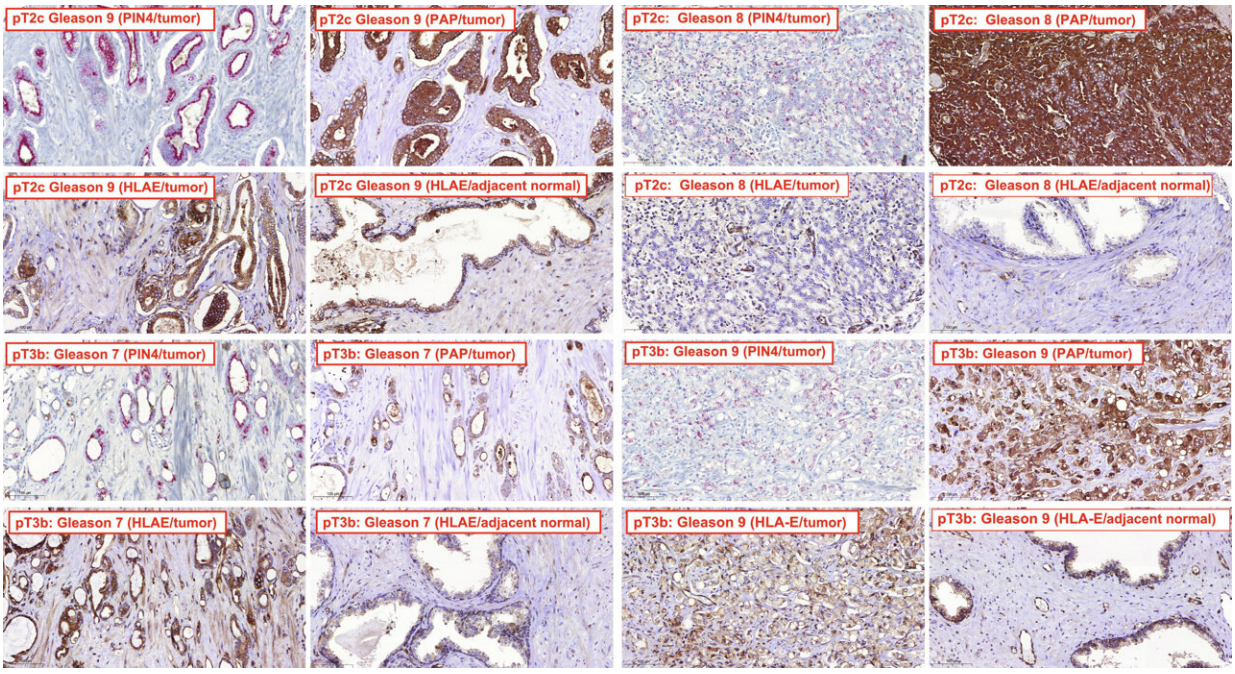
Researchers discover vaccine originally created for HIV may also combat cancer

May 29 2024, by Angela Yeager



HLA-E expression in PCa. IHC analysis of PCa or adjacent normal tissue for expression of HLA-E, PAP, and PIN4. TMAs were prepared and processed as described in Materials and Methods. Representative IHC of PCa tumor tissue and adjacent normal tissue are shown for Gleason 7, 8, and 9 tumors stained for HLA-E using a polyclonal antiserum. Pathological tumor (pT) stages of PCa are indicated with pT2c representing localized bilateral PCa, whereas pT3b represents locally advanced PCa. Staining for PAP and PIN4 is additionally shown for the tumor tissue. Credit: *Science Advances* (2024). DOI:

10.1126/sciadv.adm7515

An Oregon Health & Science University-developed platform for cytomegalovirus-based vaccines shows promise as a "shield" against cancer. The findings were recently published in the journal *Science Advances*.

Cytomegalovirus, or CMV, is a common virus that infects most people in their lifetimes and typically produces mild or no symptoms.

Cancer cells, like many viruses, often evade the immune system by escaping T cell control; T cells help protect the body from infection. OHSU researchers used CMV to transport cancer-related antigens that would cause an immune response. This triggered the production of T cells that specifically target cancer cells and established a long-lasting defense by the immune system.

"We show that cytomegalovirus can induce unconventional T cells to cancer antigens and that these unconventional T cells can recognize cancer cells," said Klaus Früh, Ph.D., professor in OHSU's Vaccine & Gene Therapy Institute, or VGTI. "The idea is that by throwing a type of T cell against the cancer that the cancer hasn't seen before, it will have a harder time evading immunity."

Früh and his colleagues Louis Picker, M.D., professor in VGTI, and Scott Hansen, Ph.D., associate professor in VGTI, have been working on developing this vaccine platform since the early 2000s. In 2016, their OHSU startup company TomegaVax was acquired by San Francisco-based Vir Biotechnology. The company is currently testing the platform

in a human clinical trial for HIV.

Their initial research focused on using the platform as an HIV T cell vaccine. While the first human clinical trials for the HIV vaccine established safety of the platform, the researchers have since modified the vaccine to elicit the desired immune responses. They expect the first batch of immune response data from the clinical trial later this year.

Expanding the platform

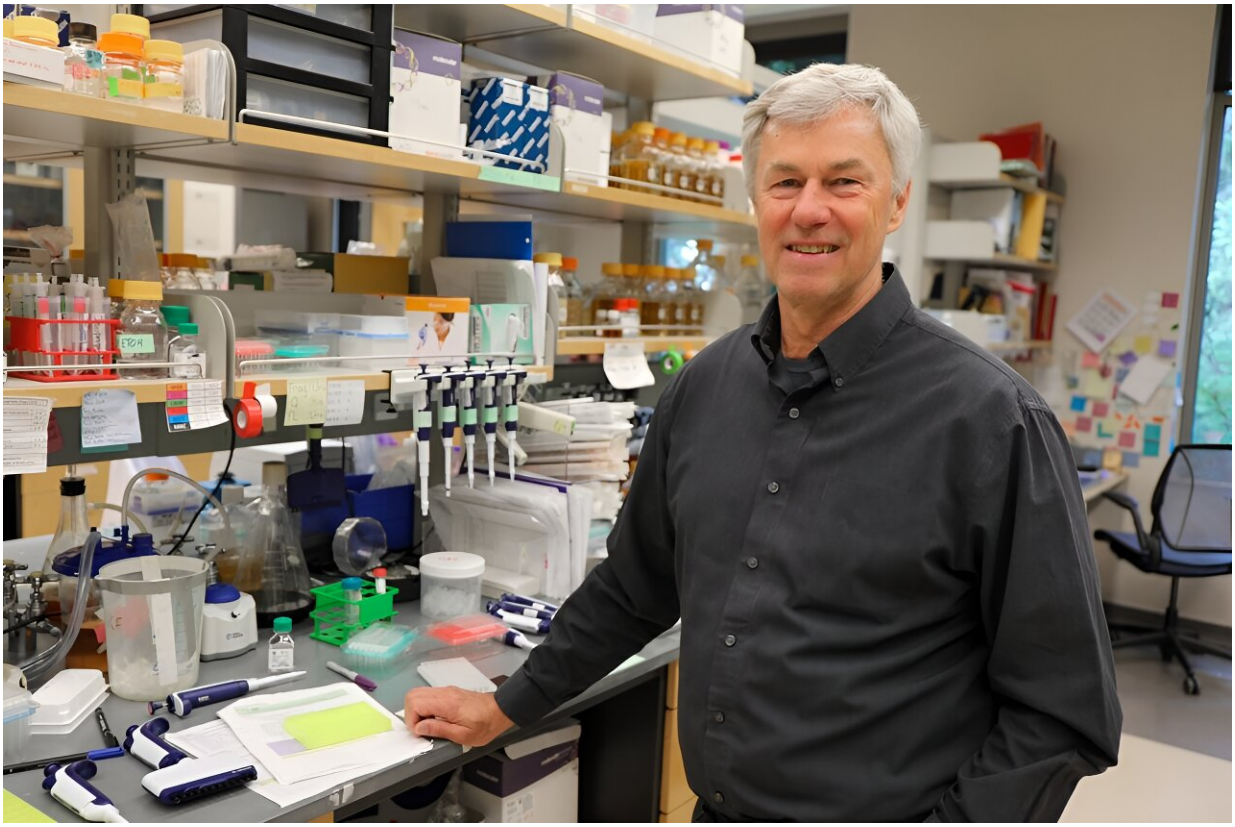
The new study expands their preclinical research, showing the promise of the CMV vaccine platform against cancer.

Researchers used genetically modified rhesus CMV to induce cancer-specific T cells in rhesus macaques at OHSU's Oregon National Primate Research Center. In their earlier preclinical research, they showed that the rhesus CMV can be genetically programmed to stimulate T cells differently from typical vaccines. These T cells recognize infected cells in a unique manner.

They aimed to answer two questions: Can the vaccine made from rhesus CMV prompt an unusual immune response against common cancer antigens? And if so, can these unique immune cells identify and attack cancer cells?

The answer to both questions is yes. The way T cells reacted to cancer-related antigens was similar to how they reacted to viral antigens, both in terms of strength and precision. Working with Mt. Sinai Hospital in New York, they also found that when the animal model was exposed to a prostate cancer antigen, T cells became activated by prostate cancer cells. This suggests that the cancer cells could be targeted by this unique immune response.

"Eliciting T-cells to cancer antigens is not easy, because you are trying to elicit an immune response to a self-antigen, which the immune system has been trained not to do," Früh said. "Overcoming this immunological tolerance is a challenge for all cancer vaccines."



Klaus Früh, Ph.D., professor in OHSU's Vaccine & Gene Therapy Institute, investigates the potential of cytomegalovirus-based vaccines. With colleagues Louis Picker, M.D., and Scott Hansen, Ph.D., both in VGTI, they have found their vaccine platform shows promise as a "shield" against cancer. Credit: OHSU/Christine Torres Hicks

The hope: Cancer vaccine

The potential for the vaccine platform to help the fight against cancer is exciting, Früh said. Since the T cells elicited by CMV vaccines are maintained for life, it might be particularly useful as a way to keep cancers such as prostate or breast cancer from reoccurring. The hope is that, if someone has had prostate cancer once, the vaccine would prevent that cancer from coming back.

"If you've had cancer, you are worried the rest of your life that it may come back," he said. "So having a vaccine that can elicit cancer-specific T cells that act as an immune shield continuously patrolling your body and that would protect you for the rest of your life, it's just really exciting."

The researchers first need to find out if the results they found in an animal model can be replicated in humans. CMVs are species-specific, so the rhesus CMV may not yield the same immune response in humans. The ongoing clinical trials for HIV will give early evidence to help decide if further testing and development would yield results. Human clinical trials for other pathogens and cancers are next on the horizon.

More information: Ravi F. Iyer et al, CD8 + T cell targeting of tumor antigens presented by HLA-E, *Science Advances* (2024). DOI: 10.1126/sciadv.adm7515

Provided by Oregon Health & Science University

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