

Viral therapy could boost limb-saving cancer treatment

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Viruses designed to target and kill cancer cells could boost the effectiveness of chemotherapy to the arms and legs and help avoid amputation, a new study reports.

Scientists at The Institute of Cancer Research, London, tested the effectiveness of a genetically engineered version of the [virus](#) used to vaccinate against smallpox.

They found use of the virus alongside isolated limb perfusion chemotherapy – given directly to blood vessels supplying the affected arm or leg as an alternative to amputation – was more effective in rats than either treatment on its own.

The study, published in the *International Journal of Cancer* today (Tuesday), was funded by the Dr Lucy M Bull Lectureship and Research Fund and supported by the NIHR Biomedical Research Centre at The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research (ICR), with additional funding from The Royal College of Surgeons of England and Sarcoma UK.

Researchers at the ICR, in collaboration with colleagues at The Royal Marsden, used a vaccinia virus known as GLV-1h68. This virus had been modified to infect and kill [cancer](#) cells.

The study suggests that the combination, if successful in the clinic, could help some skin cancer and sarcoma patients avoid radical surgery or amputation, greatly improving their quality of life. A clinical trial to test the combination in cancer patients has now been approved and is expected to take place in the near future.

Isolated limb perfusion uses a heart and lung bypass machine connected to the arm or leg to separate its blood supply from the rest of the body. This allows a high dose of a chemotherapy drug (in this case melphalan) to be given directly and specifically to the diseased limb without causing

toxic side-effects to the rest of the body.

Chemotherapy is given alongside a drug called tumour necrosis factor-alpha (TNF-?) which helps make [blood vessels](#) more leaky, allowing melphalan to get to the tumour more effectively. In this study, researchers found that TNF- ? also helped the virus get to the tumour more easily.

Researchers first tested the treatments on rat sarcoma cells in tissue culture, and found combining modified vaccinia virus and melphalan killed more cells than either treatment on its own.

They tested the combination in rats with advanced sarcoma and found it slowed [tumour growth](#) and prolonged survival by 50% compared to standard ILP therapy (melphalan and TNF-?). Rats given the combined therapy survived a median of 24 days, compared to 16 days for rats who received standard limb perfusion treatment, 15 days with the modified virus alone, and 11 days with no treatment. They saw the modified virus had no adverse effects on the rats, adding to existing evidence that the virus has a good safety profile.

Isolated limb perfusion allows drugs to be given in much higher doses than could be tolerated by the whole body. It is used by doctors as a last line of treatment for advanced skin cancer or sarcomas in the hope of avoiding amputation. However, the technique is not always successful and researchers have been searching for ways to make the approach more effective.

Professor Kevin Harrington, Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, and Honorary Consultant at The Royal Marsden NHS Foundation Trust, said: "Our research shows that a virus that targets and kills [cancer cells](#) could significantly improve an existing treatment for advanced [skin cancer](#) and sarcoma in the arms and legs. Combining modified virus and isolated limb chemotherapy doubled

survival times in the laboratory, which gives us hope that it might be effective in the clinic. We have approval to start clinical trials on the combination therapy and hope to begin testing in patients in the near future.

"The beauty of this technique is that the arm or leg is isolated, making it harder for the virus to be destroyed by the immune system – something that has been a stumbling block for virus treatments in the past. The study also showed that the virus didn't cause any adverse effects, adding to evidence that it should be safe to use as a cancer treatment.

Professor Paul Workman, Deputy Chief Executive of The Institute of Cancer Research, London, said: "Viral therapies have been suggested as a possible treatment for cancer for a number of years, but trials of cancer-killing viruses alone have not proved effective enough. Combining cancer-killing viruses with chemotherapy gives the tumour a double hit that could offer an improvement over existing treatment, and might help cancer patients avoid amputation."

Provided by Institute of Cancer Research

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