

FEEL THE BURN? THAT'S SKIN CANCER.

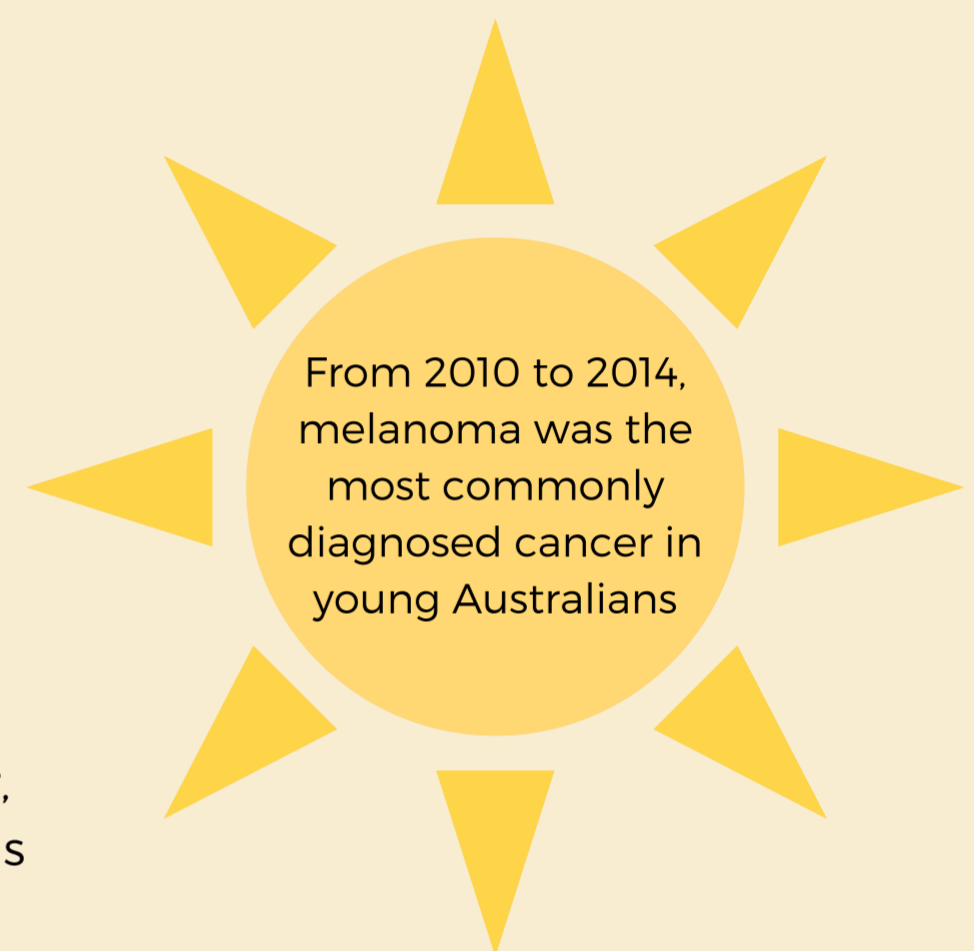
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YOU COULD HAVE CANCER RIGHT NOW AND YOU MIGHT NOT EVEN KNOW IT.

Your cells could be undergoing rapid and uncontrolled division resulting in abnormal growth that could be endangering your life. Plus, if you're in Australia and you get cancer, there's an 80% chance it's skin cancer.

Everyone is susceptible to skin cancer. However, the risk of developing it is impacted by factors that include family history and exposure to the sun. Symptoms may consist of: spots, freckles, and moles that change in color, thickness or shape over weeks or months. Sores that are crusty or don't heal, as well as small lumps that are pink, red or pearly in color could also be signs of undiagnosed skin cancer.

Basal Cell Cancer (BCC) and Squamous Cell Carcinoma (SCC) are more common in the elderly, while melanoma is more common in the youth (especially in people aged 25 to 29). Melanoma is the deadliest form of skin cancer. If not treated at an early stage, it can spread to organs, more rapidly than other types of skin cancers. The stages of melanoma range from Stage 0 to Stage IV, which are representative of the severity of the skin cancer. As skin cancer is the result of uncontrolled cell division, it is crucial to understand your cells to fully grasp the nature of this cancer.



What are Cells?

Cells are the building blocks of life and as humans, we are made of trillions of them. To produce them, cells undergo a process of division known as 'mitosis' that produces two new identical cells. Mitosis is a component of a cell's life cycle, also referred to as the 'cell cycle'.

The Cell Cycle and Checkpoints:

The cell cycle is a process which is required in order for cells to replicate. It can be broken down into two major parts (refer to Figure 1):

1. *Interphase (G₁, S, G₂)*- the longest part which involves DNA replication, cell growth and other preparations in order to divide.
2. *Mitosis*- the process in which the cell divides to form two new, identical cells.

To ensure that only healthy cells replicate, there are three checkpoints that the cell has to pass in order to successfully divide. They are located:

1. *At the end of G₁*- the cells are checked to determine if they are under environmental stress. If they are, they go into a 'resting' phase called G₀.
2. *At the end of G₂*- the cells are checked for DNA replication errors. If there are any errors, the cells will undergo programmed cell death (known as apoptosis).
3. *During mitosis*- the cells are checked to see if the chromosomes are properly attached to the spindle fibers that will separate the . If anything is wrong, the cell will undergo apoptosis.

Regular cells move through these checkpoints in a systematic manner, however cancerous cells have damaged genes - known as mutations - which alter this behaviour. A mutation commonly seen in people with cancer is on the gene TP53. When a person has a TP53 mutation in their genes, they are at a higher risk of developing cancer. This is because their body may struggle to detect and deal with cancer cells, which are rapidly proliferating.

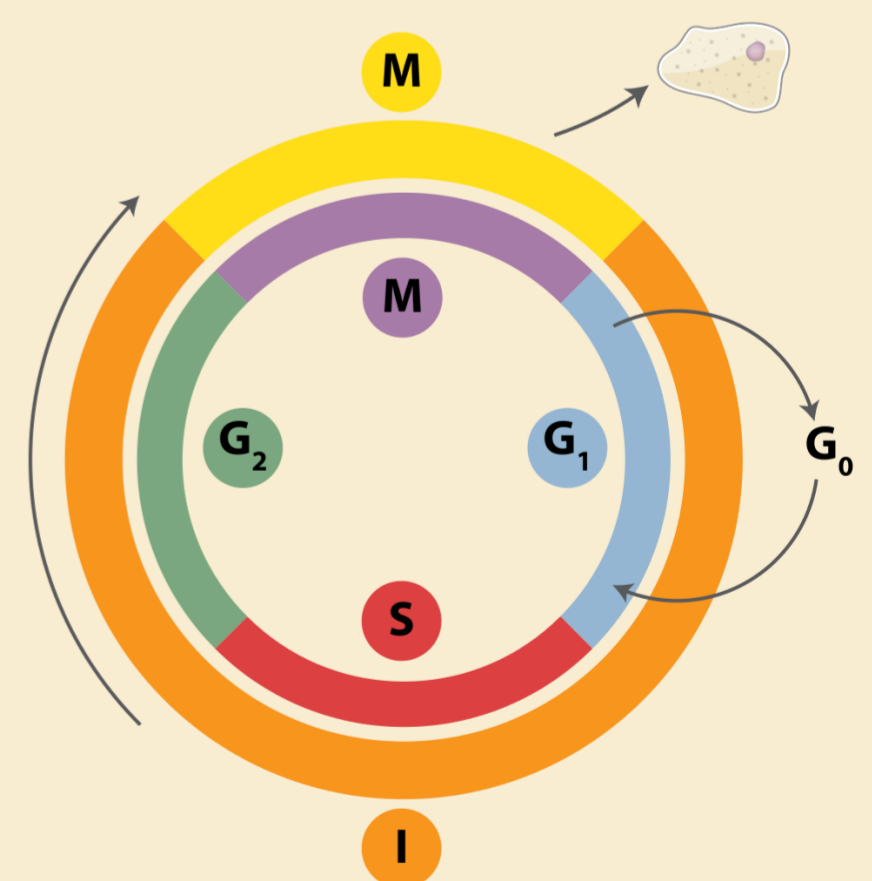


Figure 1
The cell cycle! In G₁, S and G₂, the cell prepares to divide, and in mitosis, actual division of the cell occurs.



What is Cancer?

Characteristics of Cancer:

What makes cancer so hard to detect and treat? The answer lies in the way it interacts with our immune system...

The immune system protects our body from foreign substances, so when it encounters cancer early it is able to kill it off. However, as these abnormal cells begin to replicate more rapidly, the immune system is no longer able to keep up the pace.

Furthermore, cancerous cells are able to disguise their appearance by changing the composition of their surface. This results in the immune system losing its ability to take action against them, therefore allowing extensive undetected spreads.

Some cancers have many mutations, which produce various 'wrong' proteins - making it easier for the immune system to detect and get rid of them. Other cancers don't have as many mutations, making proteins that allow it to appear as a normal cell. Thus, the fewer the mutations of a cancer cell, the harder it is to be treated.

As cancer cells are constantly growing and dividing, they require access to nutrients and oxygen. To access this, they release signals to recruit blood vessels from their surroundings. Consequently, blood vessels are diverted from normal cells to deliver substances to cancer cells. This process of fueling cancer cells is known as angiogenesis (refer to Figure 2).

Cancer cells also have the ability to break away from other cells and invade other environments. As they move, they may reach blood or lymphatic vessels and as a result, they spread and invade distant body sites. This process of uncontrollable invasion is called metastasis. Melanoma is known to metastasize at a rapid rate, which is why it's so deadly!

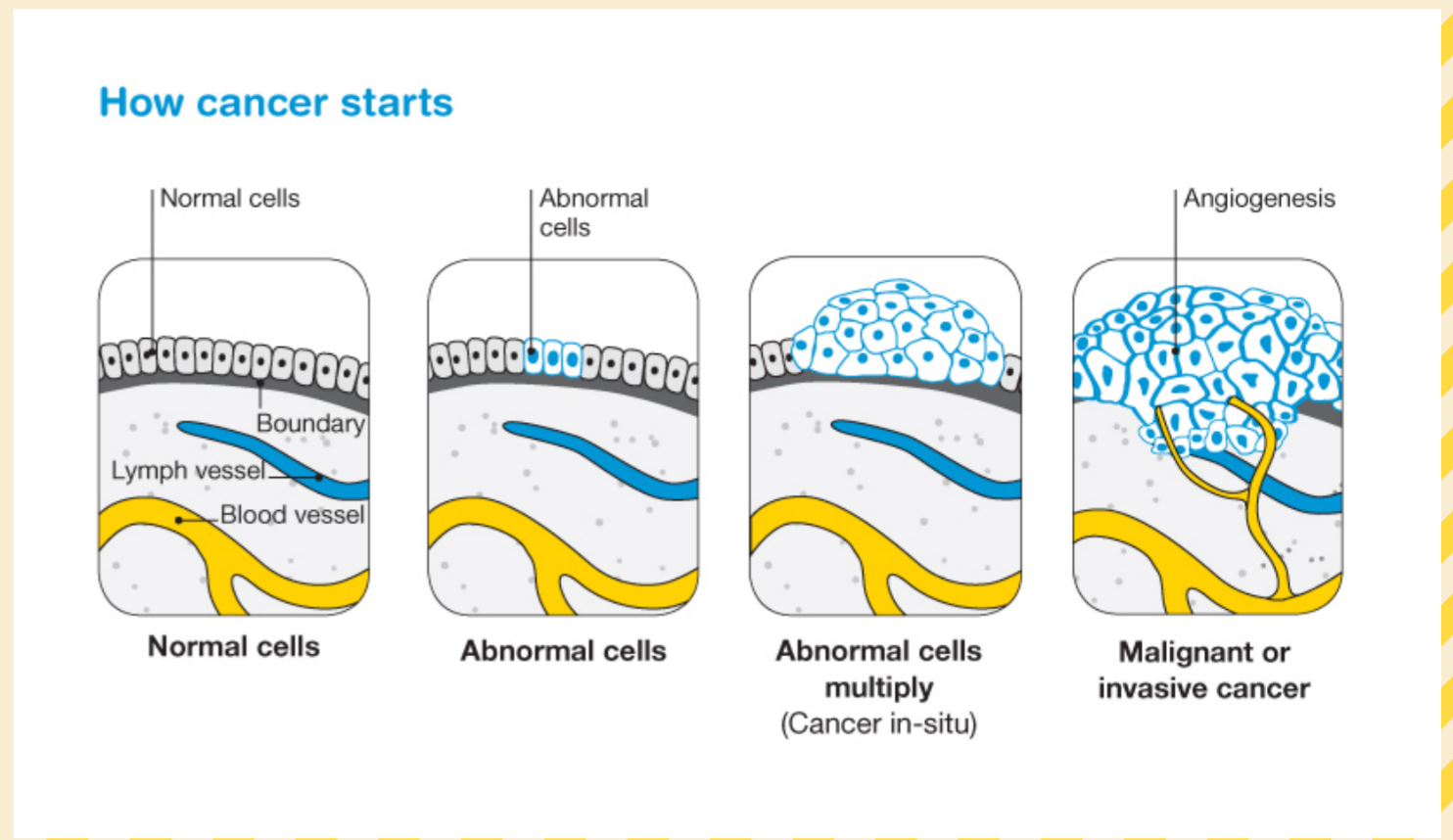


Figure 2

This diagram shows how rapidly cancerous cells spread to other regions of the body. 'Malignant' in this case refers to the tumor being able to invade surrounding tissue. On the other hand, if the tumor were 'benign,' it would only be able to grow in one place.

Myth:

If you tan but don't burn, you don't need to bother with sun protection...

There's no such thing as a safe tan. If skin darkens, it is a sign of skin cells experiencing trauma, even if there is no redness or peeling. Your skin darkens as a way of trying to protect itself because the UV rays are damaging living cells. If you tan easily, you are still at risk of skin cancer and need to use sun protection.

What is Melanoma?

Stage 0 and Stage 1 melanomas are regarded as early stages of melanoma, as they are usually localized and are yet to spread. These tumors are commonly removed by excisional surgery (using a scalpel to cut out the cancerous parts).

Stage 2 melanoma has higher risks as they are characterized by larger tumors in addition to other traits, such as ulceration (refer to the Figure 3). These factors increase the risk of spreading, however, the cancer is still localised (in one place).

During treatment, physicians may offer a more aggressive option. A sentinel lymph node biopsy (medical procedure in which your nodes are mapped and removed to be analyzed in a lab) is often recommended in addition to surgery, as cancer spread to local lymph nodes starts to increase. If melanoma is detected in your nodes, your doctor may continue to examine the rest of your nodes, removing any with cancerous cells. Depending on the severity of the situation, additional treatment such as immunotherapy or radiation may be recommended.

Stage 3 and Stage 4 are advanced melanomas. In Stage 3, the cancer will have spread to local lymph nodes or more than 2cm from the original tumor. In Stage 4, distant body areas, lymph nodes or organs are 'infected' with the cancer. Some options for treatment include immunotherapy, chemotherapy, radiation and surgery. At this stage, supplemental medicine that may enhance the effectiveness of surgery - aimed at prevention and relapse delay - becomes available. Other therapies are obtainable if treatment options are unsuccessful: shrinking tumors and delaying disease progression are some examples.

Ulcer or no ulcer?

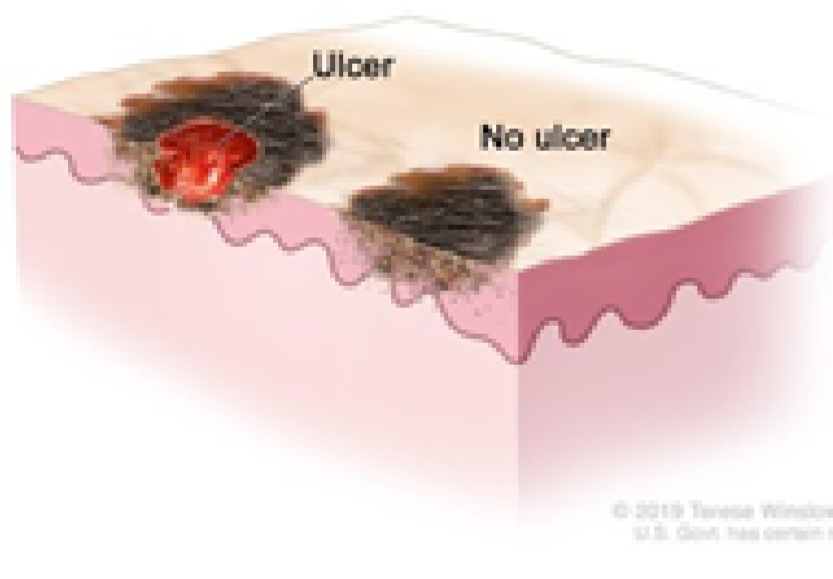


Figure 3
Comparison between melanoma with ulceration and without ulceration.

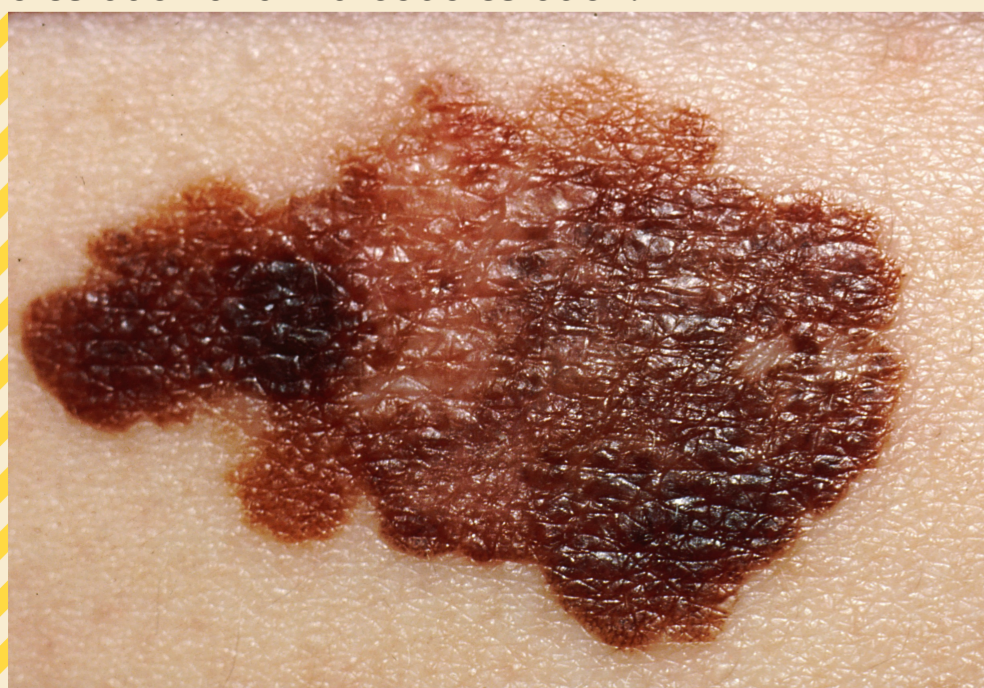


Figure 3.1
A malignant melanoma (Stage III or Stage IV).

Immunotherapy

Immunotherapy is an emerging treatment for cancer. Skin cancer was one of the first cancers that responded to it and has been useful in treatment of Squamous Cell Carcinoma (SCC) and Melanoma.

Immunotherapy involves using the patient's immune system and enhancing it so it can destroy the cancerous cells. Immunotherapies are characterized broadly into two categories: 'stimulants' that boost the immune system functions, or 'substances' that mimic the function of the immune system which, when introduced to the body, is able to detect and destroy cancer cells. More specifically, there are 4 types which are used in the treatment of melanoma and SCC:

- Immune Checkpoint Inhibitors
- Interleukin
- Oncolytic Virus Therapy
- Imiquimod Cream

Immune Checkpoint Inhibitors work by reducing the amount of undetected melanoma cells. Melanoma cells can avoid detection by binding with specific proteins that communicate with T cells (cells that kill foreign particles). Immune checkpoint inhibitors prevent this from happening by revealing the melanoma cells to the immune system. In turn, this increases the likelihood of those cells being destroyed

Interleukins are proteins (cytokines) that are naturally found in humans, and can be artificially made in a laboratory. Their general role is to increase the activity of the immune system with the hope of inducing a faster response to tumors and melanoma.

Oncolytic virus therapy is unique, as it harnesses the capabilities of viruses that kill off cancer cells. In the lab, the viruses are effectively reprogrammed to infect the cells leading to their death. What's more is that the virus also stimulates the immune system as a whole to respond to the cancer cells (refer to Figure 1).

Imiquimod cream is applied to the skin, causing an immune response in the localized area. This treatment is used at least 2 to 5 times a week for 3 months.

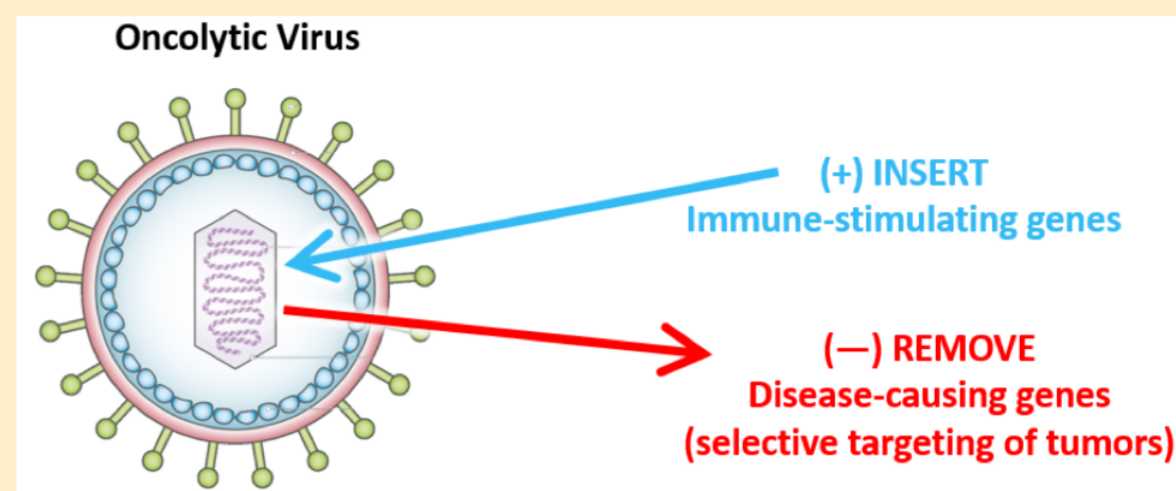


Figure 4 - In oncolytic virus therapy, virus cells are edited to have properties that aid the destruction of cancer cells.



Sun damage is not possible on windy, cloudy or cool days...

Sun damage is caused by UV radiation, not temperature. A cool or overcast day in summer can have similar UV levels to a warm, sunny day. Sun damage is also possible on cloudy days, as UV radiation can penetrate some clouds, and may even be more intense due to reflection off the clouds.

Further Treatments:

As we have already learnt, the further the stage the more monitoring and treatment is required, so let's see what treatment is provided in Stage IV melanoma.

Stage IV melanomas spread (metastasizes) to distant lymph nodes or other areas of the body. Skin tumors or enlarged lymph nodes that cause symptoms can often be removed by surgery or treated with radiation therapy. Tumors found in internal organs are sometimes removed, depending on how many there are, where they are, and how likely they are to cause symptoms. Metastases that cause symptoms but cannot be removed may be treated with radiation, immunotherapy, targeted therapy, or chemotherapy.

Further research for the treatment of melanoma is still in progress. Researchers are looking into the genes that are mutated as a result of melanoma, and are aiming to produce newer targeted therapy drugs in the form of inhibitors for a mutated gene to try and cure patients in a non-invasive way.

Due to such difficulty in treating Stage IV melanoma, patients may want to think about taking part in a clinical trial. Many studies are now looking at new targeted drugs, immunotherapies, chemotherapy drugs, and combinations of different types of treatments.

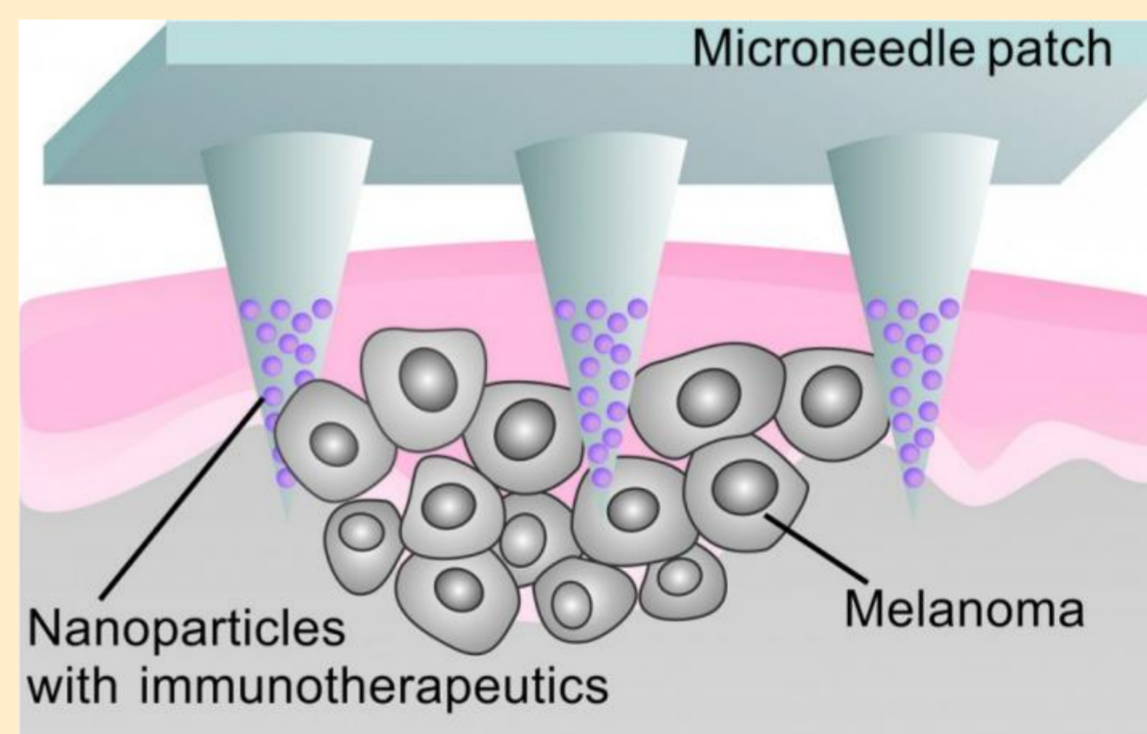


Figure 4.1 - Immunotherapeutics are injected into the skin via a microneedle patch, to enter the melanoma cells and subsequently destroy them.

References:

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