Academies of Sciences, Engineering, and Medicine has this year recommended that clinical trials of the technique be approved if preclinical data suggest that it is safe.

As many as 1 in 5,000 children are born with diseases caused by harmful genetic mutations in the DNA of their mitochondria; the diseases typically affect the heart, muscles and other power-hungry organs. Children inherit all their mitochondria from their mothers.

To prevent a mother who has harmful mitochondrial mutations from passing them to her children, the proposed remedy is to transplant the nuclear DNA of her egg into another, donor egg that has healthy mitochondria (and has been emptied of its own nucleus). The resulting embryo would carry the mitochondrial genes of the donor woman, and the nuclear DNA of the father and mother. These are sometimes called three-person embryos.

Current techniques can't avoid dragging a small number of the mother's mitochondria into the donor egg, totalling less than 2% of the resulting embryo's total mitochondria. This isn't enough to cause health problems. But researchers have worried that the proportion of faulty, 'carried-over' mitochondria may rise as the embryo develops. The UK Human Fertilisation and Embryology Authority (HFEA) — which will oversee clinical applications of mitochondrial replacement — has called for research into this possibility.

Egli's study offers some clarity (M. Yamada *et al. Cell Stem Cell* http://doi.org/bhsj; 2016). His team used eggs from women with healthy mitochondria, but otherwise followed a procedure similar to the real therapy: transplanting nuclear DNA from one set of egg cells into another woman's egg cells. The team converted these eggs into embryos using two copies of the maternal genome instead of sperm (to discount any role for paternal DNA), extracted stem cells from the embryos and grew the cells in dishes in the lab. The embryos, on average, had just 0.2% of carried-over mitochondrial DNA (mtDNA), and the resulting embryonic stem cells at first harboured similarly minuscule levels. But one stem-cell culture showed a dramatic change: as the cells grew and divided, levels of the carried-over mtDNA jumped from 1.3% to 53.2%, only to later plummet back down to 1%. When the team split this cell line into different dishes, sometimes the donor egg's mtDNA won out, but in others, the carried-over mtDNA dominated.

"I don't think it would be a wise decision to go forward with this uncertainty."

COMPETING DNA

Exactly how the carried-over mitochondria rose to dominance is unclear. Egli suspects that the resurgence happened because one mitochondrion copied its DNA faster than the others could, which he says is more likely to occur when large DNA-sequence differences exist between the two populations of mitochondria.

Iain Johnston, a biomathematician at the University of Birmingham, UK, says that this theory makes sense. He was part of a team that found that, in mice with mitochondria from lab strains and distantly related wild populations, one mitochondrial lineage tended to dominate (J. P. Burgstaller *et al. Cell Rep.* **7,** 2031–2041; 2014). If mitochondrial replacement does reach the clinic, Johnston says that donors should be chosen such that their mitochondria closely match those of the recipient mother.

But Mary Herbert, a reproductive biologist at the University of Newcastle, UK, who is part of a team pursuing mitochondrial replacement, says that mitochondria behave very differently in embryonic stem cells than in normal human development. Levels of mutant mitochondria can fluctuate wildly in stem cells. "They are peculiar cells, and they seem to be a law unto themselves," she says. She calls the biological relevance of the latest report "questionable", and thinks that data from embryos cultured for nearly two weeks in the laboratory will provide more useful information than Egli's stem-cell studies.

An HFEA spokesperson says that the agency is waiting for further experiments on the safety and efficacy of mitochondrial replacement (including data from Herbert's team) before approving what could be the world's first mitochondrial replacement in humans.

Egli hopes that the HFEA considers his team's data. He thinks that the problem can be surmounted, for instance, by improving techniques to reduce the level of carried-over mitochondria or matching donors so that their mitochondria are unlikely to compete. Until this is shown for sure, he advocates caution. "I don't think it would be a wise decision to go forward with this uncertainty." ■

EARTH SCIENCE

Carbon-sensing satellite system faces high hurdles

Space agencies plan an advanced fleet, but technical and political challenges abound.

BY JEFF TOLLEFSON

Today just two satellites monitor Earth's greenhouse-gas emissions from space. But if the world's leading space agencies have their way, a flotilla of such probes could be launched beginning in 2030. The ambitious effort would help climate scientists to improve their forecasts — and it could also help to verify whether countries are upholding their commitments to reduce greenhouse-gas emissions.

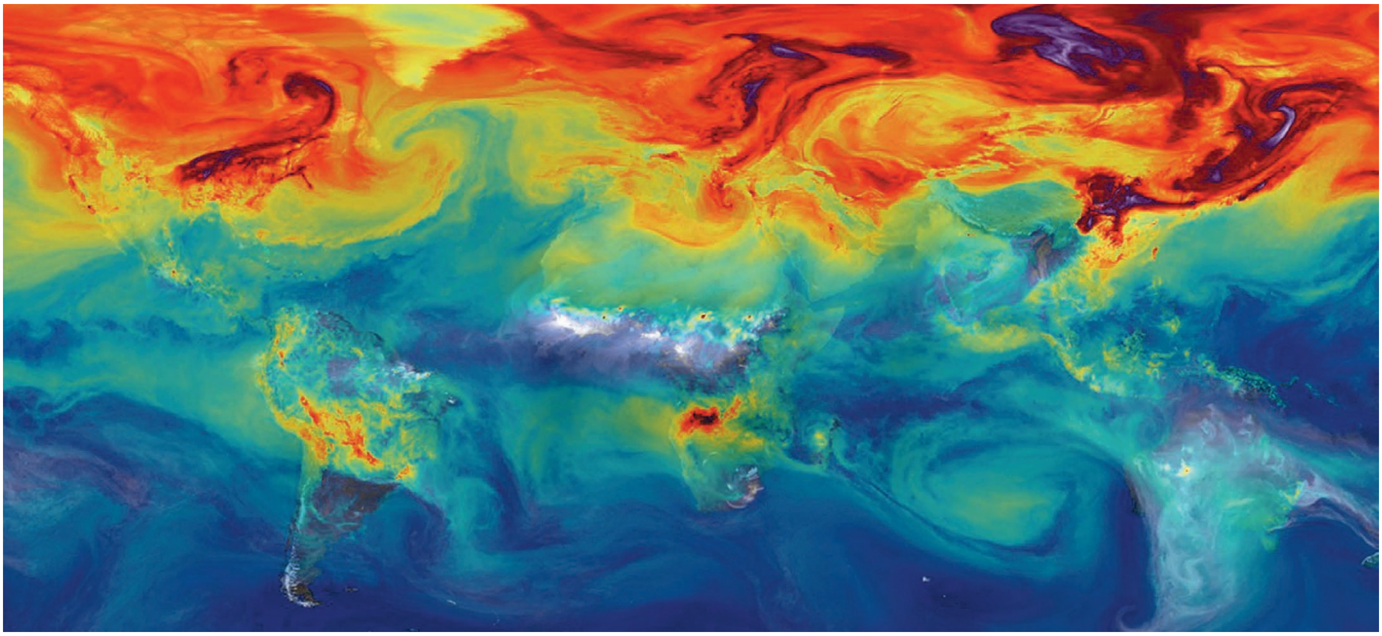
But researchers will need to clear a daunting array of political and technical hurdles if they are to get the system — estimated to cost several billion dollars — off the ground. Competition for satellite launch slots is stiff: last year, for instance, the European Space Agency shelved plans for an advanced carbon-dioxide-monitoring probe in favour of a mission to measure plant growth. And scientists must still prove that satellite measurements of gases such as CO_2 and methane can match the accuracy of data from observatories on Earth.

"We have a small fleet of satellites that are being launched, but these are all just scientific experiments," says David Crisp, science team leader for NASA's Orbiting Carbon Observatory-2 (OCO-2). "What we are trying to do now is just figure out how to monitor greenhouse gases from space."

Scientists have access to data from a pair of pioneering satellites: OCO-2, which launched in 2014 and measures CO_2, and Japan's Greenhouse Gases Observing Satellite (GOSAT), which launched in 2009 and tracks CO_2 and methane. NASA and the Japan Aerospace Exploration Agency are working to calibrate the instruments against each other and with a network of ground-based monitoring stations.

Both probes have a margin of error of about 0.5%, Crisp says. His team wants to reduce that to just 0.25% for the OCO-2 measurements.

NASA/GODDARD SPACE FLIGHT CENTER



A NASA atmospheric simulation from a computer model that traces how carbon dioxide emissions disperse in the atmosphere.

Meanwhile, nations are queuing up a new suite of satellites to lay the foundations for a larger monitoring effort (see 'Counting carbon'). China will launch a pair of CO_2-monitoring satellites this year, and Japan plans to send up GOSAT-2 in 2018. NASA is looking ahead to OCO-3, which could launch as early as 2018. Unlike its predecessor, OCO-3 will not be a free-flying satellite, but a spectrometer built from OCO-2's spare parts that will be installed on the International Space Station.

Crisp says that NASA scientists know how to build an instrument that is 20 times more powerful than OCO-2's spectrometer, but that the agency does not have the funds to construct and launch it. "I can't even compete for the money," he says, "because it doesn't exist." At present, NASA is developing a satellite called ASCENDS that would use a laser to measure CO_2; unlike OCO-2, it would be able to track the gas at night and during winter at high latitudes.

SHARPER VISION

Together, these satellites will extend a continuous record of CO_2 measurements that began in 2002 with SCIAMACHY, a spectrometer on the European Space Agency's Envisat probe. The world's space agencies want to transform this ad hoc system into a coordinated fleet of about six probes by 2030.

More than 60 agencies collaborated on a declaration finalized on 16 May that sets out a broad vision to develop and implement new monitoring technologies and to share the resulting data. France kick-started the effort last year, before December's United Nations climate summit in Paris. At that meeting, nations adopted an agreement to curb heat-trapping emissions that also commits them to develop ways to verify whether they are meeting their climate goals. The nascent satellite programme could help nations to fulfil that requirement.

"It's very general, but it's a beginning," says Jean-Yves Le Gall, the head of the French space agency, CNES. He says that the group is discussing how to distribute and use data from the system before its meeting in Mexico in September.

"We've got training wheels on for the next decade."

The space agencies' efforts are a welcome surprise to many researchers. "I think it's very important," says Heinrich Bovensmann, a remote-sensing specialist at the University of Bremen in Germany. "Now we have to see what really comes out of it."

The current generation of satellites measure how much CO_2 is in a given column of air. But what scientists and governments really want to know is where that CO_2 came from. To pinpoint emissions produced by industrial activity, researchers must also determine how much CO_2 is absorbed and released by land and ocean ecosystems.

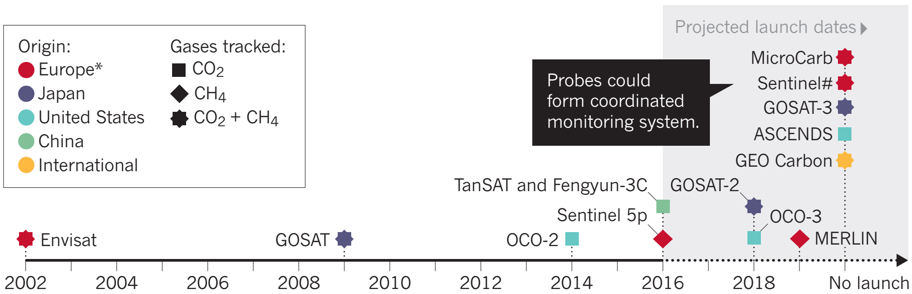
This requires combining atmospheric CO_2 measurements with accurate information about how the natural environment takes up and releases the gas, and plugging the data into detailed air-current models that can trace where the CO_2 probably came from. In essence, the task requires developing something akin to current weather forecast systems — but run in reverse.

Achieving the precision needed to verify whether nations are meeting their emissions goals is a tall order, says Stephen Pacala, a climate researcher at Princeton University in New Jersey who led a 2010 report on space-based carbon monitoring for the US National Academies of Sciences, Engineering, and Medicine. He says that satellites would need to be more accurate than current greenhouse-gas inventories, which are calculated using a variety of data on fossil-fuel consumption and economic and land-use trends.

But Crisp and his colleagues remain confident that they can deliver greenhouse-gas data that will be useful for both scientists and policymakers. "We've got training wheels on for the next decade," he says. "Once we learn how to ride, we'll build a bicycle." ■

COUNTING CARBON

The number of satellites monitoring the world's greenhouse-gas output could triple by 2030. Scientists are working to make the probes' data on carbon dioxide and methane (CH_4) as accurate as those collected by observatories on Earth.



*Includes European Space Agency projects, a French satellite (MicroCarb) and a French–German initiative (MERLIN).