

tropical diseases — a constellation of illnesses affecting roughly one billion people living in poverty around the world.

The idea for the latest study came from an analysis of the pre-emptive use of the antibiotic azithromycin in Ethiopian communities affected by trachoma — a disease that causes blindness — in the late 2000s. Researchers noticed a drop in overall deaths (T. C. Porco *et al. J. Am. Med. Assoc.* **302**, 962–968; 2009), and Thomas Lietman, an infectious-disease researcher at the University of California, San Francisco, and his colleagues followed up with the current trial, dubbed MORDOR (from the French description of the project).

As part of MORDOR, children under five in communities in Niger, Malawi and Tanzania took one dose of azithromycin twice a year for two years. Control populations received a placebo. Childhood mortality rates among treated communities in Niger dropped by 18% compared with control populations; Tanzania had 3% fewer deaths and Malawi saw a 6% reduction.

Lietman says that Niger probably experienced the greatest benefit because it has the highest childhood mortality rate of the three countries. About 9% of children die before the age of 5 in Niger, compared with about 5% in Tanzania and Malawi. Pneumonia and diarrhoea triggered by bacterial infections help to drive up childhood mortality rates, according to a 2017 report from the United Nations. Poor sanitation, unsafe drinking water and malnutrition combine to make children living in poverty especially vulnerable to disease-causing microbes. They're also more likely to die from curable conditions because health care can be unaffordable or too far away to be of help.

But this antibiotics strategy comes at a cost, says Ramanan Laxminarayan, director of the Center for Disease Dynamics, Economics and Policy in Washington DC. If resistance develops against azithromycin, diseases treated by the drug, including gonorrhoea, would become harder to combat. He hopes that, if policymakers decide to implement this approach, they will target only the populations most in need, and then just for a limited time. Groups supporting this approach should also work to reduce childhood mortality in the same way that the developed world did, he says, through improved sanitation, nutrition and health care.

For now, researchers will continue to study the effects of this antibiotics strategy. Later this year, similar trials will launch in Mali and Burkina Faso. And Lietman's team is evaluating data collected during an extension of its trial, to assess how fast antibiotic resistance develops. The WHO plans to release a statement about whether this strategy is justified, and in what circumstances, by the end of 2019. ■



The Owens Valley Long Wavelength Array in California hosts the LEDA experiment.

ASTRONOMY

Physicists trawl skies for enigmatic signal

Teams rush to find faint signature from Universe's first stars.

BY DAVIDE CASTELVECCHI

Researchers are heading to some of the most remote spots on Earth — from the Tibetan Plateau to an island in the sub-Antarctic ocean — to try to capture an enigmatic radio signal from the early Universe. This grand search includes some of the first experiments to follow up on a surprise announcement in February that astronomers had seen evidence of the Universe's first stars lighting up¹, a moment known as the cosmic dawn.

And as experimental physicists try to replicate those findings in the few places on Earth that are relatively undisturbed by radio interference, theorists are struggling to make sense of the data. “The signal does not look like anything we expected,” says Abraham Loeb, an astrophysicist at Harvard University in Cambridge, Massachusetts.

The original detection was reported by researchers at the Experiment to Detect the Global Epoch of Reionization Signature (EDGES), which uses a pair of table-sized radio antennas in the Australian outback. The experiment measures the long-wavelength part of the cosmic microwave background, the noisy afterglow of the Big Bang. The researchers were searching for a subtle dip in the background spectrum where the microwave radiation is

slightly dimmed. Cosmologists have theorized that such a dip should have been caused by the light of the first stars, which made primordial hydrogen in the Universe less transparent at a particular radio wavelength. The details of this absorption should contain information about the early interstellar matter and the stars that cast light on it.

“We might have the most radio quiet place on Earth.”

But the blip had an unexpected shape. It suggested that the absorption started to ramp up rapidly around 150 million years after the Big Bang, stayed roughly constant between 200 million and 250 million years ago, and then disappeared relatively quickly. The dip was also deeper than predicted, which implied that the gas was colder than expected during that epoch — perhaps 4 kelvin instead of 7 kelvin.

EXTRA SCRUTINY

The EDGES team spent two years cross-checking their peculiar result before deciding to go public. Researchers have posted dozens of preprints in response, trying to interpret the anomaly. Some physicists have suggested that it was a possible sign of previously undiscovered interactions between ordinary matter and dark matter². Others saw a possible indication of ▶

► the absence of dark matter³.

The EDGES researchers have now started another round of observations with a new, smaller antenna. They have “preliminary evidence” that this antenna also sees the original feature, says lead scientist Judd Bowman, an astronomer at Arizona State University in Tempe.

Competing experiments are also trying to reproduce the EDGES result. In April, Lincoln Greenhill, a radio astronomer at the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, flew to the arid Owens Valley in California to test a modified version of the Large-Aperture Experiment to Detect the Dark Ages (LEDA). The experiment — an array of antennas that look like umbrella frames — might have just missed the EDGES signal because it originally operated with filters that cut off frequencies above 82 megahertz. The EDGES signal seems to be centred at about 78 megahertz, so is very near the top of that range. The team is testing filters that allow detection of higher frequencies. If things go well, Greenhill says, it might take a few months to collect and analyse enough data.

Meanwhile, at the Raman Research Institute in Bangalore, India, Ravi Subrahmanyan and his colleagues have quickly built a version of their spherical antenna, called SARAS-2, that is sensitive to the range of the EDGES signal. They plan to deploy the new antenna in May at a site outside town, and to later move it to the Tibetan Plateau.

Places without radio interference are rare now, but “we might have the most radio quiet place on Earth”, says physicist Jonathan Sievers at the University of KwaZulu-Natal in Durban, South Africa. The spot is on Marion Island, halfway to Antarctica, and the only way to get there is on a ship that goes once a year, in April. A small KwaZulu-Natal team led by physicist Cynthia Chiang installed its cosmic-dawn experiment, Probing Radio Intensity at High-Z from Marion (PRIZM), there last year. Chiang is now at the island station again, retrieving data from the past year and upgrading their telescope for new observations.

But one of the quietest places for radioastronomy in the Solar System would be the far side of the Moon. Jack Burns, an astrophysicist at the University of Colorado Boulder, is leading a proposal to put a 10-metre-long wire antenna on a small lunar orbiter. From there, the probe should detect not only the EDGES absorption feature, but also one from an earlier epoch known as the dark ages — before stars existed. The feature would appear at around 15 megahertz, a band that is not accessible from Earth. ■

1. Bowman, J. D., Rogers, A. E. E., Monsalve, R. A., Mozdzen, T. J. & Mahesh, N. *Nature* **555**, 67–70 (2018).
2. Barkana, R. *Nature* **555**, 71–74 (2018).
3. McGaugh, S. Preprint at <https://arxiv.org/abs/1803.02365> (2018).

SYNTHETIC BIOLOGY

Genome-synthesis effort shifts focus

GP-write project to make virus-resistant human cell lines.

BY ELIE DOLGIN

A bold plan to synthesize an entire human genome has been scaled back to a more technically attainable near-term goal. Instead of synthesizing all of the human genome’s 3 billion DNA base pairs, the project will now attempt to recode the genome to produce cells immune to viral infection.

Organizers of Genome Project-Write (GP-write), a global public-private partnership that includes around 200 scientists, announced the priority shift at a meeting in Boston, Massachusetts, on 1 May.

But even the downsized ambitions might be difficult to achieve soon, because the two-year-old effort still has no dedicated funding for what’s estimated to cost tens, if not hundreds, of millions of dollars and last a decade or more.

“We thought it was important to have a community-wide project that people could get behind,” says project co-leader Jef Boeke, a yeast geneticist at New York University. When the effort launched in 2016, the creation of a virus-resistant human cell line was listed as one of several pilot projects that would develop the technology to synthesize the full genome¹. With the cell line now the focus, raising money should be easier, says Nancy Kelley, a biotechnology lawyer who is co-leading the effort with Boeke and George Church, a genome scientist at Harvard Medical School in Boston.

Onlookers generally approve of the priority shift. “This is a terrific idea,” says Martin Fussenegger, a synthetic biologist at the Swiss Federal Institute of Technology in Zurich. “It’s more geared toward utilities and applications” — not just DNA synthesis for its own sake, he adds.

A virus-proof human cell line would let firms make vaccines, antibodies and other biological drugs without risk of viral contamination. It could also help to make protein drugs with chemical ornaments similar to those in human proteins, to decrease the risk of the body’s immune system rejecting them. However, the organizers’ main goal is still to improve DNA technologies, not to create a particular product. “The idea is to develop the technologies to

do this very quickly and easily using a variety of gene-editing and synthesis techniques,” says Harris Wang, a synthetic biologist at Columbia University Medical Center in New York City, and a member of GP-write’s scientific executive committee. The “ultra-safe” human-cell-line project, Wang adds, has “the right level of complexity, difficulty and many different facets of design” to push those technologies forward.

One thing it doesn’t have going for it, however, is much dedicated funding. Although a gene-editing technology company said it would donate technical expertise at the meeting, no financial backers have stepped forward.

Church estimates that the consortium has more than US\$500 million in “related funding” — but he includes, for instance, \$40 million earmarked for his own work on synthetic-biology projects including engineered bacteria and miniature organ-like structures. He also counts \$23.4 million for an international initiative led by Boeke to synthesize the yeast genome. Both efforts started years before GP-write.

And the lion’s share of the related funding is investment money raised by loosely affiliated biotech companies. Church includes it in his estimates not because the firms have given money to the effort, but because he is tabulating what he calls “a rough-draft market summary” of the gene-synthesis “ecosystem”.

As such, he includes hundreds of millions of dollars collectively raised by eGenesis, a start-up that he co-founded in Cambridge, Massachusetts; Twist Bioscience in San Francisco, California, of which he is a shareholder; and Ginkgo Bioworks, a Boston synthetic-biology company that last year acquired another Church-backed venture, Gen9. And although leaders of eGenesis and Twist have been active in GP-write, Ginkgo senior management has not. “We’re not involved in GP-write at all, and I’m surprised to see that they included us on that list of funding,” says creative director Christina Agapakis.

Church defends his accounting. “It would be great if we accomplish the goals of GP-write entirely with pre-existing or unlabelled funds,” he says. “Companies like Ginkgo are relevant independent of their formal ties.”

When (and if) the consortium can secure funding for its ultra-safe human-cell-line project, the team plans to imitate previous efforts by Church’s lab to recode the genome of *Escherichia coli* bacteria, making it resistant to viruses.

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