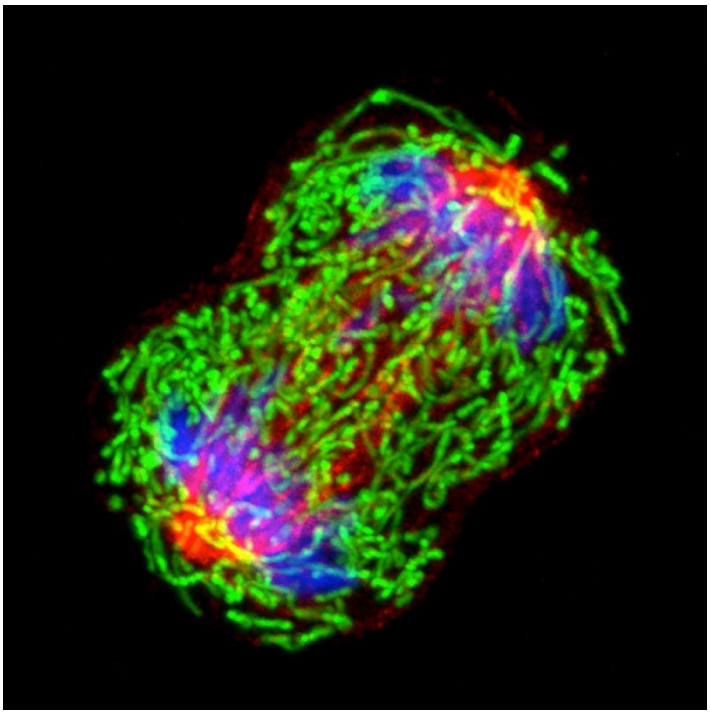
Cancer Basics

Before we can dive into treatment options it's important that you understand the basics of how cancer develops, grows, and spreads.

Without this foundation it's difficult to understand the science behind the treatment options you'll be offered and the difference between standard care and the latest advances in medical science. In this unit we'll give you the information you need to understand the role of DNA and stem cells in the development of cancer.

Cancer, at its most basic level, is a disease caused by genetic mutations and all cancers originate in stem cells. Traditional treatments, like chemotherapy and radiation, target all rapidly growing cells and fail to treat dormant cancer causing stem cells. This is a problem because if these stem cells are not treated, when they are active again they will create more cancerous cells. Newer treatments, like targeted therapies, specifically target the stem cells that cause cancer, even dormant stem cells, treating your cancer at the source.



Dividing breast cancer cell.

Source: National Cancer Institute & University of Pittsburgh

In this unit we'll cover the fundamentals of cancer so you can understand the science of your treatments and care. We'll cover what DNA and stem cells are, the normal function of DNA mutation, and how these mutations differ from Cancerous mutations. This information is key to

understanding the difference between standard treatments and advanced treatments, the role of stem cells in particular.

Our peer support team will share their experience with DNA testing, and exercise and nutrition for supporting your body as it fights cancer, and what they wish they knew about Genetic testing when first diagnosed. As always make sure you watch the peer support videos. Much of this information can seem abstract but they will help you understand how it applies to your life or that of a loved one

If you have any questions please drop them in the comments below and we'll do our best to answer them.

What is Cancer?

Cancer is a group of many diseases that share similarities and can occur anywhere in the body. What these diseases have in common is that they are the result of genetic changes within our genes.

These changes disrupt the ways our cells function and alter the systems that manage and control our cells' lifecycle. **These genetic changes result in unrestricted cell growth and stop our cells from going through their normal death process.**

Before we understand how this happens, it's important to understand our bodies are growing new cells all the time, how this process works, the role of stem cells, and what DNA is and how it fits into this process

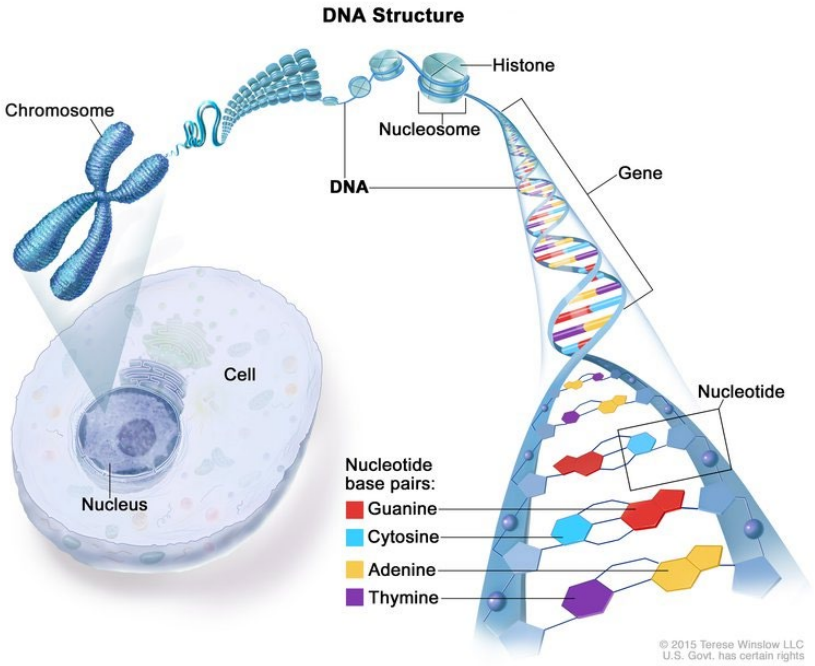
To make new cells our existing cells divide and multiply, copying themselves and passing on their exact sequence of DNA. Occasionally things go wrong in this process because of damage that has been done to our DNA. Our DNA can be damaged by radiation (the sun or cancer treatment), chemicals in the atmosphere, oxygen radicals, cosmic rays (which are small waves that come from space), but the key issue is that somehow our DNA has been physically damaged.

DNA

DNA is essentially the set of instructions that create and direct everything biological.

Our bodies are made up of trillions of cells grouped together. Within each cell is a complete strand of DNA. DNA is essentially the set of instructions that create and direct everything biological. These instructions tell our cells how to grow, work, divide, and die.

Our bodies are growing new cells and biomolecules (hair, teeth, bone, etc) all the time. To do this the DNA in our genes provide the instructions to our stem cells which then create the specific types of cell we need. It's important that we understand the role stem cells play in our bodies, because it's now widely accepted that all cancers are caused by adult stem cells (or cells with stem-cell like properties).



From Alex:

Our bodies are made of many different components. Our bodies know how to make these components because of the code (signaling molecules) within our DNA. DNA is a double helix chain of amino acids, which are the building blocks of proteins, attached to a sugar. The order of these amino acids creates the code for a new type of a protein or enzyme our bodies need. This could be a protein in our hair, skin, or a component of our blood.

DNA is composed of four different amino acids: Adenine (A), Thymine (T), Guanine (G) and Cytosine (C). Adenine and thymine connect and guanine and cytosine connect. They always connect in this pairing. It's the order, or sequence, of these pairs that determines what is created.

These pairs link two strands and create a double helix. One strand is the coding strand, the other is the template strand. Our bodies create the necessary protein or enzyme by reading the coding strand. The template strand is a redundancy that is used to repair any damage that occurs to the coding strand.

What is interesting is that genes and other transcribed elements can be encoded on either strand in either direction. So in other words genes can be inside of genes in different orientations. (what we now know is that some genes can be on the coding strand backwards, they can be in any orientation and any position. Like a crossword puzzle the words can be in any orientation and still understood by our bodies.) This adds to the complexity of how our DNA can be used.

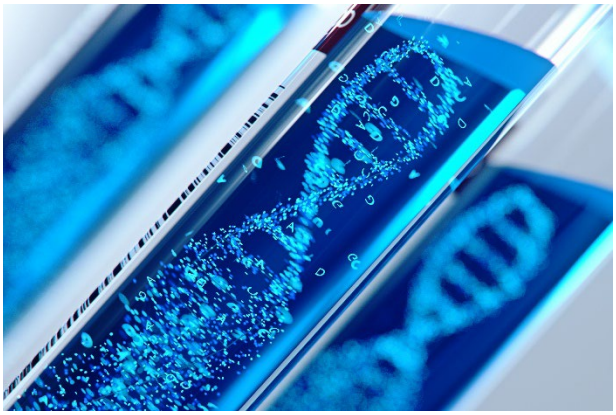
Stem Cells

Stem cells are unique cells, they are the cells from which all other cells originate.

Each type of cell and tissue has their own stem cells which are responsible for creating and replacing those cells and tissues. Our stem cells live in niches within the tissues they repair or replace.

Stem cells are dormant most of the time (a state called 'quiescence'), waking up only when we need them to produce the cells they specialize in. To give you an idea of how special these cells are there are roughly 1 stem cell for every 6 million cells in our body.

Stem cells receive their instructions from the DNA in their genes. Cancerous mutations occur within this DNA and affect the genes that are involved in repairing damaged DNA. The result of this damage is that our cells stop functioning the way they are supposed to, which can cause a tumour to develop. A tumour usually develops a short distance away from the stem cell niche where the DNA damage occurred.



From Alex

All of this protein (a general term for the product of a gene) creation is happening inside our cells. Once the protein structures are created they are released by the cells and begin to fulfil their role in our body.

While all of our cells contain DNA it is only mutations within the DNA of our stem cells which lead to cancer.

To understand how mutations occur we need to understand how our stem cells replicate. Stem cell process involves two stages

1. Proliferation
2. Differentiation

Proliferation means the stem cell makes an exact copy of itself. Proliferation creates another stem cell which lays dormant in the stem cell niche until it's needed.

Differentiation happens when the copied stem cells are converted into a normal cell (the type of cell it's destined to be), it is then given a Hayflick number - the number of times the normal cell will divide and replicate before it stops and dies. This is a process called 'pre-programed cell death'. Cell death is a completely normal process and something predetermined when new cells are created. Programmed cell death allows the body to recycle its products.

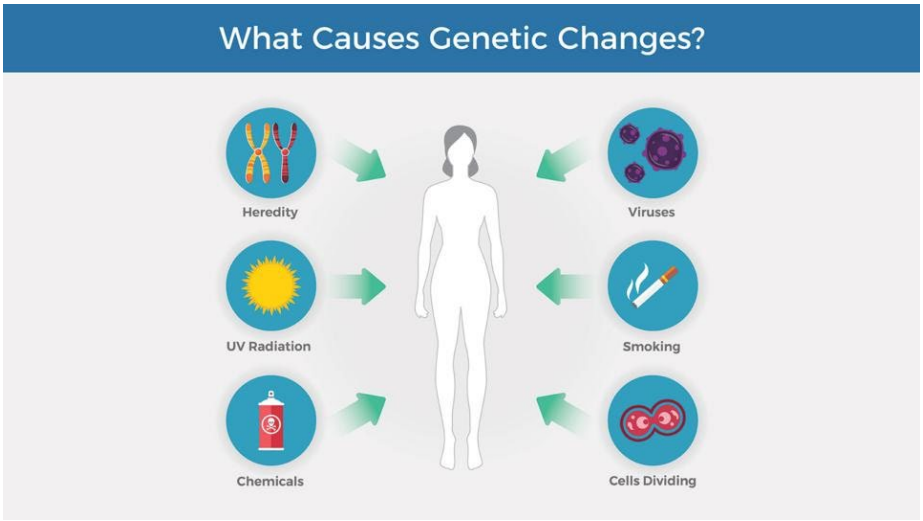
DNA Mutations

From Alex:

Mutations occur in our DNA all the time. Some lead to positive developments (evolution), some mutations are harmless (neutral/benign), some are repaired before they replicate, but some - a small amount - those within our stem cells (or cells with stem cell like properties) that are not repaired can go on to cause cancer. While only harmful mutations within stem cells lead to cancer, the process of all mutations are the same.

Mutations are the result of a physical change to the base pairs that encode for the amino acids in our DNA, that then lead to an error while our DNA is being copied. The physical damage to our DNA can be caused by many different things, but it's usually some form of radiation (the sun), oxygen radicals, chemicals in the environment around

us, cosmic rays (small molecules from beyond our atmosphere). Through various processes pieces of our DNA can be damaged; biomolecules can break off, merge together, get knocked out of place, etc.



Source: National Cancer Institute

Because this happens all the time, and because our DNA has a template strand, our body's are able to repair the damage and replicate. Even if the damage occurs to both DNA strands, or the original amino acid sequence (and therefore the repair instructions provided by the template strand), our bodies have a way to repair that as well.

With the help of a gene called the 'error prone pathway' a replacement pair of amino acids will be inserted in place of the missing or damaged acids. These amino acids are a placeholder, a band aid of sorts, they are not the correct amino acids but they fill the gap in our DNA. If the cell is able to replicate with this band aid, the replicated cells are classified as a mutation.

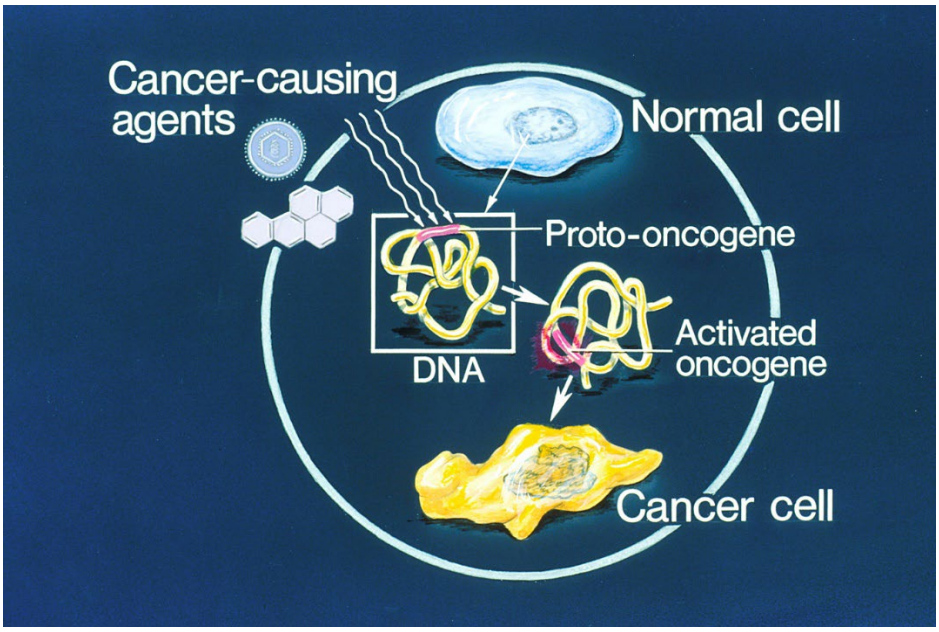
Cancerous Cell Mutations

From Alex: Gene mutations occur in the body all the time. In order for a cancerous gene mutation to occur the mutation must happen within a stem cell, and effect a gene that is involved with either 1) growth and development or 2) repair of DNA damage.

These classes of genes are referred to as **oncogenes** and **tumour suppressor genes** respectively. Specifically, mutations must occur in at least four of these signalling pathways in humans.

The types of mutations that must occur within growth and development genes are ones that:

- Affect the control region of the gene and turn it on when it's supposed to be turned off
- Cause the gene to stay in its active state longer than its supposed to
- Last in the body longer than its supposed to
- Cause it to remain attached to the signaling proteins it affects rather than detaching after its job is done (constitutive signaling).



How does an oncogene form?

Source: National Cancer Institute

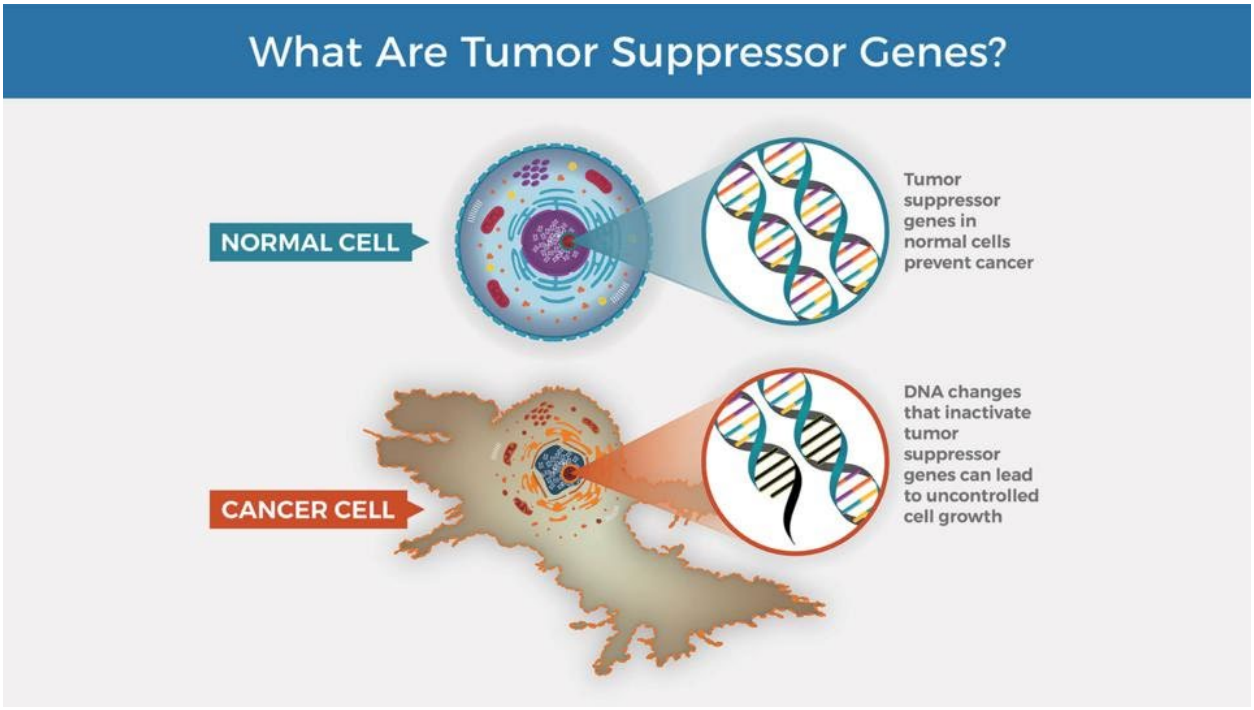
Growth and Development Genes

Normally growth and development genes are only switched on briefly to fix damage to tissue or while you're growing during childhood, otherwise these genes are turned off. **However when a mutation occurs and these genes are switched on and stuck in their production phase, called proliferation, these genes are now cancerous and called Oncogenes.**

Tumour Suppressor Genes

The second pair of genes that must mutate, tumour suppressor genes, are genes that fix and recognize DNA damage, also known as 'checkpoint genes'. These genes are supposed to be switched on all day, every day, for our entire lives. These are the genes that fix DNA damage in all genes and cells. Their job is to recognize when a random amino acids have been added and either fix the damage or stop the cell from reproducing. Mutations can happen in these genes that can:

- Cause the gene to not be expressed at a high level
- Damage the binding regions that these genes use to attach to other molecules
- Change the genes they interact with, so they turn on oncogenes rather than repair genes



Source: National Cancer Institute

You only need one stem cell niche with alterations to cause a problem.

For cancer to develop mutations must happen in **at least four** of these pathways in one stem cell niche. Once this has happened, we now have unregulated production of mutated cells.

There are hundreds of documented oncogenes and tumor suppressor genes in our bodies, due to this there are many 1000's of possible combinations of gene alterations that can lead to cancer. It is not the same for every person and this multitude of mutation possibilities is why the success rates for treatment can vary so greatly from one person to another. Each cancer is unique.
