



# FUTURE MEETS ONCOLOGY

LABORATORY DR. GANSAUGE | GERMANY





## LANEX-DC® Immunotherapy with dendritic cells

The ability to fight cancer using one's own immune system has been a great dream of medical scientists for centuries. The detection of the immunotherapy by dendritic cells in the late 90s has brought this dream considerably closer to reality. The „father of modern immunotherapy“ Professor Ralph Steinmann was therefor awarded the Nobel prize for medicine in 2011 - the highest honor achievable for a scientist.

Countless research and treatment facilities worldwide increasingly turn toward the dendritic cell therapy, more than 7,000 dissertations have been published on this topic and in some modern nations, like the USA, this therapy is already approved.

The Cabion Technologies GmbH, which was founded in 2002, was taken over by LDG maintaining the responsible team, and is able to look back on over 2,500 successfully implemented therapies with LANEX-DC®.

On behalf of our entire team, I wish you all the best for your treatment.

Prof. Dr. Frank Gansauge

# What is cancer?

Every organism consists of a harmonic structure of cells, each of which has a specific function at a specific location.

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Cancer develops when any given cell in the body escapes the strict control of growth, size and mobility, begins to multiply uncontrolled and produces offspring that can invade surrounding tissues.

Besides, today many factors are known that play a role in the development of cancer, and many more factors are at least suspected of contributing to the emergence of cancer.

This invasion stage may be followed by the formation of metastases when the malignant cells spread through the lymphatic system and the blood stream.

Therefore, it is rather questionable whether a single main cause for the development of cancer will ever be identified, although there may certainly exist general mechanisms leading up to this disease.

About one hundred different types of cancer are known in humans, and all are different from one another regarding, for instance, the average age at which they appear, the growth rate and the tendency to metastasize.

# The effectiveness of a dendritic cell therapy

## Who can benefit from treatment with dendritic cells?

Until now, the effectiveness of a treatment with dendritic cells could be proven in the case of skin, kidney, breast, pancreatic and prostate cancer. Even patients with colon or ovarian cancer benefited from treatment with dendritic cells.

For most types of cancer, however, there exist standard treatments which have been developed over decades. Therefore, we recommend to make use of these treatments and supplement them with immune therapy, since it is known that tumor cells damaged by chemotherapy or radiation are much easier to destroy with immune cells than undamaged tumor cells.

Treatment with dendritic cells is also often used when conventional therapies have not been successful.

This was demonstrated, for example, in the case of kidney carcinoma and malignant melanoma. Vaccination with dendritic cells is most promising, however, when only small

numbers of tumor cells are present. Today we know that the immune system of patients with a low tumor mass often still functions much more efficiently than that of patients with a high tumor load.

Just as with chemotherapy and radiation, the earlier dendritic cell therapy is begun, the more successful it is.



# Cancer and the immune system

## Can the immune system protect from cancer?

The immune system is our body's own defense against harmful pathogens, such as bacteria, fungi and viruses, but also against cells that have degenerated and divide uncontrolled. Every day of our life, about 8 malignant cell proliferations occur in our body. Nevertheless, only 1 cancer on average develops for every 200 years of life. This demonstrates that the human immune system recognizes and destroys almost all cells that show mutations which could lead to cancer. Scientists examined this issue. They tested the function of the immune system in 3,625 healthy persons aged over 40 for a period of 11 years. Humans with a normal or even an extraordinarily efficient immune system had about 40% less risk to come down with cancer.

An efficient immune system is, therefore, important to protect oneself from cancer.

Yet it may happen that our immune system does not recognize these cells precisely because of their mutations. Moreover, tumors exceeding a certain size can produce messenger substances leading to a weakening of the immune system. Thus, the immune system of a majority of patients with cancerous diseases is weakened. Based on this knowledge, physicians try to strengthen the immune system of cancer patients with medications, vitamins and trace elements, but also by using complementary forms of treatment.

As a result of intensive research, knowledge about the immune system, the individual factors and the cell types, that play a crucial role in the defense against pathogens or cells, has grown significantly in recent years.

Today a lot more is known about the cells of the immune system than it was 10 years ago. Amongst other things, one is aware of the fact that dendritic cells occupy a very important role in this system.

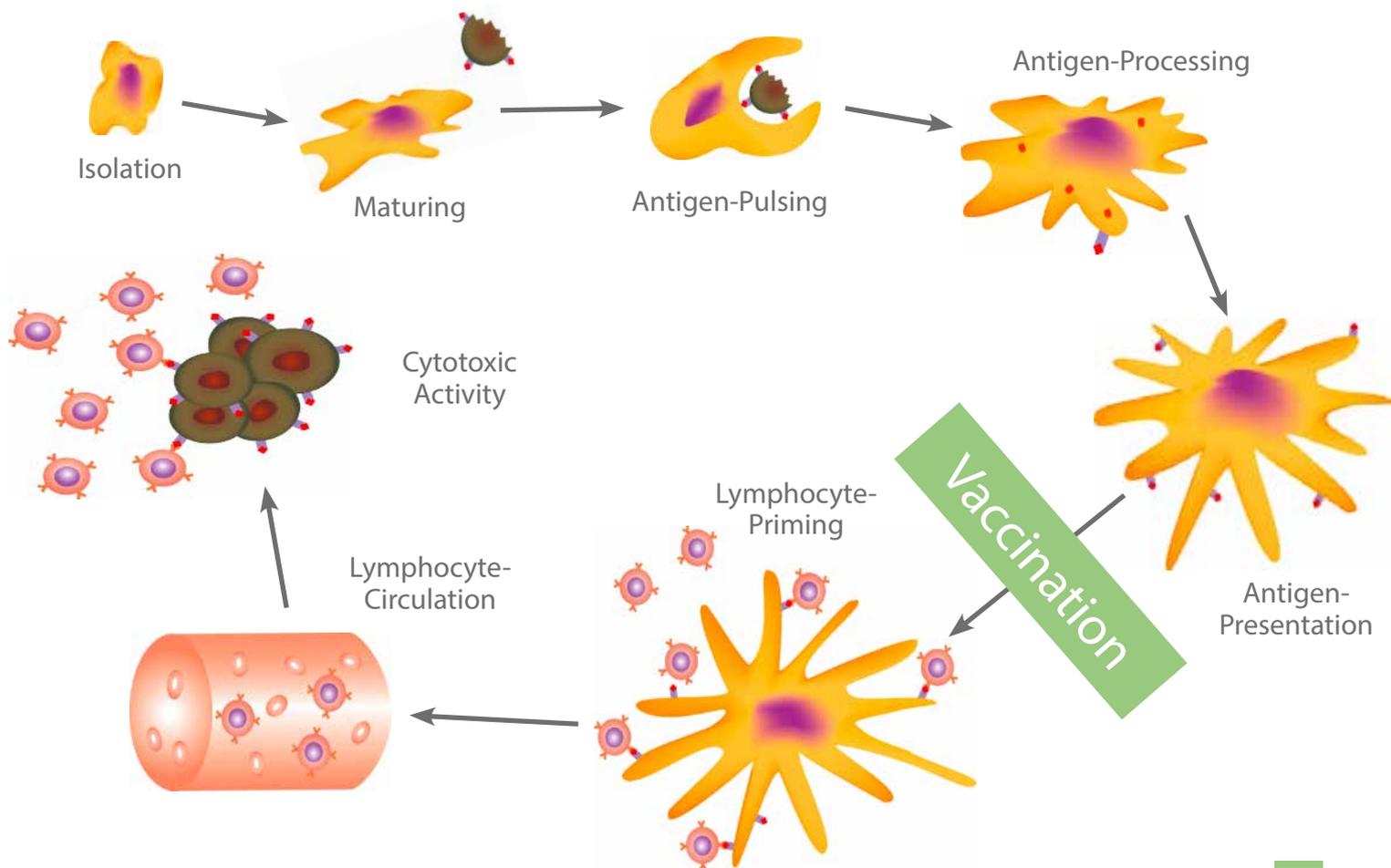
# Dendritic cells:

## The therapy's principle

- Precursor cells that have the potential of becoming dendritic cells can be isolated from the blood by a special procedure. Certain messenger substances, to which the cells are exposed in a culture dish, promote this capability.
- While the precursor cells are in the maturation phase, they are capable of absorbing protein (e.g. tumor antigens out of the patient's plasma).
- The not yet completely matured precursor cells can take up these proteins under clean laboratory conditions even outside of the body.
- Once the cells have taken up the tumor antigens, they rearrange and present them on their surface. Thus, the characteristics of these antigens can later be recognized by other immune cells.



- During this process, the precursor cells mature into fully developed dendritic cells that carry the characteristics of harmful tumor cell structures related to a special marker on their surface. The immune cells can detect and identify this marker as harmful.
- When the meanwhile fully developed dendritic cells are injected subcutaneously, they travel to the lymph nodes and activate various types of killer cells (the so-called cytotoxic T-lymphocytes) that have the capability to destroy degenerated cells.
- These activated killer cells „remember“ the foreign structure characteristics. They enter the vascular system, spread throughout the whole body and search for cells having exactly these characteristics in various tissues.
- When the killer cells encounter relevant cells during their search (in the concrete case, tumor cells), they try to destroy them and send out messenger substances that alarm other defense cells.



# A long-cherished dream of mankind

## Dendritic cells can also be grown ex vivo

To be able to fight cancer using one's own immune system has always been a dream of mankind. In the 90s, the possibility of cultivating dendritic cells has brought the dream a little closer.

Dendritic cells are cells that patrol the body's tissues and track down foreign structures. These structures are taken up by the cells and broken down into smaller components that are displayed on the cell surface.

With this „showcase“, the dendritic cells then migrate from the tissue to the lymph nodes. There, the foreign structures are offered to special „killer cells“ (cytotoxic T-lymphocytes) that subsequently become active and take off to destroy cells with precisely these structural characteristics.

Furthermore, the dendritic cells can also activate other cells, so-called T-helper cells, that arrive at the site also via blood stream and produce substances providing support for the cytotoxic T-cells.

As a result of the interplay between the dendritic cells and the T-helper cells, antibody-producing cells, like B-cells, are also encouraged to grow and produce appropriate antibodies.



# How are dendritic cells produced?

For the purpose of isolating dendritic precursor cells, 200 ml of blood is drawn from the patient, transported under stable temperature conditions and processed immediately in a clean room certified according to EU GMP directives. After centrifugation, the blood is separated into various fractions in order to separate the white blood cells from the red ones and the nonspecific defense cells, the granulocytes. The fraction containing the red blood cells and the granulocytes is discarded.

The fraction with the lymphocytes contains the cells, from which dendritic cells develop. After several cleaning steps, the isolated cells are put in a nutrient solution. These cells, among them also the precursor cells of the dendritic cells, come off. The optimal matu-

ration in the cell incubator is stimulated by a nutrient solution and specific growth factors, and even at the beginning of the maturation process autologous tumor antigens out of the patient's plasma are added to the precursor cells.

The dendritic cells are grown in the incubator for 7 days and monitored microscopically. These cells, marked by a very conspicuous form, differ from other cells due to their thin, hair-like growth.

Before the cells are harvested on day 7, the specification of the surface characteristics, the quantity of cells and their vitality in the flow cytometer is carried out. After that, the cells are harvested, cleaned several times and



put into two small syringes. The attending physician carries out the immunization with dendritic cells by injecting them subcutaneously in the groin region. Afterwards, the patient receives high dosed vitamin infusions and can then return home.

# Treatment with dendritic cells is a gentle treatment

The vaccination with dendritic cells is rather a supplementary treatment in connection with standard therapies.

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In contrast to other forms of treatment, such as chemotherapy or radiation, where foreign substances or damaging radiation are used to fight the tumor, the treatment with dendritic cells uses the body's own immune system for fighting the cancer.

Compared to other forms of treatment, side effects only occur very rarely after vaccination with dendritic cells. If they do so at all, they subside quickly and affect the patient only slightly or not at all. Therefore, no hospital stay is required for the treatment, since it can be performed on an outpatient basis.

For these reasons, the vaccination with dendritic cells can be carried out in addition to other treatments. Care should be taken, however, that the timing of the various treat-

ments is coordinated properly. Although the number of studies on the therapeutic benefit of dendritic cells in the treatment of tumors is growing constantly, standard treatments should under no circumstances be cast aside.

These forms of treatment have largely proven their effectiveness in extensive studies and represent the basic therapy for quite a number of diseases.



## What kind of side effects can occur as part of this treatment?

Even though the body's own cells are used in this treatment, side effects can occur. These side effects may be caused by the fact that, as part of an immune response by the body, inflammation messenger substances are re-

leased, just like in the case of an infection, that produce a slight fever and weakness.

Swollen lymph nodes may be another manifestation of a reaction to the vaccination.

Occasionally, redness may occur at the injection site.

However, all these symptoms are harmless.



## Who bears the costs?

The treatment with dendritic cells is a relatively new form of therapy. As with many other new forms of treatment, health insurers have not yet definitely assessed this treatment and are currently making decisions on a case-by-case basis on who is to bear the costs. Since the number of scientific studies

dealing with the dendritic cell treatment is steadily rising, however, health insurance providers are increasingly willing to assume the costs. In any case, this should be confirmed beforehand with the health insurance provider.

We will be happy to send you a selection of scientific publications to provide the decision makers at your health insurance company with information that may help them to evaluate the treatment. The application for coverage should definitely be done in writing.



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