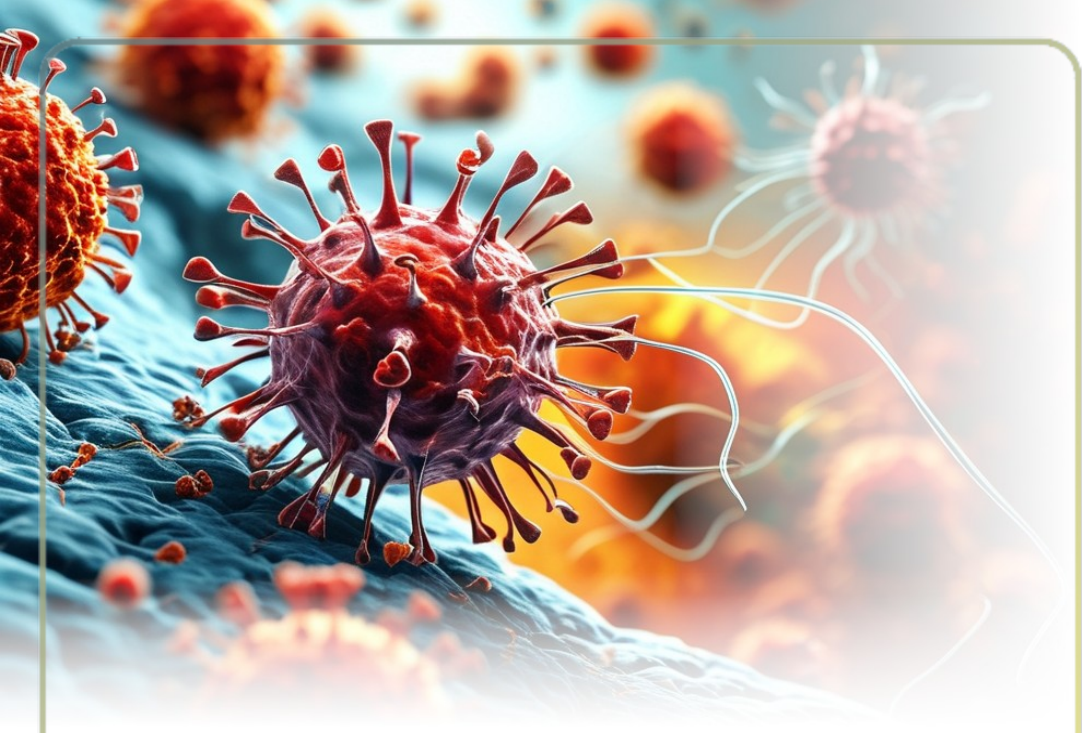
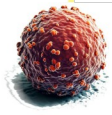


RUDOLF WANK

THE POWER OF IMMUNE CELLS

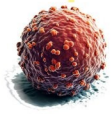


The Power of Immune Cells

First English Edition, v2024-11-01

This is the first English edition of *The Power of Immune Cells*, originally written in German as *Die Macht der Immunzellen*. The German draft of 17 January 2017 remains unpublished.

Translated, revised and updated by Christoph H. Larsen

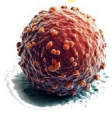


Foreword by Prof. Jurgen Freers

This book is the English translation of a manuscript that my long-time mentor, friend, and senior colleague, Rudi Wank, shared with me for feedback shortly before his untimely death. It was originally intended for his patients and supporters, offering a glimpse into his ideas, thoughts, experiences, and research that underpinned the development of the highly effective CAPRI therapy. I was struck by the simplicity and lucidity of his explanations, which rendered the complex immunological mechanisms of CAPRI therapy accessible to all. As an admirer and, not least, a beneficiary of this innovative approach, I was delighted when my close friend Christoph Larsen, who pioneered an automated method for the production of CAPRI cells, undertook to translate and update Rudi's manuscript from German into English. This translation will enable prospective patients and supporters to gain a deeper understanding of CAPRI therapy.

Cape Town, 24 October 2024

Jürgen Freers



About the Author

Figure 1: Rudolf Wank

Rudolf Wank's medical education at Ludwig Maximilian University in Munich, Germany, was followed by a diverse range of clinical experience, spanning university hospitals and rural clinics, from 1965 to 1972. This broad foundation in general and internal medicine, as well as pathology, laid the groundwork for his subsequent career in immunology, which began at the Institute of Immunology of Munich University. A four-year stint as a research associate in the USA, including a period at the Sloan Kettering Institute of Cancer Research in New York, further refined his expertise. Upon his return to Munich in 1993, he was appointed Professor of Immunology, a position that enabled him to establish a research team focused on immunotherapy. Under his leadership, the team received several prestigious academic awards, including the 2006 Science Prize of the German Society of Immunogenetics (DGI) for the development of the innovative Cascade Priming (CAPRI) method. Following his retirement in the same year, he and his team continued their research and clinical work on the CAPRI method at the Immunotherapy Research Centre in Munich until his untimely death in 2017. The CAPRI method shall be described in more detail below.

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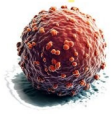


Part I: How Immune Cells Work

Discovery of a New World

Like astronauts gazing at the Earth from their spacecraft, doctors and biologists are fascinated by the world of immune cells in our bodies. For decades, scientists have been amazed by the sophisticated organisation of immune cells against invading microorganisms. Despite this, microorganisms often find weaknesses in the body's defence system and settle for permanent colonisation, causing a multitude of diseases. About fifty years ago, only antibodies, not immune cells, were credited with fighting diseases. Nowadays, we can train immune cells to combat diseases outside the body. This training of immune cells outside the body for subsequent use in the body marks a new era in medicine. After this training, immune cells can even successfully combat diseases, whose causes are still unknown. The following reports on what immune cells can do and what they can achieve with support.

Immune Cells can be Trained against Many Diseases

Trained immune cells can make the impossible possible. The stories of patients with cancer, allergies, joint, autoimmune or chronic vascular diseases that lead to heart attacks and strokes, and patients with neurological or psychiatric disorders will tell you, what trained immune cells can achieve. Often, these diseases arise from a long battle with microorganisms that find gaps in the body's defence system and that, according to estimates, cause around 80% of all diseases (1). The harmony of our immune cells with our microbial cohabitants means being healthy, even in mental terms, and feeling well enough to lead a longer life (1). Immunotherapy is a gentle revolution for the well-being of patients. Many scientists have contributed to this, and some of these contributions are cited at the end of the book.

My First Experiences with the Healing Power of Trained Immune Cells

About thirty years ago, a colleague from the University of Kiel asked me to treat chronic miscarriages with immune cells to spare a patient from Munich a thousand-kilometre trip to Kiel. I agreed. The result was a beautiful baby boy of almost four kilograms. The news spread quickly, and other patients from Munich came to me. Assuming that immune cells could

also be applied to other diseases, I asked my patients about the side effects they experienced with the immunotherapy. I only heard positive things. After a few treatments, allergies to nickel and cat hair disappeared, chronic inflammatory bowel diseases and asthma improved significantly or were cured. With my research group, initially with Dr Barbara Laumbacher, later joined by Drs Barbara Fellerhoff, Songhai Gu, and Xiaoqing Cai, we advanced the development of immunotherapy over many years. Today, our centre for immunotherapy not only treats cancer, but also diseases of the nervous system, blood vessels, connective tissue, joints, and autoimmune diseases with remarkable success. Patients report improved overall health and a renewed sense of vitality thanks to immunotherapy. Notably, cancer patients often remain able to work while undergoing radiation or chemotherapy, with many experiencing a remarkable return to their normal level of energy and well-being. We have described this in scientific journals, and our immunotherapy has also been tested in university clinics in China (2,3).

Immune Cells are All-Knowing

Chronic diseases are a major problem for patients and doctors. For doctors, because they often can only alleviate symptoms without identifying the underlying cause, and for patients, because despite treatment, the disease often recurs. Even if doctors cannot determine the cause of a disease, immune cells can detect unknown infections and damage in the body. However, immune cells often remain dormant when an infection is not actively spreading. Fortunately, immune cells can be activated against chronic, unknown infections if they are nurtured and stimulated outside the body. This is a relatively simple process, provided you know the correct approach. It is possible to obtain a sufficient number of immune cells from a blood sample, which can be trained outside the body within days or weeks for therapeutic use. After activation in an incubator, the immune cells are returned to the body in a saline solution, typically administered via injection into the skin, muscle, or vein.

Trained Immune Cells are All-Powerful

Immune cells can be trained for various tasks. For example, immune cells can take on the functions of nerve cells, as they share a common origin. Like children inheriting certain traits from their parents that are unique to their family, scientists have discovered many characteristics of a close relationship between nerve cells and immune cells in recent years. Perhaps activated immune cells can cross the blood-brain barrier into the brain, because they can recognise and respond to signals emitted by brain cells (4,5). They can

produce nerve growth factors (neurotrophins) that can reactivate dormant nerve cells in patients with depression. Activated immune cells can apparently produce substances that induce a sense of well-being (6), as almost all patients treated with activated immune cells in our centre have reported a regained sense of purpose and vitality. Immune cells are evidently capable of much more than just fighting infections.

Where Immune Cells are Born

The birthplace of immune cells is the bone. From there, they migrate into the blood. Despite this, bones are often depicted as a symbol of death. Skeletons are often shown as harbingers of death, wielding scythes to guide us into the afterlife. However, ancient cultures suspected that bones were connected to life. In ancient Jewish tradition, it was believed that the resurrection was initiated by an indestructible bone called *Luz bone*, also known as *Os sacrum* or *Sacrum* (7). In fact, we now know that bones are the site where cells are born that sustain our life. In the bone, cells mature in many small nests, which then enter the blood and continue to migrate. From these bone nests, immature cells, also called *stem cells*, migrate to replace dead cells in other organs, if needed. They can develop into egg cells in the ovaries (8), or form new brain cells in the brain, even in adults (9). The spleen acts as a large graveyard for dead cells. The disposal of these cells is a task of scavenger cells, which can also be found in the blood and other organs. During the processing of cellular waste, scavenger cells gain information about the processes in the body, including the causes of diseases. If scavenger cells are supported during the processing of cellular waste, they can pass on more accurate information to the immune specialists, the lymphocytes.

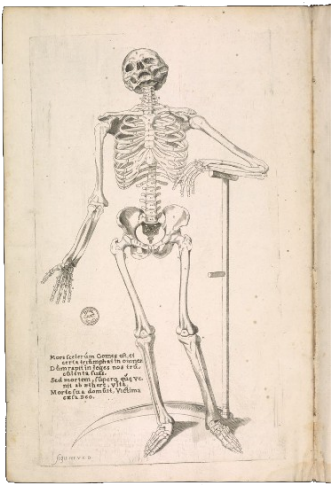


Figure 2: Coiter, Volcher (1573)

The Diverse Roles of Immune Cells and Other Cellular Players

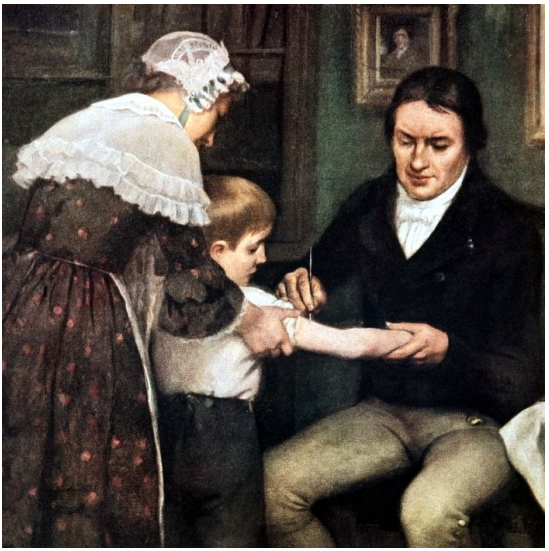


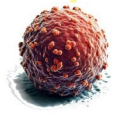
Figure 3: Ernest Boad (undated). Dr Edward Jenner

Long before the discovery of bacteria, viruses, and immune cells, therapies were developed that stimulated immune cells. Thousands of years ago, various substances were rubbed into the skin or burned into the soles of the feet in China (10), and in the 15th century, the crusts of smallpox pustules were scratched into the skin of healthy people in Turkey and China as a preventive measure. Doctors saw successes, but at the time, they did not know that a sophisticated immune response was being triggered in the skin. Even with vaccination in the 18th century using smallpox pustules from cows, the people who developed vaccination did not know that they were training immune cells by scratching them into the skin (11). The skin is a good place to prepare immune cells for their job in the body, which is why vaccines are often given as a skin injection rather than into a vein.

Our body is made up of tiny building blocks called *cells*. The importance of cells in the body and in diseases was first described by the German pathologist Rudolf Virchow. Human cells are incredibly small and can only be seen with the help of a microscope. You can even scrape cells from the lining of your mouth with your finger, place them on a small glass slide, and examine them under a microscope.

Cells in the skin and mucous membranes are connected to form a protective layer and stick together tightly. In contrast, cells in the blood flow through the body as individual cells, but are packed closely together.

When you look at a drop of blood under a microscope, you can see and count that red blood cells are about a thousand times more common than white blood cells. This is why our blood is red.



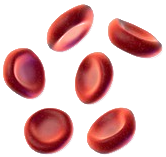


Figure 4: Red blood cells

Red blood cells become specialised when they leave the bone marrow, as they expel their nucleus, their central control centre or brain. As a result, they use very little of the oxygen they absorb in the lungs and can supply all cells in our body with the vital oxygen they need.

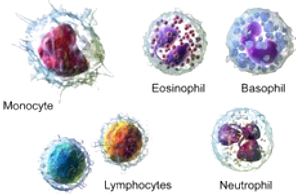


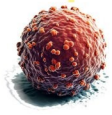
Figure 5: White blood cells

White blood cells, on the other hand, have different tasks than red blood cells. Since they retain their nucleus, their brain, they can recognise and fight against living organisms that enter our body. These organisms are smaller than our cells and can be harmful to us. Our body is surrounded by tiny microorganisms, some of which are friendly and others that are hostile, which can only be seen under a microscope and are therefore called microbes.

Bacteria and viruses are examples of such microorganisms. Many of them live as beneficial cohabitants (technically known as the *microbiome*) on our skin and in our gut, and some even in our blood. The importance of living in harmony with these cohabitants for a healthy life and a slower ageing process has recently been recognised (11).

The Main Tasks of Immune Cells

Immunity actually means maintaining purity. Immune cells are responsible for keeping the inside of our body free from hostile microorganisms. Immune cells encounter an incredible number of different bacteria, viruses, and fungi every day. Sometimes, these microorganisms can infect immune cells and live there undetected. They can hinder immune cells from defending against other microorganisms, or even cause chronic diseases themselves. An example is the AIDS virus HIV (human immunodeficiency virus), which infects immune cells and weakens their ability to fight against other microorganisms. When we are sick, we only notice the intense struggle between immune cells and microorganisms, when it comes to the destruction of cells. We experience this as inflammation or fever. Chronic inflammation in organs such as bones, liver, lungs, and other organs not only impairs the function of the infected organs but also affects our overall well-being. Chronic inflammation produces a lot of cellular waste, which is partially eliminated by fever or can be deposited in unfavourable places, such as in the arteries or brain. Chronic known and unknown inflammation accelerates ageing and shortens lifespan (1). Trained immune cells can combat many of these chronic inflammations.



Specialised Groups in the Immune Cell Population

In a society, people with different professions are entrusted with different tasks. Similarly, in the immune system, individual cell groups are specialised in specific tasks. Some cell groups are responsible for alerting the immune system to emerging infections, others combat the infection site, others support the fighters, and others try to minimise the collateral damage of the fight against microorganisms. In the therapy with activated (means: stimulated) immune cells that we use with our patients, four cell groups play a crucial role: two groups of phagocytic cells, the monocytes and dendritic cells, and two groups of lymphocytes that are trained in a small organ, the thymus.

What follows are the character profiles of the aforesaid four immune cell types that are activated step by step in the course of the CAPRI process:

The monocyte is a round phagocytic cell that digests cellular or microbial waste and reports on the digested material.

Dendritic cells originate from the phagocytic cell type of monocytes, have many tentacle-like arms, and are particularly effective at alerting T lymphocytes.

T killer lymphocytes receive highly specific information from phagocytic cells about infected cells and cancer cells and benefit from the support of T helper lymphocytes.

T helper lymphocytes may not be as effective at destroying infected cells, but are essential helpers of T killer lymphocytes and support many other cells, including brain cells, with messenger substances.

T Lymphocytes are Trained in the Thymus

How lymphocytes are trained in the thymus to attack infected cells, but spare healthy cells of their own body has puzzled scientists for generations (12). The lymphocyte graduates of the thymus school are called *T* lymphocytes. In the thymus, lymphocytes are trained to become defence specialists, and any rogue cells that would attack healthy cells of their own body are eliminated. Among these T lymphocytes, there are, as already mentioned, two main groups that we simply call T helper lymphocytes and T killer (or cytotoxic) lymphocytes.

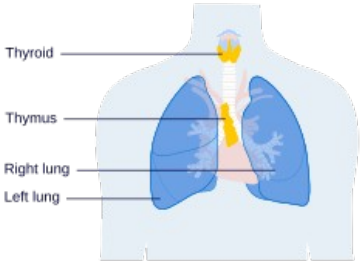
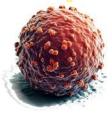


Figure 6: Position of the thymus



There is another group of cells comprising the natural killer cells (also called *NK cells*) and B lymphocytes that are not trained in the thymus school. B lymphocytes and NK cells shall not be discussed in more detail here, as they are not relevant to our method of activating immune cells. Likewise., qranulocytes, another type of phagocytic cell that engulfs microorganisms in abscesses and has a short lifespan of two to three days, only, are not used in our method of activating immune cells.

Why Immune Cells were not Trusted to Destroy Cancer Cells for a Long Time

Not too long ago, the majority of scientists assumed that immune cells were incapable of destroying cancer cells. Similarly, only antibodies, but not immune cells, were trusted to defend against microorganisms. Additionally, most cancer researchers did not believe that microorganisms could transform a normal cell into a cancer cell. Although Rous discovered a virus about a hundred years ago (13) that could cause cancer in chickens, most scientists considered this an exception in cancer development. The change in thinking was accelerated by the observation that nuns got cervical cancer much less frequently than other women. It was concluded that carcinogenic microorganisms could be transmitted through sexual contact.

Figure 7: Francis Peyton Rous

Figure 8: Armand Gaultier (undated). Three Sisters of Charity St Vincent de Paul

Figure 9: Quba Mosque, Medina

Interestingly, in Jewish and Muslim women, the circumcision of the penis foreskin led to a significantly lower incidence of cervical cancer. In cases of poor hygiene, microorganisms could apparently nest in the foreskin. Only decades later could human papillomavirus (HPV) be identified as the main cause of cervical cancer (14). The genetic material of these viruses, DNA, was found in the nucleus (brain) of cancer cells. The DNA of these viruses can completely change the, in figurative terms, socially responsible behaviour of human cells, and the resulting cancer cells form malignant tumours that invade neighbouring tissue. The name *cancer* for malignant tumours comes from the observation that these growths shear through surrounding tissue in a scissor-like manner. If cancer cells penetrate blood and lymphatic vessels, they can sometimes settle in other parts of the body. The growth of these metastases in vital organs such as the brain, liver, and lungs is a life-threatening event.

How Immune Cells Recognise Microorganisms and Cancer Cells

The body is constantly exposed to ever-changing microorganisms. Immune cells that can develop new responses to new microorganisms form the so-called adaptive immune system. But how does the adaptive immune system really work? Until about 40 years ago, it was believed that microorganisms attach to body cells and are destroyed by killer cells. Many discoveries have shown that this is not the case. The realisation began with the observation of a protrusion of the outer skin (membrane) of an immune cell. This protruded structure was crystallised. The structure was named *HLA* in humans, an abbreviation for Human Leucocyte Antigen. The name was coined at a time, when it was not known that HLA structures are not only found on the surface of white blood cells (leukocytes), but on all body cells. The HLA structure was of particular interest to researchers, because it offered an explanation, why a transplanted kidney that did not come from a twin, but from an unrelated donor was commonly rejected. Surprisingly, the crystallised HLA structure showed a small foreign body (15) in its centre. What was this foreign body? The question arose because the immune cells used for crystallisation were infected with a virus to obtain a large number of cells. The cells

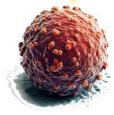
used for crystallisation were B lymphocytes, which can be stimulated to cancer-like proliferation, once infected with the Epstein-Barr virus. The above findings sparked an enormous surge in scientific interest in cell-to-cell interaction and tissue compatibility (16,17,18,19,20).

Inside the Microcosm of a Cell

More and more scientists engaged in research to uncover the complexity of tasks that are successfully accomplished inside the microcosm of a single cell. A cell is traversed by production sites and conveyor belts that transport microorganisms, as well as residues of dead cells, from the surface to the cell interior, where they are digested and then bound to the HLA structure. The HLA structure then returns to the cell surface with the digested fragment. Analyses revealed that the inclusion in the crystallised HLA structure consisted of protein fragments, also called *peptides*. In numerous experiments, it has been shown that the peptides presented by the HLA structure inform passing lymphocytes of the origin of the digested material, whether it is derived from microorganisms or from the cell's own tissues. If cells displayed a microbial peptide in the HLA structure, the passing immune cells would organise an immune response. As a result, either the infected cell is completely destroyed, or, more elegantly, the microbe within the cell is eliminated (21,22). Unfortunately, there are microorganisms that infect cells, but remain silent and are therefore not recognised. In such a case, lymphocytes do pass by infected cells, yet fail to detect any danger. Such microorganisms may multiply initially to ascertain their stealthy foothold inside the infected cell, and then remain dormant watching out for a favourable opportunity to surge, for example, during an infection by other microorganisms.

HLA-Bound Peptides Help Distinguish Self from Foreign

Not only foreign peptides, but also the body's own normal peptides, are presented in the HLA structures. Lymphocytes, as defence specialists, are adept at distinguishing between microbial peptides and their own, and can even recognise lightly altered peptide waste products from their own cancer cells. However, some individuals' immune cells struggle to differentiate between healthy peptides and those derived from cancer cell digestion. In these cases, is the immune system ineffective against only one type of cancer, and, crucially, can we provide support to their immune cells?



Immune Cells Can React Incorrectly or not at all

The intelligence of the immune system has its limits. Not only can microorganisms' cunning tactics prevent an immune response or trigger an overreaction, but the genetic variants we inherit from our parents can also play a role in immune cells' inaction or overreaction. Every population harbours billions of immune gene variants, and only identical twins and some siblings inherit identical HLA genes.

The Information Derived by Phagocytic Cells about the Same Microorganism Differ Slightly from Person to Person

Every year, we observe that not everyone falls ill, and not everyone suffers to the same extent, when a new flu strain emerges. While caution around infected individuals and the number of inhaled microorganisms play a role, the individual's immune system is also a crucial factor. The production, sorting, and transport of peptide fragments from the microorganism to the cell surface are all controlled by immune system gene variants. For example, genetically encoded variants of the immunoproteasome protein complex, which is responsible for cleaving proteins into suitably-sized peptides for processing, can affect the recognition of fragments from digested microorganisms or cancer cells. These genetic variations can also influence the transport of these fragments to the cell surface, where they are presented to the immune system by selective transporters, such as TAP 1/2 and tapasin. Without this information, T killer and T helper lymphocytes are unable to respond.

A major obstacle in cancer and other chronic diseases appears to be the stagnation of information within phagocytic cells. The consequences of poor processing of cancer material by unfavourable immune enzyme gene variants were first identified in patients with colon cancer (23). This discovery highlights the complex interplay of factors that influence the effectiveness of T lymphocytes, many of which are only now being recognised.

Is there an Ideal Immune System?

The ideal immune system would need to control billions of different microorganisms, while also eliminating hostile ones without compromising our overall health. Vaccines against life-threatening microorganisms, such as smallpox, have been instrumental in saving countless lives. However, vaccines can only be developed against a finite number of microorgan-

isms, leaving us vulnerable to the vast array of existing pathogens. A pressing question remains: How effectively can immune cells defend against the onslaught of microorganisms without external assistance?

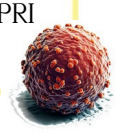
Although no one is immune to all microorganisms, some individuals are able to overcome infections with viruses such as Ebola, smallpox and AIDS (24) without exhibiting any signs or symptoms. These individuals possess optimal genetic variants, including digestion, transportation, and presentation variants, as well as HLA structure variants, that enable their immune cells to effectively combat these specific microorganisms. However, their immune cells may not respond as effectively to other pathogens. As a result, ongoing research is needed to advance the development of vaccines, immunomodulatory substances, and immune cell therapies to address the ever-evolving gaps in the immune system.

What Makes Cancer Cells so Insidious

The Cancer cells are like bad neighbours: They do not respect boundaries and can even invade blood vessels. They can also disguise themselves by wrapping themselves in a layer of normal connective tissue cells (25). But there is another problem: When monocytes, a type of immune cell, try to digest cancer cell waste, they seem to fall into a deep sleep. It is as if they need a wake-up call.

How Can we Optimise the Communication between Immune Cells to Target them Effectively?

We have found that T lymphocytes, another type of immune cell, can play the role of the proverbial prince, who wakes up the sleeping monocytes. To make T lymphocytes do their job, we first need to activate them, or get them excited. Once the monocytes are awake, they can inform T killer and T helper lymphocytes of the danger of cancer cells. This can happen in two ways: Either the monocytes can do it on their own, or they can mature into dendritic cells with many tentacles, which are even better at sending out warning signals. One of our most important discoveries was that cancer material is stored in monocytes, and that we can help these cells present cancer cell material to the rest of the immune system for further action. We have found that this is true for many types of cancer, including breast, lung, skin, stomach, colon and other cancers. In each case, we have found that monocytes fall asleep when digesting cancer cell waste. Yet, we have also discovered that we can always wake them up using our CAPRI



method, and get them to pass on crucial information about cancer cells to T killer and T helper lymphocytes for further immune action (2).

How Immune Cells can Prevent the Development of Cancer Cells

Most of the time, it is not possible to transform a cell into a cancer cell, even when exposed to microorganisms. For example, while many people carry the Epstein-Barr virus (EBV) in their B lymphocytes, their immune cells usually prevent the infected cells from becoming cancerous. However, in a few cases, the virus can succeed in transforming these cells into malignant lymphomas. On the other hand, the human papillomavirus (HPV) is more likely to trigger the development of cancer in normal cells, particularly in the mucous membranes. Some people are born with immune system gene variants that can prevent cervical cancer (26,27,28,29), probably because their immune system can destroy infected cells before they become cancerous. Since immune cells can be prepared to fight viruses with vaccines, vaccinations can be used to prevent certain types of cancer. The researcher Harald zur Hausen developed the first successful vaccine against cervical cancer, the HPV vaccine (30), and was awarded the Nobel Prize for his work. Meanwhile, microorganisms have been identified as a major factor in the development of several types of cancer. For instance, *Helicobacter pylori* is a known cause of stomach cancer and may also contribute to cancer in the intestine and pancreas (31). Fortunately, these bacteria can be effectively treated with antibiotics. The hepatitis B and C viruses have been linked to liver cancer, and vaccination against hepatitis B has significantly reduced the incidence of liver cancer in Asia (32). In summary, vaccinations against viruses can be a powerful tool in preventing cancer.

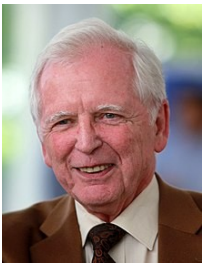


Figure 10: Harald zur Hausen

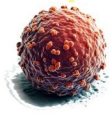
Why the Search for Microorganisms in Cancer Cells can be Difficult

Various viruses play a causative role in the development of leukæmias and lymphomas. However, identifying microorganisms in cancer cells that have transformed normal cells into cancer cells can be a challenging task. Some microorganisms appear to have the ability to alter control switches in the cell nucleus, effectively manipulating the cell's "brain", before disappearing without a trace, much like a "hit and run" operation. Despite the

lack of direct evidence, indirect indications of microbial involvement in cancer development still exist. For example, if patients with a specific type of cancer are frequently infected with a particular microorganism, it suggests a potential link. Many researchers, including myself, believe that microorganisms are the primary cause of cancer development. Given the potential benefits, it is essential to continue the search for microorganisms that can cause cancer, despite the challenges involved. To facilitate this research, state funding is necessary, as pharmaceutical companies tend to avoid long-term projects.

Classical and New Methods to Activate Immune Cells against Cancer

In classical vaccines, microorganisms are modified in the laboratory to render them non-infectious. The vaccine is then administered through a skin scratch or muscle injection, where it is further processed by phagocytic cells, including dendritic Langerhans cells in the skin. On the surface of these dendritic cells, T lymphocytes recognise the processed microbial particles as a threat and retain the experience in memory. While the exact mechanisms of this memory are not yet fully understood, it is widely accepted that T lymphocytes are the carriers of vaccine memory (33). The first vaccine specifically designed to prevent cancer is the human papillomavirus (HPV) vaccine, which targets cervical cancer (34). Interestingly, research suggests that HPV vaccination may also offer protection against other types of cancer, such as prostate cancer, as HPV has been found in these cancer cells. Furthermore, vaccination against the hepatitis B virus has been shown to significantly reduce the incidence of liver cancer in young people in Asian countries (32).



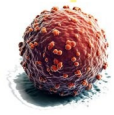
Part 2: Various Strategies of Adoptive Cell Therapy (ACT)

When you adopt a child, you want to support their development and help them thrive. Similarly, when you adopt immune cells, you isolate them from a blood sample and nurture and strengthen them in an incubator using various methods. Only a few of these methods are presented here, focusing on the essentials:

Activating Cells with the LAK or CIK Procedure

In New York over 40 years ago, Dr Doris Morgan was tasked with discovering a hormone-nutrient (cytokine) that would stimulate the development and multiplication of all bone marrow cells, including stem cells for all blood and other body cells. However, she only found a growth factor that further developed stem cells into T lymphocytes. Unfortunately, her boss did not initially recognise the significance of her discovery, and she was fired (35). Nevertheless, that newly discovered energy and proliferation substance of T cells, called interleukin 2 (IL-2), has proven to be highly beneficial for the development of those cancer therapies that use T lymphocytes.

Initially, immune cells were stimulated with extracts from beans (lectins) to produce IL-2; nowadays, IL-2 is produced genetically. With large amounts of IL-2, it became possible to stimulate large quantities of immune cells, following their isolation from the blood and multiplication in the incubator. The first patients to be treated with IL-2-activated lymphocytes were those with melanoma, with some successes (36). The activated immune cells, mainly T lymphocytes, were called LAK cells. (Lymphokin was another name for IL-2, and the name LAK stands for *lymphokin-activated killer lymphocytes*). LAK cell therapy has been improved in recent years and is mainly used in China and Japan under the name CIK. The immune cells are not only activated with IL-2, but also with an antibody against T lymphocytes. This antibody binds to an activation switch called CD3 located on the surface of T lymphocytes. When the CD3 activation switch is flipped by the antibody, signals are transmitted to the cell interior, and the T lymphocyte is activated. Unfortunately, all lymphocytes have the same activation switch, including those that put excited lymphocyte colleagues into a resting state. Even so, the aggressive lymphocytes seem to be in the majority. A Japanese group achieved a statistically significant prolongation of life in patients with liver cancer, whose T lymphocytes were only stimulated via the CD3 activation switch in a double-blind study (37).



Adoptive Cell Therapy (ACT) with Tumour-Infiltrating Lymphocytes (TILs)

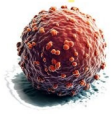
Tumour-infiltrating lymphocytes (TILs) are immune cells that can be found in cancerous tumours. However, they often struggle to effectively combat the large number of cancer cells. If these TILs are removed from the tumour and reactivated with hormone-like substances (cytokines), they can regain their ability to destroy cancer cells (38). This demonstrates that immune cells are capable of recognising cancer cells, but may require assistance to mount an effective response. Unfortunately, obtaining sufficient quantities of TILs from the tumour can be challenging, and some tumours may not be operable. Furthermore, the prolonged exposure to the tumour environment appears to weaken the immune cells, causing them to lose their aggressiveness. Overall, these hurdles pose significant challenges to developing a rapidly available and effective therapy, particularly in cases where cancerous tumours are growing rapidly.

Therapy with Dendritic Cells

In dendritic cell therapy, dendritic cells are first isolated from the blood. Then, selected tumour particles (peptides) are introduced into the dendritic cells, which are believed to activate T killer lymphocytes against cancer cells. The greatest difficulty seems to be the choice of the right, anti-cancer-stimulating tumour peptide that motivates T killer lymphocytes to fight cancer cells. The adoptive cell therapy with dendritic cells is well-tolerated, and some successes have been reported in initial studies, but the final evaluation is still pending (39).

Modifications to the Genome of T Lymphocytes: The Cultivation of "Super" T Killer Lymphocytes

The observation that tumour-infiltrating lymphocytes (TILs) can recognise cancer cells, but become weakened and inactive in the tumour has sparked the interest of genetic engineers. Indeed, researchers have been able to genetically engineer T killer lymphocytes in the laboratory to express tumour-specific tools that enable them to target and destroy cancer cells. While this approach has shown promise in preclinical studies, the first clinical trials in cancer patients have been associated with significant side effects, including fatalities (40).



Cascade Primed (CAPRI) Cells: The Reactivation of Sleeping Monocytes Creates an Effective Immune Cell Quartet

Surprisingly, a cell type that has been overlooked in other cell therapies has become a key focus in cancer therapy with CAPRI cells: the monocyte. Monocytes are believed to develop into dendritic cells, which in turn are considered ideal information mediators for T killer and T helper lymphocytes. As mentioned before, there are, however, monocytes that do not develop further, and it is postulated that these are normal monocytes that fall asleep while digesting suspiciously-looking peptides, instead of ringing an immunological alarm bell. Any such sleeping monocytes are suspected to play a key role in many chronic diseases, including cancer.

However, Once stimulated by T lymphocytes, these dormant monocytes can provide vital information about malignant cells to T killer and T helper cells. Notably, this information can only be shared with T lymphocytes that have not yet been activated, as activated T lymphocytes tend to become less receptive to new information pertaining to suspicious cells. Interestingly, once T lymphocytes are informed and activated, they appear to receive continuous updates from cancer-processing phagocytic cells. This real-time flow of information may serve as a safeguard to prevent the destruction of healthy tissue and fine-tune the ongoing destruction of cancer cells, which, after all, differ only slightly from normal cells. Acting as a well-coordinated team, each member of the cell quartet – monocytes, dendritic cells, T killer lymphocytes and T helper lymphocytes – plays a critical role at a specific point in time. For a more details, refer to the in-depth write-up by Dr Laumbacher (3).

The following depicts the steps involved in the production of CAPRI cells with a short description of the major immunological events that take place at each stage.

Step 1: Immune cells (so-called *peripheral blood mononuclear cells* or *PBMCs*) are separated from the patient's whole blood sample using a density gradient (Ficoll®).

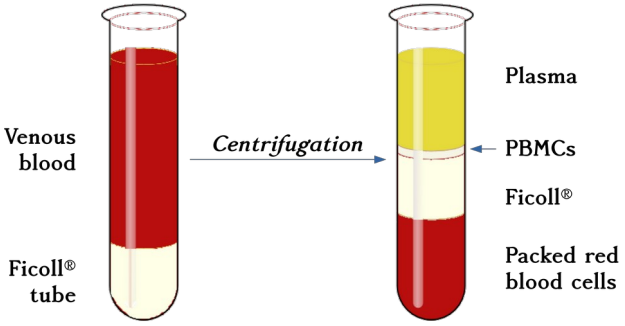


Figure II: Step 1 - Isolation of PBMCs

Step 2: The immune cells are activated using antibodies against the cell surface marker CD3. This leads to an expansion of immune cells, particularly T lymphocytes, and induces the production and release of signalling molecules (cytokines).

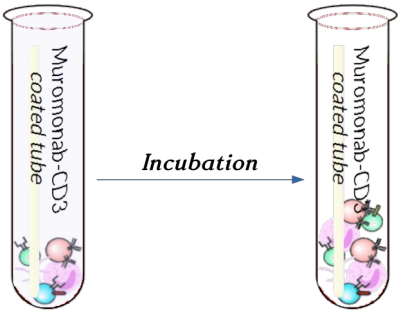


Figure 12: Step 2 - Activation of immune cells using anti-CD3

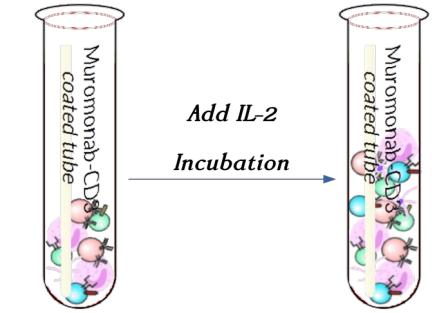


Figure 13: Step 3 - Activation of immune cells by IL-2

Step 3: The addition of the cytokine Interleukin 2 (IL-2) protects T lymphocytes from cell death and enhances the production of further cytokines. Dendritic cells develop into antigen-presenting cells (APCs) through the action of cytokines. The mixture of stimulated APCs and activated T cells, which contains many regulatory cells, is highly effective in treating autoimmune diseases and chronic infections. This cell preparation promotes a sense of well-being and is typically given in addition to other therapies.

Step 4: To generate cancer-specific CAPRI cells, non-stimulated, "naive" cytotoxic and helper T lymphocytes are added to the activated antigen-presenting cells (primarily monocytes). This initiates a complex cascade of activation steps (cascade priming), ultimately leading to a massive expansion of cell numbers, enhancement of information transfer, and increased cytotoxicity of those immune cells that become so-called *effector cells*.

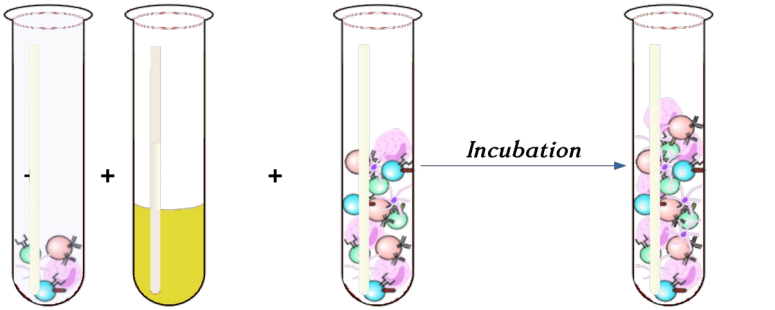


Figure 14: Figure 14: Step 4 - Activation of CAPRI cells

Part 3: Selected Patient Histories

How I was Encouraged to Treat Cancer with Immune Cells

About twenty years ago, a close friend came to me in tears, seeking help for her artist friend, Iris, who had been diagnosed with an 11cm malignant breast tumour. The gynæcologist had initially considered the smaller tumour to be benign, but it suddenly doubled in size within a few months. A renowned surgeon specializing in breast operations attempted to remove the tumuour, but cancer cells had already spread to the lymphatic vessels. He predicted that Iris had only one to two years to live. I had met Iris through her sculptures, and I wondered if immune cell therapy could help her. I had observed in the laboratory that immune cells could destroy cancer cells, and I had also seen success with immune cell therapy in women with miscarriages. I discussed my idea with Dr David Osoba, a Canadian doctor and researcher, who encouraged me to treat Iris with activated immune cells.

Figure 15: Dr David Osoba

Given the uncertainty of the new therapy and the aggressive nature of Iris's cancer, I suggested that she try chemotherapy first. However, Iris was reluctant and stopped chemotherapy after the first attempt, citing the devastating side effects that had left her feeling depressed and hopeless. She also tried hormone therapy with Tamoxifen, but it had a similar effect.

Iris then opted for adoptive cell therapy, receiving activated immune cells every week for almost seven years. While the therapy did not cure her, it improved her quality of life, and she remained enterprising and active. Unfortunately, the cancer cells continued to multiply, and six years after her diagnosis, a new tumour was removed from her second breast. Shortly thereafter, a skin metastasis appeared, which I treated with CAPRI cells. The metastasis disappeared overnight, leaving only a small blood stain on her nightgown. Although the cancer had spread too far, Iris lived five years longer than predicted and maintained a good quality of life until shortly before her death. She never regretted her decision to forgo chemotherapy and hormone therapy, and credited the immune cell therapy with giving her a longer and more fulfilling life.

My conversations with Iris were invaluable, as she was able to describe the side effects of chemotherapy and hormone therapy in detail. Her experiences led me to suggest that patients, who suffer from severe side effects of these treatments try reducing their dosages. In the case of Tamoxifen, for example, the recommended dosage was initially 50mg daily, but it has since been re-

duced to 20mg daily. Studies have shown that even lower dosages, such as 1.5mg daily, may be effective, although the side effects may persist. I now recommend a 10mg dosage to my patients, who cannot tolerate the higher dosage. In hindsight, I wonder if a lower dosage of Tamoxifen might have supported the immune cell therapy and improved Iris's outcome. Unfortunately, this was unknown at the time of her diagnosis, and all of her cancer cells had receptors for Tamoxifen, making it difficult to determine the optimal dosage.

Improved Life Expectancy and Quality of Life with CAPRI Cell Therapy in Breast Cancer Patients

Iris was fortunate to have a gynæcologist, Dr Günther, who was open to the idea of immune cell therapy. Dr Günther was a respected expert in his field, often sought out by colleagues for his broad medical knowledge. He was impressed by the visible effects of the immune cells on Iris and began recommending CAPRI cell therapy as a complementary treatment to chemotherapy and hormone therapy for his breast cancer patients. Many patients came to us through Dr Günther's referrals, as well as through word-of-mouth recommendations from satisfied patients.

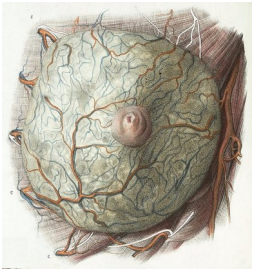


Figure 16: Jean-Baptiste Marc Bourgery (1839): Female breast anatomy

We were eager to compare the outcomes of patients who received CAPRI cell therapy with those who did not. Our study found that patients who received CAPRI cells, in addition to chemotherapy, radiation, and/or hormone therapy, lived significantly longer than patients with the same tumour stage, who did not receive CAPRI cell therapy (2). Notably, these patients already had metastases in other organs, making the results even more promising.

CAPRI Cell Therapy in Patients with Lung Cancer

The first patient with lung cancer to come to me, whom I shall refer to as Bernd, had a small-cell lung carcinoma. As the name suggests, these cancer cells are extremely small, but they infiltrate the lung very rapidly. In the past, this diagnosis typically meant a rapid decline, usually within a year. However, it is now possible to significantly prolong life with the chemotherapeutic agent 5-Fluorouracil (5-FU), as the rapidly dividing cancer cells take up much more 5-FU than healthy cells. When Bernd came to me, he was pale and emaciated, and I thought I might not be able to do anything for him. I told him that I could only try to help. He had already received chemo-

therapy and was about to start radiation therapy for the inoperable carcinoma. I contacted his clinic doctor to discuss the further treatment plans and the patient's prospects. The doctor estimated that Bernd's remaining life expectancy was at most two years, despite the effective chemotherapy, as the tumour in the lung had already caused blood vessels to become congested on his back. To my surprise, and within months, Bernd recovered incredibly under cell therapy. During subsequent X-ray examinations, Bernd was still very anxious. However, after almost twenty years, he is confident, and so am I, that he has entirely overcome the disease. I have not published Bernd's success story to date. He was, and remains, my only patient with small-cell lung carcinoma. It is possible that he may have responded particularly well to chemotherapy and radiation therapy by chance.

Let us take a view at patients with non-small cell lung carcinoma, whose treatment history has been documented (41). Non-small cell lung carcinomas are notoriously resistant to chemotherapeutic agents and radiation therapy. The prognosis is slightly more favourable, if the tumour can be surgically removed. However, only tumours of a certain size and location in the lung are amenable to surgical removal.

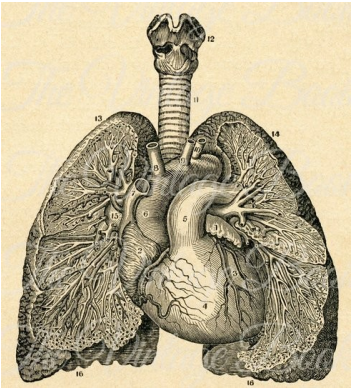


Figure 17: Anon (1885). Heart and lungs

I would like to share the story of one of these four patients, Siegfried, in more detail, as his successful treatment provided valuable insights into the optimal dose of CAPRI cells, as well as the correct therapy frequency and duration. Siegfried's tumour was discovered by a neurologist: Siegfried was experiencing significant mobility issues in his left arm, and the neurologist immediately recognised that a lung tumour was compressing the nerve that controls the arm muscles. A CT scan revealed that the cancer cells had invaded the collarbone and a nearby rib. A large lymph node above the collarbone was a direct extension of the massive tumour. Only one of many renowned surgeons was willing to operate on the tumour, but only if it would shrink or at least not grow further after combined radiation and chemotherapy. Fortunately, Siegfried had a high number of healthy immune cells in his blood, and we were able to obtain these cells before starting chemotherapy and radiation therapy. Siegfried received approximately 100 million CAPRI cells injected every weekday, with a total of around 2 billion cells per month. He attended our clinic every afternoon after undergoing combined radiation and chemotherapy. After four months, the X-ray showed a descrease in tumour size, making it possible for Siegfried to undergo surgery. The surgeon removed almost all the tumour-affected tissue, including a rib and the

collarbone, but not the cancer tissue surrounding the radial nerve, as he feared causing permanent damage to the arm. The pathologist examined all the tumour tissue removed during the operation and was astonished to find no living tumour cells. He repeated the examination, including the collarbone and rib, with the same result. This success with Siegfried provided important insights:

- Large tumour masses can be destroyed by CAPRI cells in combination with radiation and chemotherapy within three months.
- Immune cells obtained from the blood *before* they are damaged by chemotherapy and radiation therapy are highly effective, even against cancer cells altered by chemotherapy or radiation therapy.
- Continuous CAPRI cell therapy with high doses can be administered over several months without causing harmful side effects, autoimmune reactions, or a tumour lysis problem that could arise from the rapid destruction of many cancer cells.

Fifteen years after starting CAPRI cell therapy, Siegfried remains cancer-free. This is documented in detail in a case report on him and the three other patients with non-small cell lung cancer (41). Another report describes a larger number of patients with lung carcinomas, who were treated with CAPRI cells with good success at the University of Kunming in China (3).

CAPRI Cell Therapy in Patients with Stomach Cancer

For a long time, it was believed that bacteria could not survive in the stomach due to the production of hydrochloric acid and the digestive enzyme pepsin. However, most stomach cancers are caused by the acid-resistant microbe *Helicobacter pylori*. It took decades for this discovery to be recognised by scientists and eventually by health insurance companies. *Helicobacter pylori* causes the stomach to become too acidic and also leads to stomach ulcers. It can be detected in stomach juice, stool, and conveniently in the breath. In addition, the majority of patients develop a strong bad breath, which they often do not notice themselves.

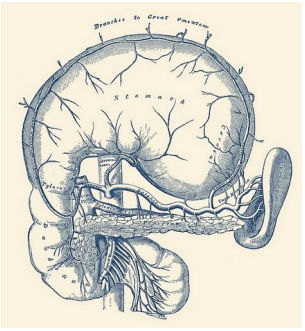


Figure 18: Anon (undated). Stomach

Of four patients with stomach cancer treated with CAPRI cells, two did not survive despite CAPRI cell therapy. One of these two patients, Erich, had an inoperable tumour and the cancer cells had already metastasised throughout the body to the liver, lungs and the brain. The CAPRI cells were unable to combat this massive combined tumour cell mass, and Erich, as an early pa-

tient to the CAPRI therapy, did not yet receive the intensive CAPRI cell therapy that is given nowadays over three months.

The second patient, Amadeus, is more difficult to evaluate, as he died from kidney failure after an attempt to dilate his œsophagus. Interestingly, no cancer cells were found in the excess abdominal fluid not uncommonly found in cancer patients.

The third patient, Horst, had a small tumour of his stomach surgically removed, and the remainder of his stomach was left intact. However, some cancer cells had already migrated to the non-operated part of the stomach. Therefore, the rest of the stomach was removed during a second operation, followed by CAPRI cell therapy over several years. Horst can only eat small servings due to the removal of his stomach and receives vitamin B_{12} injections once a month. To date, there has been no reappearance of any cancer cells.

The fourth patient, Olaf, went through a varied history of surgery and chemotherapy over a number of years before presenting to the CAPRI cell therapy. Ever since, after six years and counting, there has been no further radiological evidence with PET/CT scans of any tumour.

Visualising the Power of Patients' CAPRI Cells to Destroy their Own Cancer Cells

The efficacy of CAPRI cells in targeting cancer cells can be observed under the microscope, when cancer cells from a tissue sample have multiplied sufficiently in the incubator. While the standard preparation of CAPRI cells has proven effective in destroying cancer cells in almost all types of cancer, we found that adding an additional cytokine to the CAPRI cell cultures enhanced their effectiveness in two specific types of cancer cells, namely sarcoma and adrenal carcinoma. Therefore, we re-test CAPRI cells, whenever fresh tumour tissue grows in the incubator after an operation. Under microscopic examination, we can observe the destructive power of CAPRI cells and accurately measure the number of destroyed cancer cells using a specialised test (3).

Notably, this test appears to have limited predictive value for other adoptive cell therapy methods, such as CIK, dendritic cell therapy, or TIL therapy. Dr Barbara Laumbacher, who has successfully cultured various types of cancer cells into cell lines and developed a precise test to quantify the number of killed cancer cells, elaborates on this topic in her publication (3). Our CAPRI immune cells have demonstrated significant efficacy in destroying cancer cells from various tissues, including prostate, skin (melanomas and basal cell car-

cinomas), ovaries, muscle tissue, adrenal gland, colon and breast. These cancer types are listed in a table in our initial publication on the effectiveness of CAPRI cells in cancer treatment (2).

Adoptive Cell Therapy in Diseases of the Joints and Connective tissue

It is likely that diseases of the joints and connective tissue are largely caused by infectious diseases, which account for approximately 80% of all diseases (1). In conditions such as rheumatoid arthritis, reactive arthritis, Heberden's arthritis, ankylosing spondylitis (also known as Bechterew's disease), Reiter's disease, and soft tissue rheumatism, unfavourable variants of immune genes play a role, leading to chronic infections. These immune gene variants are not inherently bad genes, but rather are unable to mount an effective defence against certain microorganisms. Specifically, three types of bacteria – Chlamydia, Yersinia, and Klebsiella – appear to cause problems for individuals with the above immune gene variants. In ankylosing spondylitis, for example, these bacterial families can trigger symptoms such as chronic inflammation of the small joints of the spine, the joints of the pelvis and patrs of the eye, yet only in individuals with immune gene variants of the white blood cell marker HLA-B27. Historically, there were no detectable microorganisms in the joints or surrounding connective tissue, leading to the assumption that the immune cells were reacting inappropriately against the body's own tissue. However, it is now understood that debris, so-called oligonucleotides, from dead bacteria in the joints can cause painful inflammation. The effectiveness of adoptive cell therapy may be attributed to the improved removal of bacterial debris and/or the elimination of unknown microbial nests, as will be discussed in the next paragraph.

Adoptive Cell Therapy in a Patient with Ankylosing Spondylitis

Barbara Laumbacher examined the immune gene variants in 65 patients with ankylosing spondylitis in collaboration with the German Morbus Bechterew Association. One of these patients, Marlene, expressed interest in a trial therapy with activated immune cells. When she first presented, she had just received a second artificial hip joint, as her previous implant had become loose due to osteoporosis. She had also been suffering from regular bouts of iridocyclitis, a typical symptom of ankylosing spondylitis, and was treated with cortisone accordingly.

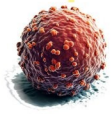


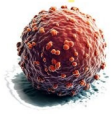
Figure 19: Skeleton showing ankylosing spondylitis

I recalled that a woman I had treated with immune cell therapy for habitual miscarriages had also experienced significant improvement in her asthma. Assuming that immune cells could have a positive effect on the autoimmune disease ankylosing spondylitis, I commenced treatment with a very low number of stimulated immune cells once a week for two months. As a result, Marlene's usual eye inflammation ceased. Interestingly, X-ray images of her second hip implant showed that the joint had remained firmly anchored in her bone ever since. This was unexpected, but further research revealed that T lymphocytes can actually prevent bone loss in mice, and may do so in humans, too (42).

It is intriguing to speculate how these few million stimulated cells can trigger such dramatic effects on the inflamed eye and bone. Perhaps they can prevent inordinate attacks by other immune cells on the inflamed tissue, much like police officers can regulate the flow of tens of thousands of vehicles with simple hand movements. It is clear that we still know far too little about such regulatory cells, which can have both positive and negative effects.

It is obvious that therapy with "good" regulatory cells can be thwarted if patients continue to infect themselves with the bacteria that cause the disease. I had to convince a sushi lover, in whom we found the white blood cell marker HLA-B27 and Yersinia in his stool, that the good effect of immune cell therapy would only last, if he avoided raw sushi fish – at least in Europe, where sushi may not be processed as hygienically as in Japan. As a result, there were no further relapses in that patient. In Marlene, we also found a chronically smouldering infection due to Chlamydia, revealed by Chlamydia pneumoniæ RNA in her blood. Marlene told us that the first eye inflammation occurred shortly after she took care of two dogs for acquaintances for four weeks.

It is unclear why treatment of the infection with antibiotics cannot prevent inflammation in the long term. It could be that even after antibiotic treatment, these bacteria survive in the body in small, secluded foci that are difficult for antibiotics to access. For example, in Reiter's disease, the eyes, urethra, and knee joints are chronically inflamed. The most common cause is a different type of Chlamydia, Chlamydia trachomatis, which can be transmitted through sexual contact. It is uncommon to find these bacteria in the blood following a recent infection. Sometimes, a small infective lesion can be found in the bladder during an endoscopic bladder examination, yet it cannot be routinely detected in the blood or urine.



This strategy of surviving in small, secluded foci makes it very difficult to detect these bacteria even with the latest diagnostic technologies. Just like immune cells, microorganisms are equally clever in constantly advancing their survival strategies. Bacterial colonies even have a cell-to-cell communication system, called quorum sensing. When the bacterial sentinels notice that it is getting uncomfortable at the fringes of the bacterial colony, they give a signal to the rest of the colony to fortify defences, for example by secreting a protective biofilm (as seen in dental plaque) that is very resistant to antibiotics.

Adoptive Immunotherapy for Joint Inflammation in a Patient with Psoriasis

Another chronic disease for which infectious causes are suspected is psoriasis, which can also lead to inflammatory swelling of the joints. Professor Jörg C. Prinz from the Policlinic of Dermatology and Allergology at the University of Munich recently discovered that streptococcal tonsillitis plays a causal role in some patients and has developed a simple and effective therapy involving a semi-annual penicillin injection (43). I was initially hesitant to treat psoriasis with CAPRI cells, but my reservations were alleviated, when I heard about a treatment for psoriasis using CAPRI cells in China. A medical colleague in China, who had treated himself with CAPRI immune cells as a precaution against cancer and also suffered from psoriasis, reported that the CAPRI cells improved his psoriasis. Unfortunately, I was unable to obtain further details about the extent of the improvement or the cell doses used. Given the unsatisfactory conventional treatment options for psoriasis, I agreed to treat a friend of an employee, whom we shall call Philippa, with CAPRI cells. Philippa also suffered from pain and swelling in her knee and ankle joints, a common accompaniment to psoriasis. The psoriasis itself was mainly visible on the extensor sides of her forearms and legs. After three weeks of therapy with CAPRI cells, the inflamed skin areas showed slight improvement, becoming less red and flatter, but the affected skin areas did not

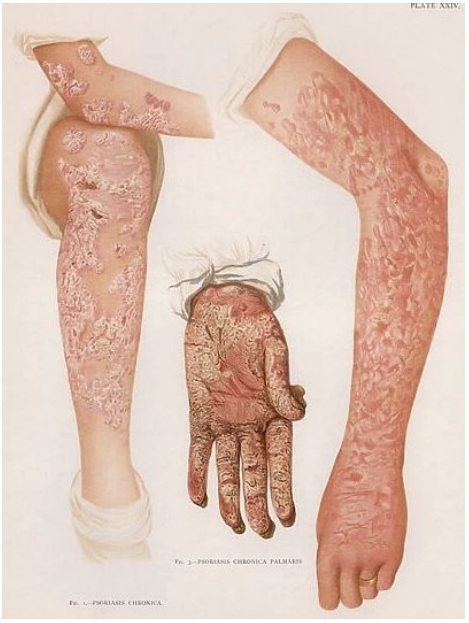


Figure 20: Anon (undated). Psoriasis

fully heal even after several months. However, the effect of CAPRI cells on the joints was pronounced: they became completely pain-free. After a year of regular weekly therapy with CAPRI cells, the inflamed skin areas had flattened further and become paler, although they remained visible. Notably, the joints remained completely pain-free for a year.

Adoptive Cell Therapy in Rheumatoid Arthritis

During the CAPRI cell treatment of a patient with breast cancer, I observed that not only were the cancer cells successfully targeted, but also that the patient's rheumatoid arthritis, affecting the finger, tœ and knee joints, showed significant improvement. In another patient, Hannelore, adoptive cell therapy proved effective even in cases of extensive joint destruction. Following the cell therapy, Hannelore has been able to tend to her garden with significantly reduced pain, despite the joint swelling having only partially receded.

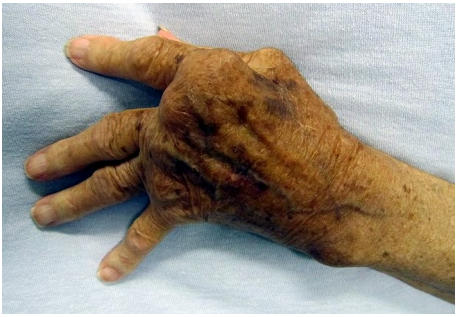


Figure 2I: Rheumatoid arthritis

Adoptive Immunotherapy for Heberden's Arthritis

In Heberden's arthritis, the finger joints become thickened, leading to a loss of mobility, although the thickened joints themselves are not particularly painful. A musician, whom we shall call Heribert, was forced to abandon not only his cello playing but also his passion for riding motorcycles, as he struggled to bend his fingers and grasp the handlebars. However, he too benefited from treatment with CAPRI cells. Within three weeks, he was able to ride his motorcycle again, and after a further six weeks, he began working on his Bach cello sonatas, a prospect he had thought was beyond hope.

Adoptive Cell Therapy for Soft Tissue Rheumatism

For joint diseases, painkillers can offer some relief, although long-term use can lead to unwanted side effects. However, in cases of soft tissue rheumatism, painkillers are often of limited benefit, and cortisone, while more effective, is also associated with significant side effects when used over an extended period. A young patient, just under twenty years old, whom we

shall call Hella, suffered from soft tissue rheumatism affecting her muscles and tendons. Fortunately, in young patients, adoptive cell therapy has been shown to have a lasting and side-effect-free impact, which can persist for years. This was indeed the case with Hella: Not only did she experience a reduction in pain following CAPRI therapy, but also an overall improvement in her sense of well-being and a restoration of her physical capabilities. Moreover, she was able to resume riding her beloved horse without experiencing pain.

ADOPTIVE IMMUNOTHERAPY FOR MISCARRIAGES

If a woman experiences recurrent miscarriages and no obvious cause can be found, such as hormonal imbalances or anatomical abnormalities, immunological issues may be to blame. The fact that a fertilised egg can implant in the uterus and develop undisturbed for nine months is a remarkable phenomenon that continues to fascinate immunologists. After all, the father's genetic material is typically foreign to the mother's immune system, which should, in theory, recognise the paternal component in the fertilised egg and reject it. However, this does not occur, and the fertilised egg is able to evade the mother's immune response.

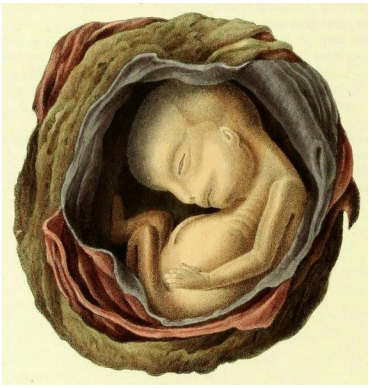


Figure 22: Joseph Perry (1834). Medical illustrations of miscarriage

Chronic, low-grade infections can also contribute to miscarriage. Undiagnosed infections in the semen can introduce infected macrophages into the uterus, triggering an immune response that may attack the fertilised egg. A patient shared with me that in some American clinics, women who have experienced miscarriages are given broad-spectrum antibiotics without attempting to identify the underlying infection before undergoing in vitro fertilisation. The clinic likely profits from this approach, as patients are refunded, if the treatment is unsuccessful. It can be assumed that antibiotics may have eliminated unknown infections in some cases.

We search for infections in both partners in cases of repeated miscarriages and treat both partners. However, antibiotic treatment is neither possible nor successful in all infections. Also, while immune cells of the phagocytic type do indeed digest microorganisms and infected cell debris, they are not sufficiently activated to stimulate T lymphocytes. For the treatment of miscarriages, we therefore proceed differently: We combine the immune cells of the man and woman in a flask with nutrient fluid and place them in an incubator. We use

the immune cells of both partners, because we do not know who of the two may be chronically infected. The mixed immune cells stimulate each other in the incubator and the lymphocytes of both the woman and the man recognise any foreign cells that may have been mixed in. In this scenario, the stimulated cells of the phagocytic type, most likely as seen in the CAPRI method, presumably train T lymphocytes to act gently and specifically against hidden microorganisms. To date, this presumed immunological mechanism could be verified in animal experiments, yet still requires confirmation in humans.

In a statistical analysis of 19 women who underwent treatment with mixed immune cells, as outlined above, presented at a gynæcology congress and published in the conference proceedings, nine out of 19 women with a history of recurrent miscarriage went on to give birth to a healthy baby (44).

Adoptive Cell Therapy in a Patient with Inflammatory Bowel Disease

Among the various bowel diseases of unknown cause (also called *idiopathic bowel diseases* or IBDs), two forms are common and significantly impair the patient's quality of life: ulcerative colitis and Crohn's disease. In both diseases, ulcers form in the inflamed intestine, and even more so in Crohn's disease, which may affect the deeper layers of the intestine. The two diseases are difficult to distinguish based solely on symptoms alone, and a definitive diagnosis is often reliant on tissue samples examined by a pathologist. This distinction is critical for determining the best course of treatment: While surgical removal of the colon can significantly improve the quality of life in patients with ulcerative colitis, Crohn's disease often leads to adhesions and fistula formation after surgery,

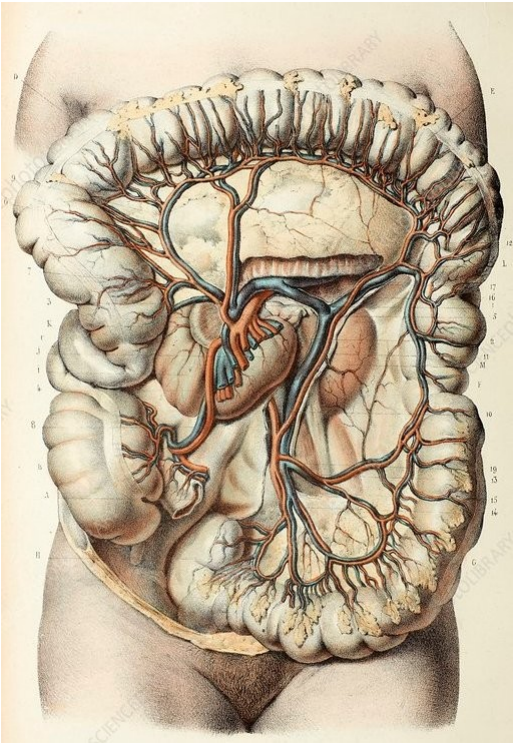


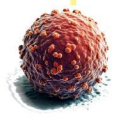
Figure 23: Constantin Bonamy, Paul Broca (1866). Intestinal vascular anatomy

making the latter a less desirable option. In both diseases, the cramp-like pains are severe, similar to the sudden onset of diarrhœa in intestinal infections.

Unfortunately, both ulcerative colitis and Crohn's disease can have a significant impact on a person's life. Wolfgang, a conductor, was forced to leave the podium repeatedly due to intestinal cramps, a symptom he had experienced several times. When Wolfgang started cell therapy, he had already been taking cortisone for several years to manage the intestinal inflammation. However, his family doctor wanted to replace cortisone with another medication that suppresses the immune system and reduces inflammation. Wolfgang was hesitant, as he wanted to have more children and was concerned that the medication could damage his sperm. Therefore, he sought an alternative. At the time, Wolfgang had already been forced to abandon his profession as a conductor due to his condition. Although I had achieved good results with adoptive cell therapy in a case of ulcerative colitis, I was less certain about its effectiveness in Crohn's disease. Wolfgang was determined to return to his profession, and I explained to him that he needed to be patient. Indeed, it was a long and collaborative process that spanned almost two years. Our shared love of classical music, including the violinist David Oistrakh and conductors Otto Klemperer and Carlos Kleiber, may have also helped to build a rapport. We even exchanged CDs. Wolfgang received CD3-stimulated immune cells, rather than CAPRI cells, which our team had found to favour the development of regulatory cells. Wolfgang continued to take cortisone, gradually reducing the dose by half every two weeks with my consent. There was no relapse, and Wolfgang was able to reduce the small dose of 5mg prednisone further to 2.5mg. Amazed by the success of the adoptive cell therapy, Wolfgang was able to return to his profession as a conductor and has been working successfully for many years. I have had the pleasure of attending some of his concerts.

Adoptive Cell Therapy in Patients with Herpes Simplex Infections

A desperate colleague contacted me to ask if I could help her young patient, Albrecht, with cell therapy. Despite trying various conventional medications, including the latest treatments, Albrecht's herpes infection had shown no improvement. The lip ulcers were not only severe, but also took several weeks to heal. The herpes healed within a few days, and Albrecht remained relapse-free for two years. The subsequent relapse was mild and short-lived. To prevent further episodes, Albrecht nowadays uses an interferon ointment with additives that I formulated, and presents for booster cell therapy once a year.



Another patient, a colleague named Frank, had himself treated with activated immune cells for his asthma. Frank had not mentioned that he occasionally developed herpes blisters on his penis. However, after a few injections, he informed me that his asthma as well as his herpes blisters had both disappeared. Ten years later, Frank has remained free of asthma and herpes.

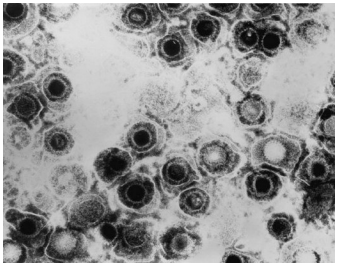


Figure 24: Herpes simplex virus

A third patient, Josef, had a rare skin disease triggered by herpes, known as erythema multiforme. Approximately ten days into each episode of herpes, a large area of skin becomes covered with red, saucer-like depressions that can form a continuous red area. We had discovered through family studies that certain traits of white blood types can affect this overreaction to herpes simplex, which we also found in Josef's parents (45). Understandably, Josef was more interested in finding a treatment for his condition rather than examining his family traits. Given our positive experience with immune cells against herpes, a successful therapy seemed straightforward. After a single injection of his activated immune cells at a moderate dose, Josef did, however, experience a peculiar side-effect, which he only told me about eight years later, when he wanted to receive immune cell therapy again: He had to urinate constantly for a day, with an urge to urinate that was so sudden and intense that it left him feeling disoriented. However, after this, Josef had no further signs of herpes and, of course, no more erythema multiforme for several years. When, after eight years, herpes blisters re-appeared on his upper lip, Josef asked me to repeat the therapy, because he wanted to prevent another episode of erythema multiforme. This time, Josef received only a quarter of the previous cell dose and experienced no adverse reaction whatsœver. His herpes disappeared entirely, and erythema multiforme has not occurred ever since.

About the calcification of blood vessels

For a long time, it was believed that ageing and cardiovascular health were closely linked, and that the hardening of blood vessels was a major contributor to this process. Calcifications were often found in the inner walls of arteries, particularly in older people. Calcification can occur uniformly, covering the entire blood vessel, or it can form individual foci, which can impede blood flow. This can be particularly problematic during exercise, when the heart needs to pump more blood. In the case of coronary arteries, calcification can lead to the death of muscle areas, resulting in a heart attack.

However, it is now clear that calcification is not just a natural part of ageing, but rather the result of several underlying factors, as will be discussed below.

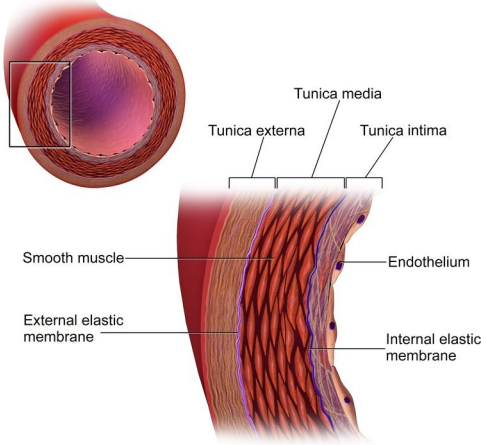


Figure 25: Structure of an artery wall

An artery's task is not only to distribute blood throughout the body, but also to be a highly adaptable vessel. With every heartbeat, blood is pushed into the large arteries in a wave-like manner, which first expand, then contract slightly, and thus push the blood further. The artery's unique architecture enables it to perform these tasks. A cross-section through an arterial tube shows an outer wall, a middle wall, and an inner wall.

The inner wall of the arteries is called intima and is a thin layer of tile-like connected cells, also known as endothelium, that forms a smooth surface for the passing blood. The inner wall of the arteries is nourished and maintained by passing blood cells. If individual blood cells are infected, microorganisms can remain in patches or arteriosclerotic plaques of the inner wall and penetrate deeper. In fact, Finnish scientists have found a specific microbe, *Chlamydia pneumoniæ*, in the arteriosclerotic plaques of almost half of people (46). *Chlamydia pneumoniæ* was, as the name implies, first found in lung infections, yet later in a variety of conditions, including schizophrenia (47). *Chlamydia pneumoniæ* preferentially infects phagocytic cells, such as monocytes and macrophages and can overwinter in these cells for a long time. Infected phagocytic cells of the lung can migrate from the lung to other parts of the body, including the inner walls of the arteries. This constitutes the first step in the formation of areas of inflammatory that can calcify. If this process occurs repeatedly, it leads to the formation of visible calcified deposits in the artery.

The middle wall of the artery should elastically absorb the pressure waves of the blood. Unlike the inner wall, it is not nourished by the blood flow, but by small arteries (arterioles) that supply blood to the middle and outer walls of the artery. If microorganisms infect these small nourishing arteries, the inside of the small arteries swells, reducing or cutting off blood supply to the middle wall of the large artery. This makes the middle wall rigid and less able to absorb pressure waves elastically. The constant stress of the pressure waves can lead to a separation of the arterial walls. For example, the pathogens of syphilis can cause the arterial walls to separate and bulge. A bulging arterial wall, also known as an aneurysm, can rupture, leading to rapid death from bleeding.

It has been proven that microorganisms can contribute to the formation of arteriosclerotic plaques and calcification through local chronic inflammation in the arterial wall. However, other important factors also play a role in the development of calcification. These include certain lifestyle factors, such as smoking, certain drugs, as well as excessively high blood fat levels, which can be particularly problematic in individuals with a genetic predisposition to high blood fat.

How can immune cells help to combat the narrowing and calcification of blood vessels? Activated immune cells can indeed play a crucial role in this process: On one hand, they can sanitise infected cells in the artery, breaking down chronic inflammation before it leads to the formation of calcified deposits. This can help to prevent the narrowing of blood vessels. But what about inflammation caused by drugs or smoking? In that case, immune cells can produce anti-inflammatory substances right on site, which can help to soothe the affected area. However, the regulatory effect of immune cells is limited, especially when irritating factors continue to be applied.

Despite the limitations of immune cells in preventing calcification, there are instances, where they have made a significant impact, as illustrated by the following two examples of a stroke patient and a patient with coronary artery disease.

Adoptive Cell Therapy in two Stroke Patients: Hemiparesis with Language Difficulties and Vegetative Coma

Rosa, a stroke patient, presented with her daughter as her carer. She was hemiplegic, able to move about her apartment with a walking stick, but struggled with speaking difficulties and depression. Despite her reservations, Rosa agreed to try immune cell therapy, largely for her daughter's sake. After the second injection, Rosa's language abilities started to improve and continued to do so significantly over the next few weeks, and she even began learning Italian. Unfortunately, the therapy had no effect on the paralysis in her right leg, and we decided to discontinue treatment.

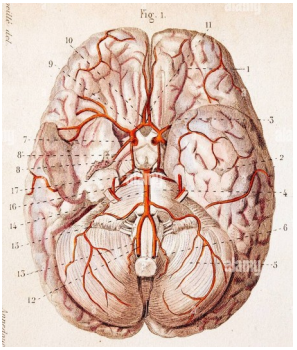


Figure 26: Anon (undated). Circle of Willis

We had a young and proactive doorman at our institute, who had given up a well-paid, demanding job to care for his mother, Maria. Maria had suffered several strokes over the years and had been bedridden for seven years, unable to swallow and requiring a gastric tube for feeding. A year ago, she could

still sit in a wheelchair and speak a few words, but her condition had deteriorated significantly. Despite this, her son and husband were eager to try immune cell therapy. During my first visit, Maria was completely motionless and had a pale yellow skin colour, which made me wonder, if I was being too optimistic about the potential benefits of the therapy. However, after the first injection of immune cells, Maria opened her eyes, and over the next few weeks, she began to show significant improvements: She turned her head to people entering the room, grasped her granddaughter's hand with her paralysed arm, and eventually began to talk to herself. Her skin colour also improved, becoming more rosy. After four and a half months, Maria was able to stick out her tongue on request, and after almost six months, she could swallow tea spoonfuls. However, despite the return of her swallowing reflex, she continued to be fed through a gastric tube. Tragically, during a morning feeding, Maria vomited the tube feeding and aspirated it into her lungs, leading to her immediate death. Her case is described in detail in a publication (48).

Adoptive Cell Therapy in Patients with Narrowed Coronary Arteries

Coronary arteries are medium-sized arteries that, among other things, supply the heart muscle with oxygen. Narrowing of the coronary arteries due to calcified deposits slows down blood flow and promotes the formation of blood clots. The blockage of a coronary artery leads to the death of the attached muscle area, a heart attack. There are various methods to prevent a heart attack. Blood thinners prevent blood clots, and the simple dilation of the artery (angioplasty) can be successful for some time. However, a more permanent solution is the placement of a plastic tube, called *stent*, inside the narrowed artery to ensure adequate blood flow.

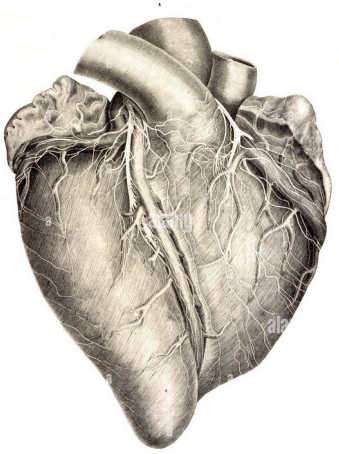


Figure 27: Anon (undated). Heart

During a conversation with a patient, the companion asked, if immune cell therapy could help with narrowed coronary arteries. The companion, Friedrich, reported that his coronary arteries had to be widened repeatedly, and the introduced stents had also narrowed again. I explained that Finnish scientists had discovered *Chlamydia pneumoniæ* in the arteriosclerotic plaques, which could be responsible for the formation of the same (46). Given that immune cells are designed to fight microorganisms, I assumed that activ-

ated immune cells could at least prevent the formation of new deposits. Friedrich, who led a large institute, had previously walked up two flights of stairs to his office, but due to the narrowing of his coronary arteries, he had to take the elevator. After a 12-week therapy with activated immune cells, the examinations showed good blood flow to the heart. Friedrich was able to resume his normal activities, including walking up two flights of stairs to his office and taking long walks. This improvement has been sustained for years.

How immune cells can protect our brain cells and preserve their performance

Activated immune cells can destroy infected cells and cancer cells, but they have many other important functions in the body. For example, when nerves are damaged, immune cells produce nerve growth factors also known as *neurotrophins*, to repair nerve pathways (49). Activated immune cells can also enter the brain and support brain cells with neurotrophins (48). Furthermore, immune cells can influence mood and have been used to treat neurological and psychiatric disorders. By nourishing nerve cells and eliminating disturbing infections, immune cells can have a significant impact on these conditions.

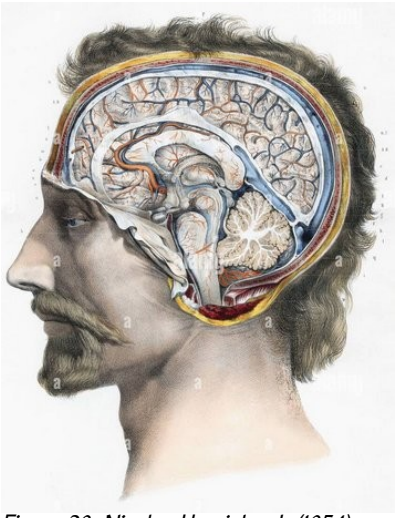


Figure 28: Nicolas-Henri Jacob (1854). Sagittal section of the human brain

Despite the growing evidence of a connection between chronic infections and neurological and psychiatric disorders, this knowledge has not yet entered the public consciousness. As a result, the search for medications that influence the psyche of patients continues without addressing the underlying cause of these disorders. The reaction to the use of activated immune cells in treating psychiatric disorders is often muted, even when there are clear therapeutic improvements. However, our reports on the treatment of patients with schizophrenia, depression, and autism have sparked public interest and been discussed in The Times (50).

One reason for the mistrust of treating psychiatric disorders with immune cells may simply lie in the relatively recent discovery that immune cells are advanced nerve cells (51). It has been discovered that immune cells communicate with nerve cells through messenger substances that can influence both immune cells and nerve cells (52). In a way, immune cells may be considered "mobile nerve cells" that can sustainably improve the quality of life in patients with neurological or psychiatric disorders.

Adoptive Cell Therapy in Patients with Multiple Sclerosis

I once did a locum for a general practitioner in a village in Bavaria, who had suffered a heart attack. As part of his practice, I visited a neighbouring community and met a woman in her mid-40s, who used a wheelchair to move around the kitchen, although her legs were not yet completely paralysed. She had multiple sclerosis (MS). Her eyes looked hopeless, and she seemed apathetic. I tried to cheer her up and asked her during the injection of the hormone ACTH, then touted as the best treatment for multiple sclerosis, if she would feel better after the injection. No, she said, she had already received ten injections and couldn't notice any improvement. ACTH stimulates the production of cortisol in the adrenal gland and was supposed to inhibit overactive immune cells that cause inflammation in the myelin sheaths of nerve fibres. There are many theories about why immune cells attack their own myelin sheaths. Like other autoimmune diseases, there are many good descriptions of what happens during the damage to the myelin sheaths, but the causes of the overactive immune reaction have not yet been found. Does MS belong to the group of diseases that are caused by an infection, like 80% of all diseases? At least, this seems to be what the pharmaceutical industry suspects, as they have marketed medications that support immune cells. These include interferons (previously interferon gamma, now interferon beta) and a vaccine that changes the balance between immune cells. This vaccine only stimulates one group of T lymphocytes, the T helper-2 lymphocytes. The latter group is supposed to prevent T helper-1 lymphocytes from destroying myelin. There are various microorganisms sus-

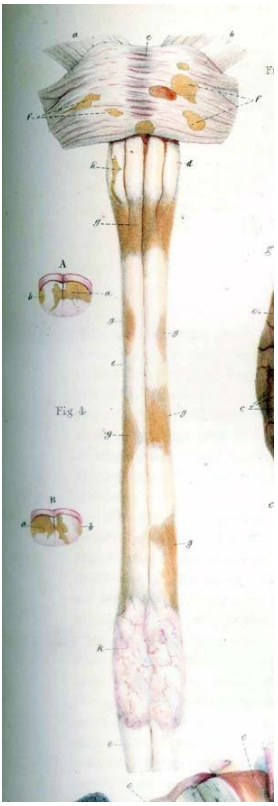


Figure 29:
Robert Carswell (1838).
Last fasciculi (MS lesions)

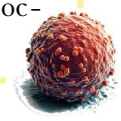
pected of triggering T lymphocytes to attack myelin cells, including Chlamydia (53). Chronic infections in the brain are difficult to detect in the blood, and even if they are detected, it does not prove that the microorganisms actually disrupt brain function or destroy brain connections. Nevertheless, we intensively searched for microorganisms in the blood of the three patients with multiple sclerosis, who wanted to undergo adoptive cell therapy.

The first of the three patients, Annabell, had studied medicine for several semesters and had deliberately chosen not to undergo the usual therapy with interferon beta. While not doubting the effectiveness of treatment with with glutamiracetate to stimulate T helper-2 lymphocytes, she decided against for fear of potential side effects. Annabell's MS diagnosis dated back several years, and she had a relatively mild course of the disease, with periods of remission. However, she had started to experience some stumbling while walking, even on obstacle-free paths. After three weeks of therapy with T helper-2-enriched immune cells, Annabell noticed a significant improvement of her symptoms. She became more relaxed overall and was able to pass her exams with good grades. She now holds a responsible position at a university and has been receiving treatment for almost 15 years.

The two other patients, Sieglinde and Ralf, received adoptive cell therapy immediately after their diagnosis. Both had a relatively mild course of MS and received no other medications besides adoptive cell therapy. Sieglinde was a student, who had failed to pass her exams twice due to excessive nervousness. After receiving T helper-2-enriched lymphocytes once a week, she passed her exams with good grades and has since worked successfully in another city. Sieglinde had no relapses under adoptive cell therapy for a year and underwent an MRI scan, which showed no new lesions in the brain.

Ralf, the third patient, worked in a factory in Munich and had increasing spasms (spasticity) in his movements. MRI scans showed the typical lesions of multiple sclerosis in the brain. Ralf had heard about adoptive cell therapy and wanted this treatment, only. He initially came twice a week and experienced a significant decrease in fatigue and spasticity. However, after a year of treatment, the spasticity returned, yet Ralf did not report it initially, assuming it was due to the natural course of the disease. After receiving adoptive immune cells once a week again, the spasticity improved quickly and eventually disappeared. Ralf is very satisfied with the immune cell therapy, which he has now been receiving for six years.

Initially, we were unable to find any evidence of an infection in Ralf. However, after the spasticity returned, we conducted a further search. Despite Ralf's initial denial of any contact with pets, he suddenly recalled not only caring for a neighbour's dog for two weeks, but also that the first spastic symptoms oc-



curred shortly after this period. Subsequent testing revealed a clear infection with the microbe *Bartonella henselæ*, which responded well to azithromycin. Notably, the spasticity resolved within two days. While this single case does not allow us to determine the true significance of this infection in Ralf's disease development, we will certainly investigate this further, if his spasticity returns. Interestingly, *Bartonella henselæ* has also been linked to an increased frequency of seizures in two of our patients with epilepsy.

Adoptive Cell Therapy in a Patient with Epilepsy

A forty year-old patient, whom we will refer to as Ludmilla, heard from one of our patients that we were investigating infections in children with epilepsy and that *Bartonella henselæ* had been found in almost half of the children. Ludmilla had a highly unusual series of illnesses. After giving birth to her child ten years ago, she fell into a coma for two weeks and subsequently experienced repeated seizures. Although the generalised seizures ceased, the severe and painful twitching of the right half of her face, including her eyelid, persisted, sometimes accompanied by unpleasant odours. Stress exacerbated the twitching and odour attacks. Ludmilla received regular Botulinum toxin injections in the muscles of the right half of her face every two months, which significantly reduced the painful twitching, which, however, left the right half of her face numb. Notably, Ludmilla had noticed a decline in her vision over the past few months, prompting us to investigate the presence of microorganisms, particularly *Bartonella henselæ*, in her blood and tear samples. It turned out that the suspected microorganism was indeed detected in both samples. Despite being a bacterium, *Bartonella henselæ* is difficult to eradicate with antibiotics, as it has the ability to enter cells, including phagocytic cells, and resist invading antibiotics. Although antibiotics halted the decline in her vision, the epileptic twitching in her face persisted. In contrast, cautious therapy with low doses of activated immune cells once a week significantly reduced the twitching and pain, rendering the three-monthly Botulinum toxin injections unnecessary.

Figure 30:
Cerrahiyetül Haniye (1465). Epileptic treatment

We also found *Bartonella henselæ* in Ludmilla's throat swab during a cold and in the biopsy sample of a small tumour on her back. The pathologists classi-

fied the tumour as a neurofibroma, typically a benign tumour that can recur even after careful removal. In another patient with recurrent tongue swelling and life-threatening shortness of breath, we detected three types of Bartonella in the blood or throat swab. This highlights that hardly any part of our body is safe from Bartonella microorganisms, not even the brain.

There has been a suspicion for some time that *Bartonella henselæ* can trigger a brain infection and epilepsy. It was even recommended that school children with epilepsy be tested for an infection with Bartonella. We have found *Bartonella henselæ* in more than a third of the sixty children with epilepsy we have examined, supporting the notion that a search for an infection with Bartonella in cases of epilepsy, as well as in other unclear and recurring disease patterns where a chronic infection is suspected.

Adoptive Immunotherapy in Patients with Schizophrenia: A Patient with Positive Symptoms

Figure 31: Anon (undated). Salmoneus

A patient who was undergoing treatment with CAPRI cells for her breast cancer approached me and asked if I could also treat a friend of hers with schizophrenia. Her friend, whom we refer to as Henry, had spent a year in a psychiatric institution due to his schizophrenia, which was characterised by so-called positive symptoms, including hallucinations, delusions, illogical changes in his thoughts or behaviour, hyperactivity, and thought disorder. For example, he had been driven to take long walks and had even swum across the Rhine river due to his restlessness.

As I believe that psychiatric diseases can often arise from infections and unfavourable immune gene variants, I asked Henry and his parents about infections he may have had before and at the onset of the disease. Diary entries revealed that Henry's persecution by inner voices began after a severe lung infection. Interestingly, an autistic child who was also treated with immune cells by us showed a similar sequence of disease development: first, a severe lung infection, followed by various thinking and behavioural disorders (54). In Henry, we found evidence of a number of recurring infections, including Chlamydia, which was described in detail in the same publication (54).

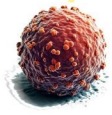
Henry contacted me just hours after the first injection, saying that he felt much better. When asked what had improved, Henry mentioned that his nervous system in his stomach, the solar plexus, had become “calmer”. After

several treatments with immune cells, another problem improved, which Henry described as a “hole in his head”. While Henry previously enjoyed visiting his parents, he now felt that these visits were more of an obligation. Henry successfully completed his university studies and is currently self-employed. He has been seeing his psychiatrist for years, who wants to maintain his current good condition with medication. Despite his improvement under immunotherapy, Henry is still afraid to reduce his psychiatric medication by even a quarter, due to concerns about the potential impact on his everyday life despite the severe side effects. Henry has remained stable overall and is able to pursue his profession daily (54,55). Although the inner voices have not disappeared, they are no longer as disturbing, but are now like well-meaning advisors, except for one less good advice: to continue smoking.

Two Patients with Negative Schizophrenia Symptoms

Two patients with a diagnosis of schizophrenia had shown little response to medication. Both exhibited negative symptomatology, a manifestation of schizophrenic symptoms that resembles symptoms of simple (unipolar) depression. Both patients lacked the motivation to engage in any activity. Alexander, an older student, had lost interest in his studies and all activities, which caused his parents significant concern. Nico, a lawyer, had abandoned his practice and also lost all drive. The parents of both patients hoped that adoptive cell therapy would bring about a turnaround.

However, the cell therapy seemed to have no effect on both patients, and both independently stopped the therapy without prior notice. Nico discontinued treatment after only a few sessions, while Alexander received one treatment per week for several weeks before stopping. However, I was surprised when I spoke with Nico's parents to gather more information. Nico's self-reported lack of progress contrasted with his parents' observations, which indicated that he had started socializing with friends again and had even resumed his law practice. Similarly, conversations with Alexander's parents several months later revealed a positive influence of immune cell therapy on Alexander. After dropping out of a language course, Alexander had been disinterested in his studies for years. However, soon after adoptive cell therapy, Alexander resumed his studies and even began looking for a job.



Infections in Schizophrenia and Depression

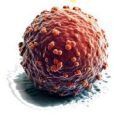
We investigated the infections we found in individual patients in larger groups using advanced diagnostic methods. In blood or brain samples from over 100 patients with schizophrenia and patients with depression, we found that *Chlamydia pneumoniæ* occurs six times more frequently and *Chlamydia psittaci* occurs four times more frequently in both blood and brain samples from patients with schizophrenia compared to controls (47,56,57). Notably, the brain samples were sent to us anonymously by the Stanley Foundation from the USA, and we did not know whether a sample came from a patient with schizophrenia, a patient with depression, or a healthy individual. Only after we had completed our analysis and reported our results did the Stanley Foundation inform us which patients and healthy individuals had been found to have bacteria.

Adoptive Cell Therapy in a Patient with Bipolar Depression

We also reported in detail the effect of adoptive cell therapy on a patient with bipolar depression, whom we will refer to as Carl (59, 60). Carl was the first patient with a psychiatric disorder to be treated with activated immune cells. His illness, bipolar depression, was characterized by phases of overactivity lasting months or years that alternated with phases of complete inactivity, resulting in extreme mood swings, from euphoria to deep depression. At the beginning of the approximately one-year immune cell therapy, Carl was bedridden and required a wheelchair to be pushed to the dinner table. Despite trying various treatments, all antidepressants had become ineffective over time, and the last-resort lithium therapy had to be discontinued due to severe kidney damage. However, after just a few weeks of adoptive cell therapy, Carl experienced a dramatic change: He suddenly got up on his own and began to take care of himself, going to the toilet, kitchen, and later the garden, and even making outings after months of being unable to do so. Additionally, he reconciled with his brother, with whom he had been estranged. Further details of Carl's remarkable response to adoptive cell therapy can be found in our previous reports (54).

Two Patients with Unipolar Depression

A patient with unipolar depression feels completely weak and joyless. Unfortunately, it can happen in medication therapies that activity returns before improved joy in life. The patient sees no sense in continu-



ing to live, but has already regained the sufficient energy to commit suicide. This risk of suicide also exists in patients with schizophrenia with negative symptoms, as in the case of patients Alexander and Nico.

The two patients with unipolar depression described below had something in common with Alexander and Nico: they were obsessed with the perception that had not yet improved. I had asked a nearly seventy year-old patient, whom we will call Josefa, who had no response to medication for depression, to keep a diary. So, I read in Josefa's diary that even under cell therapy, everything remained unchanged after eight weeks, specifically that depression sets in at 4 pm and results in a complete lack of desire to meet with any friends in the evening. In the past, she used to go out every evening. One day, she was accompanied by her husband to the consultation, who suddenly said while listening to his wife: "But Josefa, tell me, you're shopping again, you're cooking, you're meeting friends twice a week." And Josefa nodded.

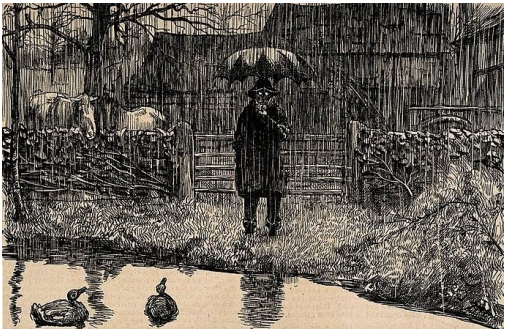


Figure 32: Punch (1869). Nervous depression

Similar were the reports of a depressive patient who had given up his design studio and retired at sixty, because he had no strength left. Let us call him George. Medications did not help or no longer helped. George came to therapy for eight weeks dressed completely in black. Towards the end of the immune cell therapy, some colourful accents appeared in his clothing. Two weeks later, he stayed away without any notice. After four more weeks, he reappeared and said that he had actually been feeling good and therefore wanted to take a family vacation in the USA; his wife later said it was the first time in years that he had wanted to take a trip. However, after a car accident on the way to the airport, he became depressed again. Now George returned all in black and decided after three injections that any further cell therapy would not make any sense. Based on my experiences with Josefa, Alexander, and Nico, who could not recognize an improvement in themselves, I called George two months later. His wife was on the phone and answered very enthusiastically, "he's doing very well, he dœsn't need any medication", and then handed the phone to her husband, who confirmed it. George's good condition lasted for three years, when he experienced a relapse, as I later learned from his wife. However, George did not return to immune cell therapy.

It seems to be a problem of immune cell therapy that it dœs not taste bitter and dœs not have, in our experience, any serious memorable side effects. Therefore, many patients, who suddenly feel well, think that it would have happened anyway, even without immune cell therapy, and in the event of a relapse, that the immune cell therapy did not help in the first place.

Adoptive Immunotherapy in an Alzheimer's Patient

Figure 33: Alois Alzheimer

Prof. Alzheimer examined the brain of a deceased patient over a hundred years ago, who had shown rapid memory loss and complete mental confusion during her lifetime. Alzheimer found numerous deposits, called *plaques*, in the brain. These Alzheimer plaques can apparently interrupt or destroy neural pathways and affect thought. A vaccine was developed from such plaques, which healed some patients, but also caused worsening and even death in some patients. It seems that the vaccine provoked an overly strong immune reaction. However, one can conclude from the healing of some patients that immune cells could possibly help, if they are stimulated correctly and not used in excessive numbers. Therefore, I told a colleague, who was caring for an Alzheimer's patient and was inquiring about the effects of immune cell therapy, that it could be used as a therapy attempt.

After Professor Alzheimer's discovery, researchers have continued to explore the potential causes of Alzheimer's disease. One area of research has focused on the role of bacteria in the development of the disease. In fact, researchers have suspected that various bacteria may contribute to the development of Alzheimer's disease. One such bacteria is *Bartonella kœbleræ*, which was found in Helga, an 86-year-old patient with Alzheimer's disease, who had been diagnosed with complete blindness in childhood. Due to frequent eye infections, her eyes were removed and glass eyes inserted. However, there were still occasional infections of the eye sockets. The diagnosis of Alzheimer's disease was made after increasing disorientation and severe memory disorders, based on various investigations in a psychiatric university clinic. Helga was looked after in a nursing home. She often quarrelled with her fellow residents and became violent sometimes, was restless at night, and was occasionally wandered off to other rooms.

I arranged with the colleague, who was caring for Helga, that he would bring her for immunotherapy once a week. A very caring nurse, whose mother had died of Alzheimer's disease, observed every change in Helga during the ensuing week. The therapy with a low number of immune cells showed a clearly

positive effect after only a few weeks. Helga became increasingly friendly and approachable towards her fellow residents and the nursing staff, who were very pleased. Although Helga was very sensitive to pain and loudly complained about the injection, she soon started to wait fully dressed every Mondays for the nurse to receive her injection. Her memory seemed to be working better again. Especially interesting was the return of her sense of touch. The blind Helga had not been able to distinguish her stuffed animals with her hands. Yet, following immune cell therapy, she regained her sense of touch.

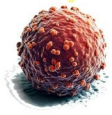
We have, of course, searched for any unrecognised infections in Helga and found bacteria from a family of bacteria that we have reported in other patients with eye problems, as well as a number of epileptic children. In Helga, it was *Bartonella kœbleræ*, in epileptic children *Bartonella henselæ*, the causative agent of cat scratch disease, both of which can cause blindness. *Bartonella kœbleræ*, which was found in Helga, may have been the reason for her childhood diagnosis of blindness.

Researchers have suspected various bacteria of contributing to the development of Alzheimer's disease. Whether *Bartonella kœbleræ* will also be found in other patients with Alzheimer's disease and whether the therapy with immune cells will also be successful in them, can only be shown by further therapy attempts. Since immune cells have developed from nerve cells, as American scientists first discovered, activated immune cells could indeed help restore destroyed nerve pathways that were not destroyed by infections (52).

Much Knowledge is Stored in Phagocytic Cells and Awaits Discovery

Humans have been discovering effective medicinal plants for thousands of years. The active ingredients of these plants could only be isolated in the last few centuries. A famous example is aspirin, whose active ingredient is obtained from willow bark. In contrast, the power of immune cells was only discovered in the last fifty years. With the transplantation of stem cells from the bone marrow in 1968 by Robert Good, immune cells were used as a therapeutic agent for the very first time.

The therapy with activated immune cells has not only proven effective in a wide range of diseases, but also showed an unexpected, yet consistent long-term “side-effect”, as it seems to improve general health and boost energy: Not only do many patients improve under CAPRI cell therapy and regain their ability to return to an independent life, but also other ailments, like migraines



and, as reported before, herpes infections, disappear, even if they were not at all the target of the cell therapy.

The advantage of therapy with one's own activated immune cells is the possibility of starting therapy with almost homeopathic cell numbers. This is a great advantage in autoimmune diseases and allergies. For example, we started with an immune cell amount in the Alzheimer's disease patient Helga, which is obtained from a thimbleful of blood. Later, we increased the dose of immune cells to ten thimbles, which apparently presented a sufficiently large number of immune cells for Helga to achieve improvements.

The production of CAPRI cells is still somewhat cumbersome, but efforts to automate this process are well underway. Last, but not least, once we have really understood the conversations of immune cells, CAPRI cells may even tell us how to get by without them.

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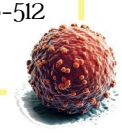

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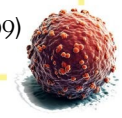

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