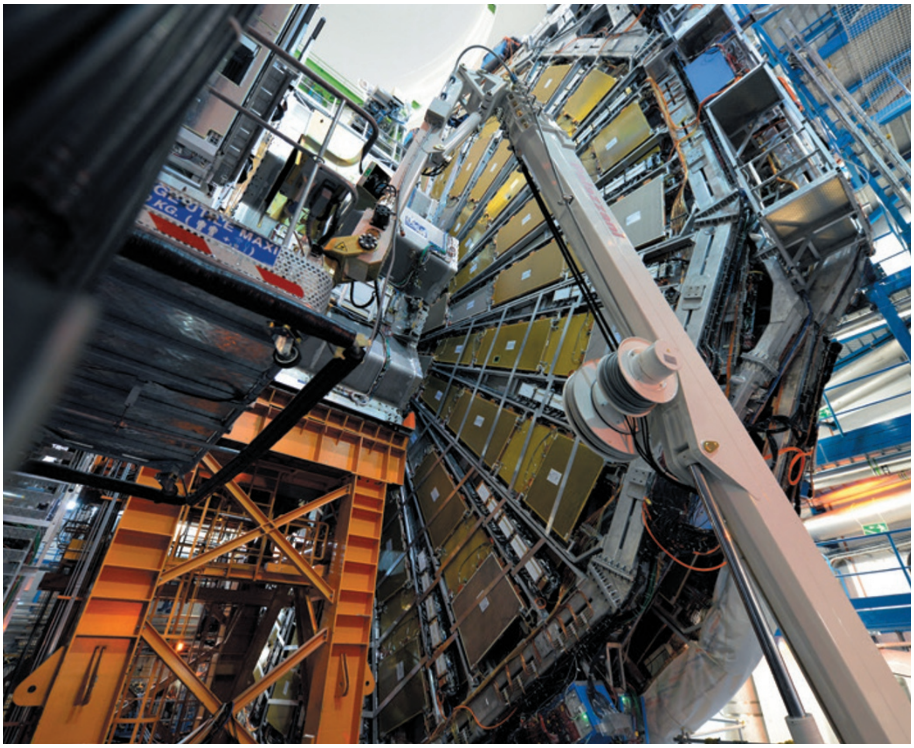

HAROLD CUNNINGHAM/GETTY

Scientists hope to create WIMPs when the Large Hadron Collider comes back online.

COSMOLOGY

Push to find dark matter's darling

Thought to make up the Universe's missing matter, WIMPs are running out of places to hide.

BY DAVIDE CASTELVECCHI

After decades of searching and multiple no-shows, it is crunch time for a leading theory of what comprises dark matter, the mysterious stuff thought to make up around 85% of the Universe's matter.

The Large Hadron Collider (LHC) at CERN, Europe's particle-physics lab near Geneva, Switzerland, is scheduled to restart in March after a major upgrade. It is widely seen as the last chance in a generation to create — and thus confirm — theoretical particles known as WIMPs, or weakly interacting massive particles. A super-sensitive 'direct-detection' experiment, which is designed to catch naturally occurring WIMPs streaming from the heavens, is also due to start this year.

At the same time, the failure so far to glimpse WIMPs at either the LHC or through direct-detection experiments, combined with surprise signals from others, is fuelling suggestions that dark matter is made of something else. A range of alternatives that were previously considered underdog candidates now look "less exotic", says Kevork Abazajian, a theorist who studies particle cosmology at the University of California, Irvine.

Whatever dark matter is, most astronomers believe that it is real. The amount of ordinary, 'visible' matter does not produce enough gravity to explain the speed at which stars move inside galaxies, or at which galaxies move inside galaxy clusters. Dark matter would solve this mystery because it does not absorb or scatter light, making its presence known only by its gravitational pull on normal matter. Different theories posit different suggestions as to what kind of particle would have these properties.

WIMPs are theoreticians' darlings. They are relatively heavy — somewhere between 1 gigaelectronvolt, or roughly the mass of one proton, and 1 teraelectronvolt — and thus would be relatively slow, or 'cold'. These properties fit well with the current best models for the evolution of the Universe, in which haloes of cold dark matter are the prime movers in the formation of galaxies and galaxy clusters. WIMPs also fix problems in two separate branches of physics: particle physics and cosmology. The mass of the WIMP and the strength of its interactions with other particles would help to explain why the Higgs boson has the mass it does. But these figures also mean that WIMPs would have been synthesized at just the right rate in the early Universe for the creation of the abundances that theory requires today — a coincidence that is dubbed the 'WIMP miracle'.

Yet despite being on physicists' most-wanted list, WIMPs remain on the run. When the LHC shut down for maintenance in 2013, its WIMP searches had come up empty. And the most sensitive of the direct-detection searches, carried out by the Large Underground Xenon (LUX) experiment at the Sanford Underground Research Facility in Lead, South Dakota, found no WIMPs during its first major run in 2013 (see *Nature* http://doi.org/zh8; 2013).

But WIMPs could show up this year. The souped-up LHC will smash together protons with combined energies of 13 teraelectronvolts — versus the 8 teraelectronvolts of the previous run: the extra energy will be capable of creating particles that were not possible to make before. Also, this summer, a WIMP detector called the XENON1T experiment, based under Gran Sasso in central Italy is scheduled to go live. It will have a sensitivity 50 times greater than LUX's, says XENON1T spokesperson Rafael Lang, a particle physicist at Columbia University in New York.

But the string of disappointments means that some theorists are already beginning to back away from WIMPs and look at alternatives, says cosmologist Scott Dodelson of the Fermi National Accelerator Laboratory in Batavia, Illinois.

One possibility is neutrinos, particles that interact weakly with other types of matter, a requirement for dark matter. The properties of the three known types of neutrino are not quite right for dark matter. But a hypothetical fourth type — called the 'sterile' neutrino, because it would interact even more weakly than its cousins — could be a suitable candidate.

In December 2014, the European Space Agency's Planck observatory released a map of ancient radiation from the early Universe that all but ruled out the existence of a sterile neutrino with a small mass like the other neutrinos, as did results from the Daya Bay neutrino experiment in China's Guangdong province.

But back in February 2014, astrophysicist Esra Bülbül of Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, and her collaborators reported a mysterious photon signal coming from 73 galaxy clusters (E. Bulbul *et al.* Preprint at http://arxiv.org/abs/1402.2301; 2014). The photons' wavelength was consistent with the decay of sterile neutrinos that weigh about 7 kiloelectronvolts — at least 30,000 times heavier than ordinary neutrinos.

Their results, posted on the arXiv repository, unleashed a flurry of proposed mechanisms by which dark matter could have produced the signal. Super-heavy neutrinos would still be light compared with WIMPs. According to conventional theories, this would make them 'warm' and they would not be a good fit with models of the Universe's evolution. But Abazajian says that the early Universe could have produced cold heavy neutrinos, and that these particles could fit with the current best models of galaxy formation, in some cases better than WIMPs (see, for example, K. N. Abazajian *Phys. Rev. Lett.* **112,** 161303; 2014). "The WIMP miracle does have a theoretical nicety to it," says Abazajian — but, he adds, a heavy neutrino solves many of the same problems as WIMPs do.

Evidence for a heavy neutrino "would be really revolutionary", Dodelson says. So far, however, teams that have attempted to reproduce Bülbül's result have had mixed success.

Another WIMP alternative is the axion, a hypothetical particle proposed in the 1970s. Axions would spontaneously transmute into photons in a magnetic field, providing a means to detect them. Although a few experiments have failed, physicists led by Leslie Rosenberg of the University of Washington in Seattle is currently upgrading the sensitivity of its Axion Dark Matter Experiment. The team says that it will make or break the case for the axion.

Even Rosenberg has not given up on WIMPs, however. "There is nervousness about WIMP dark matter," he says. But, "the LHC 2015 data set will need exploration before you should get too nervous." ■

SYNTHETIC BIOLOGY

Safety boost for GM organisms

Engineered microbes kept in check with a synthetic building block.

BY ELIE DOLGIN

Critics of genetic engineering have long worried about the risk of modified organisms escaping into the environment. A biological-containment strategy described this week in *Nature*[1,2] has the potential to put some of those fears to rest and to pave the way for greater use of engineered organisms in areas such as agriculture, medicine and environmental clean-up.

Two US teams have produced genetically modified (GM) bacteria that depend on a protein building block — an amino acid — that does not occur in nature. The bacteria thrive in the laboratory, growing robustly as long as the unnatural amino acid is included in their diet. But several experiments involving 100 billion or more cells and lasting up to 20 days did not reveal a single microbe capable of surviving in the absence of the artificial supplement.

"Our strains, to the extent that we can test them, won't escape," says Dan Mandell, a synthetic biologist at Harvard Medical School in Boston, Massachusetts, and an author on one of the two studies describing the strategy.

The microbes also do not swap their engineered DNA with natural counterparts because they no longer speak life's shared biochemical language. "Establishing safety and security from the get-go will really enable broad and open use of engineered organisms," says Farren Isaacs, a synthetic biologist at Yale University in New Haven, Connecticut, who led the other study.

Biocontainment could provide added safety in the biological production of drugs or fuels, where microbes can be kept separate from their surroundings. But the modified bacteria could also permit controlled release into the human body or the environment. "Containment might no longer be of the physical kind," says Tom Ellis, a synthetic biologist at Imperial College London who was not involved in the research.

The new technique originated in the laboratory of George Church, a geneticist at Harvard Medical School. Two years ago, Church and his team (which included Isaacs) reported the synthesis of a strain of *Escherichia coli* that had a reprogrammed genetic code[3]. Instead of recognizing a particular DNA triplet known as the amber stop codon as an order to terminate protein synthesis, the recoded bacterium read the same instruction as a directive to incorporate a new kind of amino acid into its proteins.

> ***"What we're now starting to talk about is a really, completely synthetic organism."***

Church and Isaacs have independently made this engineered microbe reliant on unnatural amino acids. The Isaacs team used genomic sequencing to identify sites in essential bacterial proteins where the microbes could incorporate synthetic amino acids without affecting overall function, whereas Church's group started with the protein structures and added elements to help integrate and accommodate the artificial amino acids.

"This is really the culmination of a decade of work," says Church.

These organisms are also more resistant to viruses than their natural counterparts because of the mismatch between the genetic code of the virus and that of its host[3]. Looking ahead, Church and his team are working to co-opt seven different codons, instead of just one. "That would be more than enough to be resistant to all viruses and to create a lot of opportunity for safety," Church says.

> **➲ NATURE.COM**
> To hear more about making safer GM organisms, visit:
> go.nature.com/jrrn2t

Isaacs has also developed a different safeguarding system, in which *E. coli* can grow only in environments containing synthetic chemicals needed for gene expression. He described the work this month in *Nucleic Acids Research*[4]. Another research team led by Jef Boeke at the New York University Langone Medical Center and Patrick Yizhi Cai at the University of Edinburgh, UK, has been working on a similar strategy in yeast. Commonly used in industry and biotechnology, yeast has its genetic material packaged in chromosomes similarly to animals and plants rather than bacteria.

"That's a strategy that is going to be more easily adaptable to other organisms beyond *E. coli*," says Isaacs. His team is now engineering a bacterium that is dependent on synthetic chemicals as well as on artificial protein building blocks. "I think ultimate solutions for robust biocontainment will involve multiple approaches that are deployed at the same time in a single organism," he says.

Such a beast will present a real challenge for regulators, says Todd Kuiken, senior research associate for the Science and Technology Innovation Program at the Woodrow Wilson International Center for Scholars in Washington DC. "What we're now starting to talk about is a really, completely synthetic organism," Kuiken says. "How do you evaluate that once you put it out into the field?" ■

1. Mandell, D. J. *et al. Nature* http://dx.doi.org/10.1038/nature14121 (2015).
2. Rovner, A. J. *et al. Nature* http://dx.doi.org/10.1038/nature14095 (2015)
3. Lajoie, M. J. *et al. Science* **342,** 357–360 (2013).
4. Gallagher, R. R., Patel, J. R., Interiano, A. L., Rovner, A. J. & Isaacs, F. J. *Nucleic Acids Res.* http://dx.doi.org/10.1093/nar/gku1378 (2015).