commonly studied yeast strains have lost PRCs through evolution[3]. Hence, yeast and human rixosomes have become integrated into two different chromatin-regulating pathways.

The rixosome also has a role in generation of the ribosome – the protein-synthesis machine of the cell[8]. However, Zhou *et al.* demonstrated that the pathway they discovered is independent of ribosome biogenesis. Thus, the rixosome has been repeatedly repurposed through evolution to fill gaps in different pathways across the nucleus. It is tempting to speculate that the rixosome could also participate in other chromatin-related pathways.

Many PRCs interact with thousands of transcripts[10], and the bound RNA seems to regulate the activity of PRCs. Various models have been proposed to explain how this regulation might occur – but the precise molecular mechanisms involved are still a subject of study[11]. Zhou and colleagues' work implies that RNA-mediated regulation of PRCs is a two-way street.

PRCs regulate each other through convoluted feedforward loops that involve their repressive histone marks. This makes it challenging to distinguish between direct and indirect effects when studying the regulation of gene repression by PRCs. Experiments by Zhou *et al.* pinpointed a subunit of PRC1 as a key determinant of the recruitment of the rixosome to facultative heterochromatin. Less was done to investigate how PRC2 regulates the rixosome, although the authors did identify physical interactions between the complexes. There are at least six subtypes of PRC1 complex and two subtypes of PRC2, each of which has different subunit compositions and functions[3]. More work will be needed to identify the subtypes of PRC1 (and perhaps PRC2) that recruit the rixosome to chromatin. Structural studies could reveal how PRCs and the rixosome interact in a way that allows these massive complexes to carry out all their molecular tasks in the context of chromatin.

Mounting evidence points to RNA as a central scaffold that moulds chromatin structure[9] and compartmentalization[5]. The new-found knowledge of the ability of PRCs to trigger RNA degradation, together with their known roles in histone modification and chromatin compaction, cements these complexes as key drivers for shaping the 3D structure and function of facultative heterochromatin.

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Nuclear physics

Cryogenic mastery aids bid to spot matter creation

Jason Detwiler

A cubic metre of tellurium held at cryogenic temperatures over many years has enabled a search for matter created in a rare nuclear process. The feat bodes well for stabilizing other complex systems at low temperatures. **See p.53**

Astrophysical observations reveal that the Universe is made almost entirely of matter, with nearly no antimatter in sight. However, laboratory and particle-collider experiments have so far observed the creation of matter and antimatter in equal parts. Big Bang theories that aim to explain the cosmic matter imbalance predict that matter could be generated without antimatter in a 'little bang', during an ultra-rare nuclear process called neutrinoless

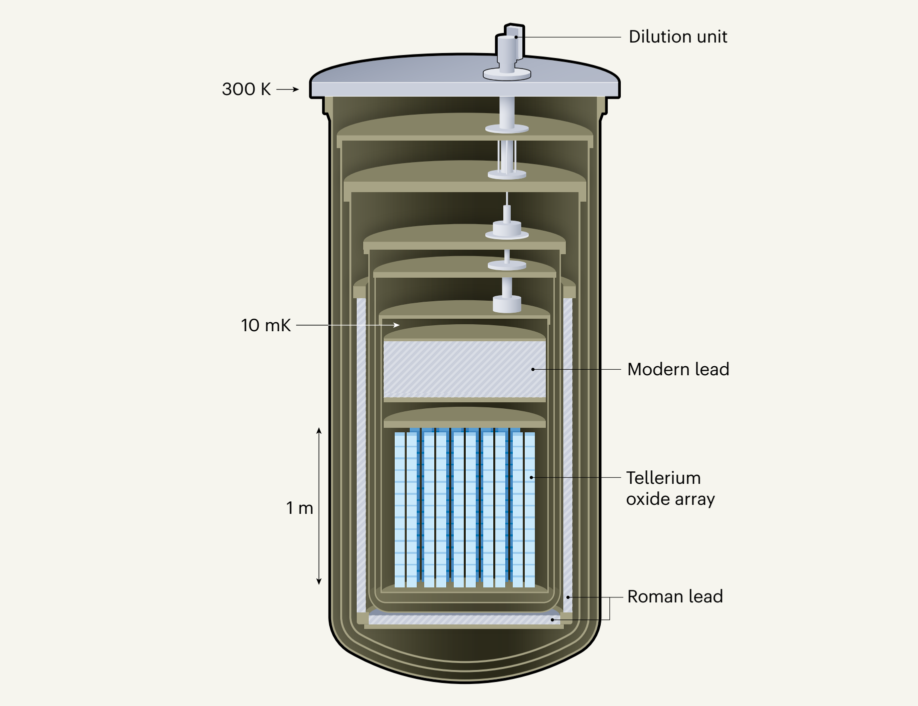

Figure 1 | The coldest cubic metre in the known Universe. The CUORE collaboration[1] searched for an ultra-rare type of nuclear decay using an array of 988 crystals of tellurium oxide, shown here in this simplified schematic. The array is housed inside the world's largest dilution refrigerator, which is a cryogenic device that uses the dilution of helium as a cooling mechanism; a multistage cooling process allowed the team to achieve temperatures of 10 millikelvin in the innermost chamber. Lead shielding was used to block external radiation that could mimic the signature of the decay. As well as modern lead, the team used lead salvaged from a Roman shipwreck in the Sardinian sea, which has lower levels of natural radioactivity. The apparatus is located 1.4 km underground, beneath the Gran Sasso mountain in Italy. (Adapted from Fig. 1 of ref. 1.)

double-β decay. On page 53, the CUORE Collaboration[1] reports the most sensitive search yet for this type of decay using isotopes of tellurium. The decay was not observed, but the engineering feat was remarkable – requiring the stable operation of more than a tonne of experimental apparatus, at cryogenic temperatures close to 10 millikelvin, over several years.


Figure 2 | The CUORE experiment involves a cubic-metre array of tellurium oxide crystals.

YURY SUVOROV

In neutrinoless double-β decay, an atomic nucleus spontaneously transforms into the lighter of its second neighbours in the periodic table of the elements[2]. The process is hypothesized to create two new electrons – and only two electrons – without creating any antimatter. Although similar decays occur in the natural world, in every case witnessed so far, the creation of the two electrons has always been accompanied by the generation of two antineutrinos.

But theories that try to explain the cosmic matter imbalance predict that the neutrino and the antineutrino are actually the same thing – they simply behave like a particle or an antiparticle depending on the direction in which they spin. Such particles are known as Majorana particles, and they have the ability to self-annihilate. Neutrinoless double-β decay could thus be interpreted as the simultaneous emission of two electrons, along with two particles that have the properties of antineutrinos, and that annihilate each other before they can escape the vicinity of the nucleus. So at the end of the decay, there are two new electrons and no new antimatter particles, meaning that the conditions for a little bang are met.

The idea that the neutrino could be a Majorana particle was considered mostly irrelevant for decades, because this property requires the neutrino, long thought to be massless, to have a non-zero mass. However, at the turn of the millennium, different types of neutrino were found to oscillate – that is, to transform into one another – and this phenomenon requires that neutrinos have mass (see go.nature.com/3dhk6hu). This led to renewed interest in the idea that neutrinos could be Majorana particles, and set off a flurry of experimental efforts to search for neutrinoless double-β decay.

The CUORE collaboration searched for this decay using an array of 988 large crystals of tellurium oxide (Fig. 1). Tellurium contains isotopes that could, in principle, undergo the hypothesized decay. The electrons that are generated when tellurium decays are highly energetic, but they come to a stop quickly in a crystal. The authors detected their presence by measuring a slight change in temperature caused by their absorption in the crystal.

Measuring such a subtle temperature change requires that the crystals be cooled to cryogenic temperatures near 10 mK, just ten-thousandths of a degree above absolute zero. To achieve this, the collaboration housed the entire array inside a single, giant dilution refrigerator, a cryogenic device in which the dilution of helium acts as a cooling mechanism. Dilution refrigerators are used widely at small scales in low-temperature research. The CUORE incarnation is the largest dilution refrigerator ever made, and is unofficially referred to as the coldest cubic metre in the known Universe[3] (Fig. 2).

The sensitivity of such experiments rests primarily on two key aspects. One concerns the existence of other physical processes that can change the crystal temperatures by exactly the amount predicted for neutrinoless double-β decay. The rate at which such processes occur is known as background, and a low background is required to minimize the chance of mistaking these mundane known processes for a little bang. The second key aspect is the experiment's exposure, which is the total detector mass multiplied by the duration of its operation. Exposure quantifies how the chance of detecting a decay increases with the number of nuclei present and the length of time they are given to decay: the higher the exposure, the more likely the decay.

The CUORE experiment's reported exposure was more than one tonne-year, which triples the collaboration's previous achievement[4]. This is no small engineering feat. CUORE is the largest, most complex experiment undertaken in a dilution refrigerator so far. Achieving such high exposure required the cooling to 10 mK of around 1.5 tonnes of crystals, along with the lead radiation shielding and supporting infrastructure, and maintaining that temperature over several years. All the while, the authors also achieved stable operation of the detectors, which remained running for an impressive 90% of the experiment's total time. And all of this was done 1.4 km underground, beneath the Gran Sasso mountain in central Italy.

The team's achievement lights the path for others facing similar engineering challenges. One notable application of dilution refrigeration is in quantum computing, in which low temperatures could mitigate errors that arise from quantum bits (qubits) interacting with their warm surroundings. The quest to build devices with high computational power is naturally driving the industry towards very large arrays containing many qubits. These efforts could benefit directly from the technological solutions developed by the CUORE Collaboration.

An upgrade of the experiment is under way[5], involving crystals that are able to identify and eliminate the dominant background observed in the present study. The upgrade has been dubbed CUPID, and it is expected to vastly improve the sensitivity of the experiment, resulting in a strong probability of observing neutrinoless double-β decay, according to a wide class of theoretical model[2]. CUPID will reuse the CUORE collaboration's giant dilution refrigerator and shielding, building directly off the team's technical success. The coldest cubic metre in the known Universe could thus very well be the pristine environment in which humans first observe a little bang.

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