Artist's conception of the European Space Agency's Trace Gas Orbiter above Mars.

will allow high-resolution mapping, which could be key to spotting methane seeps, if they exist. But the mapping mode's sensitivity is relatively low; Vandaele expects that the look-down observations won't detect concentrations below 11 ppb. "That's a big problem," says Chris Webster, the leader of Curiosity's methane detection instrument at the Jet Propulsion Laboratory in Pasadena, California, because it means the TGO won't be able to map methane if it remains at or below the levels detected by the rover. On the other hand, Webster says the TGO team should be able to convert the limb mode observations into lower-resolution maps.

Methane is not the TGO's only quarry. It will also search for sulfur-bearing compounds, a signal of volcanism that, if found in conjunction with methane, could imply that the methane has a geological rather than a biological origin. Both spectrometers will monitor how carbon dioxide and water vapor move through the atmosphere, and ACS will measure temperature. Those observations will help fine-tune martian climate models, says TGO project scientist Håkan Svedhem in Noordwijk, the Netherlands, making them "more precise and more useful for predictions."

The TGO is part of a two-mission, €1.2 billion program called ExoMars, which was originally supposed to be run jointly with the United States. But NASA pulled out in 2012 because of budget troubles. ESA turned to Russia, which in return for placing scientific instruments aboard the spacecraft offered two Proton rocket launches, the first for the TGO and the second, scheduled for 2018, for a rover that will drill into the subsurface and look for life.

The Schiaparelli lander is key to that plan, because it will test many of the technologies needed to land the rover, including a parachute and radar altimeter. Schiaparelli is scheduled to detach from the TGO 3 days before it enters Mars's orbit. Then, on 19 October, the lander will plummet for 6 minutes through the thin atmosphere, slowed by the usual but always hair-raising methods of parachute and retrorocket. A camera will snap a picture 10 seconds or so before touchdown, and as the lander strikes the surface at 10 kilometers per hour, an underbelly of honeycombed aluminum will crumple, cushioning the blow.

How confident is Thierry Blancquaert, Schiaparelli manager at the European Space Research and Technology Centre in Noordwijk, that the lander will arrive safely? "I don't have a number," he says. "I would say 'likely' or 'very likely.'" ■

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INFECTIOUS DISEASE

Evidence grows for Zika virus as pregnancy danger

Lab experiments and new clinical data suggest that fast-spreading virus attacks developing brain

By **Gretchen Vogel**

Since late last year, when doctors in Brazil warned that a wave of serious birth defects might be linked to a little-known virus called Zika, researchers have struggled to pin down the link. Some in the media have questioned whether the reported increase in birth defects is real; others, particularly environmental activists, have suggested the virus is an innocent bystander, unfairly blamed for defects caused by chemicals or other factors. With three studies published last week, chances that the virus has been wrongly accused are fading.

Two independent groups showed that, at least in the lab, the virus eagerly infects developing brain cells, suggesting a mechanism by which it could cause the most striking of the observed birth defects: microcephaly, in which babies are born with abnormally small heads and brains. The work "is going to be very important," says Madeline Lancaster, who studies human brain development at the Medical Research Council Laboratory of Molecular Biology in Cambridge, U.K. The results "are quite consistent with what you're seeing in the babies with microcephaly."

A third study, following several dozen pregnant women in Brazil who had become infected with Zika virus, directly links the infection to an increase in brain defects. It also suggests that the virus can harm a developing fetus in other ways, possibly by attacking the placenta and slowing down the supply of nutrients. "These are the data we have been waiting for," says Daniel Lucey, an expert on global health at Georgetown University in Washington, D.C.

Zika virus, named after a forest in Uganda where it was first isolated decades ago, usually causes only mild symptoms in people, including fever and rash. But the virus's spread across northeastern Brazil last year coincided with a striking increase in microcephaly (*Science*, 8 January, p. 110), and many of the mothers reported having had symptoms consistent with Zika infection earlier in their pregnancies. Researchers have also identified the virus in amniotic fluid of pregnant women whose fetuses were diagnosed with microcephaly, in the brain tissue of a fetus with the disorder, and in the placentas of women infected during their pregnancy. Still, it has

Brazil saw a sudden increase in babies born with microcephaly after the Zika virus spread there last year.

been difficult to prove a link to the birth defects, in part because blood tests for Zika virus are only accurate for about a week after infection.

To gauge the virus's possible effects on the developing brain, researchers in one of the new studies coaxed induced pluripotent stem (iPS) cells to grow into immature brain cells called human cortical neural progenitor cells. (iPS cells are adult cells that have been reprogrammed into stem cells that can grow into most of the tissues in the body.) They then exposed the neural progenitor cells to a lab strain of Zika virus. Three days later, 85% of the cells in the culture dishes were infected, neuroscientists Hongjun Song and Guo-li Ming at Johns Hopkins University in Baltimore, Maryland; virologist Hengli Tang at Florida State University in Tallahassee; and their colleagues reported on 4 March in *Cell Stem Cell*. In contrast, when the virus was applied to other kinds of cells—including fetal kidney cells, embryonic stem cells, and undifferentiated iPS cells—it infected fewer than 10% of the cells by day 3.

The virus hijacked the neural progenitor cells, Song says, using their machinery to replicate itself and spread quickly to new cells. The infected cells grew more slowly and had abnormal cell division cycles, which could also contribute to microcephaly, the team reported.

In a separate set of experiments, researchers found similar impacts on two other lab models of developing brain tissue. In a preprint posted online in *PeerJ* on 2 March, neuroscientist Patricia Garcez and stem cell researcher Stevens Rehen at the D'Or Institute for Research and Education in Rio de Janeiro, Brazil, report growing human iPS cells into clusters of neural stem cells called neurospheres, as well as into 3D organoids that resemble a miniature developing human brain. Infections with Zika virus (isolated from a Brazilian patient) killed most of the neurospheres and left the few survivors small and misshapen. Infected organoids grew to less than half their normal size.

Lancaster says the fate of the lab-grown cells mirrored what was seen in earlier studies of organoids derived from stem cells that carried gene mutations linked to microcephaly. "You have two very different causes of microcephaly, but you see something very similar happening: a depletion of neural stem cells, and that would lead to fewer neurons" in the developing brain, she says.

The first published clinical data from infected pregnant women suggest that microcephaly is not the only type of damage the virus can cause. In an ongoing study, researchers at the Oswaldo Cruz Foundation in Rio de Janeiro have been enrolling pregnant women who develop a rash. Of the first 88 women, 72 tested positive for Zika virus, the team reported on 4 March in *The New England Journal of Medicine*.

Although none of the fetuses of the 16 women who tested negative for Zika have shown any abnormalities on ultrasound examinations, 12 of the 42 infected women who agreed to receive additional ultrasounds developed complications. Five had fetuses with abnormal brain growth, and one baby was born with microcephaly and eye problems. Several other fetuses were small for their developmental age. Two whose mothers were infected late in pregnancy were stillborn. Other issues included a lack of amniotic fluid and eye problems that may indicate blindness. This range of problems suggests that risks for pregnant women could be broader than doctors have realized, says Karin Nielsen of the University of California, Los Angeles, who helped coordinate the study with colleagues from the Oswaldo Cruz Foundation. In particular, she says, Zika infections late in pregnancy seem able to attack the placenta, producing damage that can kill an otherwise healthy fetus. Nielsen proposes a new name for the suite of symptoms: Zika virus congenital syndrome.

Still, many scientists suspect that Zika has accomplices that exacerbate its effects. Both Garcez's and Song's teams are now repeating their experiments with other viruses, including dengue, a relative of the Zika virus that is prevalent in the same regions. Previous exposure to other related viruses—even the vaccine for yellow fever—might also affect how Zika infection affects pregnant women and their babies. Genetic factors may also play a role.

> ***"The news isn't just bad. It's terrible."***
> **Daniel Lucey**, Georgetown University

Even if other factors contribute to the prenatal damage, the new findings are sobering news for countries across the Americas where Zika has spread in the last half-year: They are bracing for their own waves of birth defects. Colombia has seen its first Zika-related cases of microcephaly in recent weeks. "The news isn't just bad," Lucey says. "It's terrible."

Public health officials are rushing to respond to the threat and identify questions that need answering. The World Health Organization (WHO) convened a meeting last week in Washington, D.C., to outline Zika virus research priorities. That was followed this week by a WHO meeting in Geneva, Switzerland to discuss how to spur companies to develop better diagnostic tests, a vaccine, and ways to control the mosquitoes that spread the virus.

At the Geneva meeting, WHO physician Bruce Aylward, who the agency has tapped to lead its responses to major new outbreaks, noted that in February WHO declared an international public health emergency based on just the possibility of an association between Zika virus and microcephaly. Although WHO isn't ready to formally declare the virus guilty, he said, "a lot has happened since then. The data are all moving in one direction." ■

GRAVITATIONAL WAVES

In search of spacetime megawaves

Timing in celestial radio beacons could reveal gravitational tsunamis

By **Daniel Clery**

Last month, the detection of gravitational waves from merging black holes made headlines and tweetstorms around the world. But a hunt for much bigger game was already afoot.

The black holes responsible for last month's discovery weighed a few dozen times as much as our sun. Black holes millions or billions that massive, however, lurk at the centers of most galaxies—and they merge, too. Spotting the ensuing gravitational tsunamis takes an entirely different kind of detector from the Laser Interferometer Gravitational-Wave Observatory (LIGO), the Earth-based device that triumphed last month—one that stretches to the stars.

Three teams of radio astronomers are watching the heavens for hints of these megawaves, and their latest results suggest that increasing sensitivity could lead to a detection sometime in the next decade. "Eventually we will detect something," says Michael Kramer, director of the Max Planck Institute for Radio Astronomy in Bonn, Germany. "It's like peering through fog. We'll clear the smokescreen in time."

Astronomers think that over the history of the universe, galaxies have grown by consuming smaller galaxies or merging with their neighbors. When that happens, the supermassive black holes at their centers wind up orbiting each other, just like the pair of black holes LIGO detected. Because such dark behemoths move much more slowly, they produce long, loping gravitational waves. Whereas LIGO detected waves thousands of kilometers long, supermassive black holes would throw off waves measured in light-years.

To detect these much longer waves requires a much bigger detector. LIGO measured differences in the length of its two 4-kilometer arms caused by a passing gravitational wave. For waves from a supermassive binary, observers need "arms" hundreds of light-years long.

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Editor's Summary