

News in focus

attributed the resilience of the antibody to its target: a particular region of the spike protein that does not tend to accumulate mutations.

VIR-7831 joins a list of monoclonal antibodies that have been tested against COVID-19, some of which – including Lilly's combination – have already been authorized for use in the United States and elsewhere. But there has been relatively little uptake by US physicians and their patients, says Angus.

One problem, he says, is that although results have been press released, companies have yet to publish data from key clinical trials in peer-reviewed journals. The drugs are also expensive and must be administered by infusion in a specialized facility, such as a hospital or outpatient-treatment centre – a difficult task when medical resources have already been stretched by a surge in cases.

Mixed messages

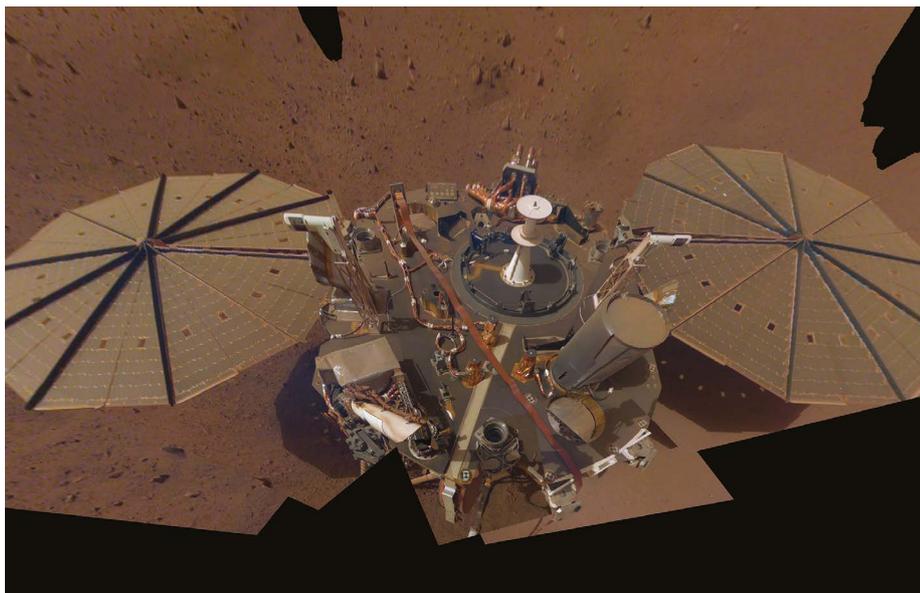
Another challenge has been mixed messaging. Earlier in the pandemic, some key clinical trials involving people who had been hospitalized with COVID-19 found no benefit from monoclonal antibodies. Many researchers had anticipated that result: monoclonal-antibody therapy is expected to work best early in disease, and the late-stage symptoms of severe COVID-19 are sometimes driven more by the immune system itself than by the virus.

Even so, those clinical-trial failures created a narrative that competed with positive results in studies of milder infections, says Angus. "People would say, 'But I thought it didn't work,'" he says. "It's totally getting in the way."

And although studies in mild infections have shown promise, they are too small to allow researchers to draw definitive conclusions, says Saye Khoo, a pharmacologist at the University of Liverpool, UK, who is leading the UK AGILE Coronavirus Drug Testing Initiative. Only a small fraction of people with mild COVID-19 will progress to severe disease, meaning that although the trials enrolled hundreds of participants, the number of those who were hospitalized or died was low.

But it will be a long wait until everyone is vaccinated, and monoclonal antibodies could provide an important bridge between vaccines and the treatments that work for people who are hospitalized, says Jens Lundgren, an infectious-disease physician at the University of Copenhagen and Rigshospitalet. "It is not a replacement for vaccines, but it is a plan B," he says, adding that the drugs could be particularly important for those who cannot mount an immune response to vaccination.

The speed with which these monoclonal antibodies were developed holds a lesson for future pandemics, says Khoo. "These compounds are without a doubt exciting," he says. "There will be other pandemics coming to us. This has been a real lesson in how to be prepared."



NASA/JPL-CALTECH

InSight snapped this dusty selfie in early 2019 after deploying its seismometer.

MARS'S CORE HAS BEEN MEASURED — AND IT'S SURPRISINGLY LARGE

Mars becomes the first inner planet after Earth to have the size of its core estimated.

By Alexandra Witze

Scientists have peered into the heart of Mars for the first time. NASA's InSight spacecraft, sitting on the Martian surface with the aim of seeing deep inside the planet, has revealed the size of Mars's core by listening to seismic energy ringing through the planet's interior.

The measurement suggests that the radius of the Martian core is 1,810–1,860 kilometres, roughly half that of Earth's. That's larger than some previous estimates, meaning the core is less dense than had been predicted. The finding suggests the core must contain lighter elements, such as oxygen, in addition to the iron and sulfur that constitute much of its make-up. InSight scientists reported their measurements in several presentations last week at the virtual Lunar and Planetary Science Conference, based in Houston, Texas.

Rocky planets such as Earth and Mars are divided into the fundamental layers of crust, mantle and core. Knowing the size of each of those layers is crucial to understanding how the planet formed and evolved. InSight's measurements will help scientists to determine how Mars's dense, metal-rich core separated from the overlying rocky mantle as the planet cooled. The core is probably still molten from

Mars's fiery birth, some 4.5 billion years ago.

The only other planetary bodies for which scientists have measured the core using seismology are Earth and the Moon. Adding Mars will allow them to compare and contrast how the Solar System's planets evolved. Similar to Earth, Mars once had a strong magnetic field generated by liquid sloshing around its core, but the field's strength dropped sharply over time, causing Mars's atmosphere to escape into space and the surface to become cold, barren and much less hospitable to life than Earth's.

Simon Stähler, a seismologist at the Swiss Federal Institute of Technology in Zurich, reported the core findings in an 18 March presentation for the virtual conference. Stähler declined an interview request from *Nature*, saying the team intends to submit the work for publication in a peer-reviewed journal.

The work builds on earlier findings from InSight that detected layers in the crust. "Now we start to have that deep structure down to the core," said geophysicist Philippe Lognonné in another pre-recorded talk. Lognonné, at the Paris Institute of Earth Physics, heads InSight's seismometer team.

The spacecraft, which cost nearly US\$1 billion, landed on Mars in 2018 and is the first mission to study the red planet's interior. The stationary lander sits near the Martian

equator and listens for ‘marsquakes’, the Mars equivalent of earthquakes. So far, InSight has detected around 500 of these, meaning the planet is less seismically active than Earth but more so than the Moon. Most marsquakes are small, Lognonné said, but nearly 50 have been between magnitude 2 and 4 – strong enough to provide information on the planet’s interior.

Just as seismometers do on Earth, InSight measures the Martian core size by studying seismic waves that have bounced off the deep boundary between the mantle and the core. With information from enough of these waves, InSight scientists were able to calculate the depth of the core–mantle boundary and hence the size of the core. The seismic data also suggest that the upper mantle, which extends to around 700 to 800 kilometres below the surface, contains a zone of thickened material in which seismic energy travels more slowly.

In an effort to replicate conditions inside planetary cores, other researchers have squeezed combinations of chemical elements at high pressures and temperatures in the laboratory. InSight’s estimate of Mars’s core density agrees with many of their results, says

Edgar Steenstra, a geochemist at the Carnegie Institution for Science in Washington DC.

InSight might be running out of time to make discoveries. Dust has been piling up on its 2-metre-wide solar panels, cutting down the amount of power the spacecraft can generate. Mars is also moving towards the farthest point from the Sun in its orbit, which will further limit the craft’s opportunity to recharge.

“This is going to cause us to reduce our instrument usage,” says Mark Panning, InSight’s project scientist at the Jet Propulsion Laboratory in Pasadena, California.

In January, the team already had to give up on its German-built ‘mole’, a thermal probe that was supposed to bury itself in the soil and measure heat flow, but which encountered problems with friction and couldn’t dig deep enough.

Drastic temperature changes on Mars that occur when day turns to night, and vice versa, create noise in the signals that InSight’s seismometer collects. That’s because the tether connecting it to the lander lies exposed on the planet’s surface. So InSight is now trying to bury the tether by scooping dirt on to it, with the aim of insulating it.

found ways to grow a menagerie of organoids, including miniature livers, cervical cancers and snake venom glands.

Welling up

Tear glands, which are also called lacrimal glands, are a particular challenge to study, says Darlene Dartt, who studies tear production at Massachusetts Eye and Ear in Boston. The glands are located above each eyeball, behind the bony orbit of the eye, making them difficult to biopsy. Clevers’ lab used their expertise to work out culturing conditions for cells from mouse and human lacrimal glands. To stimulate tear production, they then exposed their organoids to several chemicals, including the neurotransmitter noradrenaline, that relay messages between nerve cells and glands.

Because the organoids lack ducts, ‘tear’ production causes them to swell. “If there had been a little duct, there would have been droplets,” says Clevers. And when the team transplanted the organoids into mice, the assemblages matured and developed duct-like structures containing proteins found in tears.

The team hopes that the cells can be used to study tear glands, and to screen for drugs that affect tear development. Clevers and his colleagues have already used CRISPR genome editing to study tear-gland development, and have found that a gene called *Pax6* is important in guiding cells to take on a tear-gland identity. *Pax6* is a known regulator of eye development: expressing the fly version of *Pax6* on the leg of a fruit fly will cause an eye to develop there.

Clevers’ lab is now teaming up with Dutch naturalist and television-show host Freek Vonk to study structures resembling tear glands in crocodiles. The team hopes to use the organoids to study actual ‘crocodile tears’, which the reptiles use as a way to excrete salt.

Transplant potential

Organoids derived from human cells could also eventually provide material for transplants, to replace diseased or damaged tear glands. Clevers’ group and its collaborators have developed salivary-gland organoids that will be tested in clinical trials starting this summer for people who suffer from dry mouth, a condition that can cause tooth decay and difficulty in chewing and tasting.

Those salivary-gland trials could serve as a testing ground to work out methods that could then be adapted for future tear-gland transplants, says Dartt. In the meantime, she says, the work that Clevers’ team has done in characterizing tear glands – including creating a detailed cell-by-cell map of the structures and their organoids – has demonstrated that the glands are more heterogeneous than was previously appreciated and could send researchers back to reinterpret old data. “That has implications for a lot of studies.”

SCIENTISTS GROW TEAR GLANDS IN A DISH — THEN MAKE THEM CRY

Organoids made of tear-producing cells offer chances to study, and possibly treat, eye disorders.

By Heidi Ledford

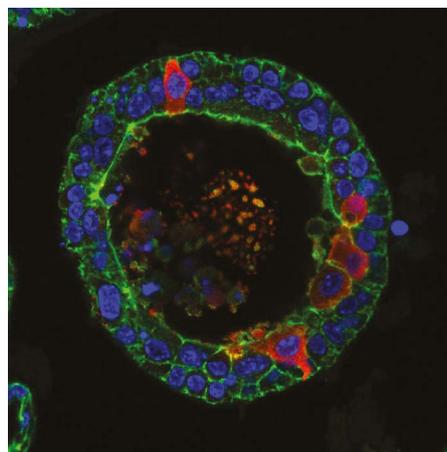
At first, it took a long time – up to a day – to make the cells cry. But, with experience and a little prodding, the researchers eventually made them weep in only half an hour.

The tearful cultures, reported in *Cell Stem Cell* on 16 March (M. Bannier-Hélaoui *et al. Cell Stem Cell* <https://doi.org/10.1016/j.stem.2021.02.024>; 2021), are the first tear-gland ‘organoids’ – 3D assemblages of cells that are designed to resemble miniature versions of organs. Organoids of the glands that produce tears could be used to study and eventually treat disorders that cause dry eyes, including an autoimmune condition called Sjögren’s syndrome.

“It’s very promising,” says ocular pathologist Geeta Vemuganti at the University of Hyderabad in India.

In addition to their role in displaying emotion, tears help to lubricate and protect the eye. Dry eyes can be painful, inflamed and

prone to infection. To study tear production, developmental biologist Hans Clevers’ laboratory at the University Medical Center Utrecht in the Netherlands developed a way to grow tear-gland cells as organoids. The group has



The organoids produce a tear-like fluid (red).

Correction**Mars's core has been measured — and it's surprisingly large**

This story erroneously stated that the only planetary bodies to have their cores measured were Earth and the Moon. In fact, this is true only for seismological measurement; other bodies have had their cores measured using different techniques.