a process that correlated with fusion of the sutures in the mice. These findings prompted the authors to look for cells other than CTSK^{+} CSCs that could build bone.

Bok and colleagues' thorough analysis revealed that the observed fusion occurs through a process called endochondral ossification, which involves the initial formation of cartilage and its subsequent substitution by bone. This raised the question of where the cartilage-producing cells (chondrocytes) come from. Under normal conditions, there are no chondrocytes in sutures (with the exception of one type of cranial suture, which has a different developmental origin from that of the other types[10] and therefore is not relevant to the current findings).

Further investigation revealed the presence of another population of CSCs characterized by the expression of the *Ddr2* gene (DDR2^{+} CSCs), which normally generate cell types similar to those produced by CTSK^{+} CSCs (Fig. 1). However, the authors found that, in the absence of CTSK^{+} CSCs, DDR2^{+} CSCs differentiate into chondrocytes that contribute to the observed fusion of the sutures. Notably, an independent study published this year also identified DDR2-expressing cells as potential CSCs in sutures[11].

From a scientific perspective, it is tremendously exciting to discover a case in which two distinct populations of stem cells with the same developmental origin are located in the same tissue and generate similar types of cell. The finding underscores the complexity of stem-cell biology and, if similar arrangements occur in other organs, could have important implications for our understanding of how stem cells are involved in tissue regeneration more broadly.

Nevertheless, several questions still need to be answered. The observation that altering the size of one population of CSCs affects the behaviour of another indicates an interaction between these populations, the underlying mechanism (or mechanisms) of which remains to be explored. Bok *et al.* identify one mechanism, which involves secretion of the hormone IGF1 by CTSK^{+} CSCs; binding of this hormone by receptors on DDR2^{+} CSCs prevents cartilage formation. However, the interaction is probably considerably more complex than this, and might well involve other proteins[7,12] known to influence stem cells.

Another issue that requires further investigation is a partial discrepancy between different findings. Genetic ablation of *Gli1*-expressing cells, which probably include both the CTSK^{+} and the DDR2^{+} CSCs, leads to abrupt fusion of sutures[4], contradicting the conclusion that DDR2^{+} CSCs are required for fusion. By contrast, the ablation of *Prrx1*-expressing cells, which also probably include both populations of CSCs, does not cause craniosynostosis[6]. And although Bok *et al.* found that ablation of the *Twist1* gene in CTSK^{+} CSCs leads to suture fusion, ablation of the same gene in *Gli1*-expressing cells does not[8] — suggesting that *Twist1* in DDR2^{+} CSCs might have a role in promoting the differentiation of these cells into chondrocytes. These discrepancies and possibilities remain to be explored.

> **"The finding could have implications for our understanding of how stem cells are involved in tissue regeneration."**

From a clinical perspective, Bok and co-workers' remarkable discovery greatly improves our understanding of the processes underlying craniosynostosis. The conventional treatment involves surgically opening the fused sutures, but refusion often occurs[13], a phenomenon that clearly requires investigation. In this context, further characterization of the relationship between the two populations of CSCs, as well as of other cell sources that potentially underlie refusion, is of considerable interest. This would build on the finding that cells of the dura mater (a fibrous membrane underlying the skull) can prevent refusion[8]. Perhaps Bok and colleagues' discovery will open up fresh avenues of research aimed at developing new therapies for craniosynostosis.

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Particle physics

Antimatter falls

Anna Soter

A test performed on antihydrogen atoms has shown that gravity acts on matter and antimatter in a similar way. The experimental feat is the latest in efforts to probe the crossover between theories of relativity and particle physics. **See p.716**

Isaac Newton's now-famous revelation in an apple orchard makes the nature of gravity seem obvious. But would an apple made of antimatter also fall to the ground? On page 716, Anderson *et al.*[1] (members of the ALPHA collaboration) answer in the affirmative. Although there was already some theoretical and indirect experimental[2,3] evidence to suggest that antimatter is subject to the same gravitational pull as matter, the authors have made the first direct observation of free-falling antimatter. Whether the fall is completely indistinguishable from that of a normal apple has yet to be determined.

The underlying physical principle behind the ALPHA collaboration's experiment is the universality of free fall. This idea was first formulated in the sixteenth century by Galileo Galilei, who reportedly observed that spheres that were dropped from the Leaning Tower of Pisa hit the ground at the same time, irrespective of their size and composition. The first precise measurements proving this universality came around the turn of the twentieth century, when Hungarian physicist Loránd Eötvös compared objects made from different materials suspended on a pendulum[4]. A century later, a satellite-borne microgravity experiment showed that titanium and platinum are subject to the same gravitational acceleration as each other, within 15 digits of precision[5]. The universality of free fall has also been tested on very small scales using atom interferometry[6], and on large scales by investigating the Moon's orbit[7].

Why are such measurements so intriguing? Simply because it cannot be assumed that an object's inertial mass, which measures its resistance to acceleration, is the same fundamental property as its gravitational mass,

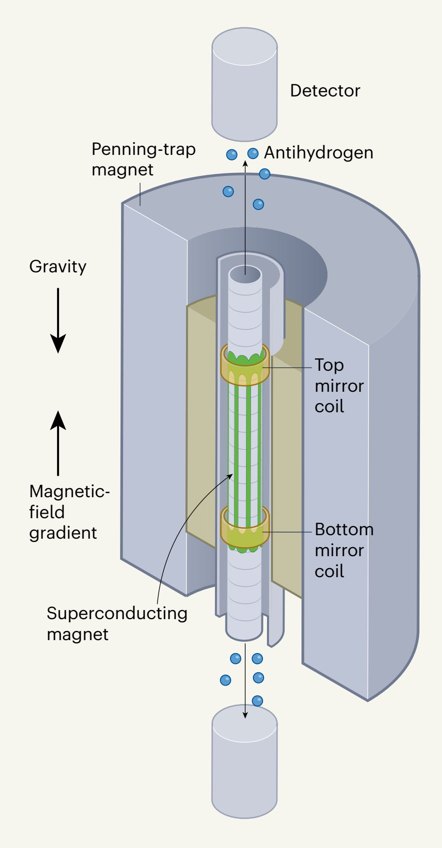

Figure 1 | An experiment to test the effect of gravity on antimatter. The ALPHA collaboration[1] observed the free fall of antihydrogen atoms, formed from particles that were manipulated with a device called a Penning trap. The atoms were trapped in a magnetic field that was generated by a superconducting magnet (one with zero electrical resistance) and by two electromagnets called mirror coils. The authors applied a voltage across the two mirror coils to create a magnetic-field gradient that mimicked the effect of gravity. They then released the antihydrogen atoms and detected them at the walls of the apparatus. Similar numbers of atoms were found on the top and bottom walls when the magnetic-field gradient balanced out the acceleration due to gravity, indicating that antimatter is subject to the same gravitational pull as matter.

which determines the magnitude of the gravitational force that it experiences. In modern physics, inertial mass is encoded in the standard model of particle physics, whereas gravitational mass is dealt with in Einstein's general theory of relativity. The assumed equivalence of inertial mass and gravitational mass is incorporated in the weak equivalence principle, which is the cornerstone of general relativity – but no proposal has yet succeeded in unifying the theories.

So far, the weak equivalence principle has been tested only on normal matter, consisting of protons, neutrons and electrons – and all attempts have supported the equivalence. A breakdown of the principle on large scales would pose serious problems for our understanding of gravity and the standard model[2], so the prospect of extending these studies to larger objects is exciting. The ALPHA collaboration took this leap by observing the free fall of charge-neutral antihydrogen atoms, which consist of an antiproton and a positron (the antiparticle of an electron). The authors first created and confined these atoms at low temperatures in a device called a Penning trap. They then released the atoms in a controlled way, and compared the number of atoms that escaped towards the bottom and towards the top of their apparatus.

Although seemingly straightforward, the experiment required highly specialized equipment and expertise. Researchers in the collaboration developed a vertical nested trap called the ALPHA-g apparatus[8] for this purpose (Fig. 1), building on their previous success with a horizontal design for antihydrogen spectroscopy[9]. After catching, accumulating and cooling antiprotons in their first Penning trap, they recaptured and recooled them in the new vertical set-up. Cold positrons were also injected into ALPHA-g, and the two cold plasmas combined at high densities to produce antihydrogen.

Some of these antihydrogen atoms were sufficiently cold to be trapped by magnetic-field gradients acting on their magnetic moments. The trapping field was generated by a superconducting magnet (one with zero electrical resistance) in the radial direction, and by two electromagnets called mirror coils in the vertical direction. This set-up provided exquisite control, but it also posed some problems. Specifically, the strong currents in the mirror coils needed to be ramped down over a period of 20 seconds, to allow the antihydrogen atoms to 'spill' gently out of the apparatus. A tendency to do so from the bottom more than from the top would indicate that the effect of gravity on antimatter is similar to that on normal matter.

The ALPHA collaboration measured this tendency by manipulating the vertical magnetic field through careful control of the currents in the mirror coils. A small vertical gradient in the field can imitate the effect of gravity, and the authors used this principle to systematically modify the acceleration experienced by the atoms. They did so by applying a small voltage across the two mirror coils, which were connected in series to the main power supply. After the antihydrogen atoms were released from the trap, they were detected when they eventually hit the walls of the apparatus. When the authors tuned the magnetic-field gradient so that it balanced out the acceleration due to gravity, similar numbers of atoms were found on the top and bottom walls.

> **"A small vertical gradient in the field can imitate the effect of gravity."**

The precision of the authors' experiment was high enough to determine the direction of gravity for antihydrogen. Future experiments could provide support for the findings by using antihydrogen atoms that are cooled with lasers[1], or perhaps even by using antihydrogen ions, if they can be synthesized and cooled to microkelvin temperatures[10].

The study is a first step towards investigating gravity in the framework of the standard model, but more advanced questions await. The experiments performed so far have all involved hadrons, which are composite particles, such as neutrons and protons, that each consist of three quarks, as well as many 'virtual' particles that generate the hadron's mass in a model-dependent way. Scientists are therefore keen to investigate atoms in which virtual particles have a less dominant role[11,12]. Such atoms would provide Newton's orchard with ever more exotic varieties of apple, providing scope for discovering previously unknown physics beyond gravity[13].

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