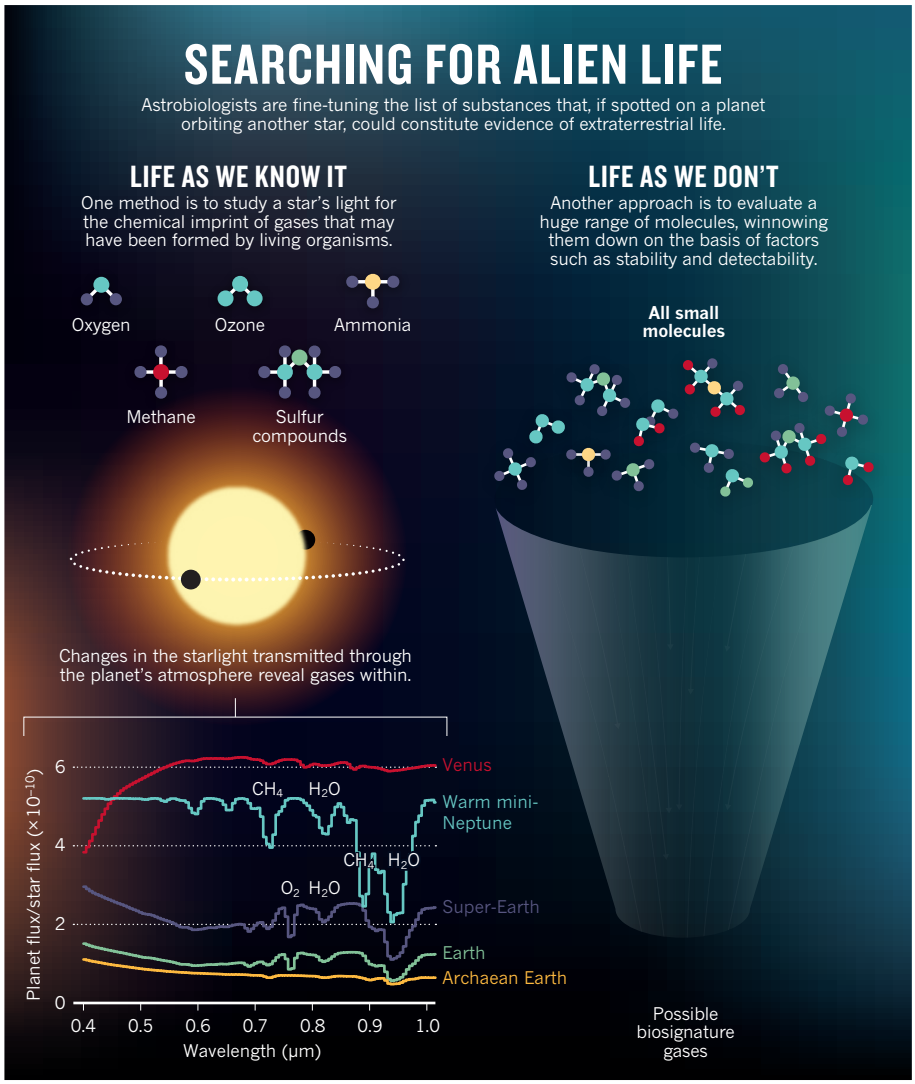

SOURCE: CHART: S. SEAGER & W. BAINS *SCI. ADV.* **1**, E1500047 (2015); CONE: REF. 5

if it came from living organisms, but results from a runaway greenhouse effect.

There are ways to tell. The runaway greenhouse would create an atmosphere thousands of times denser than Earth's, in which O_2 molecules collide to produce O_4. So spotting O_4 in a planet's atmosphere could be a clue that the oxygen does not, in fact, come from life, Meadows' team reported this year[2].

Another method is to draw up a list of alternative biosignature gases — things not as obvious as oxygen that might be made by organisms under certain conditions. These include dimethyl sulfide[3], which is produced by Earthly phytoplankton, or even ammonia[4]. On a cold alien planet, organisms might make the gas using the same chemical process as industrial manufacturers.

At the Massachusetts Institute of Technology in Cambridge, astronomer Sara Seager has begun to examine 14,000 compounds that are stable enough to exist in a planetary atmosphere. She and her colleagues are winnowing down their initial list of molecules using criteria such as whether there are geophysical ways to send the compound into the atmosphere[5].

"We're doing a triage process," says Seager. "We don't want to miss anything."

The Seattle meeting aims to compile a working list of biosignature gases and their chemical properties. The information will feed into how astronomers analyse data from NASA's James Webb Space Telescope, slated for launch in 2018. The telescope will be able to look at only a handful of habitable planets, but it will provide the first detailed glimpse of what gases surround which world, says Nikole Lewis, an astronomer at the Space Telescope Science Institute in Baltimore, Maryland.

No single gas is likely to be a slam-dunk indicator of alien life. But Domagal-Goldman hopes that the workshop will produce a framework for understanding where scientists could trip themselves up. "We don't want to have a great press release," he says, "and then a week later have egg on everybody's faces." ■

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EPIDEMIOLOGY

Brazil's birth-defects puzzle

Zika virus might not be only factor in reported microcephaly surge.

BY DECLAN BUTLER

Government researchers in Brazil are set to explore the country's peculiar distribution of Zika-linked microcephaly — babies born with abnormally small heads.

Zika virus has spread throughout Brazil, but extremely high rates of microcephaly have been reported only in the country's northeast. Although evidence suggests that Zika can cause microcephaly, the clustering pattern hints that other environmental, socioeconomic or biological factors could be at play.

"We suspect that something more than Zika virus is causing the high intensity and severity of cases," says Fatima Marinho, director of information and health analysis at Brazil's ministry of health. If that turns out to be true, it could change researchers' assessment of the risk that Zika poses to pregnant women and their children.

The idea has long been on Brazilian researchers' radar, but the enquiry marks the first time that scientists at the health ministry have taken up the hypothesis. The ministry has asked Oliver Brady, an epidemiologist at the London School of Hygiene & Tropical Medicine, ▶

and Simon Hay, director of geospatial science at the Institute for Health Metrics and Evaluation in Seattle, Washington, to collaborate with researchers in Brazil. "The aim is to understand why we are only observing elevated rates in the northeast," says Brady, who flew into Brasilia this month to begin work.

The northeast was where the first reported surge in microcephaly cases in Brazil began a year ago. Health officials had expected that they would later see the same high rates in other parts of the country. "We were expecting an explosion of birth defects," says Marinho.

FELIPE DANA/AP

A health worker sprays insecticide to combat the mosquito that spreads Zika.

But as of 20 July, almost 90% of the 1,709 confirmed cases of congenital microcephaly or birth defects of the central nervous system reported in Brazil since last November were in a relatively small area: in the coastal hinterland of the country's northeastern tip. Particularly surprising, says Marinho, is that just three cases have been confirmed in Brazil's second-most populous state, Minas Gerais, which borders the most-affected part of the northeast region. Poor data on the scale and timing of Zika outbreaks across Brazil make it hard to tell whether increases in microcephaly elsewhere might have been delayed — but ministry scientists now think that the northeast represents a marked outlier, she says.

There are many hypotheses about what might be going on. Marinho says that her team's data, submitted for publication, hint that socio-economic factors might be involved. For example, the majority of women who have had babies with microcephaly have been young, single, black, poor and tend to live in small cities or on the outskirts of big ones, she says.

Another idea is that co-infections of Zika and other viruses, such as dengue and chikungunya, might be interacting to cause the high intensity of birth defects in the area.

In a paper published last month, researchers from Brazilian labs noted a correlation between low vaccination rates for yellow fever and the microcephaly clusters (L. P. de Goes Cavalcanti *et al. J. Infect. Dev. Countries* **10,** 563–566; 2016). Because yellow fever and Zika are in the same virus family, the scientists speculate that the vaccine might provide some protection against Zika.

And the Brazilian doctor who was the first to report a firm link between Zika and microcephaly — Adriana Melo at IPESQ, a research institute in Campina Grande — has another idea. In a preprint posted on the bioRxiv server on 15 July, Melo and her colleagues at the Federal University of Rio de Janeiro reported finding bovine viral diarrhoea virus (BVDV) proteins in the brains of three fetuses with microcephaly (F. C. S. Nogueira *et al.* Preprint at bioRxiv http://doi.org/bm4c; 2016).

BVDV causes birth defects in cattle but is not known to infect people. Melo and her team suggest that Zika infection might make it easier for BVDV to cause infections; however, they haven't ruled out the possibility that their findings might be due to contamination.

The Brazilian health ministry's study will test for BVDV among other ideas, says Brady. Researchers will reanalyse raw data on microcephaly cases, and will model connections with possible cofactors such as socio-economic status, water contamination and mosquito-borne diseases. Most of this information comes from health-ministry databases, but the team will also study experimental data, such as how people's immune response may change after past infection with other viruses such as dengue.

Until more is known about Zika and the causes of increased microcephaly rates in Brazil's northeast, public-health actions and advice must err on the side of precaution, says Ian Lipkin, a virologist and outbreak specialist at Columbia University in New York City. ■

BIOMEDICINE

First trial of CRISPR in people

Chinese team approved to test gene-edited cells in people with lung cancer.

BY DAVID CYRANOSKI

Chinese scientists are on the verge of being first in the world to inject people with cells modified using the CRISPR–Cas9 gene-editing technique.

A team led by Lu You, an oncologist at Sichuan University's West China Hospital in Chengdu, received ethical approval to test the cells in people with lung cancer on 6 July, and plans to start the trial next month.

That timeline puts the proposal ahead of a planned US trial to test CRISPR–Cas9-modified cells, also for the treatment of cancer.

"It's an exciting step forward," says Carl June, a clinical researcher in immunotherapy at the University of Pennsylvania in Philadelphia.

Last month, the US trial was approved by an advisory panel of the US National Institutes of Health (NIH) but had yet to receive a green light from the US Food and Drug Administration (FDA) and a university review board. There have also been a number of human clinical trials using an alternative gene-editing technique, including one led by June, that have helped patients to combat HIV — but none so far has used CRISPR.

The Chinese trial will enrol patients who have metastatic non-small cell lung cancer and for whom chemotherapy, radiation therapy and other treatments have failed. "This technique is of great promise in bringing benefits to patients," says Lu.

CHROMOSOME SNIP

Lu's team will extract immune cells called T cells from the participants' blood, and use CRISPR–Cas9 technology — which pairs a molecular guide able to identify specific genetic sequences on a chromosome with an enzyme that can snip the chromosome at that spot — to knock out a specific gene in the