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Boosting the immune system can improve cancer prevention and treatment

The activation of the body's immune system to fight cancer is not only a promising therapeutic concept, but is already used in medical practice. The first immunotherapies have been approved and many more are either in the experimental stages or already undergoing clinical testing. Vaccines to prevent certain types of cancer are already being used successfully around the world.

Regulatory T cell under the scanning electron microscope.

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Cancer immunotherapy aims at using the T lymphocytes (T cells) of the immune system, which are responsible for producing antibodies and eliminating cells infected with bacteria or viruses, in order to provoke an immune response against a cancer. Research into using this impressive therapeutic approach has been going on for many decades. However, many attempts have failed because tumour cells have sophisticated strategies that prevent them from being recognised and destroyed by the T lymphocytes. For example, cancer cells secrete specific substances to keep T lymphocytes at bay or prevent them from intruding into the tumour tissue.

Regulatory T cells are a specific population of T cells that maintain self-tolerance to the body's own tissue in order to prevent autoimmune diseases and allergies. However, this means that they also suppress the body's ability to defend itself against tumour cells. Tumour cells carry immunosuppressive molecules on their surface that ensure that the body's own cells are not attacked by immune cells. However, in order for T cells to be able to recognise and attack a tumour, they need to have features that make them look different from healthy cells. It is not easy to identify suitable tumour antigens for use as target structures for vaccines or other immunotherapies due to the fact that tumour cells differ greatly from person to person as well as within a single tumour.

A breakthrough in cancer immunotherapy is close

Numerous strategies for overcoming the aforementioned difficulties have been developed and many experts believe that a breakthrough in cancer immunotherapy is close: T cells are genetically modified to be able to recognise specific structures in cancer cells; antibodies that inhibit the immunosuppressive molecules on cancer cells are used to induce a specific immune response against a cancer; the ability of the cancer cells to evade the body's immune system can now be overcome by suppressing messenger substances that are secreted by the tumour, thus making the tumour visible to the immune system. Patients with advanced cancer usually have a weaker immune response, and attempts are being made to strengthen the immune system by stimulating the formation and proliferation of T lymphocytes. A combination of different approaches seems to have the best effect.

A cancer cell spreads in the body by way of an opening in the blood vessel wall. If it is not recognised and eliminated by the body's immune system, it can settle in an organ and establish itself, i.e. form a metastasis.
© DKFZ

An immunotherapy for treating metasising melanoma (black skin cancer), which is based on an antibody against a checkpoint protein on the surface of cytotoxic T cells that suppresses an immune response, has already been approved for human application. Clinical studies to test the efficiency of immunotherapies for the treatment of advanced kidney and lung cancer are under way. A therapeutic vaccine for treating a specific type of brain tumour, i. e. low-grade gliomas that are characterised by a specific mutation in a key enzyme, is also undergoing clinical testing.

The company Vaximm is currently testing vaccines for the treatment of pancreatic cancer by targeting the tumour vasculature, which is essential for tumours to grow. Without a blood supply, the tumour cells die off. Other researchers are screening proteins on the surface of tumour cells or T helper cells for the presence of epitopes, i.e. specific peptide structures that induce an immune response and are excellent immunotherapy targets. Such peptides can then be synthesised in the laboratory and screened using bioinformatics and mass spectrometric tools.

Modified, genetically optimised antibodies and antigen-antibody complexes such as those that were previously only used as vaccines against infectious diseases, can also be used for cancer therapy, under certain conditions. Immunotherapies for the treatment of leukaemias and B-cell lymphomas have shown promising results.

Unfortunately, existing immunotherapies do not help all patients equally, and it is difficult to find out why. Some tumours have been resistant to all attempts at immunotherapy, and research is under way to change this by tailoring treatment to the personal requirements of individual patients, as is done with chemotherapies. This can only be achieved with reliable biomarkers. A test has been developed that shows whether a sought-after tumour-specific peptide is presented on the surface of tumour cells in a form that T cells can recognise. This approach might help determine prior to treatment whether a patient is likely to respond or not to the cancer vaccine.

In Germany, young girls can now protect themselves from cervical cancer.

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From prophylactic to therapeutic cancer vaccines

The first vaccine against human cancer was one that effectively prevents infection with high-risk type 16 and 18 papillomaviruses (HPV), which Harald zur Hausen had shown to be the cause of cervical cancer. Since the approval of the first HPV vaccine in 2006 (a second one was licensed in 2009), millions of girls and young women in America, Europe and Australia have been immunised and the incidence of cervical cancer has dropped dramatically in these countries. The vaccines are purely prophylactic, and therefore ineffective in women infected with HPV who have potentially already developed cervical cancer. Carcinogenic papillomaviruses may also lead to the development of skin cancers and other mucous membrane neoplasias. A prophylactic and therapeutic vaccine against white skin cancer (which occurs quite frequently) has already been shown to be effective in the animal model; clinical trials will be undertaken to assess the efficiency of the vaccine in people with compromised or weakened immune systems that are at particular risk of developing cancer. As for the development of therapeutic vaccines against cervical cancer, research is currently specifically focused on identifying suitable HPV epitopes on the surface of virus-transformed tumour cells and T helper cells.

In the past, vaccine development was mainly geared towards infectious diseases caused by viruses or other microbes. As viruses have also been shown to be one of the most important risk factors for cancer development in humans, research has therefore focused specifically on the development of vaccines that prevent or treat cancers caused by viral pathogens. In addition to HPV, these include Epstein-Barr virus (EBV) which leads to the development of different types of carcinomas. In order to develop an EBV vaccine, EBV surface proteins were used for the recombinant production of antigen-antibody complexes for activating – by mimicking an EBV infection – the immune system against B-cell lymphomas. This was the first time ever that such complexes were used for this purpose. Previously, antigen-loaded antibodies were only used for vaccines designed for immunisation against infectious diseases. Another revolutionary cancer immunotherapy approach is the development of vaccines based on messenger RNAs that code for tumour antigens and stimulate the immune system to produce macrophages and antibodies against the tumour. Curevac, a biotechnology company based in Tübingen, has developed an RNA-based vaccine for treating metastasing prostate carcinoma which is already undergoing clinical phase IIb testing.

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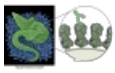

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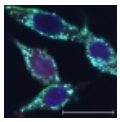

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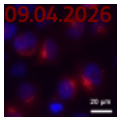

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