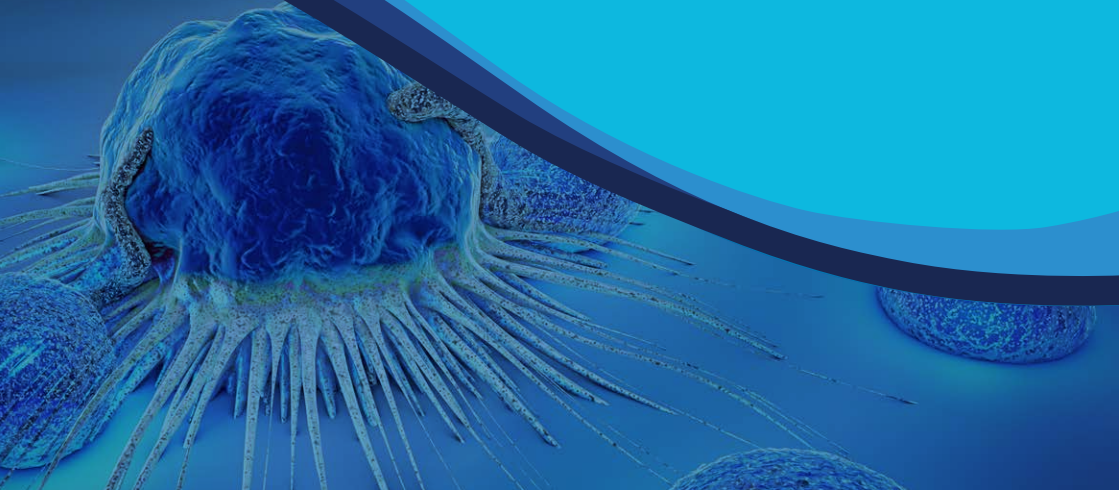




DENDRITIC CELLS IN CANCER IMMUNOTHERAPY





Contents

What is cancer?.....	3
Cancer and the immune system	5
Dendritic cells: The therapy's principle.....	6
When can dendritic cells be used?	8
How are dendritic cells produced?	9
What is the follow-up procedure?	12



What is cancer?

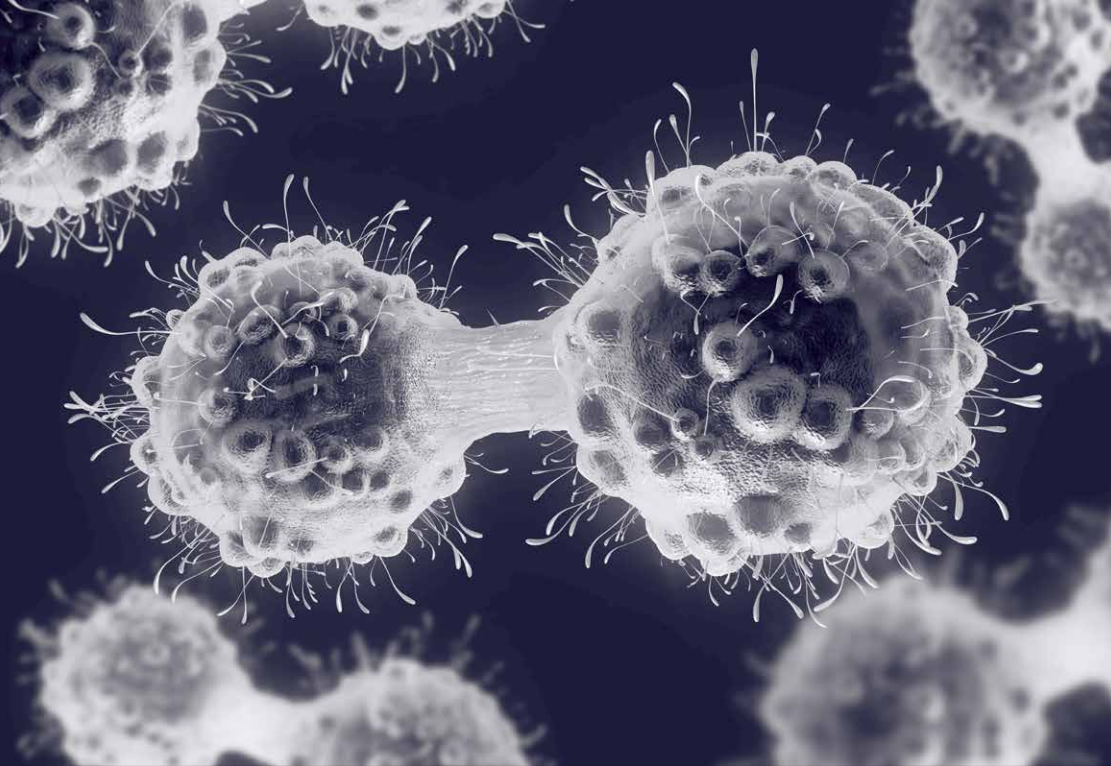
The cells in our body are continually renewed, albeit at different rates. For instance, the cells lining our guts are renewed every three and a half days, skin cells every four weeks and red blood cells every 120 days. The process of renovation is strictly controlled and every cell is instructed when to proliferate and when to stop.

New cells are produced by the division of stem cells that are available in every tissue and function according to a genetic template in the nucleus of the stem cell.

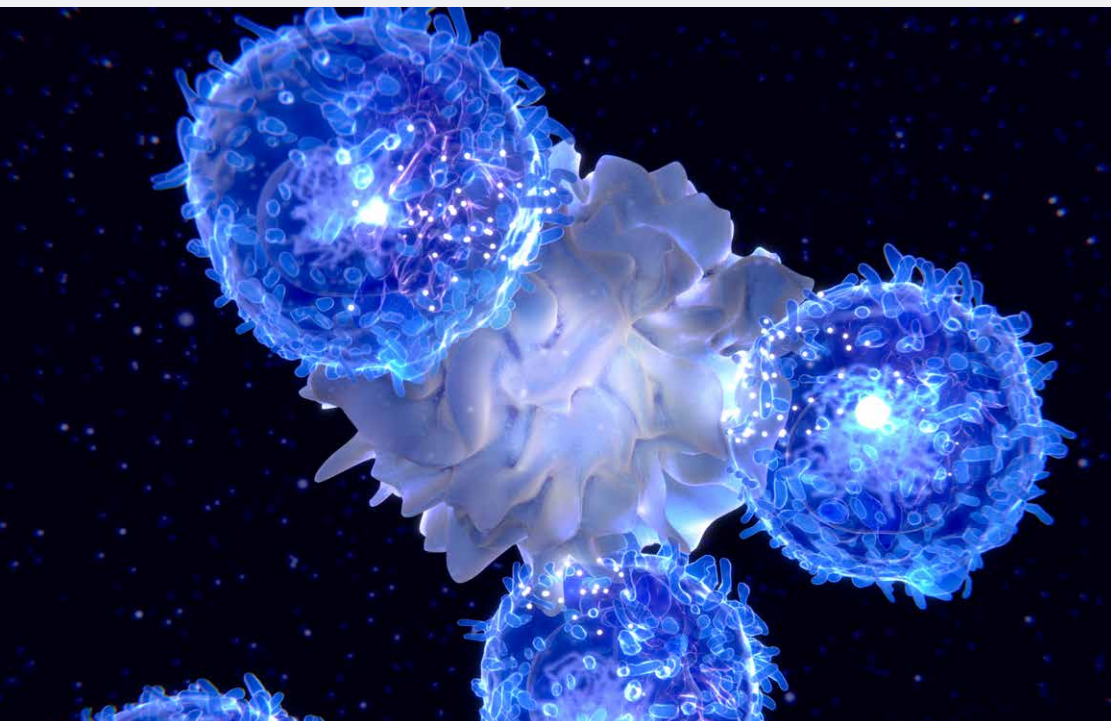
While millions of exact cells are produced in our body regularly, sometimes a mistake is made and a faulty cell is produced.

Our immune system has our body under surveillance and examines the newly produced cells thoroughly, destroying any malformed cells or foreign bodies, such as microbes, entering our body. Although our immune system is mostly very efficient, sometimes a defective cell that does not obey the body's stop signal escapes the immune system's surveillance and persists. Such a cell continues to proliferate and may lead to cancer formation.

Defective cells are produced in all living organisms but cancer develops only in a small number of those cells. Since cancer is developed from the body's own cells it can influence and further weaken the immune system. A weakened immune system will not be able to fight cancer effectively.



Cancer cells multiplying by mitosis



Dendritic cell presenting an antigen to T-lymphocytes

Cancer and the immune system

Cancer is invasive by nature so, in the majority of cases, it will spread or metastasize to other tissues via the lymphatic and cardiovascular systems. While localised cancer can be treated with surgery or radiotherapy, metastatic cancer which is spread throughout the body cannot be treated with such therapies and has to be treated systemically.

Chemotherapy is such a therapy, comprising of a systemic administration of a toxic substance to kill the cancer cells while also damaging the normal tissues of the body.

An alternative method would be the utilisation of the body's own immune system to combat cancer.

White blood cells are the functional cells of the immune system.

Dendritic cells are a subtype of white blood cells that are available in different tissues of the body including peripheral blood.

Dendritic cells are not involved directly in killing cancer cells. Instead they identify the target cells and present this information to natural killer cells (another type of immune cell) and instruct them to attack.

Certain cytokines produced by the tumours have an inhibitory effect on the production and secretion of important regulatory molecules and prevent the maturation process of dendritic cells.

Activation of the dendritic cells in the absence of the inhibitory molecules and introduction of mature dendritic cells into cancer-bearing bodies is a feasible method of fighting cancer.

This is the method employed in dendritic cell mediated immunotherapy of cancer, a treatment also sometimes called a dendritic cell vaccine.

Dendritic cells: The therapy's principle

Stage 1

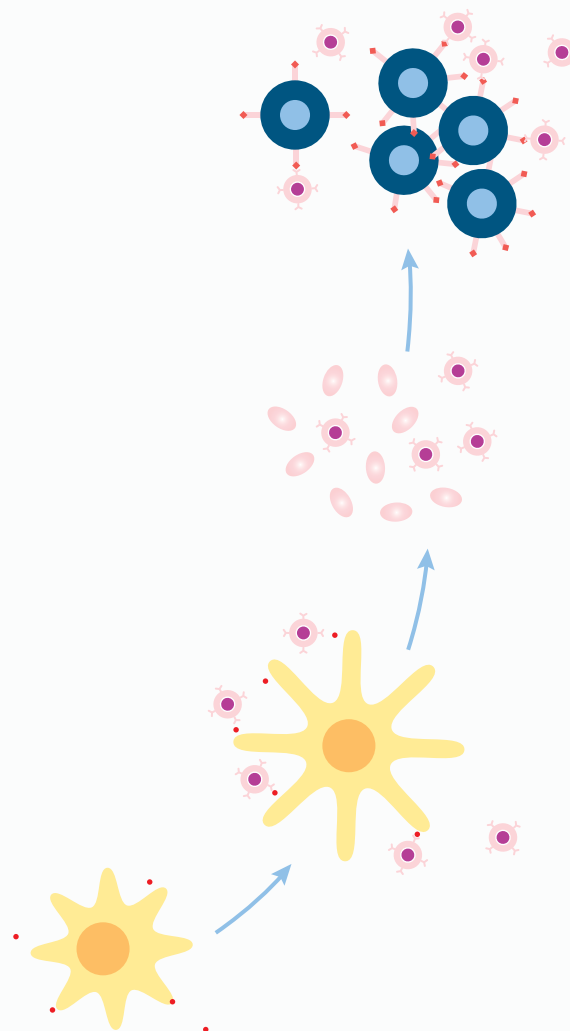
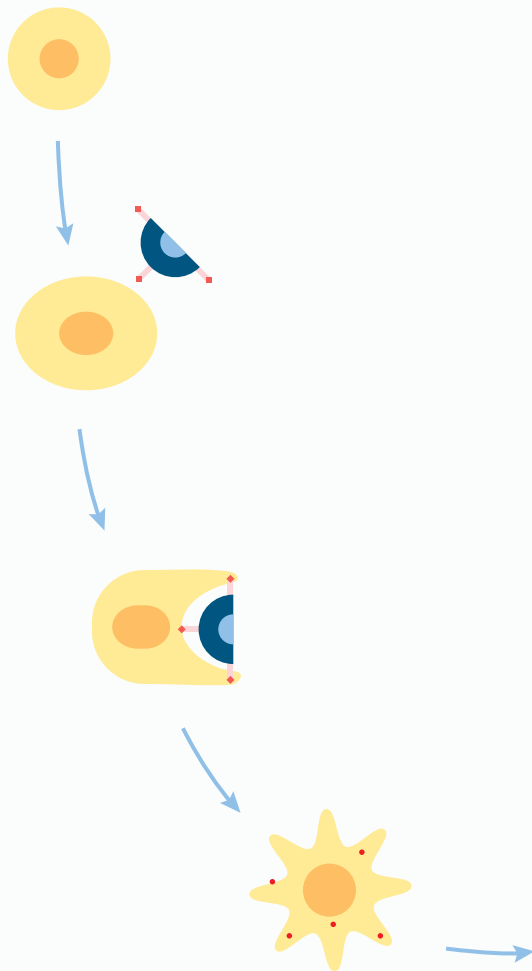
Precursor cells that have the potential to become dendritic cells are isolated from the blood by a special procedure.

Stage 2

Precursor cells are treated in the laboratory.

Stage 3

During the process, the precursor cells mature into dendritic cells capable of instructing natural killer cells to attack cancer cells in the body.



Stage 6

The process of destroying cancer cells sends messages to activate the whole immune system by signalling other resident immune cells in the body.

Stage 5

These activated killer cells enter the vascular system, spread throughout the whole body and destroy cancer cells.

Stage 4

When the dendritic cells are injected subcutaneously, they travel to the lymph nodes and activate various types of killer cells such as cytotoxic T-lymphocytes.

When can dendritic cells be used?

According to the American Cancer Society, of the various types of cancer immunotherapy vaccines, dendritic cell mediated treatment “has shown the most success so far in treating cancer”. Its effectiveness has been demonstrated in multiple cases, and, furthermore, it has been able to do so at every stage in the battle against cancer.

Firstly, it has been shown that injection with dendritic cells can actually act as a preventative measure and stop cancer from forming in the first place.

Secondly, it has been demonstrated that treatment with dendritic cells is a viable alternative to conventional approaches in early stage cancers where there is still some effective immune activity and there are fewer tumour cells to fight.

Thirdly, dendritic cell mediated immunotherapy has been shown to be effective when used after debulking of the primary tumour by one or a combination of conventional methods such as surgery, radiotherapy and chemotherapy, effectively cleaning up any remaining cancer cells.

Finally, dendritic cell therapy can provide one more option in advanced cancer cases where all other approaches have failed.



How are dendritic cells produced?

Stage 1

For the purpose of isolating dendritic precursor cells, about 200ml of blood is drawn from the patient in the presence of an anticoagulant. The blood is transported to the laboratory under controlled conditions and processed immediately.



Stage 2

The blood is processed and the white blood cells isolated.



Stage 3

The fraction containing the precursor dendritic cells are kept and the rest of the cells discarded. The dendritic cells are developed from these precursor cells.



Stage 4

After several cleaning steps, the isolated cells are transferred to a tissue culture dish containing a nutrient solution. Many cells, among them the precursor cells of the dendritic cells, attach themselves to the dish.

**Stage 5**

During the entire growth phase, the cells are kept in a cell incubator. This incubator maintains a constant temperature and ideal growth conditions that are continuously monitored.

**Stage 6**

In order to initiate the maturation process, special growth factors are added to the nutrient solution. During the maturation phase autologous (taken from the patient) plasma components are also added to the cells. These will contain information about the nature of the tumour that will be picked up by the dendritic cells.

**Stage 7**

On day seven, the cells are checked by a flow cytometer for certain markers typical of dendritic cells.

**Stage 8**

The dendritic cells are grown in the incubator for a total of seven days. The maturation of the cells can be monitored with a microscope, since their shape differs markedly from other cells. They have a distinctive form, covered with many thin, hair-like structures.

**Stage 9**

After this check, the cells are harvested and repeatedly cleaned. Half of the harvested cells are put into small syringes for the first injection and transported to the clinic. The physician then injects the cells under the skin near a lymph node. After a short observation period, the patient returns home. The remaining cells are saved for future injections.



What is the follow-up procedure?

After the first injection with the dendritic cells, your treating physician will have your blood checked at regular intervals to see how your immune system is reacting to the injection. Initially, the number of those cells that are capable of destroying the tumour cells increases significantly.

After a certain time, their number decreases again. These results will be used to evaluate any further treatment options.

This type of cancer therapy, compared with conventional approaches, is very gentle and no hospitalisation is required. Overall, dendritic cell therapy should be seen as complementary to the conventional treatment.

Side effects occur only very rarely after injection with dendritic cells. Although the dendritic cells are your own cells, their injection may initiate a slight immune response such as fever, weakness, swollen glands or redness at the site of the injection. If they occur, they subside very quickly and affect the patient minimally.

