

► WT1190F was detected by the Catalina Sky Survey, a programme based at the University of Arizona, Tucson, aimed at discovering asteroids and comets that swing close to Earth. At first, scientists didn't know what to make of this weird body. But they quickly computed its trajectory after collecting further observations and unearthing 2012 and 2013 sightings from telescope archives, says independent astronomy-software developer Bill Gray, who has been tracking the debris with astronomers at NASA's Jet Propulsion Laboratory in Pasadena, California.

WT1190F travels in a highly elliptical orbit, swinging out twice as far as the Earth–Moon distance, Gray says. His calculations show that it will hit Earth at 06:20 UTC, entering the ocean about 65 kilometres off the southern tip of Sri Lanka (see 'Splashdown'). Much, if not all, of it will burn up in the atmosphere, but "I would not necessarily want to be going fishing directly underneath it", Gray says.

The object is only 1 to 2 metres in size, and its trajectory shows that it has a low density, and is perhaps hollow. That suggests an artificial object — "a lost piece of space history that's come back to haunt us," says Jonathan McDowell, an astrophysicist at the Harvard–Smithsonian Center for Astrophysics in Cambridge, Massachusetts. It could be a spent rocket stage or panelling shed by a recent Moon mission. It is also possible that the debris dates back decades, perhaps even to the Apollo era. An object seen orbiting Earth in 2002 was eventually identified as a discarded segment of the *Saturn V* rocket that launched the second mission to put humans on the Moon.

WT1190F is a rare breed of space object. Researchers are currently tracking only 20 or so artificial objects in distant orbits, says Gareth Williams, an astronomer at the Minor Planet Center in Cambridge, Massachusetts. There are probably many more such pieces of space junk in orbit around the Earth–Moon system, but it is impossible to say how many. No others are known to have made the return trip to Earth, although it is likely that some have done so without anyone noticing, McDowell says.

Drolshagen plans to get spectral information on the object, which may help to identify it, and he hopes to coordinate impact observations conducted on ships or aeroplanes. But that may be the end of the concerted effort to study this class of object. Unlike near-Earth asteroids, space debris that flies well away from Earth has not commanded significant amounts of funding or attention. The US military, which tracks space debris, says that it lacks the ability to identify WT1190F or to predict its path.

"There is no official, funded effort to do tracking of deep-Earth orbits the way we track low-Earth orbit," McDowell says. "I think that has to change". ■

## ONCOLOGY

# Cancer-fighting viruses near market

*Anticipated approval in Europe and the United States could spur a promising field with a chequered past.*

BY HEIDI LEDFORD

An engineered herpesvirus that provokes an immune response against cancer seems poised to become the first treatment of its kind approved for use in Europe and the United States. On 23 October, advisers to the European Medicines Agency endorsed the approval of a genetically engineered virus called talimogene laherparepvec (T-VEC) to treat advanced melanoma. In April, advisers to the US Food and Drug Administration (FDA) did the same, and the agency is expected to approve T-VEC this month.

With dozens of ongoing clinical trials of similar 'oncolytic' viruses, researchers hope that such an approval could generate the enthusiasm and cash needed to spur further development of the approach. "The era of the oncolytic virus is probably here," says Stephen Russell, a cancer researcher and haematologist at the Mayo Clinic in Rochester, Minnesota. "I expect to see a great deal happening over the next few years."

Many viruses preferentially infect cancer cells. Malignancy can suppress normal antiviral responses, and sometimes the mutations that drive tumour growth also make cells more susceptible to infection. Viral infection can thus ravage a tumour while leaving abutting healthy cells untouched, says Brad Thompson, president of the pharmaceutical-development firm Oncolytics Biotech in Calgary, Canada.

## EARLY ATTEMPTS

The strategy builds on a phenomenon that has been appreciated for more than a century. Physicians in the 1800s noted that their cancer patients sometimes unexpectedly went into remission after experiencing a viral infection. These case reports later inspired doctors, particularly in the 1950s and 1960s, to raid nature's viral cupboard. Clinicians injected cancer patients with a menagerie of viruses. Sometimes the therapy

destroyed the tumour, and sometimes it killed the person instead.

Unlike the wild viruses used in those mid-twentieth-century experiments, some of today's anti-cancer viruses are painstakingly engineered. T-VEC, for example, has been altered to drastically reduce its ability to cause herpes. Researchers also inserted a gene encoding a protein that stimulates the immune system, which makes the virus even more potent against cancer (see 'Going viral against cancer').

As more researchers entered the field and initiated small clinical tests, they began to produce enticing anecdotes. Russell recalls the case of an individual with myeloma who remained sick after undergoing two stem-cell transplants. A tumour on the left side of her forehead had degraded the bone underneath and was putting pressure on her brain. Yet treatment with an experimental virus sent her into complete remission (S. Russell *et al. Mayo Clin. Proc.* **89**, 926–933; 2014). "She's a star patient who convinced us that this oncolytic paradigm can really work," he says.

But statistics — not anecdotes — rule over drug approvals. In 2005, regulators in China approved an oncolytic adenovirus called H101 to treat head-and-neck cancer, after evidence showed that the treatment could shrink tumours. Those trials stopped short of assessing improvements in patient survival — a measure often required for FDA approval. Since then, a medical-tourism industry has built up in China for people who cannot get the therapy in their home countries.

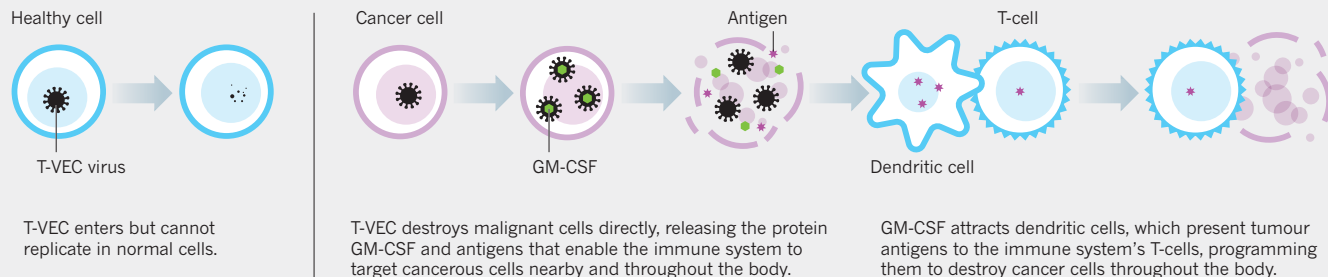
Then, in May this year, a team supported by biotechnology giant Amgen of Thousand Oaks, California, published promising results from a large clinical trial of T-VEC (R. H. Andtbacka *et al. J. Clin. Oncol.* **33**, 2780–2788; 2015). The virus both shrank tumours in people with advanced melanoma and extended patient survival by a median of 4.4 months. Yet statistically, survival benefits fell just a hair's breadth of significance. "That raised the question, 'Well, what is statistical significance? Is this an active agent or not?'" Russell says.

He and others note that the therapy — which must be injected directly into tumours — seemed to rein in cancer elsewhere in the

**Viral infection can ravage a tumour while leaving abutting healthy cells untouched.**

## GOING VIRAL AGAINST CANCER

The virus-based cancer therapy T-VEC infects tumour cells and destroys them by stimulating the immune system to direct an attack against malignant cells in the body.



body as well. This is a sign that results are real and that the virus sparked an immune response as intended, Thompson says.

### ROOM FOR IMPROVEMENT

Administering T-VEC in combination with cancer immunotherapy could prove particularly effective, notes Stephen Hodi, an oncologist at the Dana-Farber Cancer Institute in Boston, Massachusetts. In June 2014, a small clinical trial by Amgen suggested that this combination may boost effectiveness over that of the immunotherapies alone.

And researchers continue to look for ways

to improve T-VEC. In particular, they would like to be able to deliver the therapy systemically, so that the virus could target tumours in organs that are difficult to reach with an injection. This would require a technique to prevent the body from mounting an immune response to the virus prematurely, which would disable it before it could reach and kill tumour cells, says Howard Kaufman, a cancer researcher at Rutgers Cancer Institute of New Jersey.

To that end, those in the field are experimenting with a smorgasbord of viruses — from poxviruses to vesicular stomatitis virus, which does not normally infect humans but causes a

blistering disease in cattle. Oncolytics Biotech is studying a virus that hitch-hikes through the body on certain blood cells, camouflaged from the immune system.

If cancer-killing viruses could be delivered to their targets through the bloodstream, rather than via injection directly into the tumour, they could be used to treat a greater range of cancers. Thompson envisions a day when physicians will be able to peruse a menu of oncolytic viruses and select the best fit. "Each virus interacts with the immune system differently," he says. "They could have a role in pretty much all cancer therapy." ■