BEY311

Nutrition and Cancer

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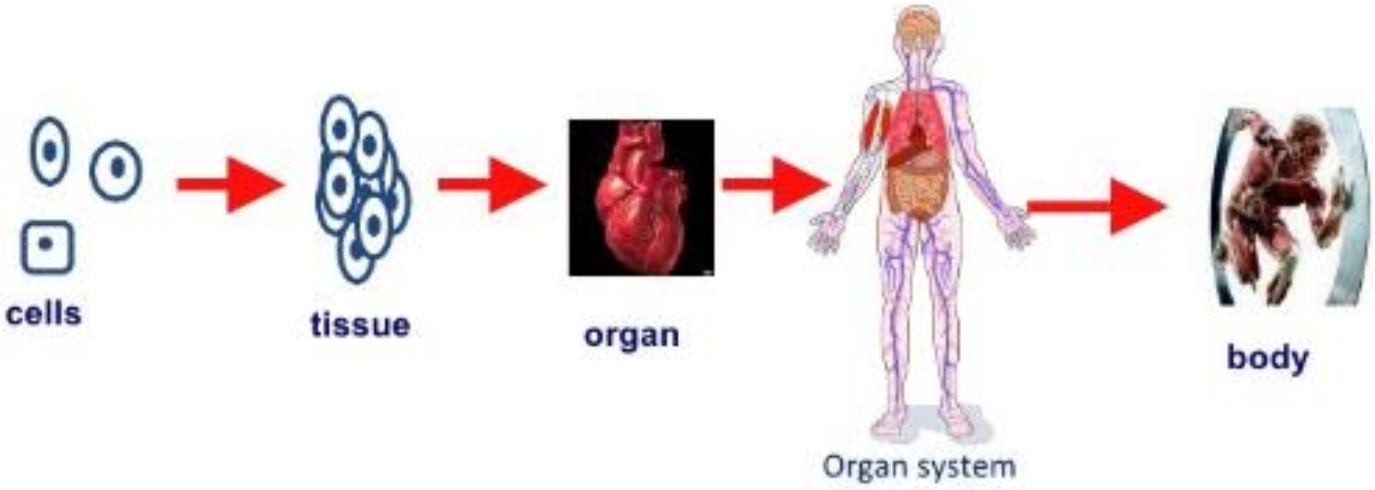
General Reading List

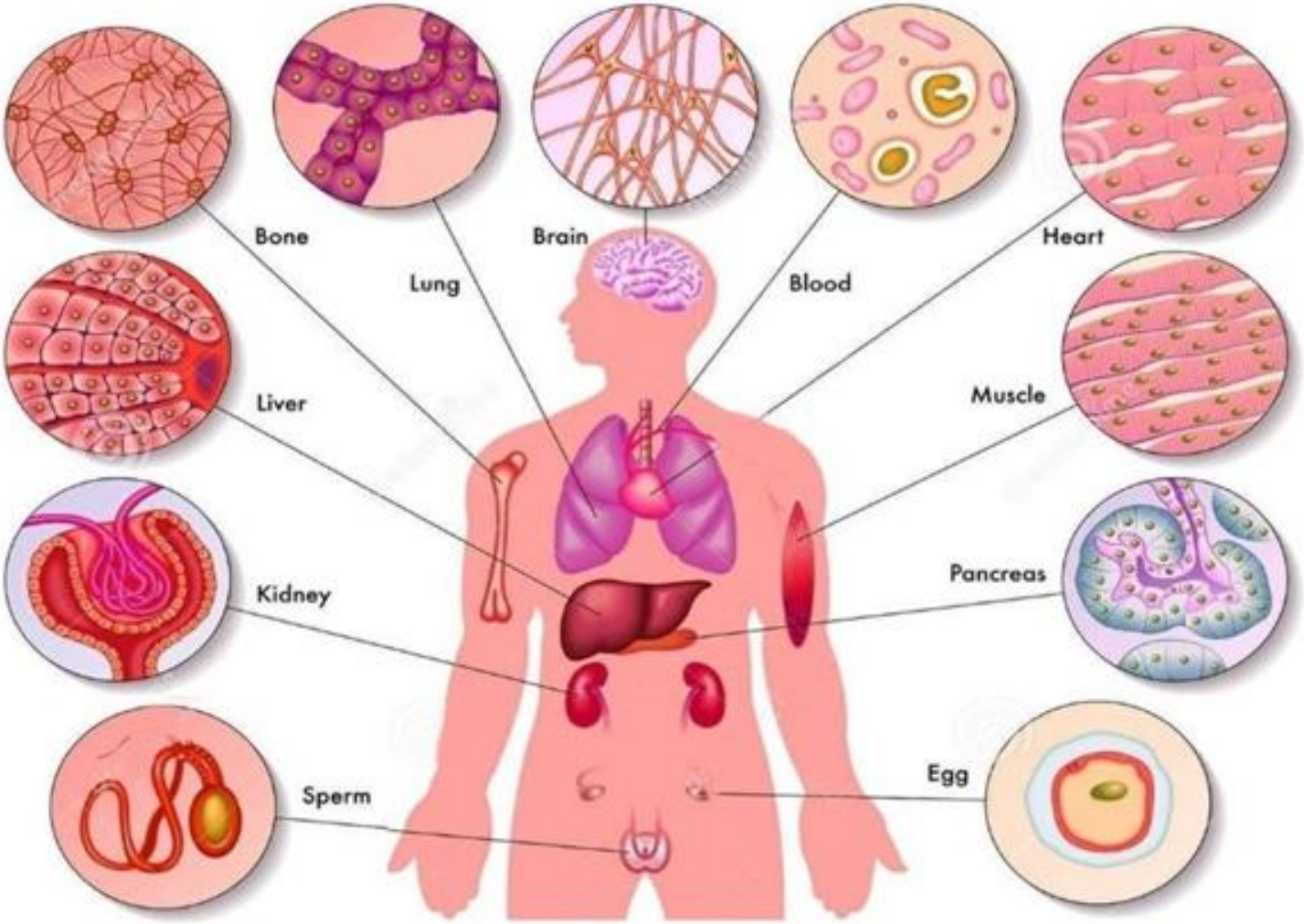
- **Nutrition and Cancer Prevention** by *Atif B. Awad and Peter g. Bradford* (Taylor and Francis)
- **Cancer Biology** (2000; 2nd ed) by *RJB King* (Prentice Hall Publishers)
- **Advances in Nutrition and Cancer** byVincenzo Zappia · Salvatore Panico Gian Luigi Russo · Alfredo Budillon Fulvio Della Ragione Editors (Springer)

How cells and tissues grow

Cells and tissues



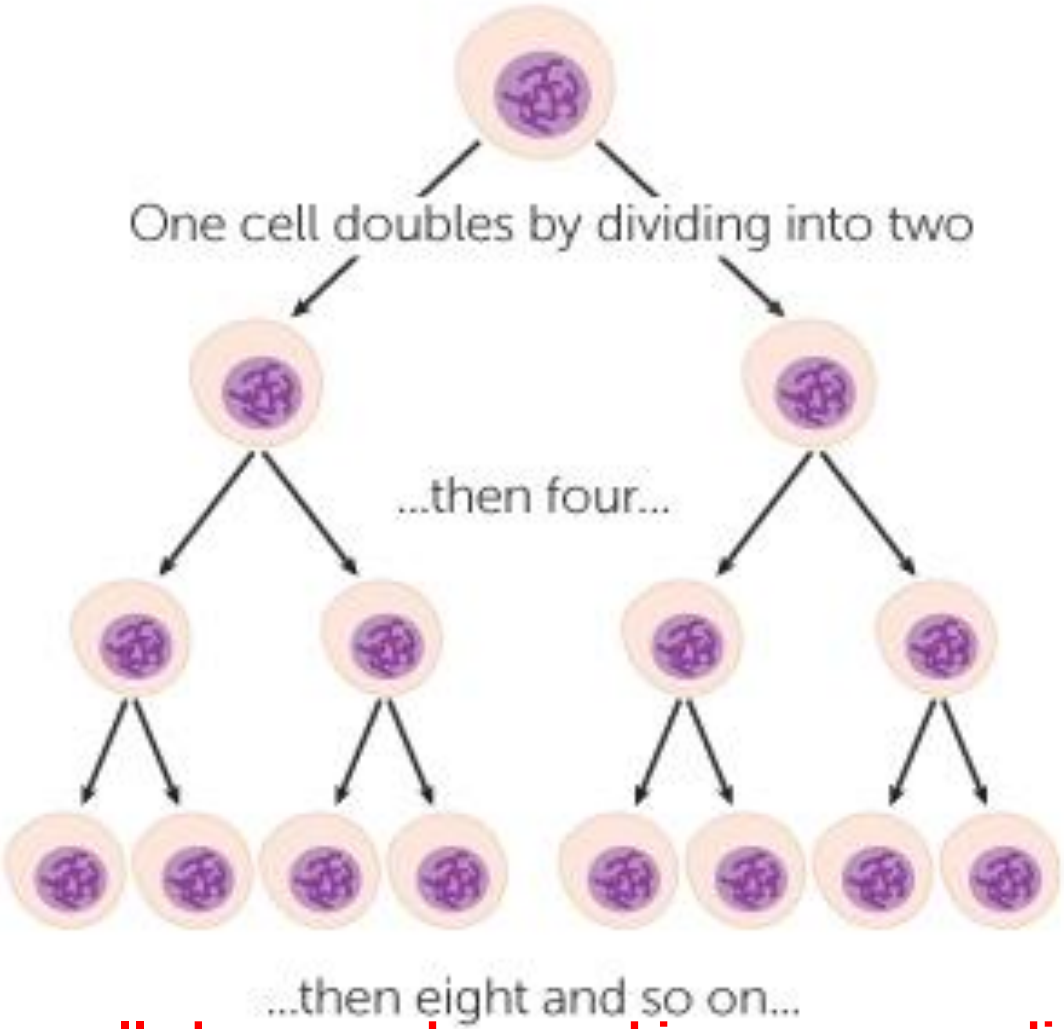
Human Cells


Bone
Lung
Brain
Blood
Heart
Liver
Muscle
Kidney
Pancreas
Sperm
Egg

How body tissues grow

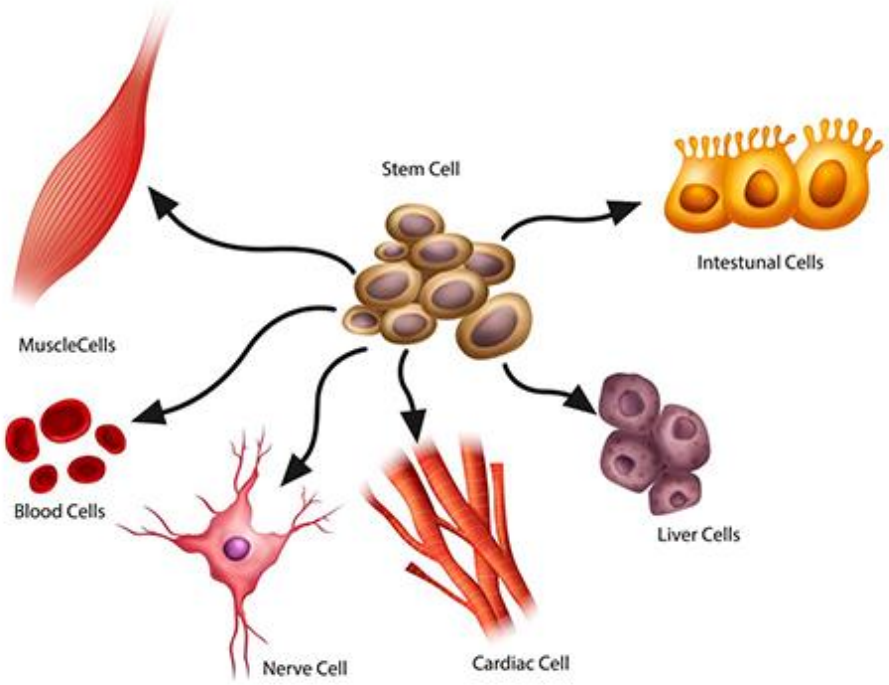
Body tissues grow by increasing the number of cells that make them up.

Cells in many tissues in the body divide and grow very quickly between conception and adulthood. Once we are grown up, many cells mature and become specialised for their particular job in the body and they don't reproduce so often. But some cells, such as skin cells or blood cells are constantly dividing.



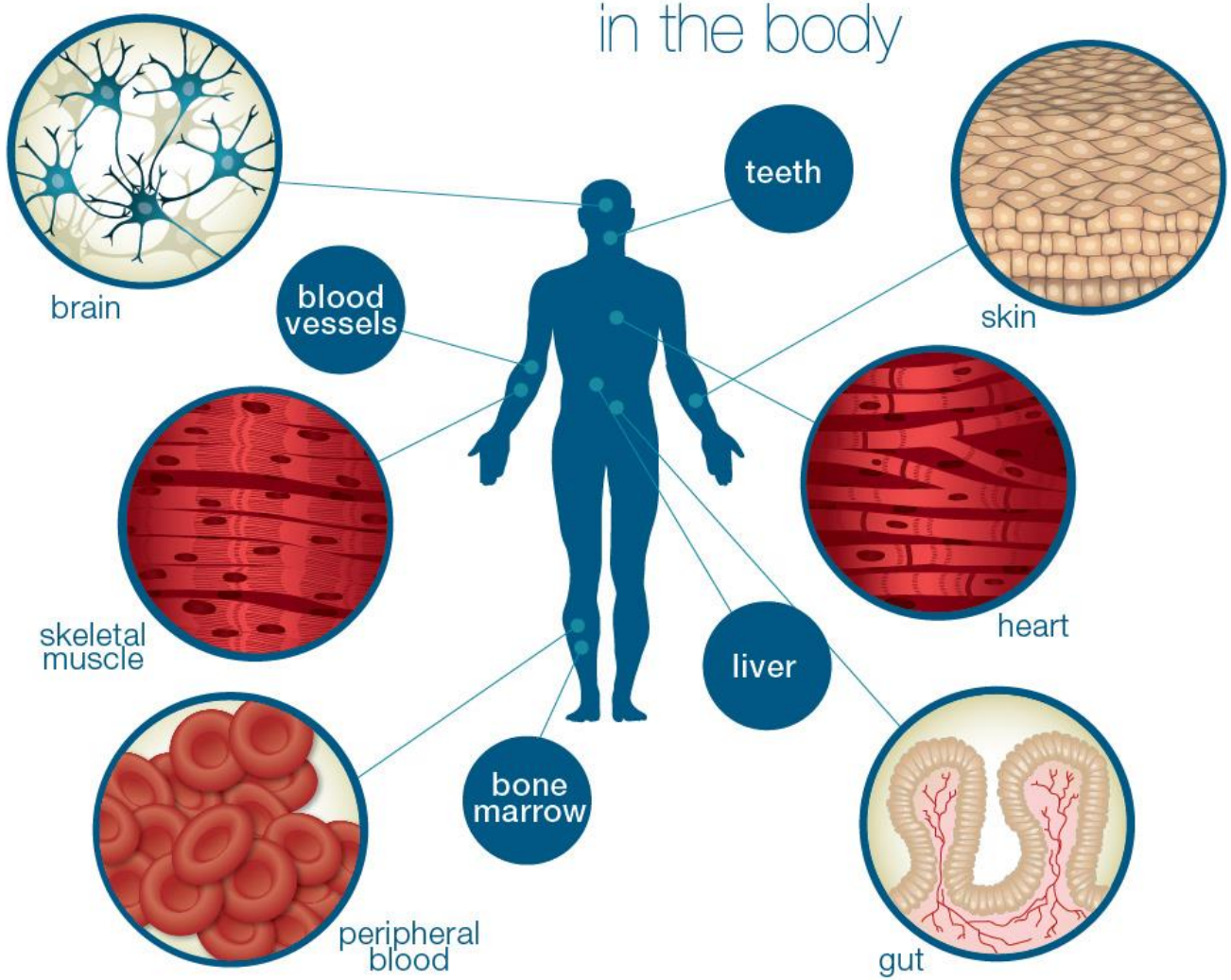
When cells become damaged in any way or die, the body produces new cells to replace them. This process is called cell division. One cell doubles by dividing into two. Two cells become four and so on. It seems that human cells can reproduce up to 50 or 60 times at most. Then they usually die.

Stem cells



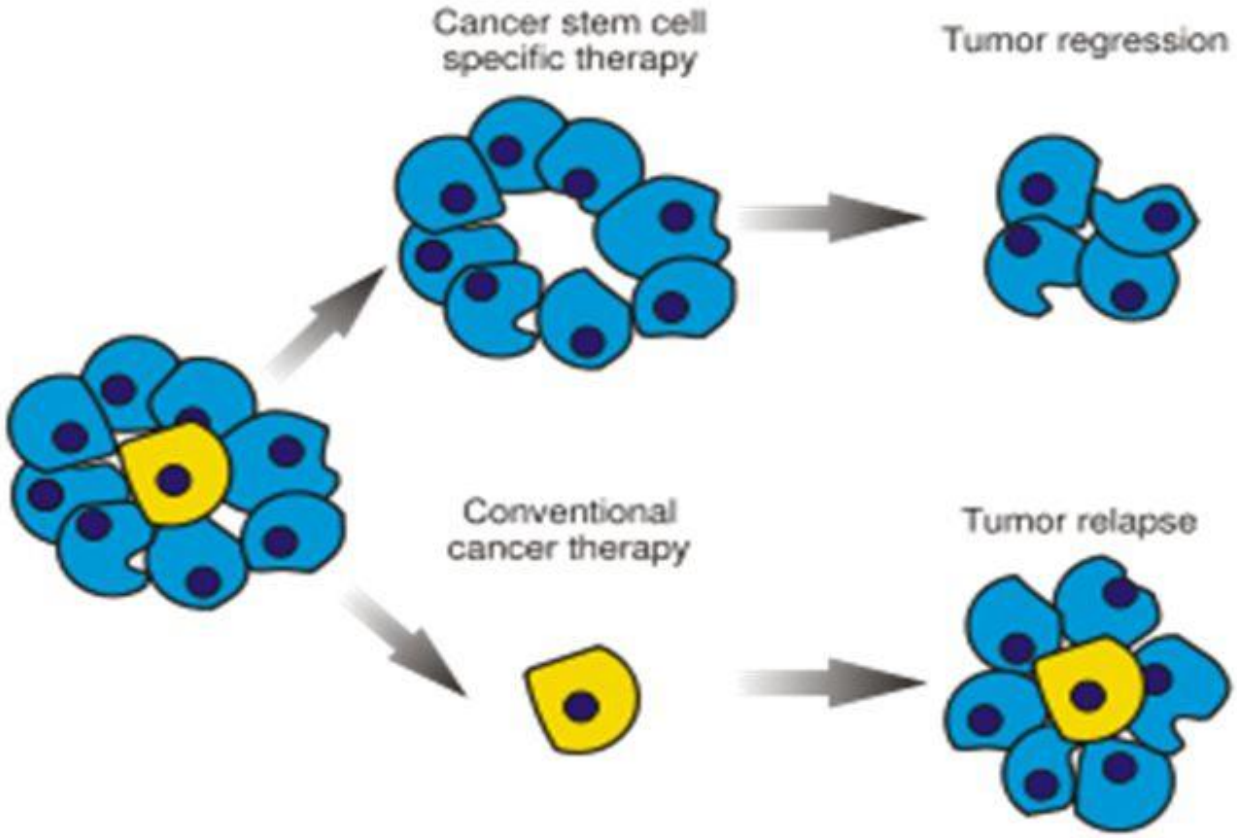
Stem cells provide a pool of dividing cells that the body uses to restock damaged or old cells. Stem cells are a kind of 'starter cell'. They have the potential to develop into different cell types in the body. When a stem cell multiplies, the resulting cells may remain as stem cells. But under the right conditions, they become a type of cell with a more specialised function, such as a muscle cell, red blood cell or brain cell.

Locations of **Somatic Stem Cells** in the body



Stem cells occur naturally in the body in various places and stages during our lifetime. In the embryo, they give rise to all the different tissues and organs of the body. In adults, each type of stem cell is usually only able to develop into a few specific types of cell. For example, adult stem cells in the bone marrow, known as haematopoietic stem cells, usually only give rise to different types of blood cell.

WRONG TARGET. Traditional cancer therapies (top) kill rapidly dividing tumor cells (blue) but may spare stem cells (yellow) that can give rise to a new tumor. In theory, killing cancer stem cells (bottom) should halt a tumor's growth lead to its disappearance.



Stem cells may play a role in the development of cancer. Some tumours develop from faulty stem cells. This has led to the idea of cancer stem cells, which scientists have now identified in a range of cancer types. The types include bowel, breast and prostate cancer as well as leukaemia. Researchers are looking at whether some treatments could target cancer stem cells. Halt=stop this is growing tumor cells in stem cell around.

How cells grow and divide

When cells divide and grow they do this very precisely so that the new cells are exactly the same as the old ones.

Each cell makes copies of all its genes. Then each cell splits into 2 with one set of genes in each new cell. During the process, there are lots of checks to make sure that everything has copied correctly. But sometimes mistakes happen, which can lead to cancer.

How healthy cells divide

https://www.youtube.com/watch?v=zR8rIPcOZMY

Here is a cell, one of millions in the body. Within the cell's nucleus are chromosomes made of DNA. Chromosomes contain genes, the cell's instructions. Most human cells have 46 chromosomes (23 pairs), but only one is shown here. When a cell gets ready to divide its DNA is copied...

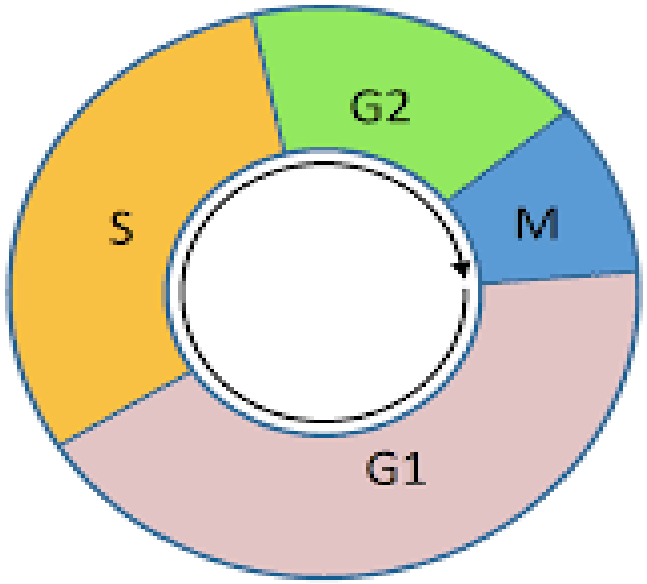
The cell checks whether everything is okay with the DNA. Is it damaged? Has it been copied correctly?

If everything is correct, then the cell can continue.

The cell gets ready to divide. It builds a molecular scaffold, called the spindle, which attaches to the DNA. The cell checks whether everything is okay with the spindle. Is the DNA attached properly?

If everything is correct, then the cell can divide. The cell splits, forming two new cells. Healthy new cells divide in a controlled way, replacing damaged or dead cells as needed. This process happens millions and millions of times every day in your body.

The cell cycle



G1 - Growth

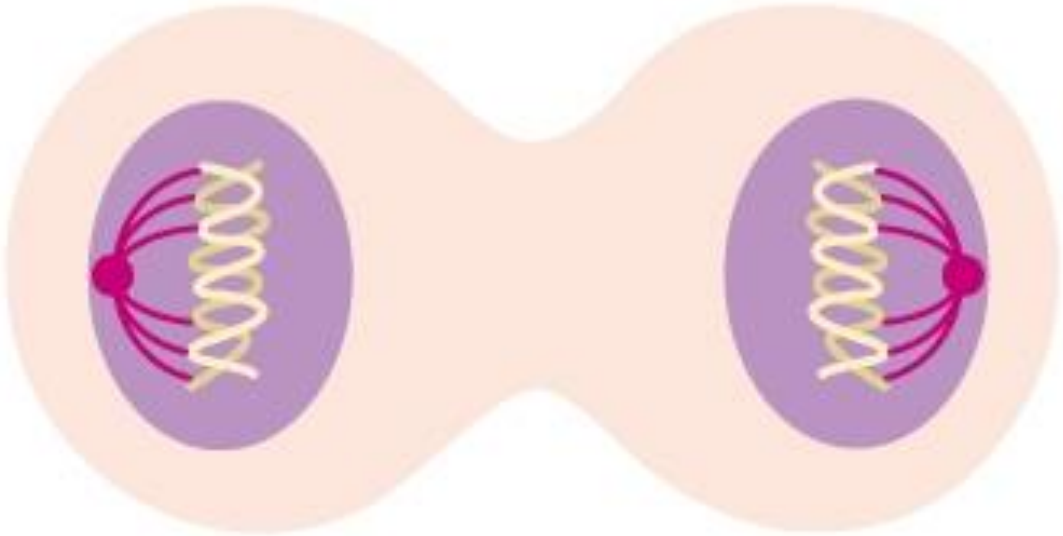
S - DNA synthesis

G2 - Growth and preparation for mitosis

M - Mitosis (cell division)

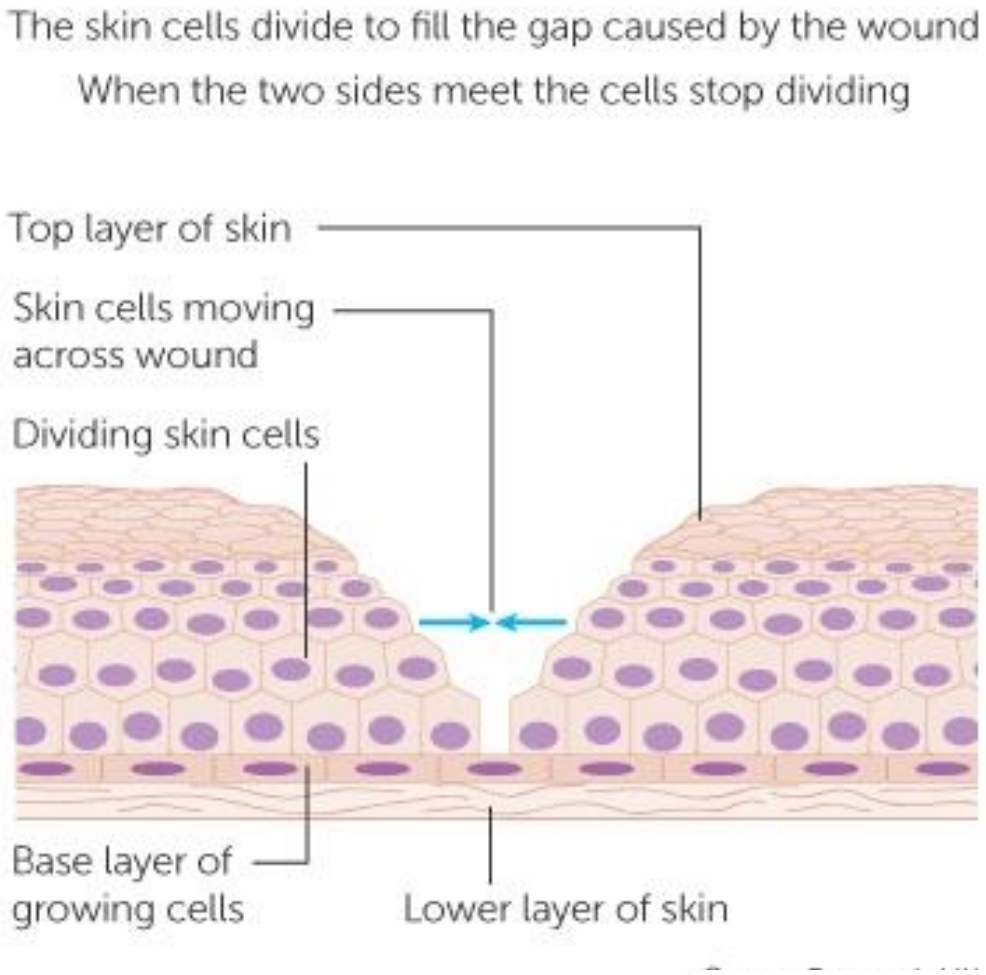
- **Gap 1 or G1 phase, where the cell grows in size, and checks that everything is OK for it to divide.**
- **Synthesis or the S phase, where the cell copies its DNA.**
- **Gap 2 or G2 phase, where the cells check that all its DNA has been correctly copied.**
- **Mitosis or M phase, where the cell finally divides in two.**

During mitosis, the cell shares the copied DNA equally between the 2 new cells.



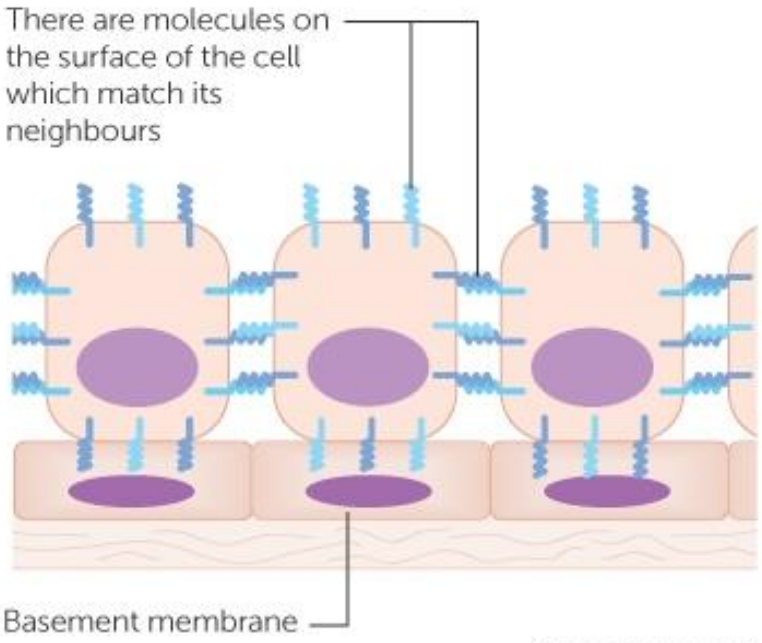
The cell separates all the duplicated chromosomes into 2 full sets, one at each end of the cell that is splitting in two. The other material that makes up the cell also splits in two. The result is two identical daughter cells.

How cells stop growing



The cells know when there are enough new cells to mend a cut or when a structure such as a finger is fully grown. They send chemical messages to each other so that they stop growing and dividing when growth or healing is complete. The diagram shows this happening

How cells stay in the right place



Cells in the body have a natural ability to stick together in the right place so that the tissues and structures of the body form correctly.

Molecules on the surface of the cell match those on its neighbours. It is a bit like having a postcode. The code makes it very difficult for the cell to move to the wrong place. But if the cell does find itself in a place where its postcode is different from its neighbours, it dies

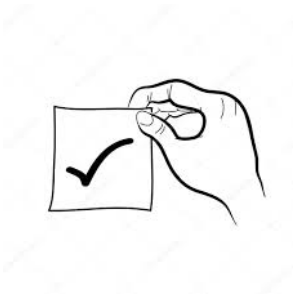
How cells die

When cells become damaged or worn out, they will self destruct.

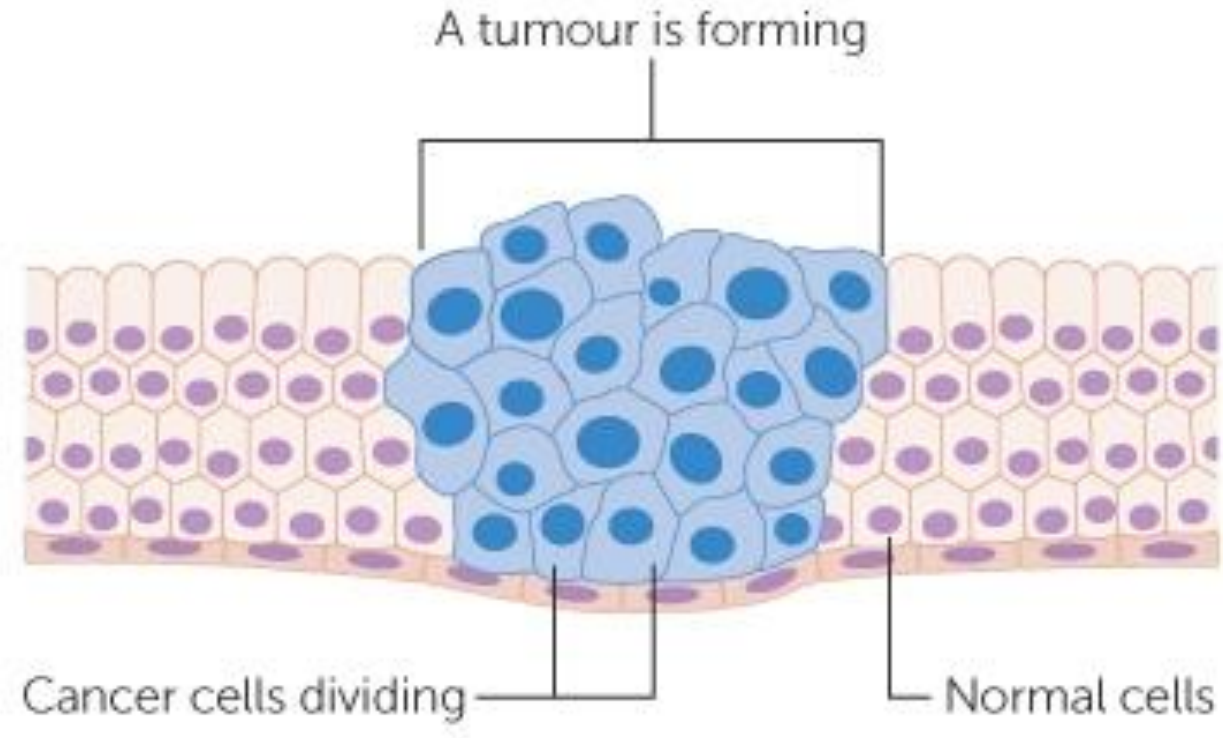
This process called as apoptosis and it helps to protect us from developing cancer. Cells can also undergo apoptosis if they have broken away from their proper place in the body.

Features of normal cells

- Reproduce when and where it's needed
- Stick together in the right place in the body
- Self destruct when they become damaged or too old become specialised (mature)



Cancer cells are different to normal cells in various ways. Unlike normal cells, cancer cells don't stop growing and dividing when there are enough of them. So the cells keep doubling, forming a lump (tumour) that grows in size



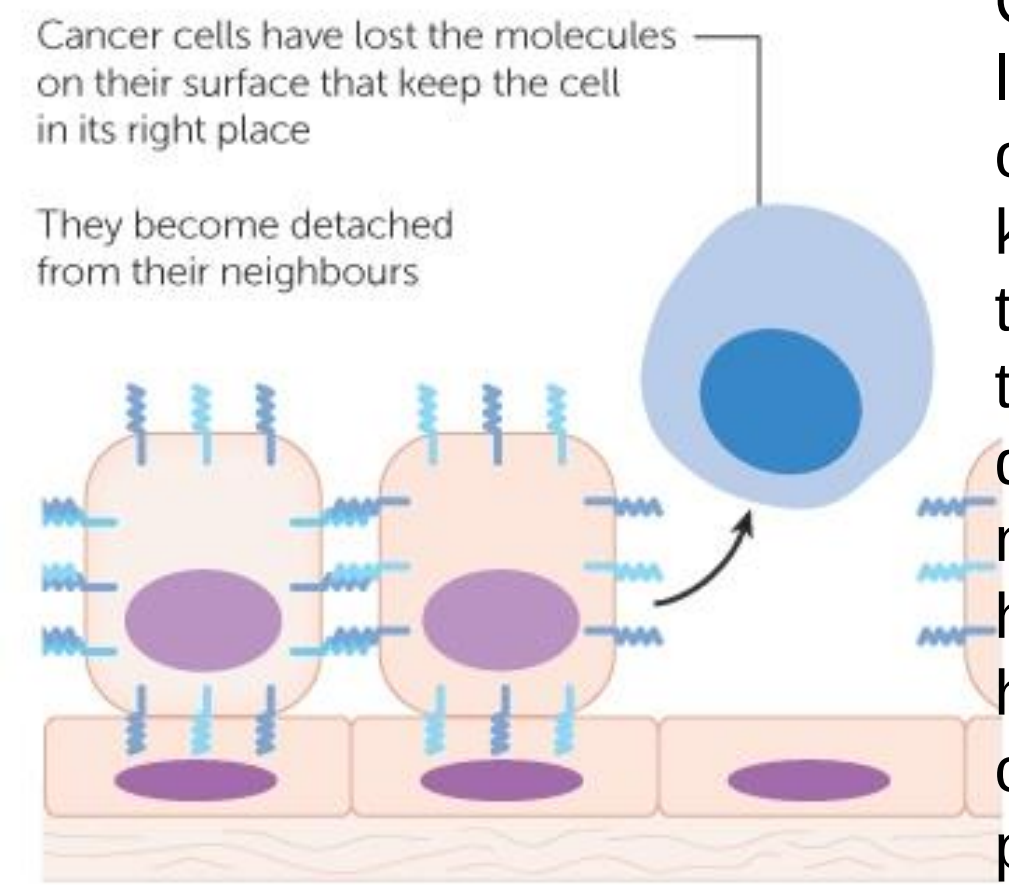
Eventually, a tumour made up of billions of copies of the original cancerous cell forms. Cancers of blood cells (leukaemias) don't form tumours, but they make many abnormal blood cells build up in the blood.

Cells send chemical signals to each other all the time. Normal cells obey signals that tell them when they have reached their limit and will cause damage if they grow any further. But something in cancer cells stops the normal signalling system from working

When cells cause cancer by giving the wrong messages

https://www.youtube.com/watch?v=e1V-JzMknfA

Cancer cells don't stick together



Cancer cells can lose the molecules on their surface that keep normal cells in the right place. So they can become detached from their neighbours. This helps to explain how cancer cells can spread to other parts of the body

Cancer cells don't specialise

Unlike healthy cells, cancer cells don't carry on maturing or become specialised.

The cells are not able to work properly.

There's a higher chance more mistakes in their genes.

They divide and grow even more quickly.

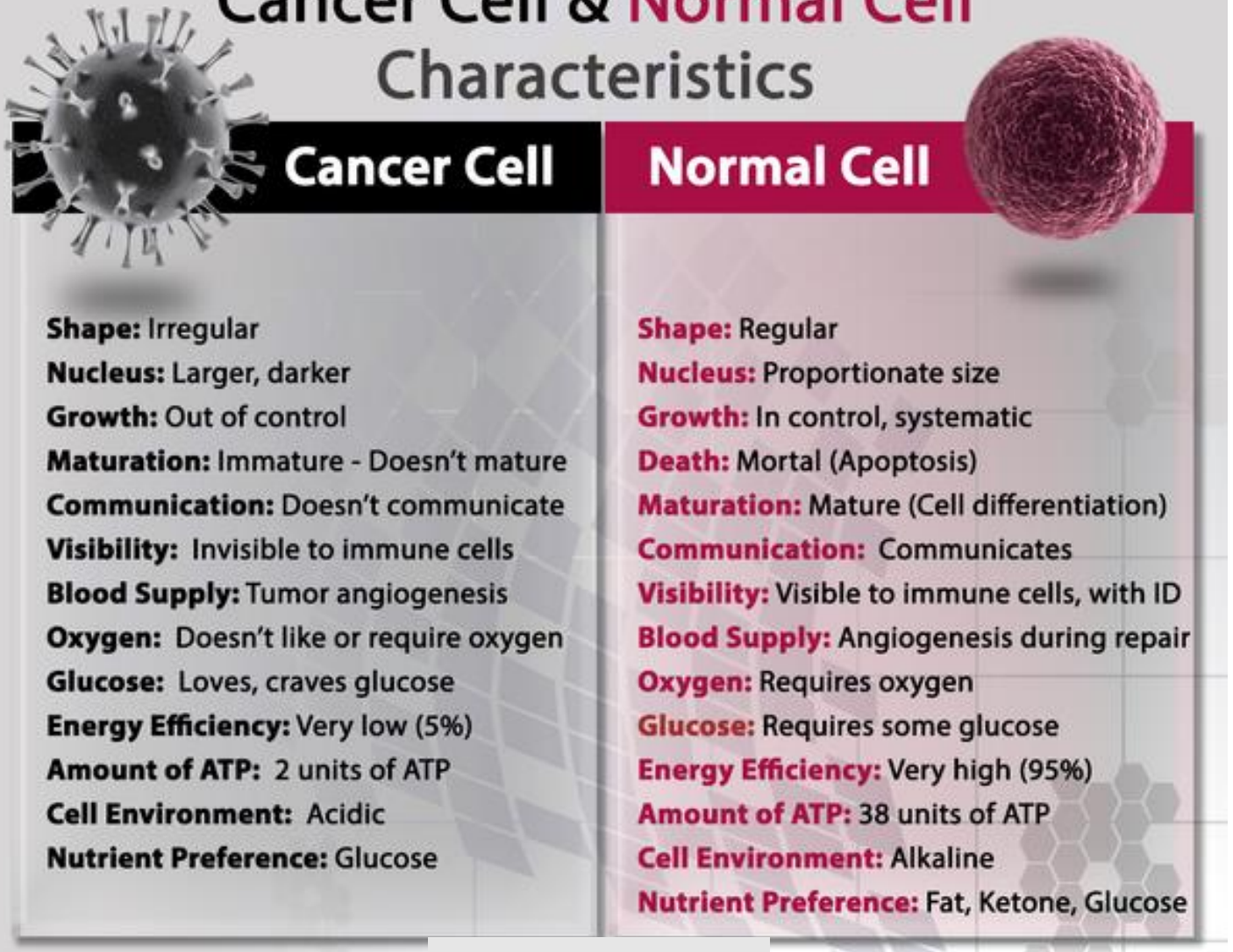
Cancer cells don't repair themselves or die

In cancer cells, the molecules that decide whether a cell should repair itself are faulty.

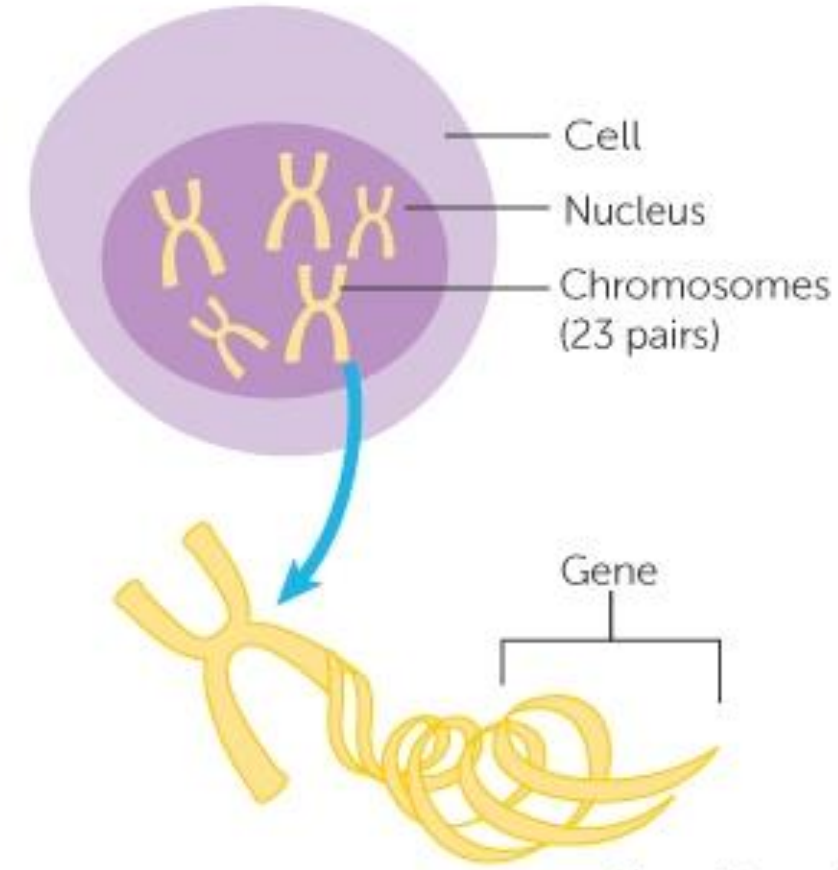
New gene faults, or mutations, can make the cancer cells grow faster, spread to other parts of the body, or become resistant to treatment.

Cancer cells can ignore the signals that tell them to self destruct.

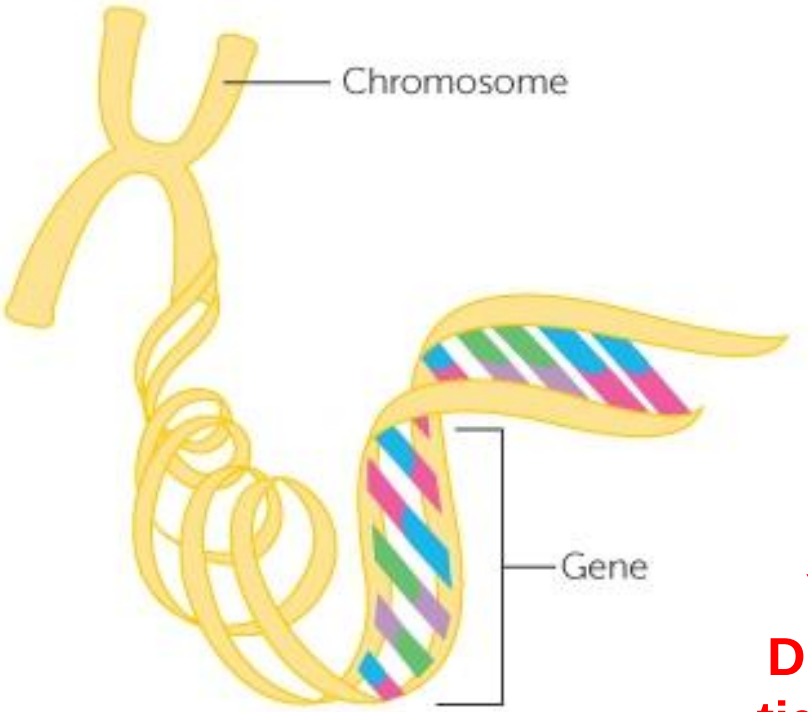
Cancer cells look different



Genes, DNA and Cancer



Inside almost every cell in your body is a structure called the nucleus, which is the control centre of the cell. Inside the nucleus are 23 pairs of chromosomes. These are long strings of DNA.



You inherit half your DNA from your mother and half from your father, so you have 2 copies of every gene.

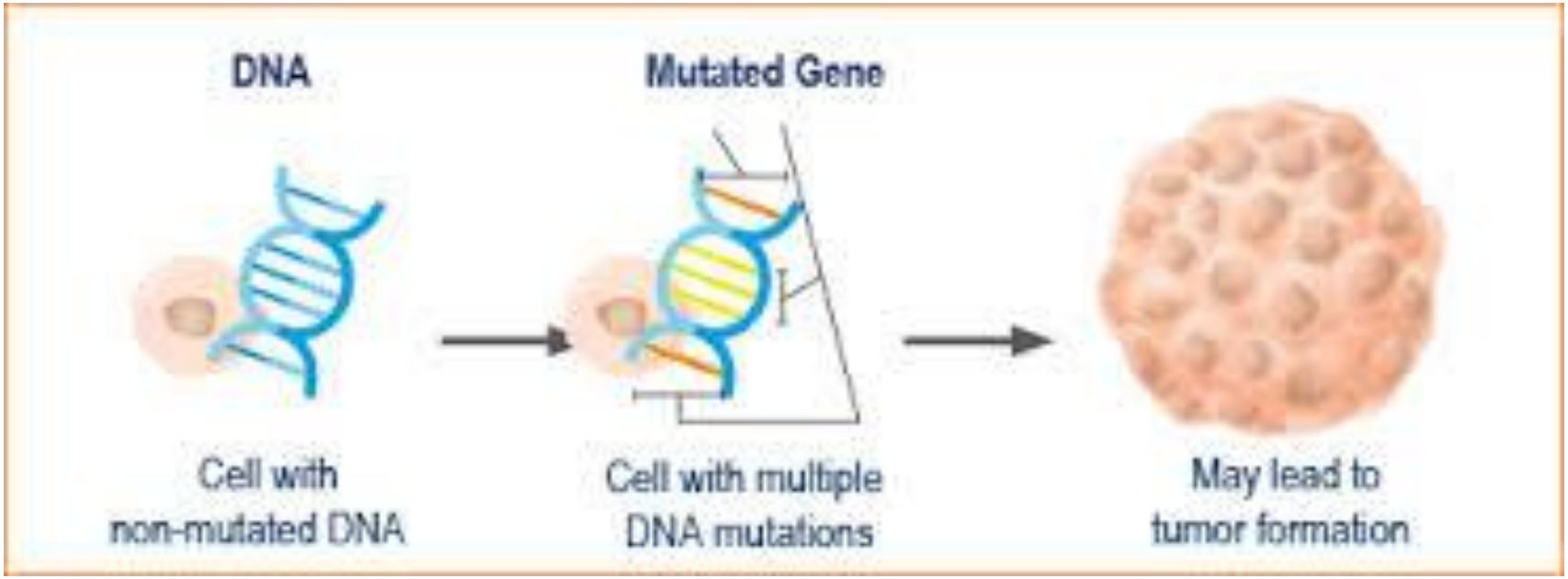
You have more than 2 metres of DNA inside every cell, but it is very tightly coiled up so it all fits. DNA is like a code containing all the instructions that tell a cell what to do. It is made up of genes. Humans have around 25,000 genes in total.

Your genes carry all the information that makes you!!!!!

How faulty genes lead to cancer

Mutations can happen throughout our lives, during natural processes in our cells. Or they can happen because of other factors such as;

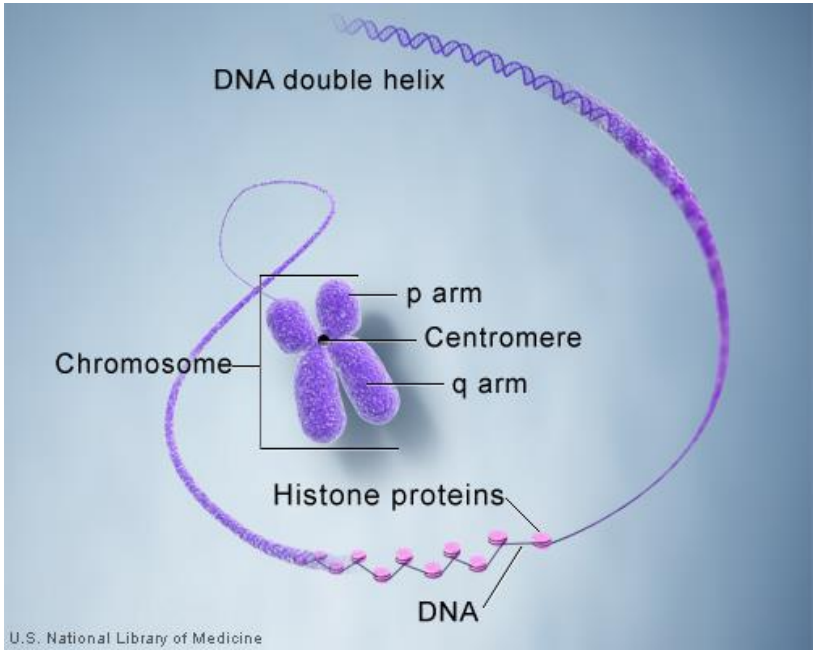
- **TOBACCO SMOKE**
- **RADIATION**
- **ULTRAVIOLET RADIATION FROM THE SUN**
- **SOME SUBSTANCES IN FOOD**
- **CHEMICALS IN OUR ENVIRONMENT**



The cell can start to multiply out of control. It doesn't repair itself properly, and it doesn't die when it should. Mutations in genes can lead to cancer.

What is a;

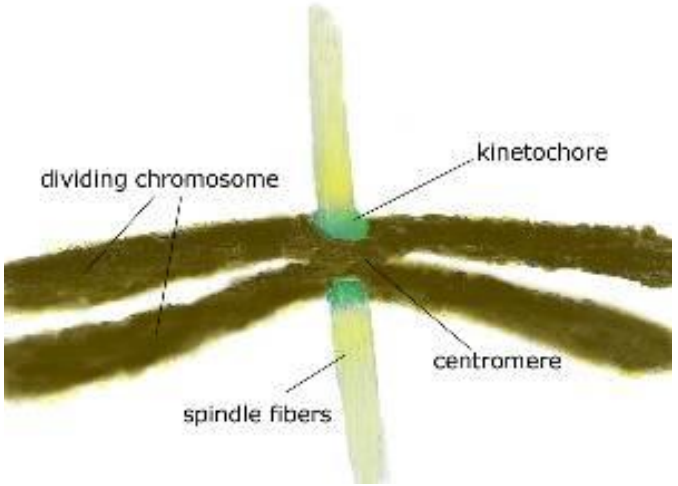
- **Gene;** the basic pysical and functional unit of a heredity. Genes are made up DNA.
- **Chromosome;** in the nucleus of each cell the DNA molecule is packaged into thread-like structures. The resulting condensed body is a chromosome, which usually resembles a large X.
- The four arms of the X join at the central portion called the **centromere**.
- **Chromatin;** Chromatin is a combination of **DNA, ribonucleic acids and proteins called histones** that fill the cell nucleus. The histones attach to and compress the double-helical strands of DNA.



- **Chromatid;** A chromatid is one of two identical halves of a replicated chromose. The chromosome consists of two identical structures called sister chromatids, which are joined at the centromere.

What is a;

- **Centriole;** All animal cells have two small organelles known as centrioles. The centrioles help the cell to divide. Centrioles are seen the process of mitosis and meiosis. The centrioles together are typically located near the nucleus in the centrosome. Centrosomes is granular mass that is the organizing center for the microtubules. The position of the centrosome within the centrosome is at right angles to each other. Centrioles are made of nine bundles of microtubules, that are arranged in a ring.
- **Microtubules;** They function both to determine cell shape and in a variety of cell movements, including some forms of cell locomotion, the intracellular transport of organelles, and the separation of chromosomes during mitosis.

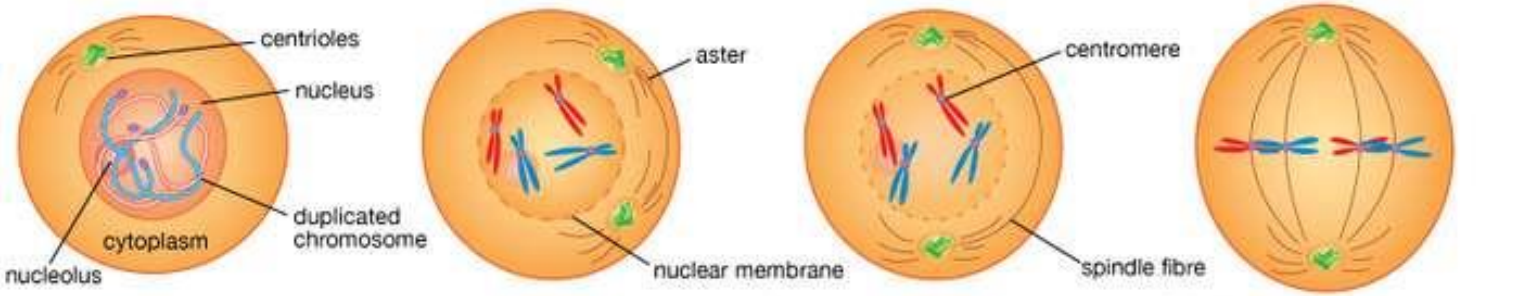


- **Kinetochores;** The kinetochore is the structure where the spindle apparatus attaches to a chromatid during cell division in eukaryotes. It is usually located in or near the centromere.

What is mitosis?

Mitosis is nuclear division plus cytokinesis, and produces two identical daughter cells during prophase, prometaphase, metaphase, anaphase, and telophase. Interphase is often included in discussions of mitosis, but interphase is technically not part of mitosis, but rather encompasses stages G1, S, and G2 of the cell cycle.

Mitosis, or somatic cell division

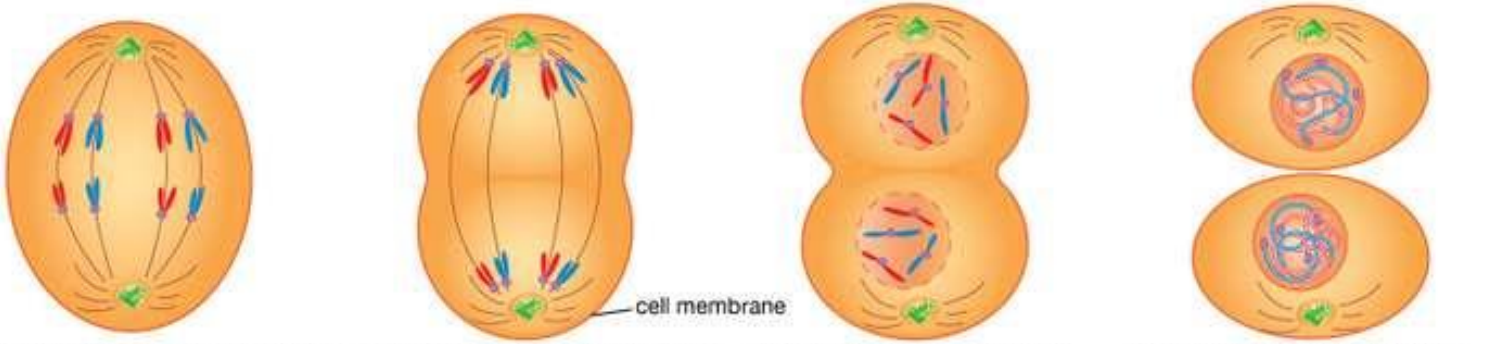


Prior to mitosis, each chromosome makes an exact duplicate of itself. The chromosomes then thicken and coil.

In early prophase the centrioles, which have divided, form asters and move apart. The nuclear membrane begins to disintegrate.

In late prophase the centrioles and asters are at opposite poles. The nucleolus and nuclear membrane have almost completely disappeared.

The doubled chromosomes—their centromeres attached to the spindle fibres—line up at mid-cell in metaphase.



In early anaphase the centromeres split. Half the chromosomes move to one pole, half to the other pole.

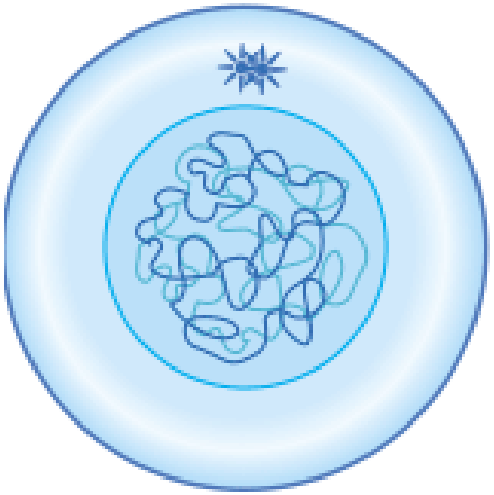
In late anaphase the chromosomes have almost reached their respective poles. The cell membrane begins to pinch at the centre.

The cell membrane completes constriction in telophase. Nuclear membranes form around the separated chromosomes.

At mitosis completion, there are two cells with the same structures and number of chromosomes as the parent cell.

Interphase

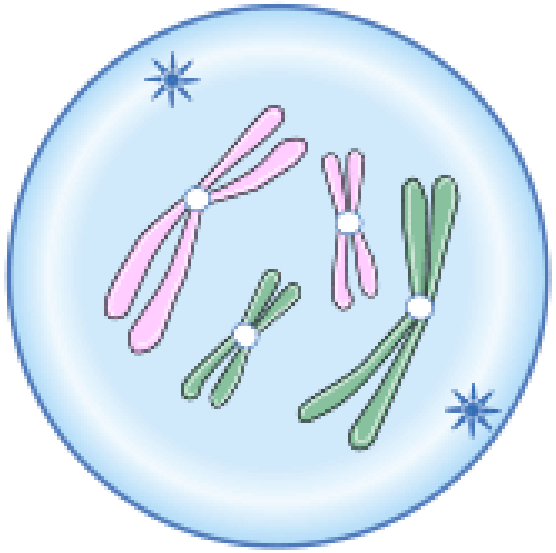
The cell is engaged in metabolic activity and performing its prepare for mitosis (the next four phases that lead up to and include nuclear division). Chromosomes are not clearly discerned in the nucleus, although a dark spot called the nucleolus may be visible. The cell may contain a pair of centrioles (or microtubule organizing centers in plants) both of which are organizational sites for microtubules.



Interphase

Prophase

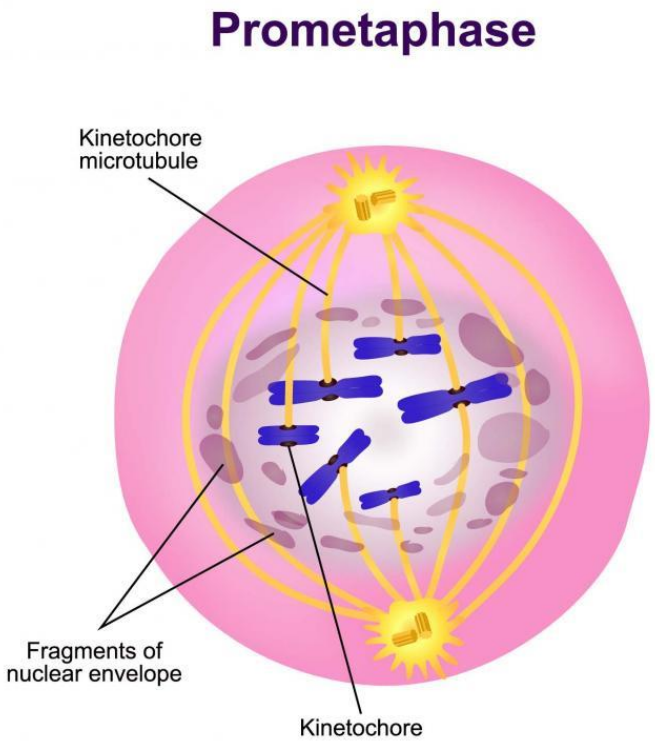
Chromatin in the nucleus begins to condense and becomes visible in the light microscope as chromosomes. The nucleolus disappears. Centrioles begin moving to opposite ends of the cell and fibers extend from the centromeres. Some fibers cross the cell to form the mitotic spindle.



Prophase

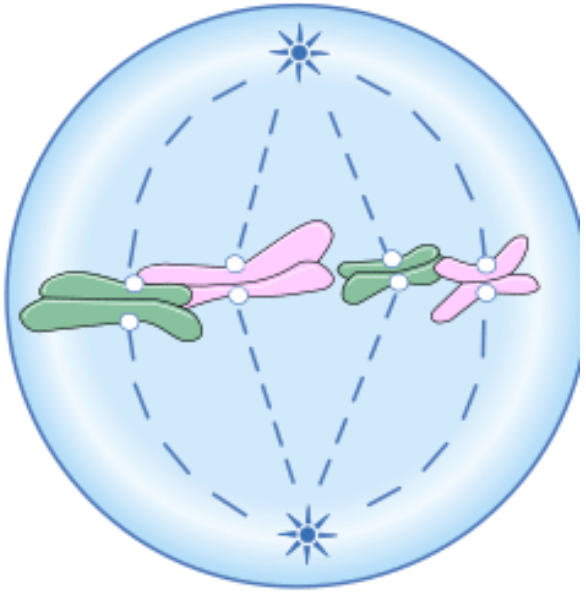
Prometaphase

The nuclear membrane dissolves, marking the beginning of prometaphase. Proteins attach to the centromeres creating the kinetochores. Microtubules attach at the kinetochores and the chromosomes begin moving.



Metaphase

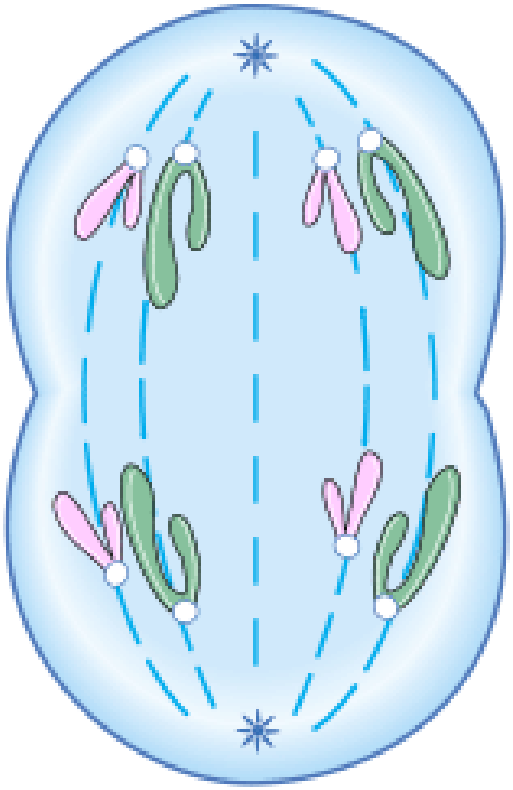
Spindle fibers align the chromosomes along the middle of the cell nucleus. This line is referred to as the metaphase plate. This organization helps to ensure that in the next phase, when the chromosomes are separated, each new nucleus will receive one copy of each chromosome.



Metaphase

Anaphase

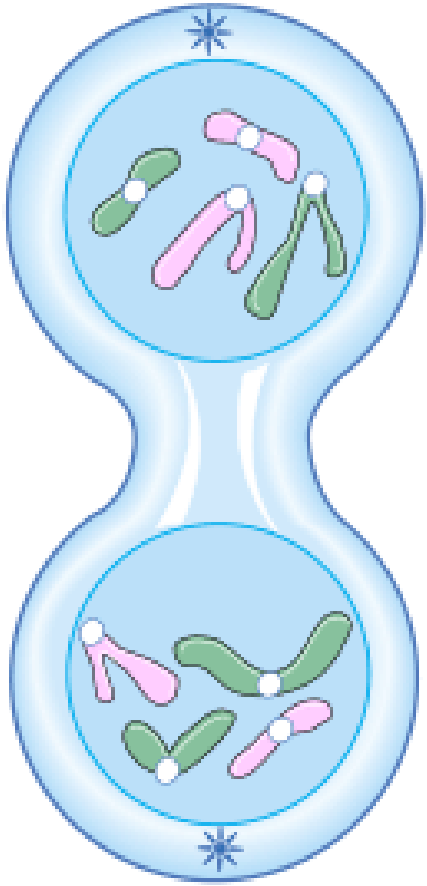
<u>The paired chromosomes separate at the kinetochores and move to opposite sides of the cell.</u> Motion results from a combination of kinetochore movement along the spindle microtubules and through the physical interaction of polar microtubules.



Anaphase

Telophase

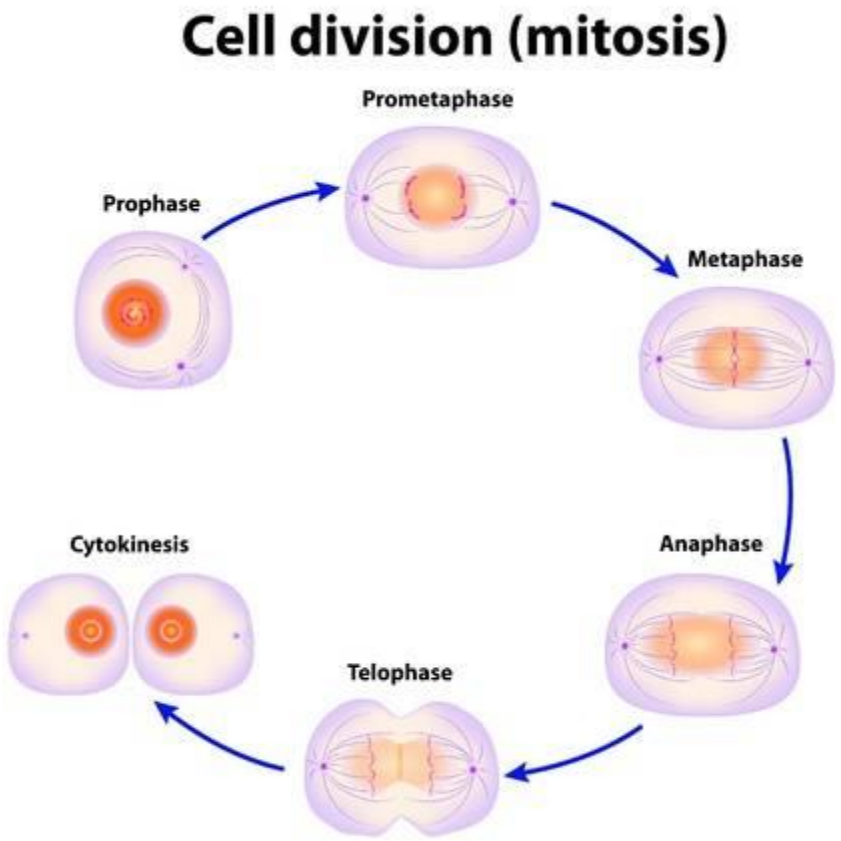
Chromatids arrive at opposite poles of cell, and new membranes form around the daughter nuclei. The chromosomes disperse and are no longer visible under the light microscope. The spindle fibers disperse, and cytokinesis or the partitioning of the cell may also begin during this stage.



Telophase

Cytokinesis

In animal cells, cytokinesis results when a fiber ring composed of a protein called actin around the center of the cell contracts pinching the cell into two daughter cells, each with one nucleus. In plant cells, the rigid wall requires that a cell plate be synthesized between the two daughter cells.

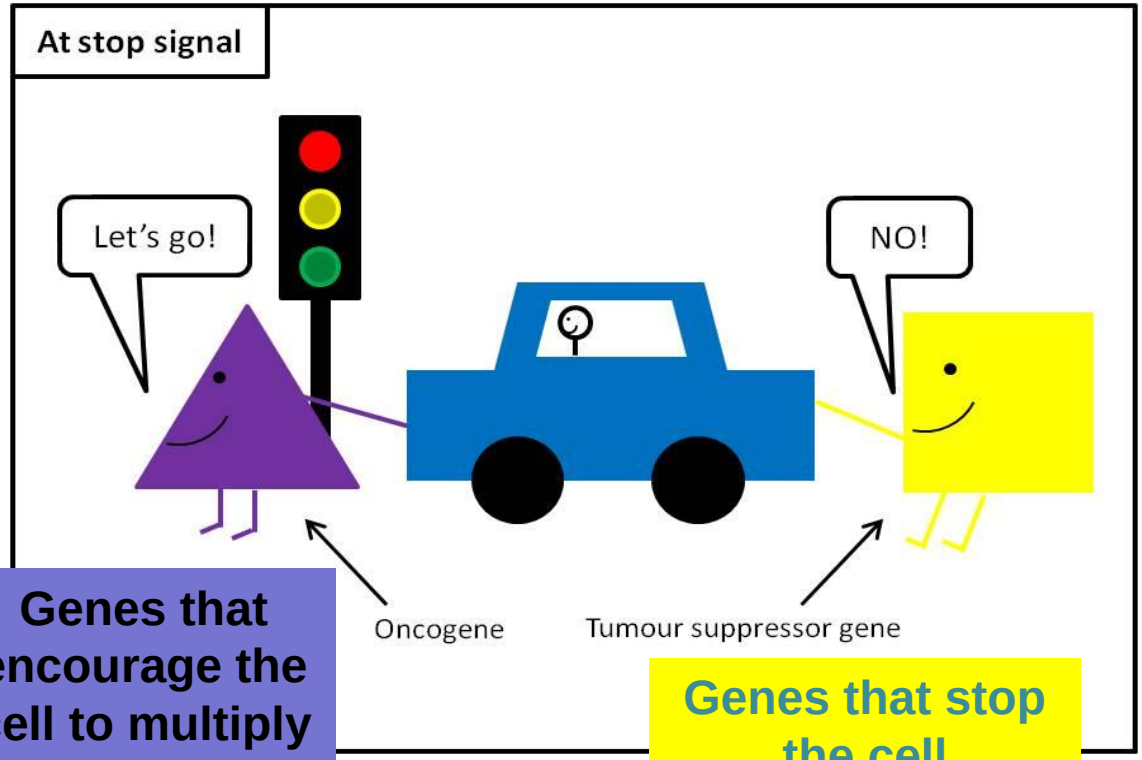


Cytokinesis is the physical process of cell division, which divides the cytoplasm of a parental cell into two daughter cells.

ONCOGENES

Uncontrolled proliferation…..

Oncogenes are genes that, under normal circumstances, tell cells to multiply and divide. Usually in adults, this would not happen very often.



Genes that encourage the cell to multiply

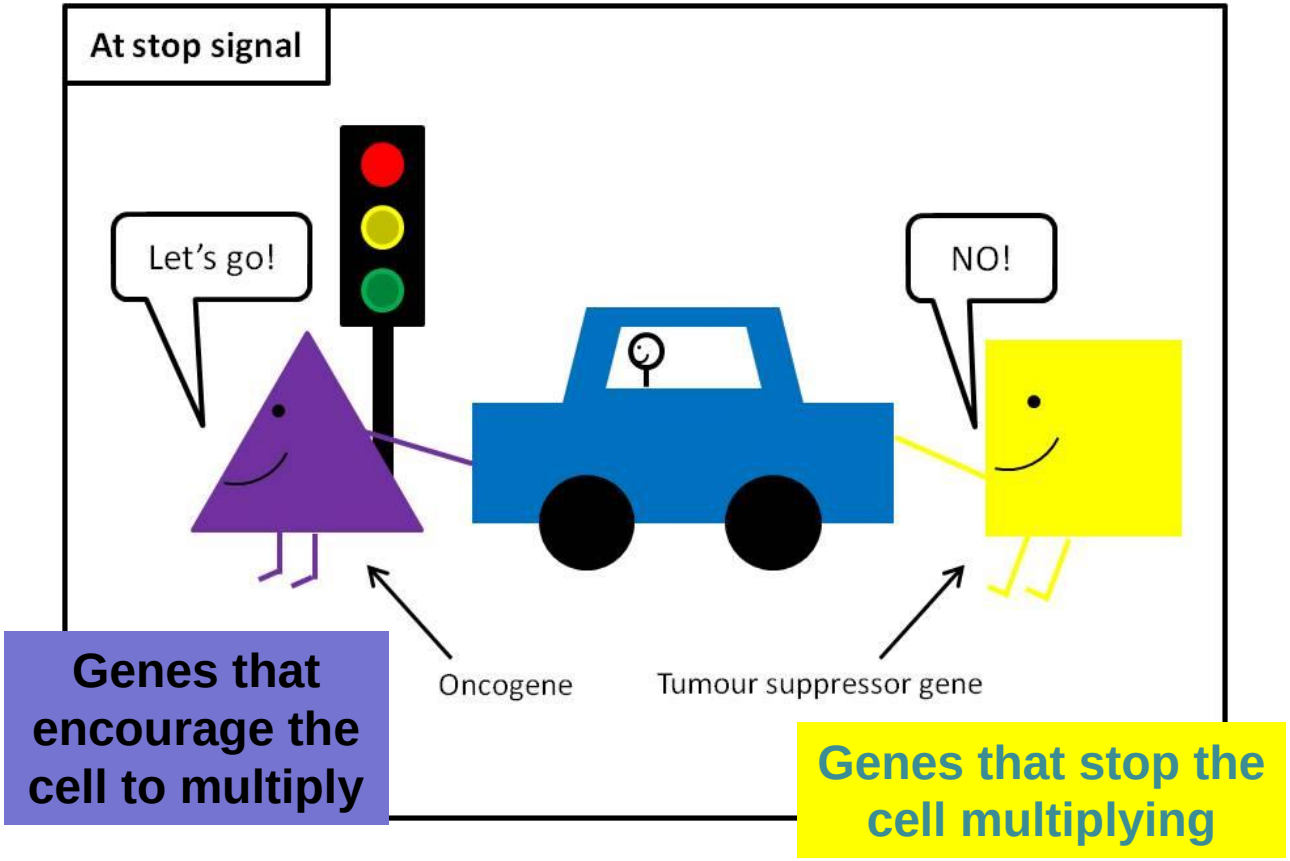
Genes that stop the cell multiplying

We can think of oncogenes as being a bit like the accelerator pedal in a car. When they become active, they speed up a cell's growth rate. When one becomes damaged, it is like the accelerator pedal becoming stuck down. That cell, and all the cells that grow from it, are permanently instructed to divide. So a cancer develops.

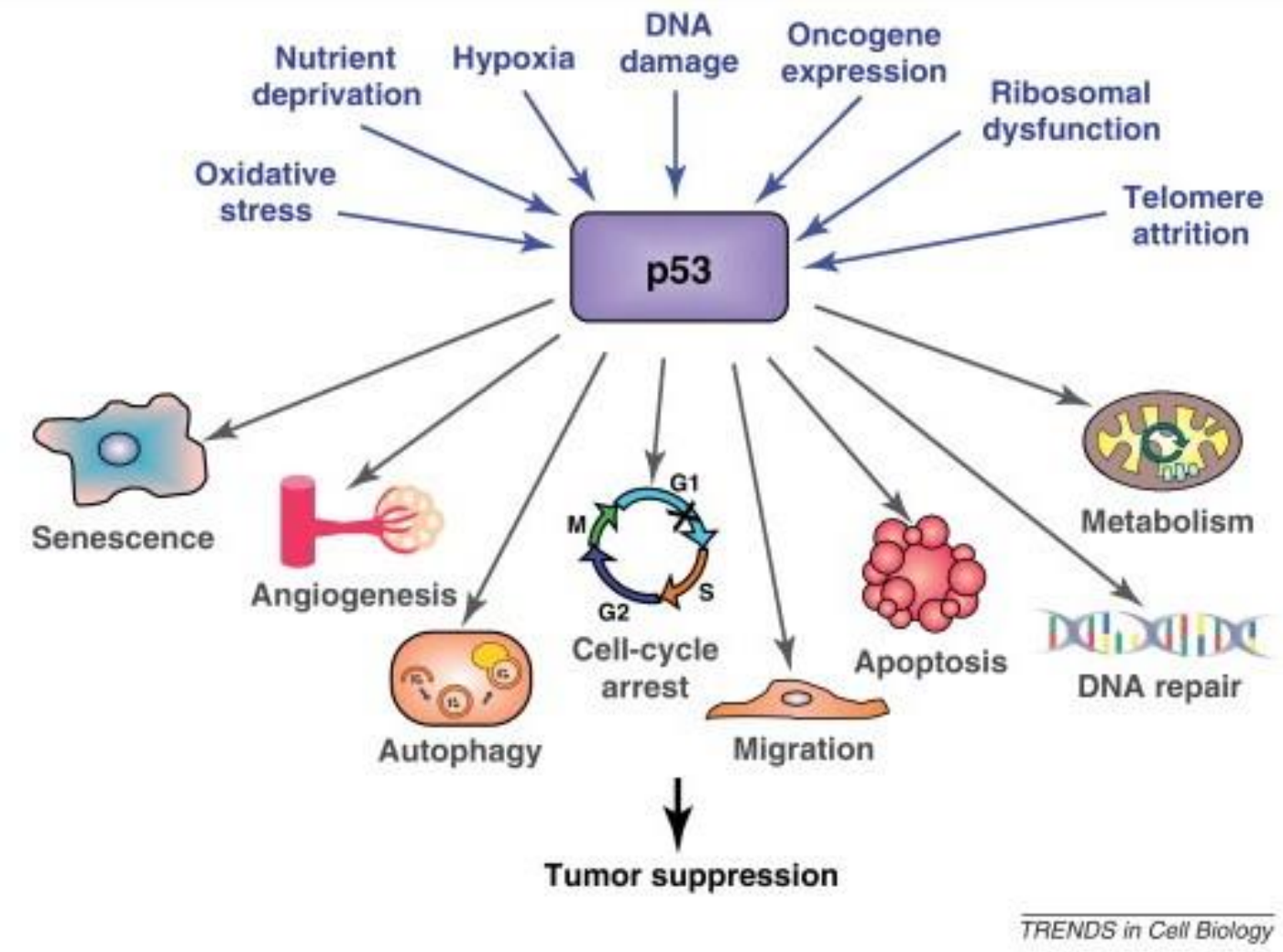
TUMOUR SUPPRESSOR GENES

Genes that stop the cell multiplying

Cells can repair faults in their genes. When the damage is very bad, tumour suppressor genes may stop the cell growing and dividing.



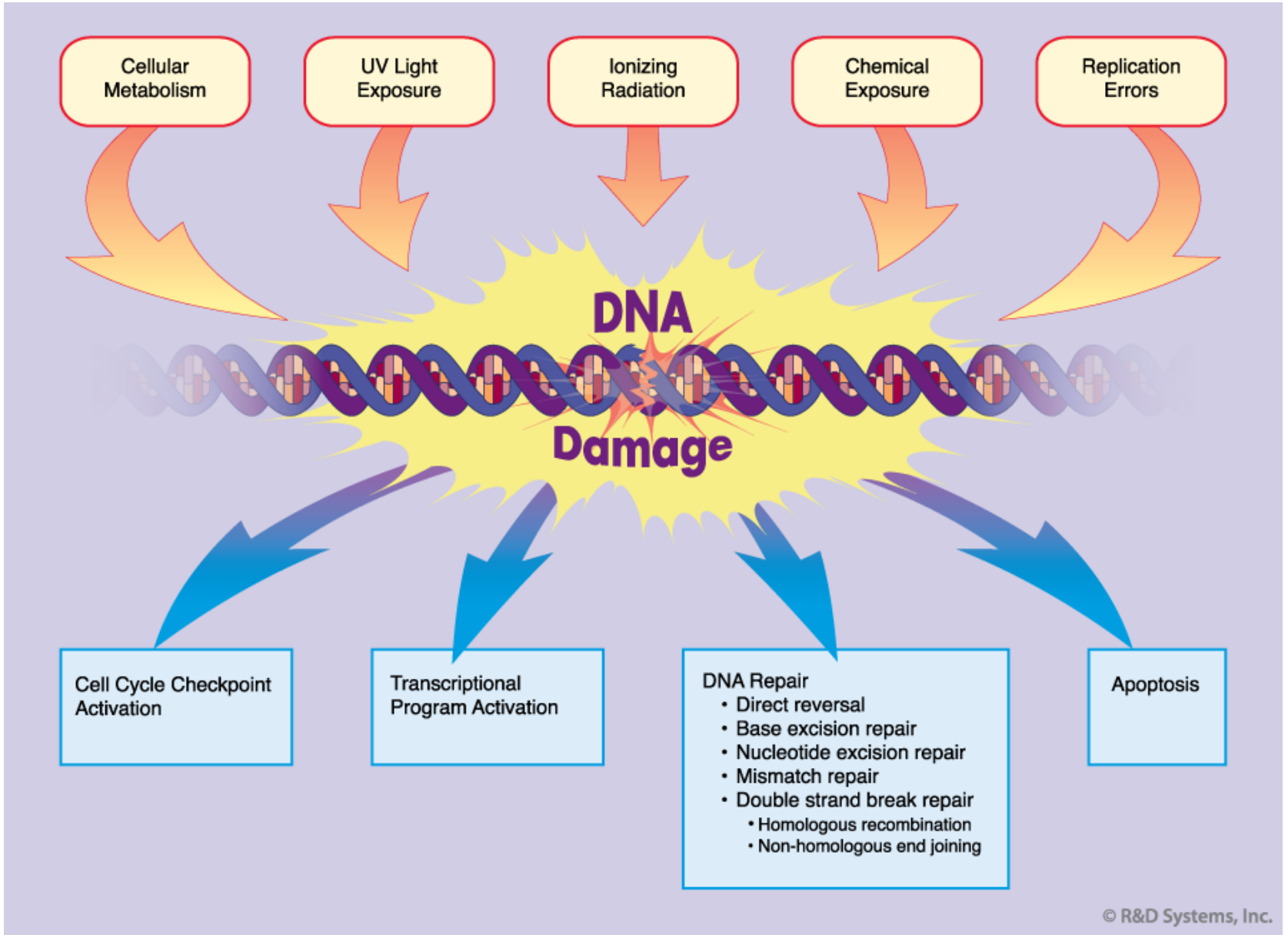
Mutations in tumour suppressor genes mean that a cell no longer understands the instruction to stop growing. The cell can then start to multiply out of control. This can lead to cancer.


Nutrient deprivation
Hypoxia
DNA damage
Oncogene expression
Ribosomal dysfunction
Oxidative stress
Telomere attrition
p53
Senescence
Angiogenesis
G1
M
S
G2
Cell-cycle arrest
Autophagy
Migration
Apoptosis
Metabolism
DNA repair
Tumor suppression
TRENDS in Cell Biology

DNA Repair Genes

Genes that repair other damaged genes

The DNA in every cell in our body is constantly in danger of becoming damaged. But cells contain many different proteins whose job is to repair damaged DNA. Thanks to these proteins, most DNA damage gets repaired immediately, with no ill effects.


Cellular Metabolism
UV Light Exposure
Ionizing Radiation
Chemical Exposure
Replication Errors
DNA
Damage
Cell Cycle Checkpoint Activation
Transcriptional Program Activation
DNA Repair
• Direct reversal
• Base excision repair
• Nucleotide excision repair
• Mismatch repair
• Double strand break repair
• Homologous recombination
• Non-homologous end joining
Apoptosis
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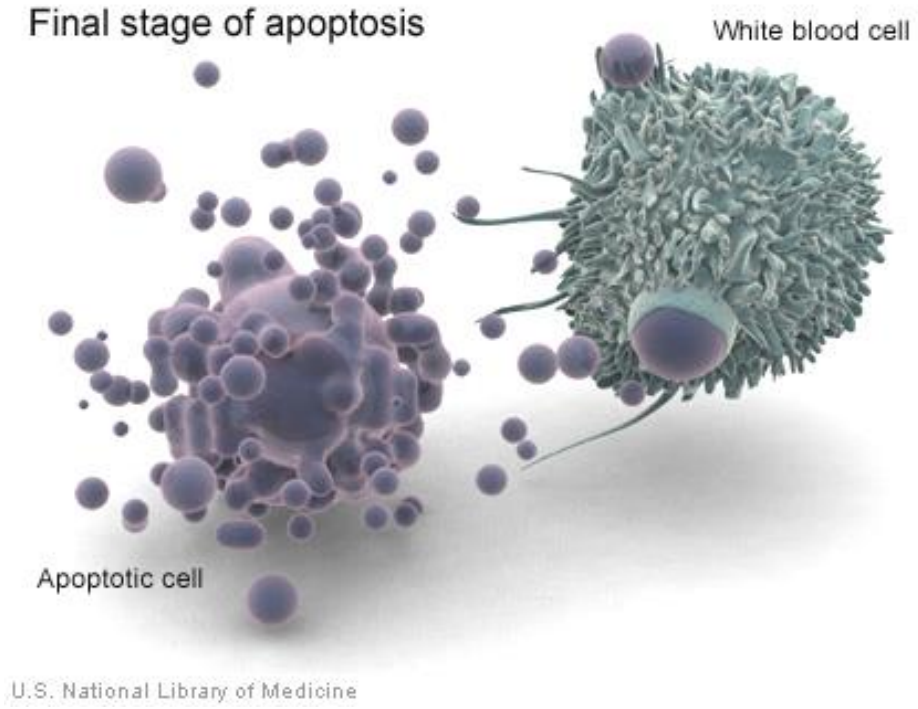
SELF DESTRUCTION GENES

Genes that tell a cell to die

PROGRAMMED CELL DEATH!!!!

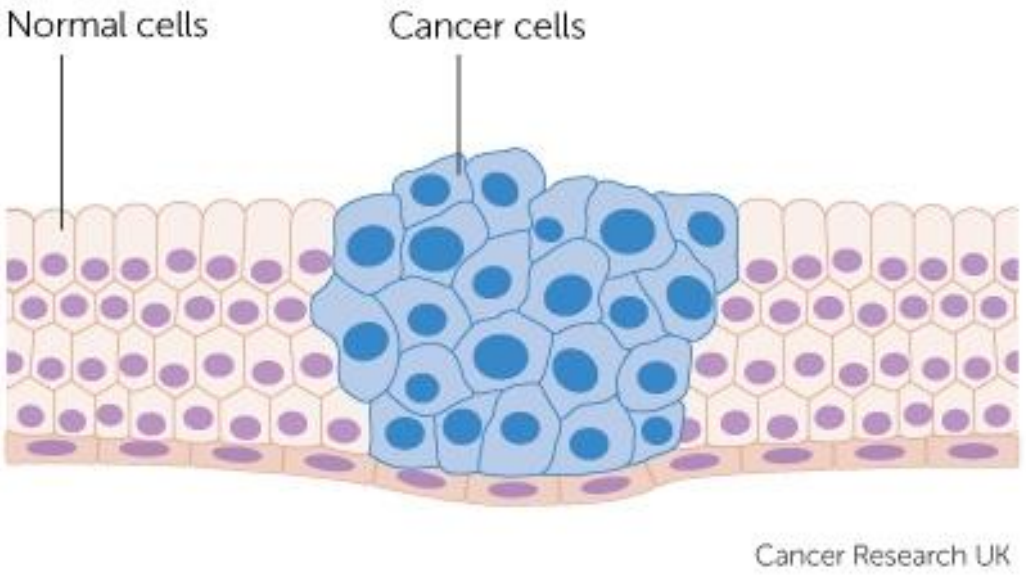


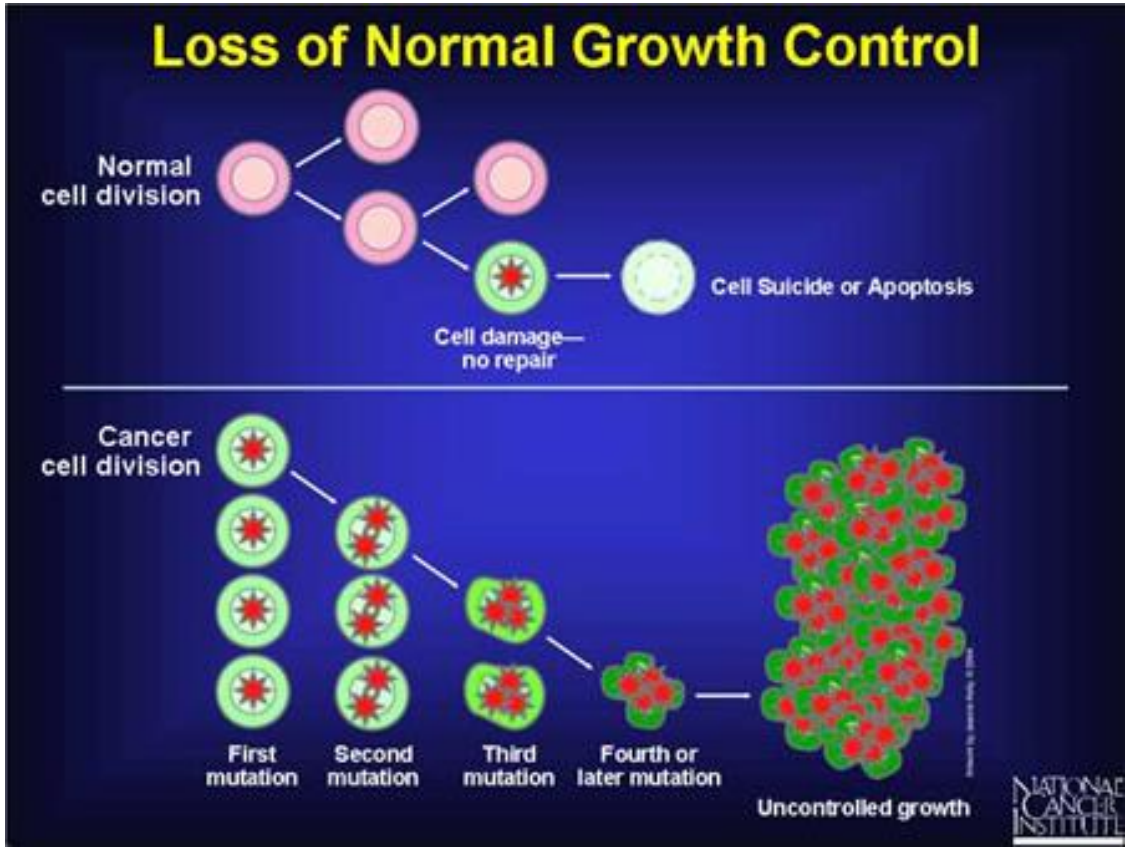
This is called apoptosis or programmed cell death. It is a highly complex and very important process. Cells usually die whenever something goes wrong, to prevent a cancer forming.There are many different genes and proteins involved in apoptosis. If these genes get damaged, a faulty cell can survive rather than die and it becomes cancerous.

How cancer starts????

Cell changes and cancer

- **Cancer starts with changes in one cell or a small group of cells.**



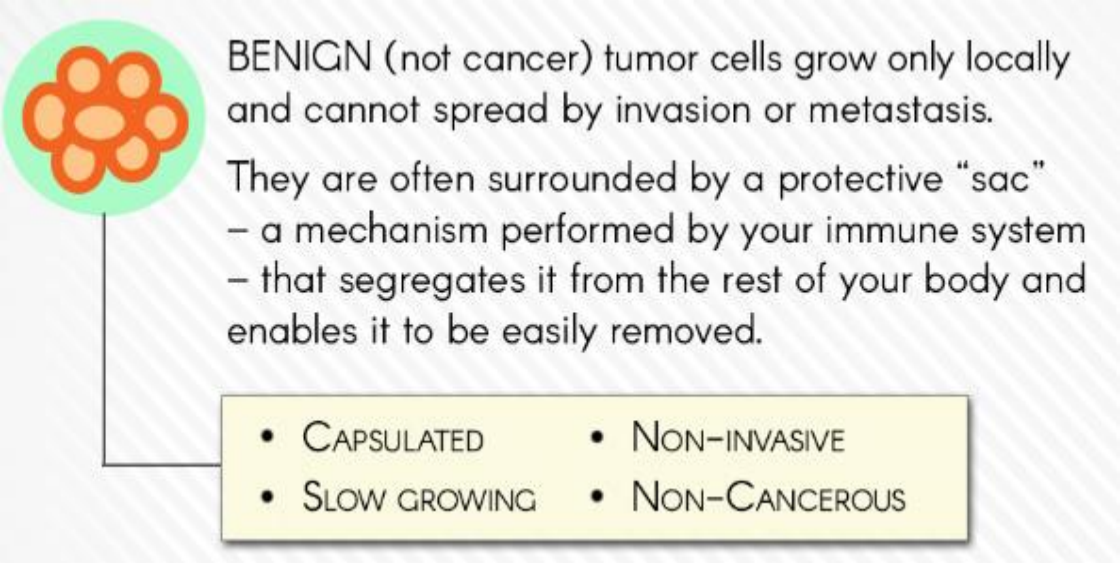


Cells may start to grow and multiply too much and form a lump called a tumour.

We have just the right number of each type of cell. This is because cells produce signals to control how much and how often the cells divide. If any of these signals are faulty or missing, cells may start to grow and multiply too much and form a lump called a tumour. A primary tumour is where the cancer starts. For a cancer to start, certain changes take place within the genes of a cell or a group of cells.

Benign Tumors

A tumor is an abnormal growth of cells that serves no purpose. A benign tumor is not a malignant tumor, which is cancer. It does not invade nearby tissue or spread to other parts of the body the way cancer can. In most cases, the outlook with benign tumors is very good. But benign tumors can be serious if they press on vital structures such as blood vessels or nerves. Therefore, sometimes they require treatment and other times they do not.



Benign tumors are often surrounded by a protective "sac" – a mechanism performed by your immune system – that segregates it from the rest of your body and enables it to be easily removed.

What causes a benign tumor to form?

- Environmental toxins, such as exposure to radiation
- Genetics
- Diet
- Stress
- Local trauma or injury
- Inflammation or infection

Treatment of Benign Tumors

In many cases, benign tumors need no treatment. Doctors may simply use "watchful waiting" to make sure they cause no problems. But treatment may be needed if symptoms are a problem. Surgery is a common type of treatment for benign tumors. The goal is to remove the tumor without damaging surrounding tissues. Other types of treatment may include medication or radiation.

Most Common Types of Benign Tumors

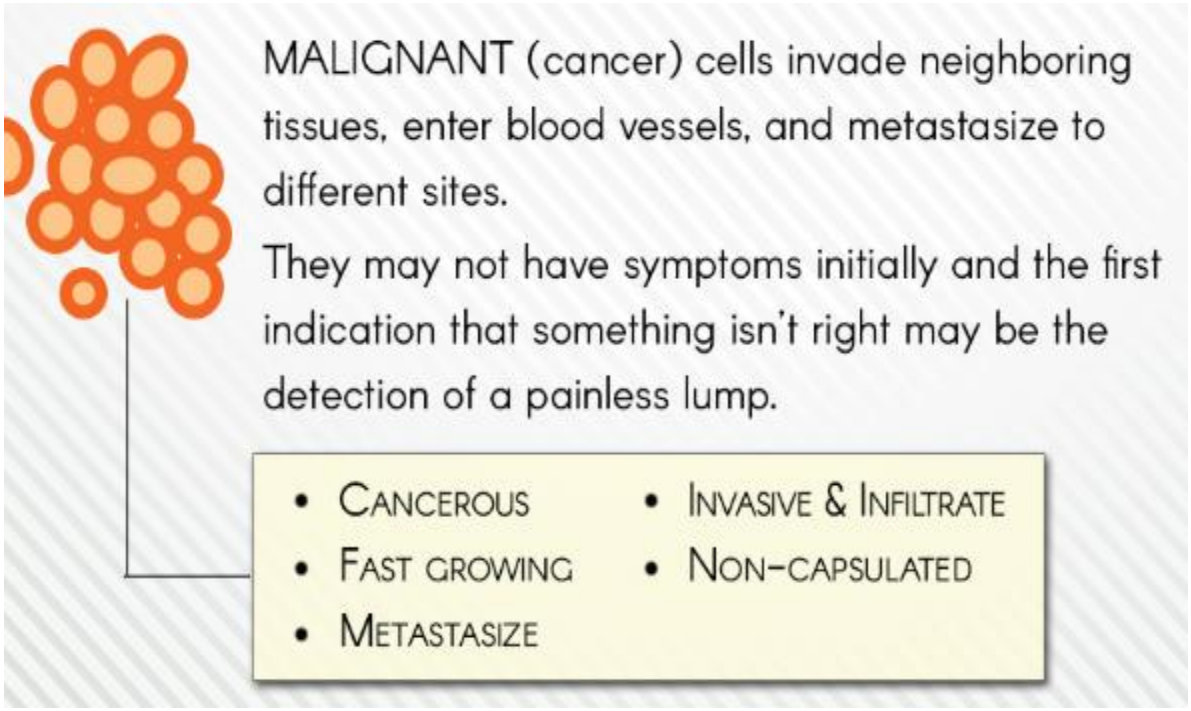
- Adenomas (epithelial tissue that covers the organs and glands)
- Meningiomas (brain and spinal cord)
- Fibromas or fibroids (connective tissue of any organ – most commonly found in the uterus)
- Papillomas (skin, breast, cervix, and mucus membranes)
- Lipomas (fat cells)
- Nevi (moles)
- Myomas (muscle tissue)
- Hemangiomas (blood vessels and skin)
- Neuromas (nerves)
- Osteochondromas (bones)

Benign and Malignant Tumors: What is the Difference?

A benign tumor is not a cancerous tumor. Unlike cancer tumors, a non cancerous tumor is unable to spread throughout the body. A non malignant tumor can be serious if they are pressing a primary nerve, a main artery, or compresses brain matter. Overall, benign tumors respond well to treatment and the prognosis is usually favorable.

If you are diagnosed with a benign tumor, altering your diet to an anti-cancer regimen is sound advice. Some benign tumors can become malignant but it's rare.

You have a malignant tumor, **that means the mass is cancerous**. This type of tumor has the ability to multiply uncontrollably, to metastasize (spread) to various parts of the body and invade surrounding tissue.



Malignant tumors are formed from abnormal cells that are highly unstable and travel via the blood stream, circulatory system, and lymphatic system. Malignant cells do not have chemical adhesion molecules to anchor them to the original growth site that benign tumors possess.

Obesity, smoking, alcohol consumption, poor diet, environmental pollution, heavy metal exposure, and household toxins are a few culprits that may lead to cancer in your body.

Most Common Types of Malignant Tumors

- Sarcomas (connective tissues such as muscle, tendon, fat, and cartilage)
- Carcinomas (organs and gland tissue such as the breast, cervix, prostate, lung, and thyroid)

What is pirmary tumor?

the original, or first, tumor in the body.

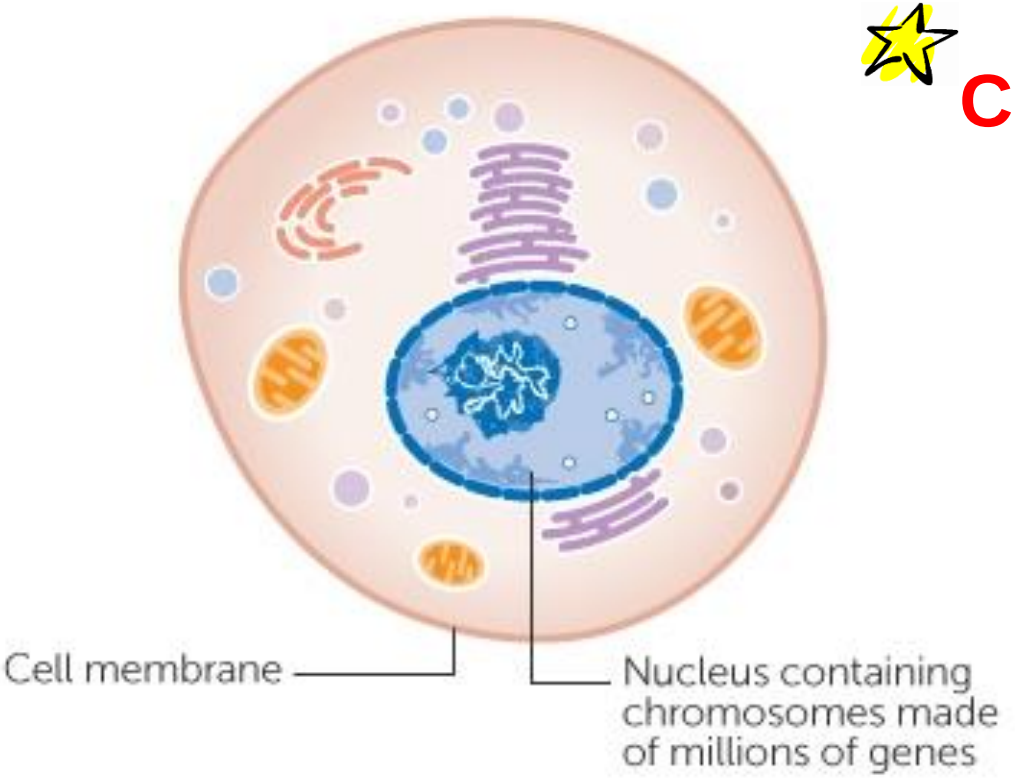
Cancer cells from a primary tumor may spread to other parts of the body and form new, or secondary, tumors. This is called metastasis. These secondary tumors are the same type of cancer as the primary tumor. Also called primary cancer.

What is Metastasis?

Cancer spreads to a different part of the body from where it started.

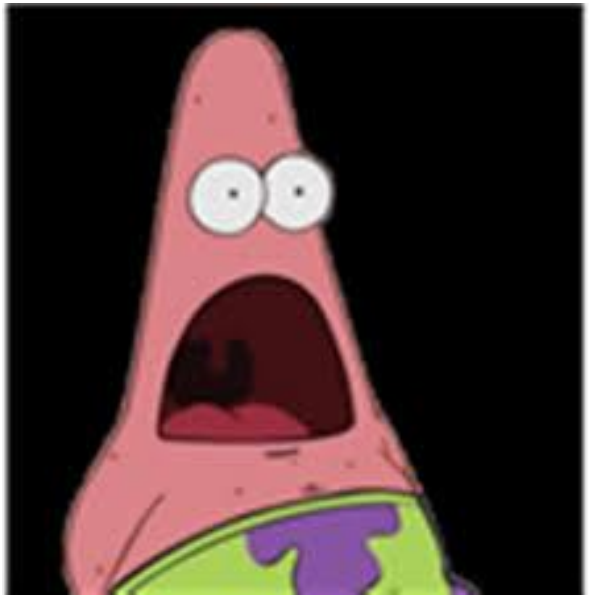
Metastases (the plural form of metastasis) most commonly develop when cancer cells break away from the main tumor and enter the bloodstream or lymphatic system. These systems carry fluids around the body. This means that the cancer cells can travel far from the original tumor and form new tumors when they settle and grow in a different part of the body. Metastases can also sometimes develop when cancer cells from the main tumor, typically in the abdominal (belly) cavity, break off and directly "seed" other areas within the abdominal cavity.

Genes and cell division



Control centre called a nucleus

Different types of cells in the body do different jobs, but they are basically similar. They all have a control centre called a nucleus. Inside the nucleus are chromosomes made up of thousands of genes. Genes contain long strings of DNA, which are coded messages that tell the cell how to behave.



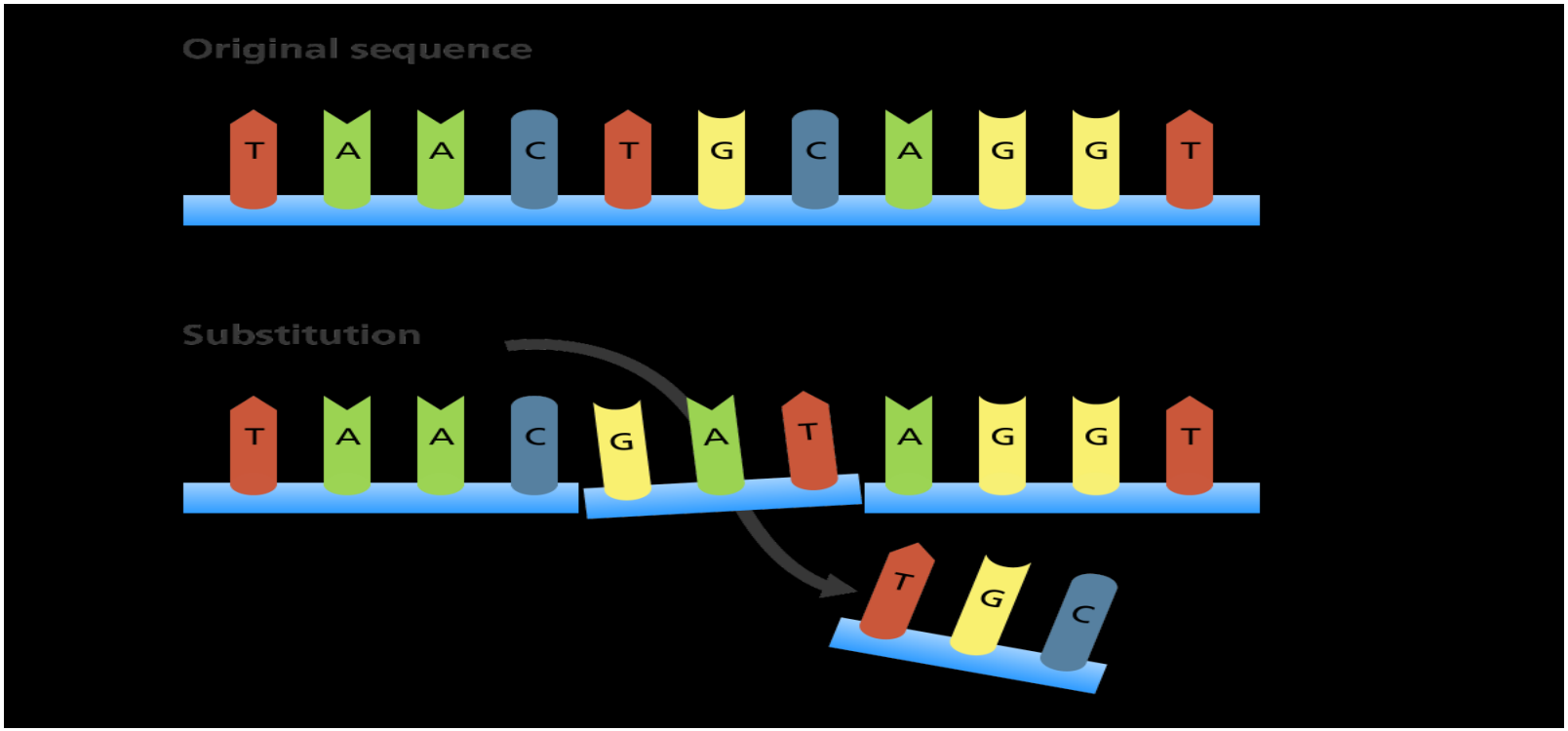
Together, proteins and RNA

- ✓ control the cell
- ✓ what sort of the cell
- ✓ what the cell does,
- ✓ when the cell will divide
- ✓ when the cell will die

MUTATIONS

Gene changes within cells

Normally genes make sure that cells grow and reproduce in an orderly and controlled way. They make sure that all the cells produced are needed to keep the body healthy. Sometimes a change happens in the genes when a cell divides. This is a mutation. It means that a gene has been damaged or lost or copied twice. Mutations can happen by chance when a cell is dividing. Some mutations mean that the cell no longer understands its instructions and starts to grow out of control. There have to be about half a dozen different mutations before a normal cell turns into a cancer cell.



Mutations in particular genes may mean that a cell starts producing too many proteins that trigger a cell to divide. Or it stops producing proteins that normally tell a cell to stop dividing. <u>Abnormal proteins may be produced that work differently to normal.</u>

How mutations happen

Mutagen- anything that causes a mutation in DNA in a cell.

- UV light
- Radiation
- X rays
- chemicals in tobacco smoke, synthetic materials, pollution
- viruses

Mutations can happen by chance when a cell is dividing. They can also be caused by the processes of life inside the cell. Or by things coming from outside the body, such as the chemicals in tobacco smoke. And some people can inherit faults in particular genes that make them more likely to develop a cancer. Some genes get damaged every day and cells are very good at repairing them.

But over time, the damage may build up. And once cells start growing too fast, they are more likely to pick up further mutations and less likely to be able to repair the damaged genes.

How does cancer start???

https://www.youtube.com/watch?v=m5_yo6uEeEc

Types of cancer

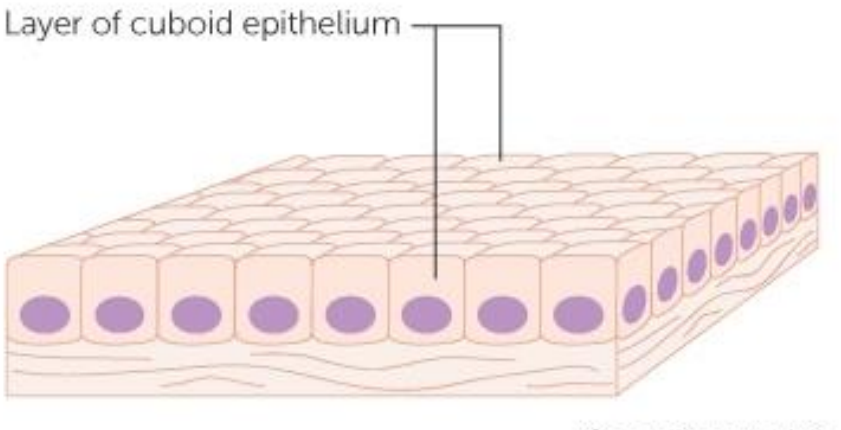
The main types of cancer

Cells group together to make up the tissues and organs of our bodies. They are very similar but vary in some ways because body organs do very different things. For example, nerves and muscles do different things, so the cells have different structures.

Carcinoma
Sarcoma
Lymphoma And Myeloma
Brain And Spinal Cord Cancers

Carcinomas

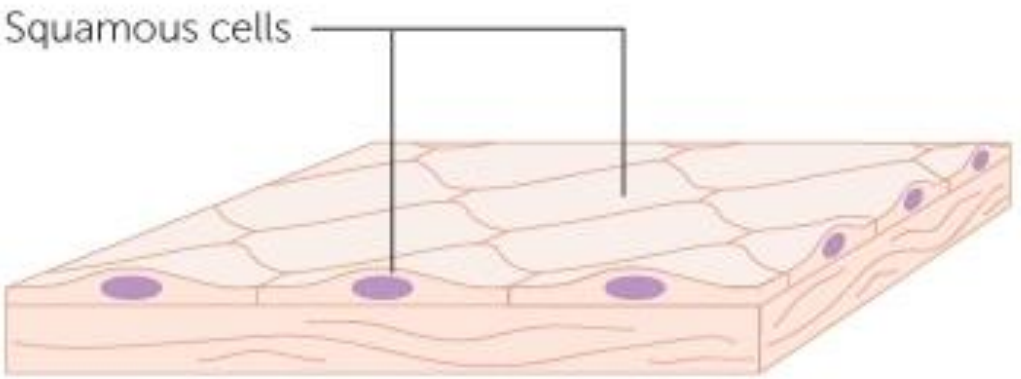
Carcinomas are the most common type of cancer. Carcinomas start in epithelial tissues.



Carcinomas start in epithelial tissues. These cover the outside of the body as the skin. They also cover and line all the organs inside the body, such as the organs of the digestive system. And they line the body cavities, such as the inside of the chest cavity and the abdominal cavity.

Squamous cell carcinoma

Squamous cell carcinoma starts in squamous cells. These are the flat, surface covering cells found in areas such as the skin or the lining of the throat or food pipe (oesophagus)



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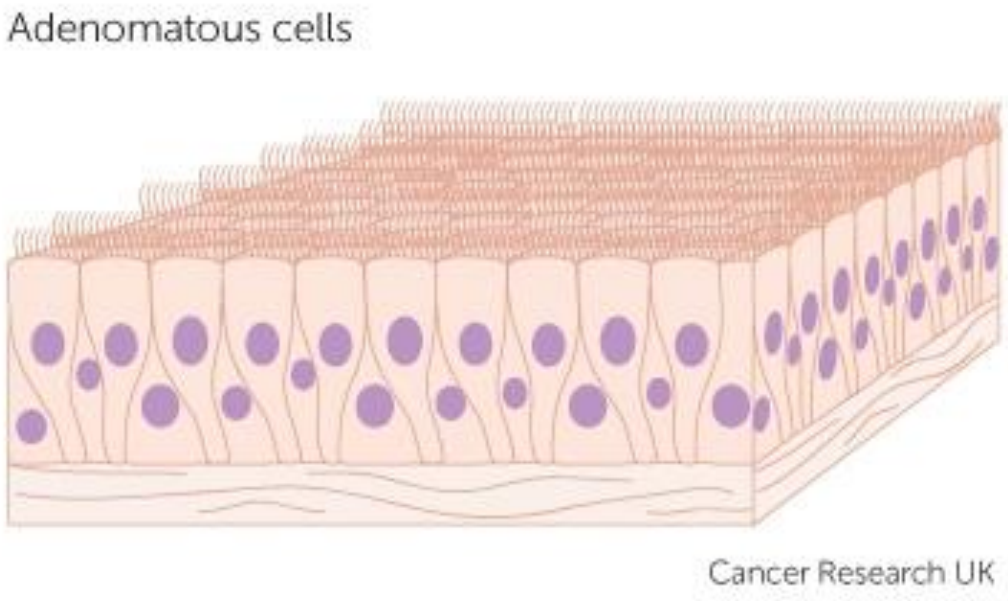
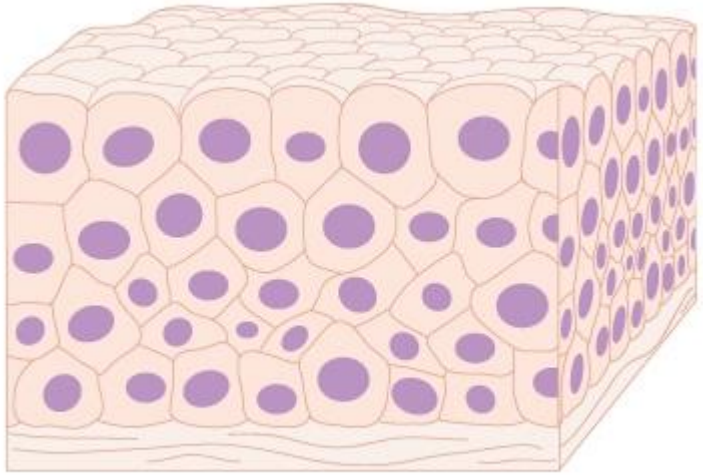
- **Adenocarcinoma**

Adenocarcinomas start in glandular cells called adenomatous cells. Glandular cells produce fluids to keep tissues moist.



- **Transitional cell carcinoma**

Transitional cells are cells that can stretch as an organ expands. They make up tissues called transitional epithelium. An example is the lining of the bladder. Cancers that start in these cells are called transitional cell carcinoma.



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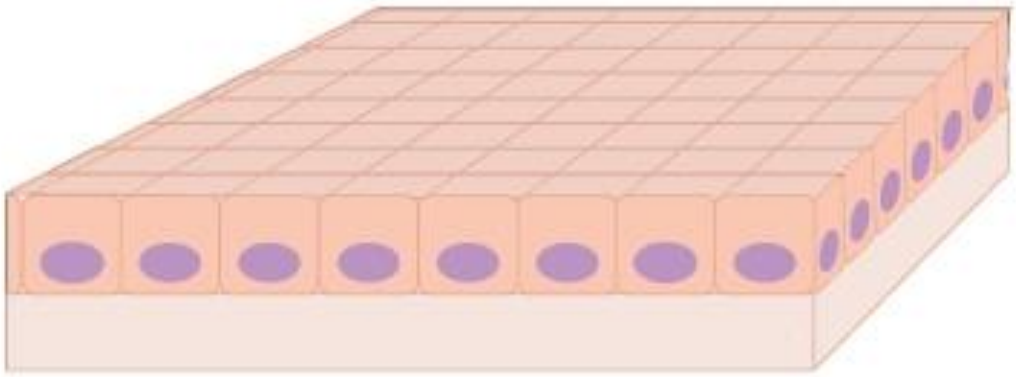
- **Basal cell carcinoma**

Basal cells line the deepest layer of skin cells. Cancers that start in these cells are called basal cell carcinomas.



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Sarcomas

- Sarcomas start in connective tissues, which are the supporting tissues of the body.
- They are usually grouped into 2 main types:

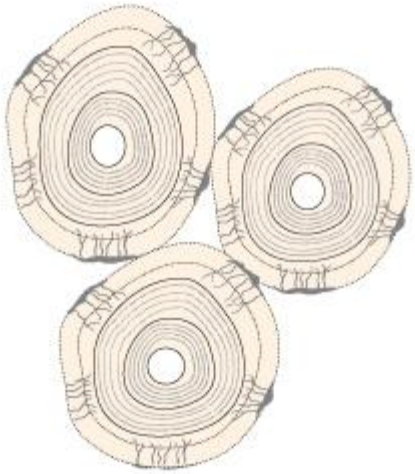
-bone sarcomas (osteosarcoma)

-soft tissue sarcomas

Bone sarcomas

Sarcomas of bone start from bone cells.

Bone cells called osteocytes



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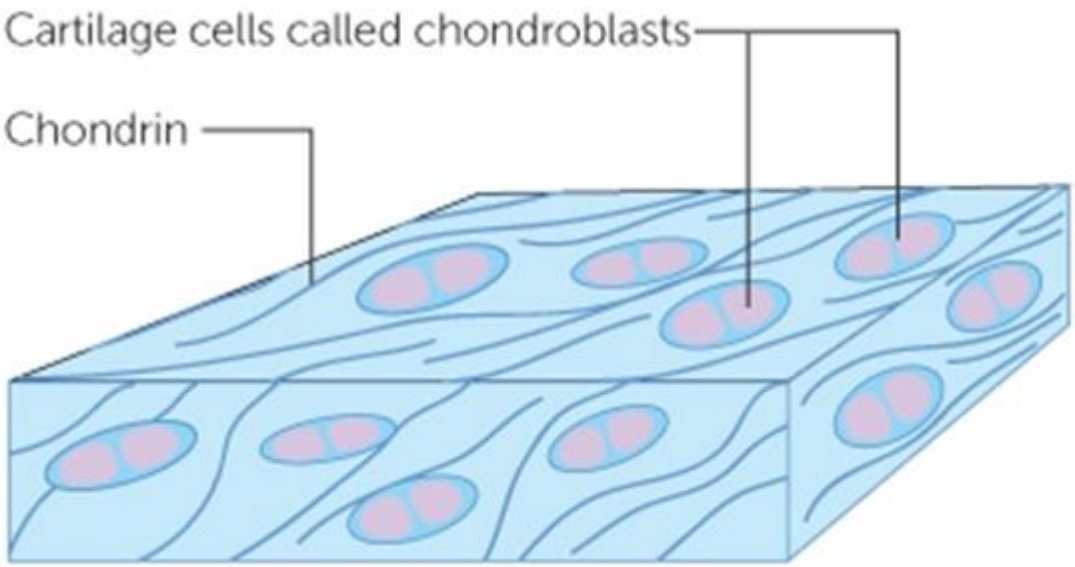


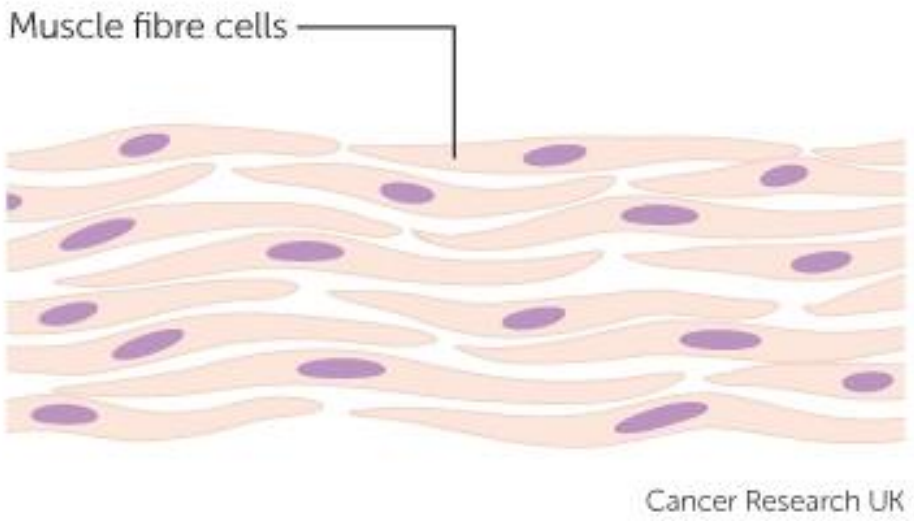
Soft tissue sarcomas

Soft tissue sarcomas are rare but the most common types start in cartilage or muscle.

Cartilage Cancer of the cartilage is called chondrosarcoma.

Muscle

Cancer of muscle cells is called rhabdomyosarcoma or leiomyosarcoma.



Leukaemias – cancers of blood cells

Leukaemia is a condition in which the bone marrow makes too many white blood cells. The blood cells are not fully formed and so they don't work properly. The abnormal cells build up in the blood.

White blood cell
(leucocyte)

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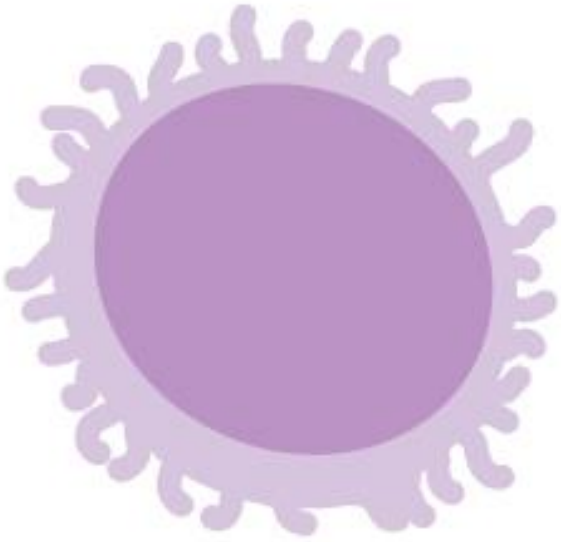
Lymphomas and myeloma

Lymphomas and myeloma are cancers of the lymphatic system.



Lymphocyte

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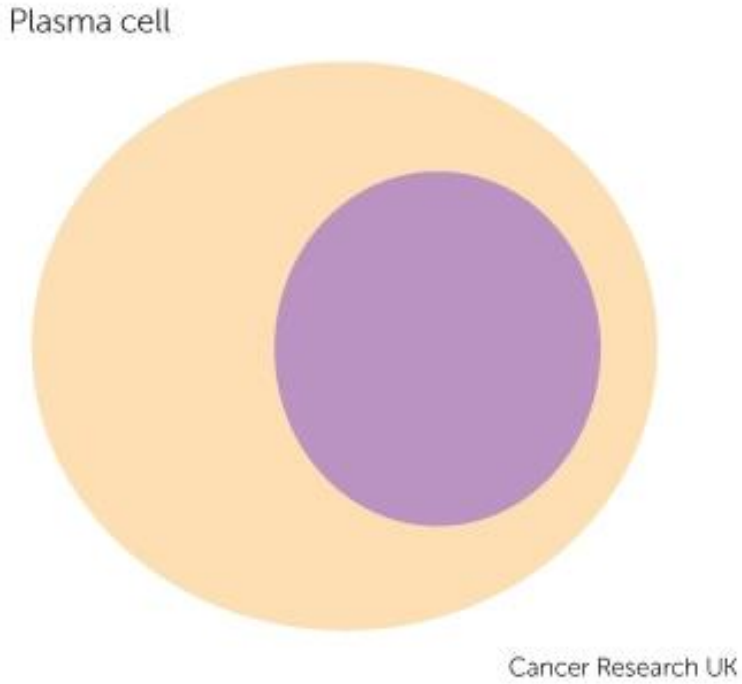
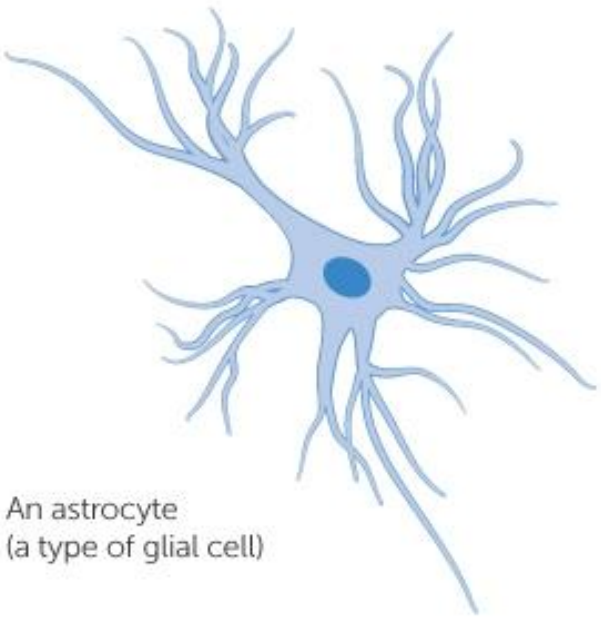
Myeloma

Myeloma is also known as multiple myeloma. It is a cancer that starts in plasma cells.



Brain and spinal cord cancers



An astrocyte
(a type of glial cell)

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The brain and spinal cord form the central nervous system. The brain is made up of billions of nerve cells called neurones. It also contains special connective tissue cells called glial cells that support the nerve cells.