Herpes virus to be weaponized to fight cancer

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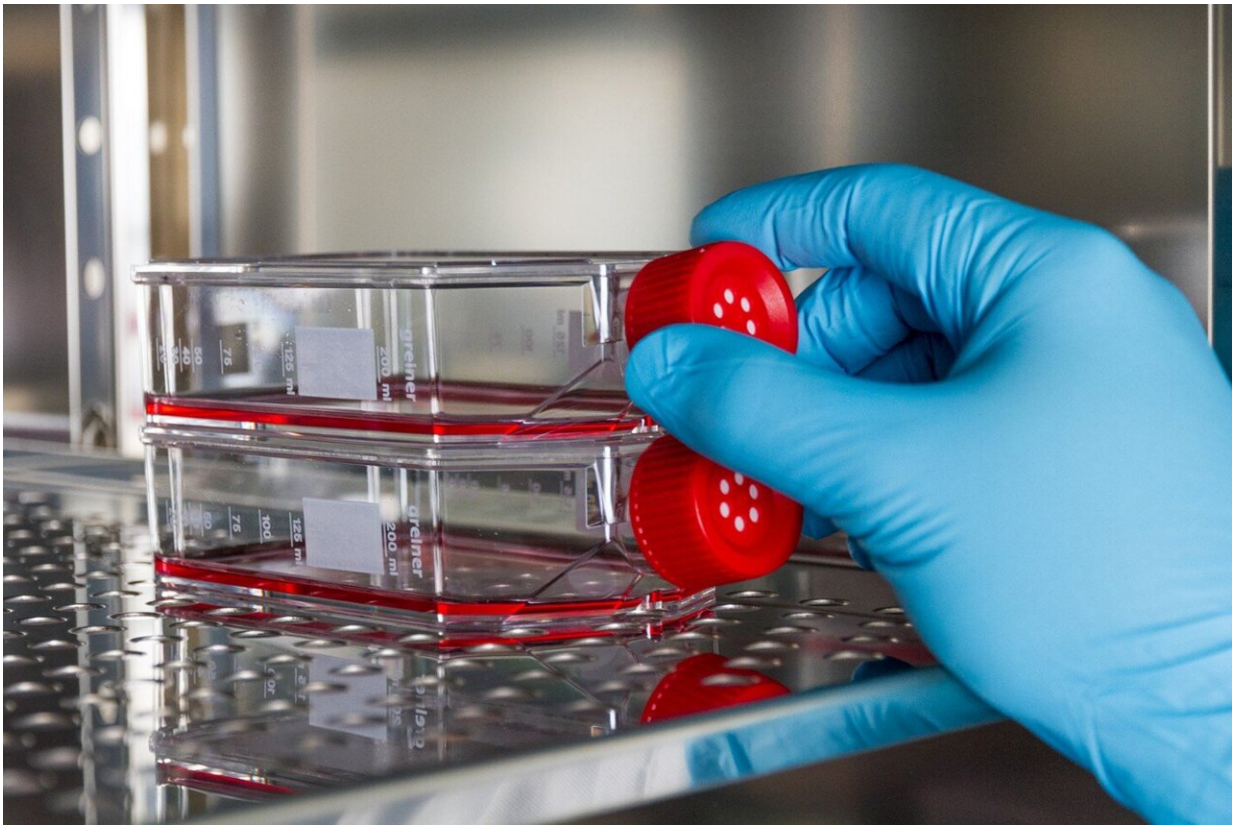

For experimental purposes, the programmable herpes simplex virus is propagated in cell cultures in an incubator. Credit: Fraunhofer-Gesellschaft

Viruses are simple in structure: They consist of a small amount of genetic material wrapped in proteins and lipids. Measuring just 20 to 200 nanometers in size, they can only be detected with an electron microscope. Yet their ability to hijack living cells and exploit them for

multiplication is what makes viruses unique. They often destroy their host cells in the process, and that's when animals and humans get sick—or now, healthy: Prof. Susanne Bailer and her team at Fraunhofer IGB in Stuttgart have succeeded in genetically modifying the herpes simplex virus type 1 in such a way that it can be used as an effective weapon against tumor cells.

Stopping disease-causing genes in their tracks

The herpes virus is known for the painful, unsightly blisters it causes on the lips. However, herpes viruses can also induce encephalitis, especially in those with a weakened immune system. Prof. Bailer, who heads up the Virus-based Technologies innovation unit at Fraunhofer IGB, has pulled off a real feat: She has managed to deactivate the genes of the virus that cause disease, thus rendering it suitable for treatment. The genetic material of the herpes virus consists of DNA, not RNA as in the case of the SARS-CoV-2 coronavirus, for example.

"The DNA genome is much larger than the RNA genome, meaning that numerous additional genes can be accommodated there. So when we're looking to reprogram the virus, we have a lot of genes at our disposal," explains Prof. Bailer, who has been researching herpes viruses for 20 years. A further advantage here is that the core technologies that can be used to genetically modify herpes viruses already exist.

Buoyed by the development of the COVID-19 vaccine, significant progress has been made in this field of research over the past few years. The AstraZeneca vaccine is based on adenoviruses, which cause colds in chimpanzees but are harmless to humans. The modified viruses pass the information required to develop vaccine antigens into human cells, at which point SARS-CoV-2-specific antibodies are formed. Overall, Prof. Bailer believes that AstraZeneca's success has bolstered research into genetically modified viruses and largely dispelled previous concerns.

Oncolytic virotherapy to stimulate the body's own immune defense

Prof. Bailer and her team have succeeded in improving the genetic engineering methods used to manipulate the herpes viruses, thus allowing them to incorporate a target control. "This ensures that our viruses enter cancerous cells when we inject them directly into the tumor, rather than healthy ones. They then multiply and cause the cells to burst." This process releases tumor markers that enable the body's own immune system to fight the cancer. "In addition, we activate the immune response with specific proteins that our viruses release when they reproduce. The immune system then recognizes the tumor cells and eliminates them."

Prof. Bailer is also hoping to use this process to combat undetected metastases outside the tumor site. "The immune system is the most powerful weapon we have to fight cancer. Using our virus and the released tumor markers, we are aiming to stimulate the immune system in a targeted way so that the body can basically treat itself."

Initial success stories in the fight against lung cancer

Initial preclinical tests using what is being referred to as the oncolytic virus were carried out by the Fraunhofer IGB team as part of the TheraVision project, in cooperation with the Fraunhofer Institutes for Cell Therapy and Immunology IZI, for Toxicology and Experimental Medicine ITEM, and for Silicate Research ISC. The researchers engineered the virus specifically for use in the treatment of non-small-cell lung cancer. The mortality rate for this type of cancer is high. Only 22% of all female patients and 17% of all male patients survive the first five years after a lung cancer diagnosis, and the prognosis is even worse for non-small-cell carcinoma because of its early metastasis.

Viral immunotherapy could also prove effective against metastases

The results of the studies are promising. The tumor cells were successfully eliminated, and the viral immunotherapy may also be effective against metastases. "We need to explore this further," says Prof. Bailer. It is still too early for clinical trials. "However, the prospects in this regard are good, because the herpes simplex virus has another decisive advantage over other viruses—we can press an 'emergency stop button.' If unforeseen side effects occur during the treatment of weakened cancer patients, there is a reliable way of stopping the viral multiplication process using an extremely effective antiviral drug that has been tried and tested for almost 50 years."

However, further studies will need to be carried out before it can be used in clinical settings: "We need to better understand the mechanisms of action to unlock the full potential of viral immunotherapy. In any case, we have now developed a viral platform technology that can be used for other types of tumors in the future."

Provided by Fraunhofer-Gesellschaft

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