remain a persistent threat. The receptor protein is present in very similar versions in many mammals, including bats, non-human primates, and various domestic animals. The virus might therefore easily jump between species, and humans might continue to be reinfected from a potentially wide range of animal reservoirs. This aspect of DPP4 is consistent with results published last year[5] showing that hCoV-EMC could infect bat, pig and human cells *in vitro*, an interspecies promiscuity not seen in the SARS virus or other coronaviruses.

From a public-health standpoint, it will be important to learn whether human cases of hCoV-EMC — so far largely centred on the Middle East — are caused by occasional jumps from animal reservoirs, or whether the virus has adapted and is now a distinct human virus spreading between people. The answer could dictate whether control measures should focus on human-to-human transmission or on transmission from livestock.

Tests in people who were in close contact with patients made ill by hCoV-EMC suggest that it does not, in fact, pass easily between humans. Volker Thiel, a coronavirus researcher at the Kantonal Hospital in St Gallen, Switzerland, and an author of the study[4] showing that the virus easily infects human cells, says that animal models are needed to better understand the factors affecting transmission.

Non-human primates are often used in coronavirus research, but researchers are also keen to study hCoV-EMC in more manageable species such as mice and ferrets. Bart Haagmans of the Erasmus centre, an author of the most recent *Nature* paper, says that this is difficult. Up to now he has been unable to infect ferrets, which he admits is "a bit surprising". It is unclear whether features of the virus or of the animal are the obstacle, he adds.

***"What we need is classic gumshoe epidemiology."***

Many of the human cases seen up to now cluster in families, which often indicates spread between humans but can also result from exposure to the same animal or environmental source. But cases in three members of the same family in the United Kingdom last month seemed to show unequivocal human spread. "What we need is classic gumshoe epidemiology," Lipkin says — to learn whether the virus is present in other animals, how prevalent it is, how people contracted it and whether it is shed into the environment, for example in faeces.

Genomic data from viruses isolated from infected people would also help, Drosten says. If the nucleic acid sequences of hCoV-EMC from different human cases are very similar, that might suggest an ancestral virus that has become an established human virus. But if the virus is only occasionally jumping to humans from an animal reservoir, one would expect to see far greater genetic diversity.

The biggest question is whether the novel coronavirus is truly the killer that the current data suggest — the mortality rate is more than 50% — or whether there are many undetected mild or asymptomatic cases. To answer this requires large-scale testing of the population, in particular of people living near outbreaks who have not fallen ill, to see if they have antibodies to the virus in their blood. That would indicate that they have been infected.

The assays needed have been developed in Drosten's and other labs, and Drosten insists that they are ready to use. Other researchers worry, however, that some tests might generate false positives by detecting other coronaviruses. Perlman says that it is urgent to start testing, especially in the Middle East. "This is the key issue." ■


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BIOTECHNOLOGY

# DNA tool kit goes live online

*Standard control sequences aim to make genetic engineering more predictable.*

**BY EWEN CALLAWAY**

The latest shopping website is open for business, offering unusual wares: DNA tools to help biologists to engineer life.

The DNA sequences — which allow precise control of gene activity in the bacterium *Escherichia coli* — are the first output of BIOFAB, based in Emeryville, California, which calls itself "the world's first biological design-build facility". Launched in 2009 with a US$1.4-million grant from the US National Science Foundation, BIOFAB aims to advance synthetic biology by creating standard biological 'parts' in the form of DNA sequences that control gene expression. These standard sequences should allow biologists to engineer cells that can make medicines and perform other useful tasks simply by plugging in various sets of genes.

The sequences are meant to overcome a key barrier to synthetic biology: genes inserted into an organism do not behave predictably, even in such a well-understood workhorse as *E. coli*. "You would think after a generation of genetic engineering, expressing genes with precision in an organism as well utilized as *E. coli* would be pretty straightforward. It turns out it's not," says BIOFAB co-director Drew Endy, a synthetic biologist at Stanford University in California.

MARGOT HARTFORD

**BIOFAB's directors Drew Endy (left) and Adam Arkin hope that their facility will help to industrialize synthetic biology.**

For a cell to express a gene — that is, transcribe it into an RNA molecule and then translate that RNA into a protein — other sequences recognized by the cell's machinery must precede it. A promoter sequence is needed to make an RNA transcript, and a ribosome binding site (RBS) is crucial for protein translation.

Over the past three decades, scientists have amassed collections of these sequences and used them to express genes in which they are interested. Some sequences tend to be 'strong' and others 'weak', resulting in varying levels of RNA and protein being produced.

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But a team led by Endy and BIOFAB co-director Adam Arkin, of Lawrence Berkeley National Laboratory in Berkeley, California, has found that the activities of those sequences are far from predictable. In two papers published online this week in *Nature Methods*[1,2], the team reports inserting many different combinations of promoters and RBS sequences in front of genes encoding fluorescent proteins, and then measuring the level of protein that was made. "It was a bloody mess," says Arkin, with each promoter–RBS combination having varying effects depending on the gene.

He and Endy also cite an earlier finding that a scientist hoping to express a protein at a particular level has just a 50% chance of producing the required amount within a factor of two. Such hit-or-miss expression poses a major challenge to synthetic biologists who would like to create genetic circuits involving dozens of genes.

As a solution, the BIOFAB team designed promoter and RBS sequences for *E. coli* that do not interfere with downstream DNA, so that their effects are independent of the specific gene they are paired with. The sequences should provide scientists with a much tighter grip on gene expression, offering around a 93% chance of hitting a desired level of expression within a factor of two[2]. Researchers can obtain the sequences for free online (see http://www.biofab.org/data), and Arkin says that some of his colleagues are already finding them useful.

Endy and Arkin's team also devised a statistical method[1] to measure the variability in the performance of their promoter and RBS sequences, and indeed any genetic part to be used in synthetic-biology applications. The method should allow researchers to create a kind of specification sheet for each biological part, making it easier for scientists to develop and share their work.

Randy Rettberg, a synthetic biologist at the non-profit organization the iGEM Foundation in Cambridge, Massachusetts, who has worked with Endy on similar projects, says that more labs should follow BIOFAB's lead and industrialize the production of biological parts. And synthetic biologist Alistair Elfick of the University of Edinburgh, UK, says that the BIOFAB products should help synthetic biologists to design bigger and more complicated circuits.

"I think the community is very aware that we've got a long way to go before we can fulfil our dream of *in silico* design of genetic circuits we can just pop into a cell and run like an app," Elfick says. ■

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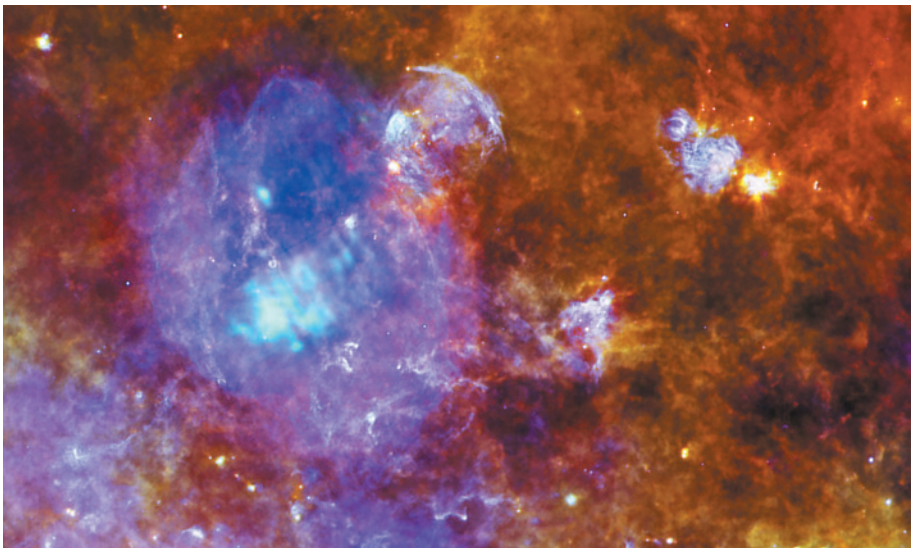

HERSCHEL: Q. NGUYEN LUONG/F. MOTTE/HOBYS KEY PROGRAM CONSORTIUM/HERSCHEL SPIRE/PACS/ESA CONSORTIA. XMM-NEWTON: ESA/XMM-NEWTON

**Herschel captured the shells of dust (orange) generated in supernovae (blue, from an X-ray image).**

ASTRONOMY

# Cold telescope faces hot death

*Herschel space observatory nears its end after unravelling star formation and tracking dust from supernovae.*

**BY GEOFF BRUMFIEL**

After more than three years of observations, astronomy's premier infrared space telescope is about to catch a fever and die. Later this month, Europe's Herschel space observatory, which has helped astronomers to revise theories about the birth and death of stars, will exhaust its stores of liquid-helium coolant, and its instruments will begin to heat up. At that point, "all the scientific instruments will shut down within hours", says Göran Pilbratt, the mission's project scientist at the European Space Research and Technology Centre in Noordwijk, the Netherlands.

Astronomers are hailing the legacy of the €1.1-billion (US$1.4-billion) mission, which has made some 22,000 hours of observations in the far infrared and submillimetre wavelengths, a part of the electromagnetic spectrum blocked by Earth's atmosphere. In an era when scientific spacecraft are increasingly specialized, the 3.5-metre Herschel telescope was a rare general-purpose observatory, used by more than 2,500 astronomers. "Anyone you ask who's been involved with Herschel has their own favourite results," says Matthew Griffin, an astronomer at Cardiff University, UK. "There's something for everybody."

Herschel orbits the L2 point, 1.5 million kilometres away in the cold shadow of Earth, where the combined gravity of the planet and the Sun create a 'gravitational well'. This shady perch, together with 2,300 litres of liquid helium, allowed Herschel to cool its instruments to a chilly 2.2 kelvin. At that temperature, the spacecraft could observe the low-temperature glow of gas and dust in stellar nurseries and in the shells of supernovae.

The cold Universe has held surprises. For example, astronomers thought that young stars form from long filaments of gas that collapse smoothly under their own gravity. Herschel painted a more complicated picture. When it looked at star-forming regions, it saw swirling, churning flows of gas driven by turbulent winds. Researchers now think that turbulence, rather than gravity, creates dense patches in the filaments that eventually collapse into stars, says Griffin. "That's a challenge for theoreticians."

The deaths of stars yielded other revelations. Astronomers had thought that most of the dust in the Galaxy forms in red giants, which puff it into space as they shrink in their waning years. Instead, Herschel detected massive amounts of dust ▶

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