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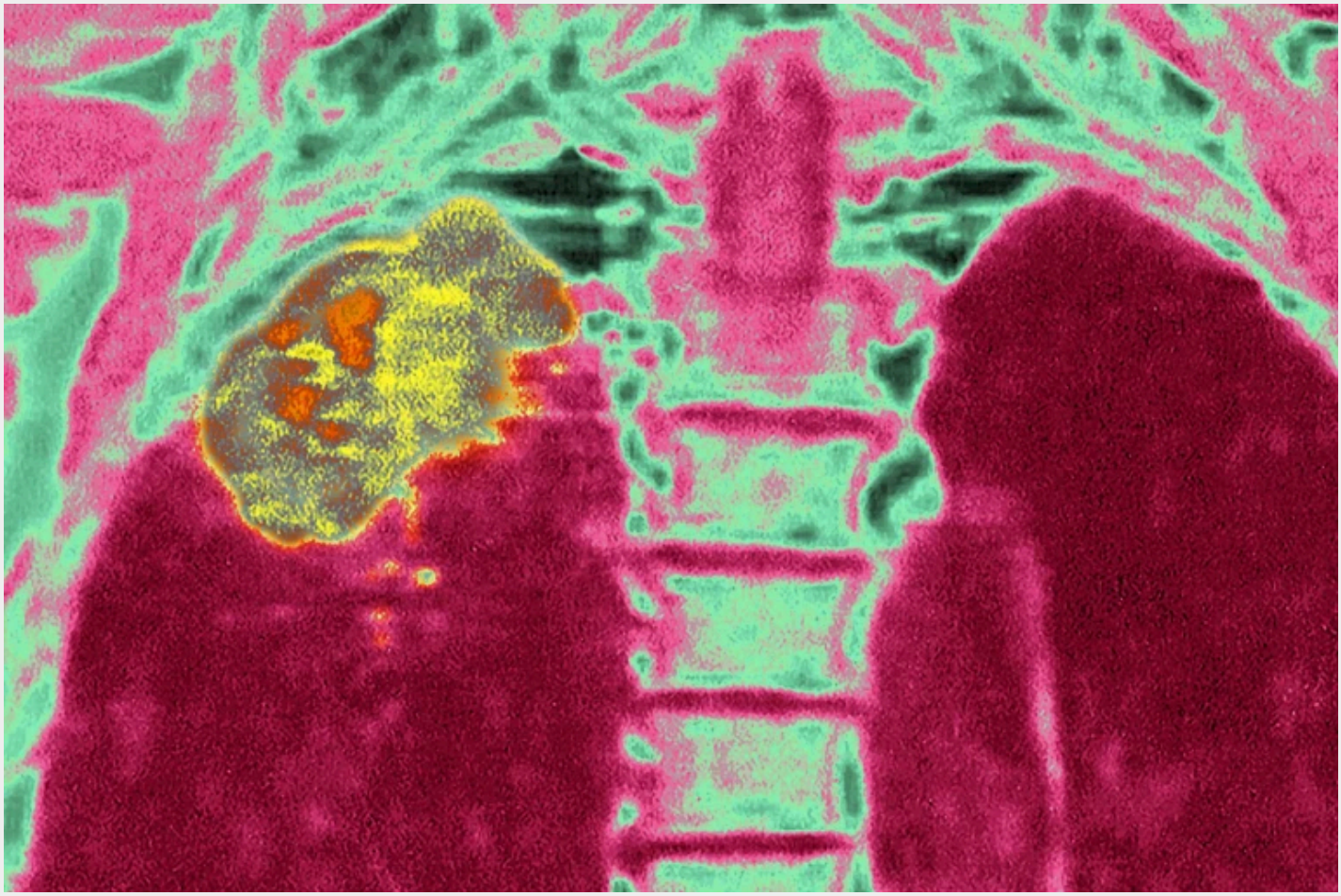
How to trick the immune system into attacking tumours

Lab-grown viruses make cancer cells resemble pig tissue, provoking an organ-rejection response.

By Saima Sidik



A tumour (yellow; artificially coloured) grows in a person's lung. Credit: Avallini James/BSIP/SPL

Scientists have disguised tumours to 'look' similar to pig organs — tricking the immune system into attacking the cancerous cells. This ruse can halt a tumour's growth and even eliminate it altogether, data from monkeys and humans suggest. But scientists say that further testing is needed before the technique's true efficacy becomes clear.

It's "early days" for this novel approach, says immuno-oncologist Brian Lichty at McMaster University in Hamilton, Canada. "I hope it stands up to further clinical testing," he adds. The work is described today in *Cell*[1].

Viral trickery

To devise a strategy against cancer, the authors took a cue from a challenge facing people who receive organ transplants: the human immune system recognizes transplanted organs as foreign objects and tries to eliminate them.

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This challenge is especially acute for transplanted pig organs, which could supplement the supply of donated human livers, kidneys and more. But human antibodies immediately attach to sugars that stud the surfaces of pig cells, leading to rapid rejection of the transplanted tissue. (Pig organs transplanted into humans are bioengineered to forestall the antibody response.)

Immunologist and surgeon Yongxiang Zhao at Guangxi Medical University in Nanning, China, wondered whether he could harness this runaway immune response and direct it against tumours.

To do so, Zhao and his colleagues combined lessons from transplant medicine with an anti-cancer strategy called oncolytic virotherapy, which has been around for decades,

Lichty says. This approach harnesses viruses to either attack cancer cells or provoke the immune system into doing so.

Co-opting a poultry pathogen

For this therapy, Zhao's team chose Newcastle disease virus, which can be fatal to birds, but causes only mild disease or none at all in humans. Applied to tumours on its own, the virus fails to elicit an immune response that is strong enough to be helpful clinically. So the team engineered Newcastle disease viruses to carry the genetic instructions for an enzyme called α 1,3-galactotransferase. This enzyme decorates cells with certain pig sugars — the very ones that provoke a fierce antibody attack in humans who receive a pig-organ transplant.

The researchers first tested the therapy in cynomolgus monkeys (*Macaca fascicularis*). Five monkeys with liver cancer that received only saline died an average of four months after treatment. But five monkeys with cancer that received the enzyme-encoding virus survived for more than six months.

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The researchers then tested the enzyme-encoding virus in 23 people who had a variety of treatment-resistant cancers, including those of the liver, oesophagus, rectum, ovaries, lung, breast, skin and cervix. Results were mixed. After two years, two people's tumours had shrunk, but had not completely disappeared. Five people's tumours had stopped growing. Other participants' tumours stopped growing but then began expanding again. Only two participants did not receive any benefit from the treatment, although two other people dropped out of the trial before the end of the first year.

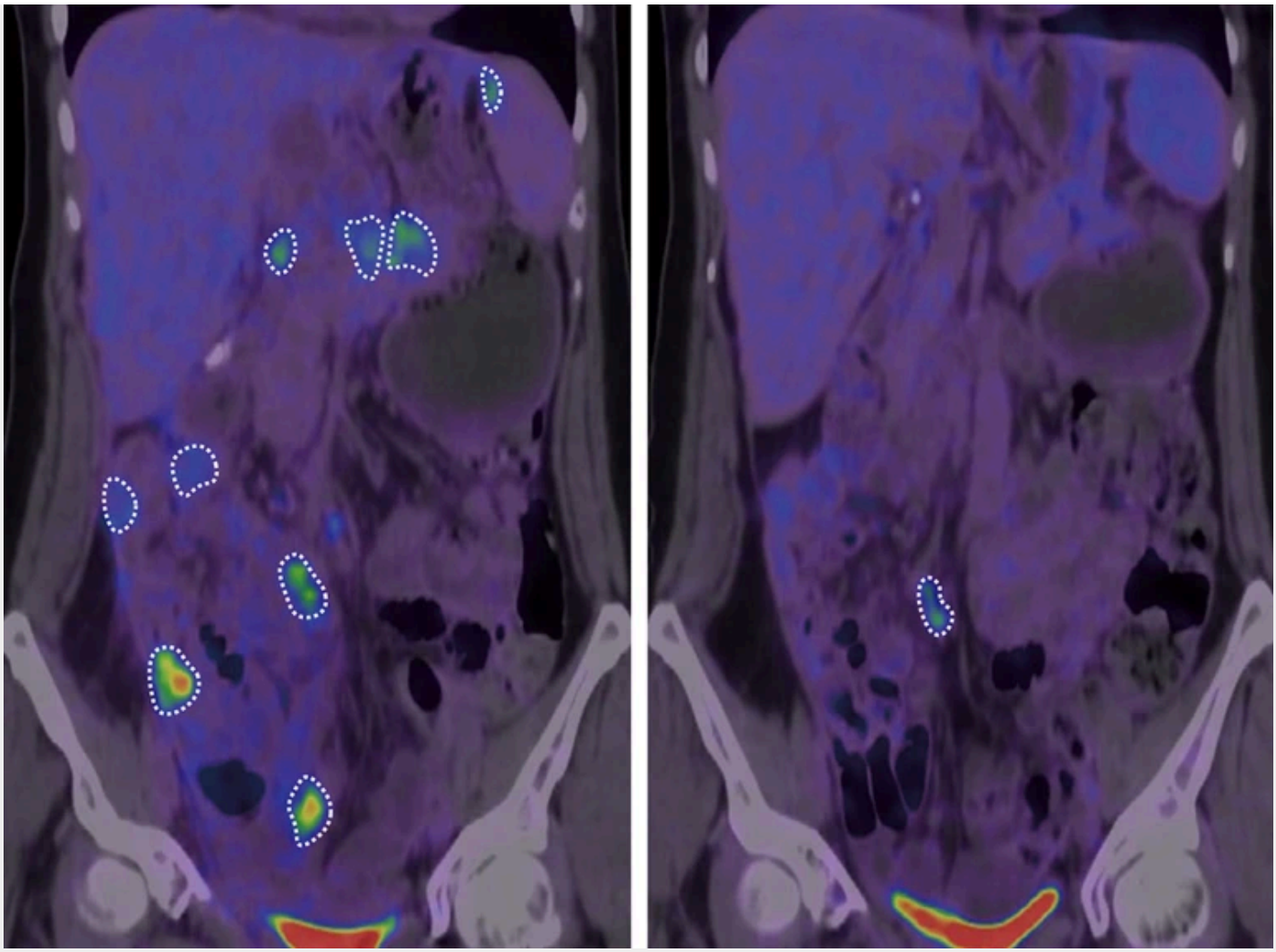
It's "a little unusual" for a treatment to show promise across such a wide range of cancer types, Lichty says. He muses that perhaps infection with just a small amount of enzyme-

encoding virus sparks a self-perpetuating immune response, potentially explaining the broad applicability of the approach.

For the people who did not benefit much from the treatment, it might have been because their disease had progressed too far and the treatment worked too slowly, Zhao says. He and his colleagues have plans to test the system further, in phase II and III clinical trials, over the next few years.

Hopeful but hesitant

Cancer researchers are intrigued by the approach, but caution that it's too early to say how effective it will be. "I'm very hopeful," says molecular virologist Masmudur Rahman at Arizona State University in Tempe. But cancers are highly variable diseases, and further work is needed to investigate who is most likely to benefit from this treatment, he says.



Cancerous tissue (left; circled in white) in the abdomen of a clinical trial participant had dwindled (right) three months after treatment with an anti-cancer virus. Credit: L. Zhong *et al./Cell*

One possibility is that immune responses initiated by the enzyme could be maintained with checkpoint inhibitors — drugs that stop immune responses from turning off — to yield effective treatments, says immunologist Samuel Workenhe at the University of Guelph in Ontario, Canada. "I think that there is some sort of synergy you can expect," he says.

If the people receiving treatment shed engineered viruses into the environment, it might infect wild birds or poultry, Rahman says. Zhao and his colleagues did not observe shedding, but Rahman says that, ideally, the virus used clinically would be engineered to not infect birds.

It will also be important to assess whether the body's typical immune responses are enough to protect healthy organs from Newcastle disease, Rahman says. If not, the enzyme might turn the immune system against healthy tissue. The authors "have not even discussed that", Rahman says. Zhao adds that this is a point he and his colleagues plan to address in future studies.

doi: https://doi.org/10.1038/d41586-025-00126-y

References

1. Zhong, L. *et al. Cell* https://doi.org/10.1016/j.cell.2024.12.010 (2025).

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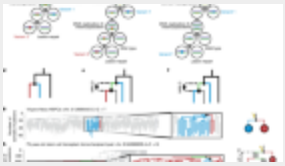

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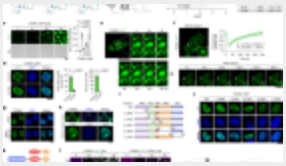

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