



Immun-
Onkologische
Forschung

IOZK Stiftung

The role of the immune system in cancer

An introduction by Dr Wilfried Stücker



Understanding cancer means understanding the immune system

A cancer diagnosis raises many questions. Alongside the immediate medical situation, it usually causes a desire to understand what is actually happening in the body – why tumours develop and what role the immune system plays in this. Particularly regarding immunotherapy, there are often fundamental questions: How does it work? How does it differ from chemotherapy or radiotherapy? And what does it mean in practice for the individual patient?

This publication aims to help non-specialists get a first overview. It explains the biological principles behind how our immune system detects and corrects countless deficient or malignant cells every day, why tumour cells can evade this system, and how the immune system can nevertheless be activated. We also describe how immunotherapies are carried out at the IOZK – from diagnostics and the collection of tumour information through to the production of dendritic cells and the use of oncolytic viruses.

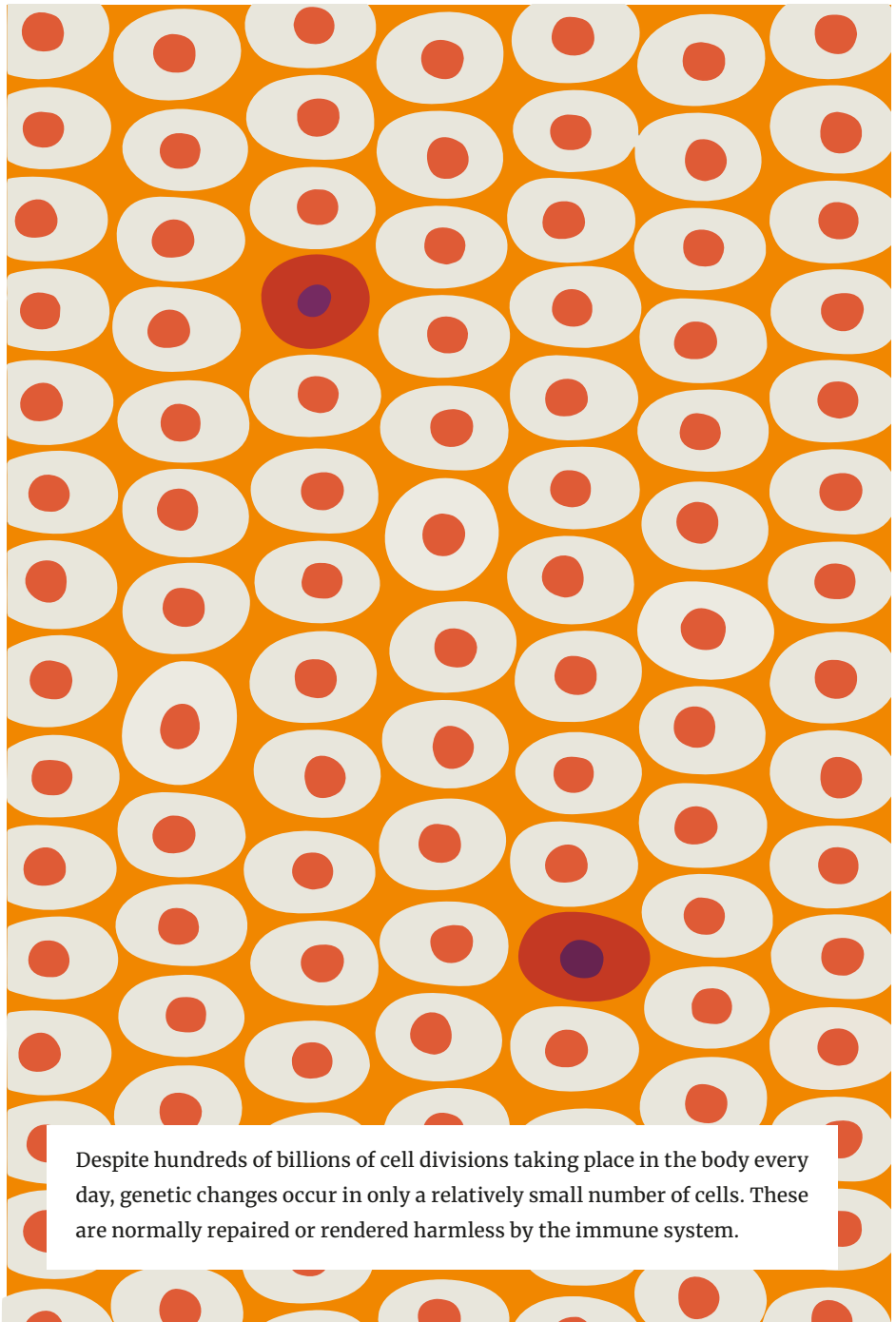
This content is based on a lecture given by tumour immunologist Dr Wilfried Stücker at an information event held in late 2025. It is intended to provide a better understanding of how closely cancer and the immune system are linked, and why modern immunotherapy is a valuable component in the treatment of solid malignant tumours.

The daily work of the immune system

Our entire body only functions thanks to cell division and cell communication. Over the course of a lifetime, an unimaginable number of these divisions take place; extrapolated over a lifespan of eighty years, this amounts to around 10 to the power of 16, or roughly ten quadrillion cell divisions, which occur within our bodies.

Not all of them go smoothly: around a billion of these divisions are ‘not quite right’. This means that around 35,000 altered cells are produced every day; although these are not malignant, they do not function as they should. The immune system normally recognises such cells immediately. It detects when a cell is new, foreign or unknown, and clears it away before it can cause any harm. Given the enormous number of cell divisions that take place every day, this is an astonishingly reliable mechanism.

Many of these cells are repaired by special enzymes, eliminated by the immune system or undergo programmed cell death. For cancer to develop at all, several adverse factors must take place at the same time, since the immune system normally keeps everything in balance. And it is precisely this power of the immune system that we want to harness once a tumour has already developed – to slow down or stop tumour growth.



Despite hundreds of billions of cell divisions taking place in the body every day, genetic changes occur in only a relatively small number of cells. These are normally repaired or rendered harmless by the immune system.

Why the immune system doesn't simply attack a tumour

The immune system always targets cells that are foreign, new or unknown. That is why it is virtually impossible for tumour cells to develop at all. If they still do so, it is only because the immune system classifies them as “our own” – it recognises nothing foreign, nothing new, nothing unusual – and leaves them alone.

This is because the immune system is fundamentally not allowed to attack the body's own cells. There is a special type of immune cell for this purpose – regulatory T cells. They ensure that the body's own structures are not attacked. If this special type of T cell does not function properly, autoimmune diseases such as multiple sclerosis, rheumatism, Crohn's disease or ulcerative colitis can develop.

With a tumour, the opposite happens: altered, self-cells are no longer recognised as foreign. Once the tumour starts to grow, the train has, so to speak, left the station – the immune system is no longer allowed to attack the tumour. Nevertheless, there are ways to draw its attention back to these cells; one of them uses an oncolytic virus that can infect tumour cells exclusively.

The virus that makes tumour cells recognisable

The Newcastle disease virus can invade any human cell. In healthy cells, it is stopped immediately because they produce a substance called interferon to combat it. The cells of solid malignant tumours cannot produce interferon in sufficient quantities; they lost this ability because they detached from their original cellular structure and can embed in foreign tissue. Healthy cells recognise the virus and stop it. Tumour cells cannot do this – which is why the virus can only replicate within them.

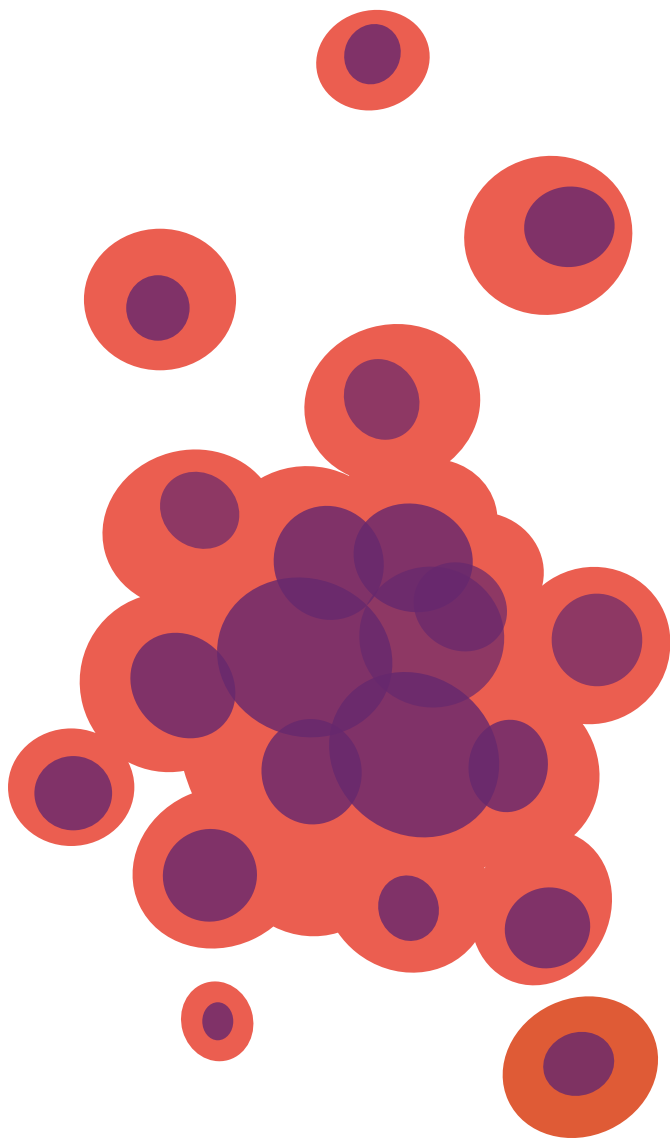
This poses no danger to humans; it originates from bird life – to put it tongue-in-cheek: as long as humans don't lay eggs or cluck about, nothing will happen to them.

What cancer means biologically

When we talk about cancer, in this case we mean solid, malignant tumours. Their distinctive feature is that they can actively leave the tissue in which they originally developed. They migrate into other tissues and settle down there.

This ability – to migrate and settle elsewhere – is what is known as malignancy. If it were merely a case of cells multiplying in one place, a tumour would form that could be removed, and the matter would be done and over with. But as soon as cells leave their original location and settle elsewhere, metastasis can occur.

A tumour is often only detected once it has grown large enough to be visible or to cause symptoms. By this stage, many tumour cells have already been circulating for some time – some lie dormant in other parts of the body and may not become active until years later. This explains why, for example, in the case of breast cancer, metastases can still occur fifteen years after a successful operation. The cells had been circulating for a long time but were simply inactive.



Malignant tumour cells can leave the original tumour mass, travel through the body and settle in other tissues. This is how metastases develop – often long before a tumour is detected.

Why chemotherapy does not reach all cells

One might think that chemotherapy solves the problem: it attacks fast-growing cells, and tumour cells do grow quickly. Some of them are indeed destroyed. However, cells that have already left the primary tumour, settled in other tissues and are lying dormant there, are not affected by chemotherapy because they did not divide at the time the treatment was administered. These migrating and nesting tumour cells are a kind of stem cell; they carry the programme for further cell growth within them. When they divide, a daughter cell is created which remains a stem cell – this ensures its survival – whilst the other half develops into hundreds of thousands of tumour cells.

Such tumour stem cells can even survive chemotherapy because they actively expel the toxins. They literally ‘vomit’ them out or flush them away to avoid being destroyed. During some courses of chemotherapy, hair may fall out but grow back after the treatment: the cells that know how to make hair were not destroyed, and likewise, the cells that know how to generate tumour cells are also preserved.

This is why patients whose cancer has spread often require long-term treatment. Chemotherapy can temporarily reduce the tumour, but it does not destroy its roots. If it is used for too long, tumour cells continue to mutate – either the patient can no longer tolerate the treatment, or the tumour adapts.

The immune system distinguishes and learns

An interesting question is why many people do not develop cancer at all, despite the enormous number of cell divisions that occur over the course of a lifetime. The key factor is the immune system: it can learn and distinguish, and it is precisely these abilities that can be harnessed therapeutically.

In 2005, a French research team examined tumour samples from 900 patients with colon or rectal cancer. The sections were stained with antibodies to see whether immune cells were present in the tumour tissue. The result was clear: if there were many immune cells in the tumour, around 85 % of patients were still alive after five years. If there were only a few, around 35 % survived. All patients had received the same treatment; the only decisive factor was whether the immune system had recognised the tumour or not.

This shows what is at stake: the immune system must be informed about the tumour cells. It must get to know them – but in a way that prompts it to take action against them.

How the immune system communicates

The body's own defence system functions in many ways similarly to the nervous system. Whilst the latter processes experiences from the environment, the former learns at a molecular level what is normal in the body and what is not. Children often suffer from infections early on; once they have had them, the system recognises the pathogens again and eliminates them a lot faster. Over time, this defence becomes increasingly reliable.

This learning principle can also be used to trigger a targeted response against tumour cells. One approach involves infecting tumour cells with a virus so that they become recognisable as dangerous to the immune system. The underlying principle – the interaction between tumour, virus and immune response – was awarded the Nobel Prize in Medicine in 2011.

Fundamentally, the functioning of the immune system is based on communication and learning. Some immune cells gather information, and others pass it on. Dendritic cells play a particularly central role in this process. In a sense, they act as the 'teachers' of this system. These cells present to other immune cells what they have discovered in the body – that is, which structures or changes they have detected. This principle was described as early as the 1970s, but was initially met with scepticism. It was not until many years later that the researcher Ralph M. Steinman was awarded the Nobel Prize for this discovery.

.

How the immune system processes information

Simply presenting information is not enough to trigger an active immune response. A danger signal must also be recognised. If a tumour cell is presented without such a signal, no reaction occurs. Although the cell is recognised, it is not attacked – on the contrary, it may even be tolerated. The situation is different when tumour cells are presented together with a virus. In this case, the system recognises that something is wrong and reacts accordingly.

It produces specialised immune cells that have a licence to kill – so-called tumour-specific cytotoxic T cells. These cells can multiply, leave the lymph nodes and specifically seek out cells with the matching structure. Some of them remain in the bone marrow and form an immunological memory. These memory cells can later recognise and attack tumour cells that reappear or are dormant. This creates a long-term protective effect.

The importance of diagnostics

When a patient comes to see us, we first focus on the immune system: which immune cells are present, how many are there, and how well do they function? You can think of it like the population of a country – there are teachers, craftsmen, professors, police officers – each group of cells has its own role. Since the 1980s, it has been possible to distinguish between individual cell types. To do this, we use so-called monoclonal antibodies, which act as markers, allowing us to identify which immune cells perform which tasks.

In the laboratory, the patient's immune cells are also placed in contact with tumour cells that they do not actually recognise; this reveals whether they react, whether they can learn, or whether they are blocked. In addition, tumour cells circulating in the blood can be examined: Which drugs do they not tolerate? To which substances are they resistant? Cell-free DNA is also analysed for possible changes that could be exploited therapeutically.

To ensure the immune system has no excuse for being deficient, it is also important to check the patient's intake of vitamins and minerals. The end result is a personalised assessment aimed at supporting the patient's own immune system so that it can fight the tumour on its own.

Every tumour is different

Every patient is an individual – and so is every tumour. It used to be thought that if you knew one tumour cell, you knew them all. Today we know that there are significant differences even within a single tumour. There can be up to fifty different stem cell mutations.

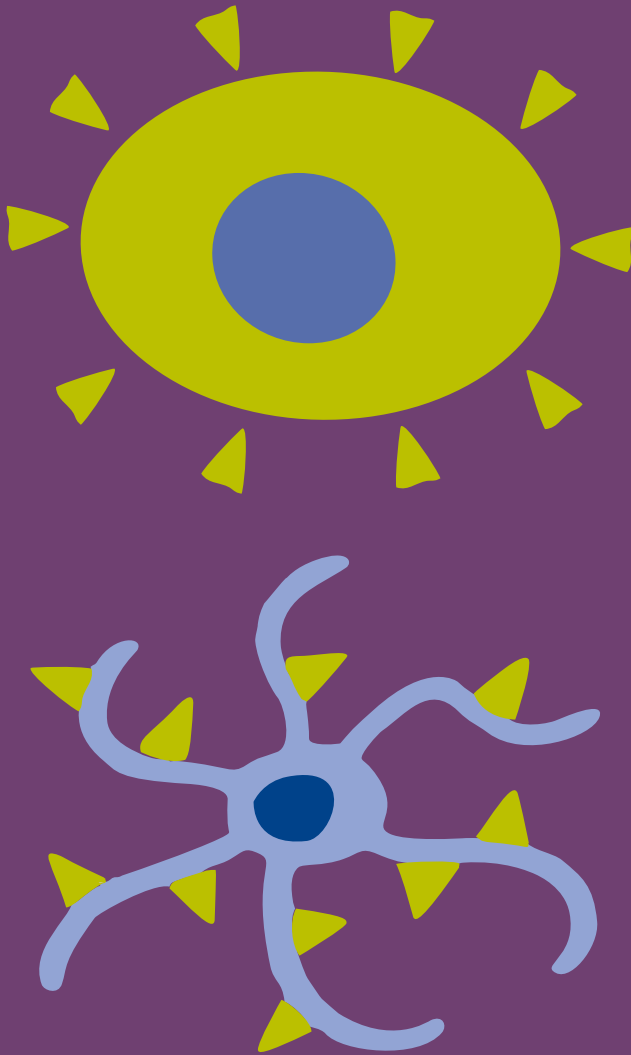
This explains why chemotherapy often has only partial or temporary effect. Even if it is initially effective, the cells continue to change. Sometimes it can even happen that a chemotherapy that is not really working helps indirectly: during treatment, the tumour cells change so much that they suddenly appear foreign to the immune system again. Then a natural defence reaction can occur.

Every tumour has unique biological characteristics – there can be significant differences even within a single tumour. This diversity explains why treatments have varying effects and why the targeted activation of the immune system plays a central role in cancer treatment. Tumour cells can change over the course of a disease and adapt to treatments. An effective treatment must take this dynamic into account and respond flexibly to it. Modern immuno-oncology approaches therefore rely on personalised diagnostics to detect changes in the tumour at an early stage and continuously adapt the treatment to the current situation.

The vaccine from the clean room laboratory

Once the criteria have been met, a blood sample is taken from the patient and a specific subgroup of white blood cells – the monocytes – is isolated from it. They make up around 10 % of white blood cells. These cells can be transformed in the laboratory so that they develop into antigen-presenting cells, i.e. information cells. Their mature form is called dendritic cells – from the Greek word for tree, because they have many branches. They need this surface area to pass on as much information as possible.

These specialised cells are grown in the IOZK's own clean-room laboratory. On the fifth day, whilst they are still immature, they are exposed to the tumour information that they are later intended to pass on. They take up components of the tumour cells, but do not destroy them; instead, they present them on their surface. On the eighth day, they are fully mature and are injected into the patient's skin in a small dose. The cells then migrate via the lymphatic system to the lymph nodes. There, all the white blood cells gather – as if at a large conference – and exchange the latest information. This is how the actual immune response begins.



Dendritic cells act as information relays: they take up components of tumour cells and display them on their surface to T cells, so that the immune system can recognise cancer cells.

Effects and side effects

Normally, this interaction ensures that the immune system tolerates the body's own cells – in other words, that it does not attack them. When tumour components are presented alongside the oncolytic virus, the situation is different: the immune cells recognise that something is wrong and produce cells that actively target the tumour cells. The aim is to generate a response that is as precise and targeted as possible.

In the past, the saying went: 'No effect without side effects.' Today we know that the opposite is true: the more precise a therapy is, the fewer side effects it has. In chemotherapy, all cells that divide rapidly are attacked. This is why blood counts drop, as red and white blood cells as well as platelets are affected. This does not happen with a targeted immune response. Here, only the cells that the immune system actually recognises as targets are attacked.

That is precisely the advantage of immunotherapy: it acts in a targeted manner, meaning that it only attacks the cell structure that is intended to be targeted. There are no side effects as with chemotherapy or radiotherapy; in isolated cases, a mild flu-like infection may occur immediately after vaccination. No serious side effects have been observed to date, nor are they described in the scientific literature.

Where the tumour information comes from

The question is: how does the necessary information reach the dendritic cells? In the past, tumour material was taken from a surgical procedure, the cells were destroyed and used in the laboratory. Today, it is possible to isolate tumour components directly from the blood.

These particles are called immunogenic microparticles or exosomes – small fragments released by tumour cells. If the patient has a tumour burden, we can extract them from their blood. We use this to inform the dendritic cells in the laboratory – always with the current material, i.e. what the tumour is right now, not what it once was.

In parallel, the tumour region is treated with locoregional electro-hyperthermia, i.e. radio waves that generate an electric field. This field stresses the tumour cells, whilst at the same time the virus is injected. The tumour cells undergo what is known as immunogenic cell death, meaning they become recognisable to the immune system. After a few days, there are many tumour particles in the blood, which are used to provide information to the dendritic cells. This creates a cycle: tumour information – immune response – adaptation. In this way, the therapy remains up to date.

When the immune system takes preventive action

It is easy to imagine that such targeted immunotherapy would be particularly effective if administered immediately after surgery, i.e. before new metastases develop: This is known as secondary prophylaxis.

A real or primary form of cancer prevention only exists for a few types of tumour – such as liver cancer, which can be caused by hepatitis B infection, or cervical and laryngeal cancer, which are linked to the papilloma virus. Vaccination can prevent these.

For all other types of tumour, the following applies: the immune system can only respond effectively once it recognises the tumour cells. That is why we need material from the tumour itself – or from the fragments it releases into the blood.

What happens inside the tumour

Tumour cells have one characteristic that sets them apart from normal cells: they do not die when their time is up. Every healthy cell has a built-in programme known as programmed cell death, or apoptosis. Tumour cells have switched this programme off. They multiply but do not make way for others – and this is how the tumour develops.

Conditions at the centre of such clusters of cells are poor: low oxygen, few nutrients. The cells die off there, and the immune system attempts to clear them away. It sends out phagocytes, known as macrophages. But the situation takes a turn: these cells stimulate the formation of new blood vessels to nourish the tissue – and in doing so promote tumour growth.

The immune system treats the tumour tissue as if it were a wound that refuses to heal. It suppresses the immune response so that ‘calm is restored’ and the tissue can heal. This allows the tumour to grow unchecked.

Tumours thus exploit the body’s otherwise beneficial repair mechanisms for their own growth. The misguided immune response creates an environment that protects the tumour rather than fighting it.

How exactly does the Newcastle disease virus work?

This is where the aforementioned Newcastle disease virus comes into play: in cell cultures, it can be seen that after a few days, no tumour cells remain. A single tumour cell can release around 10,000 new viral particles, which in turn infect further tumour cells. In the body itself, the situation is more complicated because the tumour tissue is surrounded by other cells that the virus does not infect. The decisive effect is not the destruction itself, but the immune response that it triggers.

Patients with autoimmune diseases tolerate this therapy well. It is active and specific, meaning it targets tumour cells exclusively. Non-specific activation, on the other hand, can be dangerous because it overstimulates the immune system as a whole.

The therapy only works on solid tumours, i.e. those that can form metastases. It is ineffective against leukaemia or lymphomas that multiply in the blood, because these cells produce enough interferon to ward off the virus.

What can be said about efficacy?

If tumour antigens are present in the body and the patient has an active immune system, the treatment approach can be applied to all solid cancers. In everyday clinical practice, patients with breast, ovarian and uterine cancer are treated this way; the spectrum also includes patients with lung cancer, pancreatic cancer or liver cancer, whilst in urology it covers prostate tumours or kidney and bladder cancer. Another key area is neuro-oncology, such as brain tumours.

The best data on efficacy are available for glioblastoma, a malignant brain tumour. Without additional immunotherapy, the average life expectancy following diagnosis is around twelve months. With standard treatment – radiochemotherapy followed by chemotherapy – survival improves to 14.8 months. If immunotherapy is used in addition to standard treatment, around 80 % of patients are still alive after two years, and around 20 % even survive in the long term. These figures are so clear-cut because the disease usually follows a predictable course – so the effect can be seen directly. With other types of tumours, this is more difficult because the courses of the disease vary greatly.

Recent findings also show that immunotherapy in the early stages of the disease yields the best long-term results. In cases of advanced tumour disease, a cure is still difficult to achieve, but a significant slowing of the disease is evident.

What does the process involve?

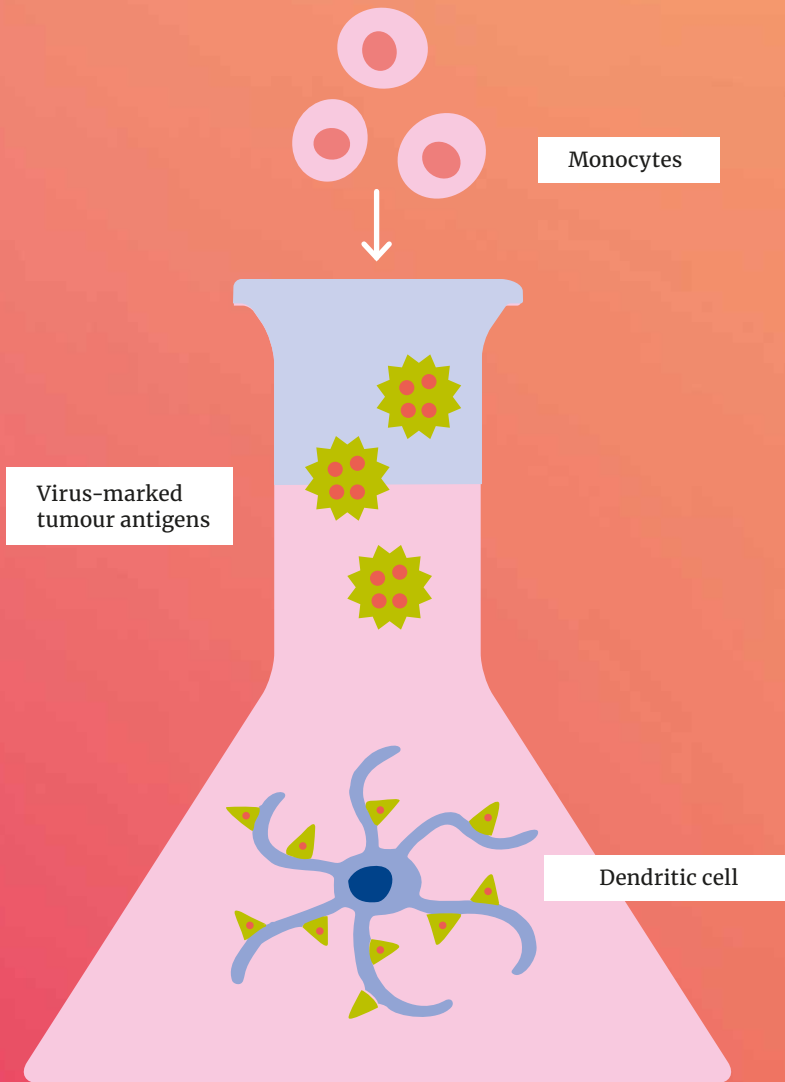
How much does it cost?

Patients usually require two doses of the vaccine, administered about a month apart. Three weeks after the second dose, the immune system's response is assessed. Depending on the results, the treatment can then be continued or adjusted.

Producing the cells is a complex process. Each dose of the vaccine is derived individually from the patient's blood and is subject to the Medicines Act. The effort involved is the same as if one were manufacturing an industrial drug – only in this case for a single person. A single dose costs around 25,000 euros; two doses are usually required. The production of the vaccine is subject to the strict requirements of the Medicines Act.

The time and financial investment required is due to the fully personalised production of the therapy. Each treatment is a bespoke medicinal product and consequently requires significant regulatory, technical and human resources.

German statutory health insurance does not usually cover the costs; however, in individual cases where no other treatment is effective, a claim may be valid. Supplementary and private health insurance policies usually cover the costs – depending on the insurance plan.



White blood cells isolated from the patient's blood are differentiated into dendritic cells – the sentinels of the immune system – through a complex process. They carry the distinguishing features of the cancer cells and can thus trigger a targeted immune response within the body.

About the IOZK

Dr Wilfried Stücker – the founder of the IOZK – has been working in the field of immunotherapy since the 1980s. Initially, the focus was on treating viral infections. With the emergence of AIDS, it became clear just how powerful the immune system is – and what happens when it fails. Since the mid-1990s, the work has focused on harnessing this power in the treatment of cancer.

Today, around seventy staff members work at the IOZK – biologists, virologists, geneticists, pharmacologists and doctors. The aim of this translational research centre is to understand each individual patient's immune system so that it can be specifically activated to combat cancer.



About the IOZK Foundation

The IOZK Foundation is dedicated to promoting the translation of immunological research into clinical practice – with the aim of ensuring that scientific advances are directly incorporated into patient care. The aim is to strengthen the link between the laboratory and the clinic: through optimised therapeutic approaches and a growing understanding of immunological communication.

By making a donation, you support innovative projects and contribute to the further development of immuno-oncology. Whether a small amount or a larger sum – every contribution helps to support the IOZK Foundation's vision of combating cancer with the help of the immune system, thereby improving people's quality of life and life expectancy.

www.iozk-stiftung.org

Donation account:

IOZK Stiftung gGmbH, Volksbank Köln Bonn

IBAN: DE29 3806 0186 8304 2140 16

BIC: GENODED1BRS

Our PayPal



Online donation on our website



Immun-
Onkologische
Forschung

IOZK Stiftung

IOZK Stiftung
Hohenstaufenring 30-32
50674 Cologne
Telephone 0221-420 399 90
Email: info@iozk-stiftung.org

Mitglied im



Bundesverband
Deutscher
Stiftungen