grow. It becomes an oncogene when a cell has too many copies of this gene. When this happens, the cells make too much HER2/neu protein and the cancer is said to be HER2 positive. Patients with breast cancer with cells that are HER2 positive do not respond as well to certain chemotherapy drugs. But newer drugs such as trastuzumab (Herceptin), lapatinib .and several others, have been designed to specifically attack cells that are HER2 positive. These drugs can slow cancer cell growth and improve outcomes in patients with HER2 positive cancers. Breast cancers are now Routinely tested to see if they are or the HER2 positive to identify which patients will benefit from these drugs. Other cancers also can be HER2 positive. Anti-HER2 therapy has also helped people with stomach cancer that is HER2-positive.

In chronic myeloid leukemia (CML), the cancer cells have a gene change called *BCR-ABL* that Makes a type of protein called a tyrosine kinas. Drugs that target the BCR-ABL protein, such as imatinib are often very effective against CML. They lead to remission of the leukemia in most patients treated in the early stages of their disease.

Drugs targeting certain mutations are useful in a number of other cancers including acute Lymphocytic leukemia, gastrointestinal stromal tumors, non-small cell lung cancer, a certain kind of non-Hodgkin lymphoma, and melanoma.

Oncogenic Viruses in AIDS: Mechanisms of Disease and Intrathoracic Manifestations…

Infection and malignancy constitute the bulk of AIDS-related disease. Although the HIV virus is not itself oncogenic, HIV infection renders patients vulnerable to develop in malignancies, especially those transmitted by oncogenic viruses. The important role that infection with oncogenic viruses plays in the development of malignancy has become well recognized in the past decade. Understanding the mode of viral transmission sheds light on the epidemiology of these malignancies. Three oncogenic viruses are strongly linked to HIV-related malignancy: human herpesvirus8 (HHV-8), Epstein-Barr virus, and human papilloma virus .As a rule, the risk of malignant transformation is related to the degree of host immunosuppression.

The mechanisms of disease and imaging feature of several AIDS-related oncogenic viruses and illustrate their typical and unusual thoracic imaging manifestations.

Tumor	Virus
Kaposi sarcoma	Human herpesvirus 8
Primary effusion lymphoma	Human herpesvirus 8
Castleman disease	Human herpesvirus 8
Non-Hodgkin's lymphoma	Epstein-Barr virus
Hodgkin's lymphoma	Epstein-Barr virus
Nasopharyngeal carcinoma	Epstein-Barr virus
Spindle cell tumors	Epstein-Barr virus
Cervical cancer	Human papillomavirus
Anal cancer	Human papillomavirus
Papillomatosis	Human papillomavirus
Adult T-cell lymphoma	Human T-cell lymphoma virus
Hepatoma	Hepatitis B and C viruses
Lung cancer	Human papillomavirus (rarely), unknown
Germ cell tumor	Unknown
Nonmelanoma skin cancer	Unknown
Plasma cell neoplasm	Unknown

Human tumor viruses

Tumor-viruses are known to be associated with discrete human malignancies. They have been broadly classified into two distinct groups, DNA- and RNA-tumor viruses, on the basis of their genetic make-up. Human DNA tumor viruses include EBV, HBV, Kaposi's sarcoma herpes virus (KSHV), human papilloma virus (HPV) and Merkel cell polyoma virus (MCV), whereas RNA tumor viruses comprise retroviruses like human T-cell leukaemiavirus-1 (HTLV-1) and human immunodeficiency virus-1 (HIV-1), and flavi virus such as hepatitis C virus (HCV).