other rocky bodies melted to form a mantle and a crust, with a denser, metallic core. Although most people think of molten rock as being unlikely to evaporate, laboratory experiments[7] have shown that such material exposed to the vacuum of space does indeed evaporate, with more-volatile elements evaporating faster than less-volatile ones. In addition, the rapidly vibrating lighter isotopes of an element evaporate faster than the more languid heavy isotopes, resulting in an excess of heavy isotopes in the melted rock that remains.

Hin *et al.* report an impressive set of high-precision data on the relative abundances of two stable isotopes of magnesium, ^{24}Mg and ^{25}Mg, showing that Earth and similar rocky bodies are slightly enriched in the heavier isotope ^{25}Mg, relative to the chondrites from which they formed. The enrichment is precisely what would be expected if molten rock in planetary precursors had evaporated, conjuring up images of lava floating in the vacuum of space. The authors' data breathe new life into earlier suggestions[8] that Earth and chondrites differ in their magnesium isotopic compositions.

Magnesium isotopes are especially useful for such analyses because magnesium is a lithophile (rock-loving) element. Consequently, this element is not lost to planetary atmospheres, nor does it dissolve in metallic cores at temperatures relevant to planetary formation. It is therefore an unambiguous tracer of the history of rock. Hin *et al.* show that if the evaporation of molten rock was slow enough to allow for thermodynamic equilibrium to occur between the rock and its vapour, previously documented enrichments of the heavy isotopes of silicon[9] and iron[10] in some melted bodies could also be explained by vapour loss, rather than by sequestration in the core, as previously suggested[11–13].

In a separate but related study, Norris and Wood melted basaltic rock in a furnace under controlled conditions. They discovered that the evaporation of moderately volatile chalcophile elements accounts for several vexing observations regarding the relative concentrations of these elements in the rocky portion of Earth. In particular, the authors found that the experimentally determined volatilities explained the pattern of depletion of these elements in the rocky Earth[14] if the partial pressures of oxygen at the time of evaporation were relatively high, similar to those intrinsic to planet formation (partial pressure is the pressure generated by a component of a mixture of gases). Such conditions could have prevailed only after the hydrogen gas left over from the formation of the Sun had been dispersed by strong stellar winds. Because this dispersal took several million years[15], Norris and Wood's experiments not only point to evaporation as a key process, but also constrain the timing of the evaporation events.

But how did the molten rock form? According to both studies, cataclysmic collisions of planetesimals caused the melting and vapour loss (Fig. 1). Both teams correctly point out that the velocities of hot gas can overcome the force of gravity only for small planetesimals — those with a mass about half that of Pluto. Therefore, Earth and other large bodies might have inherited the chemical imprints of vapour loss from these smaller building blocks. Alternatively, computer simulations of giant impacts such as the one that formed the Moon[16] allow for vapour loss through more-complicated scenarios.

The conclusions of the two studies differ in important, if nuanced, ways. Hin *et al.* propose a series of liquid–vapour equilibrium events triggered by planetesimal collisions, in which the rates of condensation and evaporation become equal before the vapour escapes. The question arises as to whether the collisions would really lead to such episodic equilibration and vapour loss. Conversely, Norris and Wood invoke the kinetics of evaporation, rather than equilibrium in the strictest sense. It remains to be seen whether these conclusions are in serious conflict.

The results of the two studies are not yet universally applicable. Mars and Earth, for example, have different silicon isotope ratios that are not easily explained by the authors' models. Moreover, the isotopic effects of elements such as silicon and iron dissolving in the cores of planetary bodies must be accounted for. Distinguishing the effects of core formation from those of vapour loss on isotopic compositions will take further study.

Unresolved problems notwithstanding, the physical chemistry of melting and evaporation could ultimately prove to be a key arbiter in competing models of planet formation. The current studies are not the first to suggest that volatile-element depletion and isotope separation resulted from collisions[17], but their relative success should encourage further exploration of the potential role of collisions in determining the chemical and isotopic compositions of planets. ■

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LEUKAEMIA

Vitamin C regulates stem cells and cancer

It emerges that high levels of vitamin C in blood-forming stem cells influence the number and function of the cells and affect the development of leukaemia, through binding to a tumour-suppressor protein, Tet2. SEE ARTICLE P.476

PETER G. MILLER & BENJAMIN L. EBERT

The substrates, intermediates and products of cellular metabolism have the potential to influence cellular identity and transformation to cancer[1,2]. Two papers (one by Agathocleous *et al.*[3] on page 476 and the other by Cimmino *et al.*[4] in *Cell*) now find a previously unknown role for one such metabolite, vitamin C, in stem-cell biology. They show that levels of vitamin C, also known as ascorbate, regulate the number and function of blood-forming haematopoietic stem cells, largely through effects on the Tet2 protein. This change, in turn, alters the progression of leukaemia.

Researchers' ability to profile metabolites in stem cells has previously been limited by the fact that such analyses typically require millions of cells. Mouse blood cells, for instance,

consist of less than 0.01% haematopoietic stem cells (HSCs)[5], making it difficult to obtain sufficient numbers for study. Agathocleous *et al.* overcame this problem by developing a method for analysing metabolites in as few as 10,000 cells. Using this technique, they found clear differences between the metabolic profiles of mouse blood cells at various stages of differentiation.

The authors discovered that levels of vitamin C are between 2 and 20 times higher in populations of immature stem cells and progenitor cells than in more-differentiated cell types. Consistent with this finding, they showed that expression of the gene *Slc23a2*, which encodes a protein that imports vitamin C, was higher in HSCs than in more-differentiated cells. Importantly, the researchers confirmed their observations in human blood cells.

Agathocleous and colleagues next sought to determine whether vitamin C levels regulate HSC numbers and function. Unlike humans, who cannot synthesize vitamin C and rely entirely on dietary sources, mice produce the enzyme gulonolactone oxidase (Gulo), which generates vitamin C in the liver. Mice lacking the *Gulo* gene therefore also depend on dietary sources of vitamin C. The authors demonstrated that mice lacking *Gulo* developed vitamin C deficiency when fed a diet low in the vitamin. These mice had more HSCs than controls, and their HSCs had increased function, as defined by the cells' ability to repopulate the blood system of recipient mice in bone-marrow-transplant experiments.

Vitamin C is a cofactor for the enzyme Tet2 (ref. 6), which regulates the modification of DNA by methyl groups — a regulatory mechanism that can lead to changes in gene expression. Specifically, Tet2 catalyses an intermediate step in DNA demethylation[7], converting the molecule 5-methylcytosine to 5-hydroxymethylcytosine (5hmC). Genetic inactivation of *Tet2*, much like vitamin C depletion, leads to increased HSC numbers[8], as well as a block of HSC differentiation. In line with this, Agathocleous *et al.* found that vitamin C depletion results in decreased levels of 5hmC, suggesting a decrease in Tet2 activity. The authors next compared mice lacking *Tet2*, *Gulo* or both, and found only slight differences in 5hmC levels and HSC function between them, implying that the effects of vitamin C depletion are mediated in large part — although not entirely — by Tet2 (Fig. 1).

Cimmino *et al.* reached a similar conclusion by taking an alternative approach. They investigated whether sustained inactivation of *Tet2* is required for the increased HSC activity and susceptibility to leukaemia that occurs in mice completely lacking *Tet2*, by generating mice in which *Tet2* could be depleted and then restored. Restoration of *Tet2* expression in these animals reversed the enhanced HSC function and block of HSC differentiation caused by *Tet2* loss. The researchers next demonstrated that they could achieve the same effect pharmacologically, using vitamin C to restore Tet2 activity *in vitro* and *in vivo*. The treatment led to higher 5hmC levels, to reduced HSC self-renewal and to a partial reversal of the differentiation defects seen in *Tet2*-mutant animals.

Tet2 mutations are common in acute myeloid leukaemia (AML) in humans[9]. Both groups therefore examined the effects of vitamin C on this cancer. Agathocleous *et al.* made use of a mouse model in which AML is driven by two mutations — *Tet2* inactivation and overexpression of the gene *FLT3-ITD* (a mutation found in 20–30% of human cases of AML)[10]. The authors found that depletion of vitamin C accelerated the growth of these leukaemias, partially owing to impairment of Tet2 function. This effect could be reversed with dietary vitamin C.

Cimmino *et al.* used AML cells taken from humans, which they studied *in vitro* or transplanted into mice. In both cases, vitamin C supplementation induced differentiation and the death of leukaemia cells. In mice, these changes led to decreased rates of AML progression.

The effect of vitamin C on human health in general, and on cancer in particular, has been a subject of debate since the 1970s. Epidemiological studies have found varied associations between low vitamin C and decreased overall survival and deaths related to both cardiovascular disease and cancer[11,12]. By contrast, clinical trials of cancer treatments have provided no evidence that vitamin C supplements have beneficial effects on tumour growth or survival[13]. One explanation for this discrepancy might be that vitamin C supplementation is efficacious only in people truly deficient in vitamin C, a group that represents just 7% of the US population[14].

Vitamin C and Tet2 function have previously been linked to inflammation, a condition also associated with altered stem-cell function, cardiovascular disease and cancer risk[15,16]. Indeed, our group and others have defined a clinical state in which mutations — commonly including *TET2* — that arise in HSCs are prevalent in the blood systems of healthy individuals. This state increases in frequency with age (increasing to more than 10% in people over 70)[17], causes inflammation and is associated with a significantly increased risk of both cardiovascular disease and the development of leukaemia[18].

The current studies provide support for the hypothesis that vitamin C deficiency alters HSC function and may influence the risk of leukaemia and other diseases. In the future, large-scale population studies that include comprehensive clinical, genomic and metabolic data may define therapeutically relevant associations between vitamin C and cancer, cardiovascular disease and death. Such studies could prove particularly useful in further defining the relationship between Tet2 mutations, vitamin C, inflammation and cancer.

Lemons will probably not do for leukaemia what they did for scurvy. Nonetheless, we are a step closer to understanding what makes stem cells, both normal and cancerous, tick. ■

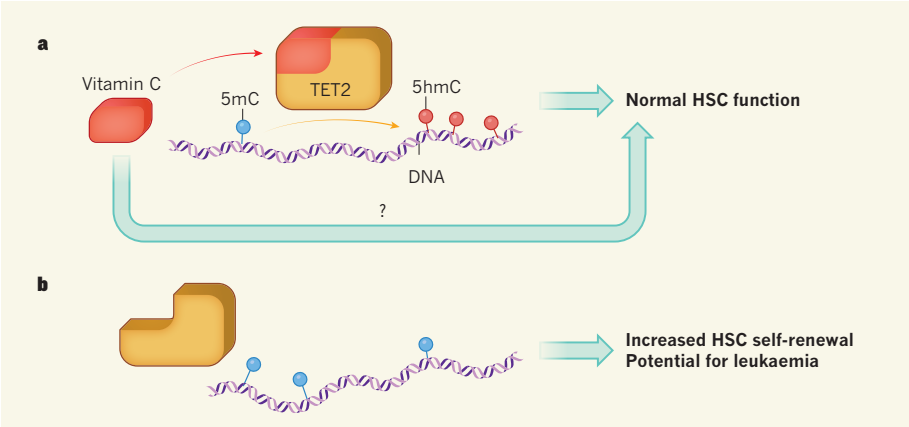

Figure 1 | The effects of vitamin C on stem-cell biology and leukaemia. **a**, Vitamin C is a cofactor for the enzyme Tet2 — interaction between them enables Tet2 to oxidize methyl groups in the modified DNA base methylcytosine (5mC) to produce 5-hydroxymethylcytosine (5hmC), leading to changes in gene expression. Agathocleous *et al.*[3] and Cimmino *et al.*[4] demonstrate that this pathway maintains the normal function of blood-forming haematopoietic stem cells (HSCs). Vitamin C also maintains HSC function through unknown, Tet2-independent mechanisms. **b**, By contrast, vitamin C depletion leads to impaired 5mC demethylation and expansion of the HSC population owing to excessive self-renewal. This, in turn, increases the potential for HSCs to give rise to leukaemia.

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CONDENSED-MATTER PHYSICS

Taking control of spin currents

Conventional wisdom dictates that an electron's magnetic moment and momentum are strongly coupled only in materials made of heavy elements. An experiment demonstrates a striking counterexample. SEE LETTER P.492

ZHI-XUN SHEN & JONATHAN SOBOTA

Spintronic devices promise enhanced performance over conventional electronics by simultaneously exploiting the flow of electric charge and of the magnetic moment (spin) in a material. Realizing this level of mastery requires the identification of materials in which each electron's spin and momentum are strongly coupled. Such materials are generally composed of heavy elements, for example gold or bismuth. But on page 492, Sunko *et al.*[1] report surprisingly strong spin–momentum coupling in electrical pathways comprised of oxides of transition metals, such as cobalt, that lack heavy constituents. The authors explain the observed coupling as being due to symmetry properties of electronic states at the material's surface. In addition to its fundamental interest, this discovery could lead to strategies for designing material interfaces that will lie at the heart of tomorrow's spintronic devices.

When a wire is hooked up to the terminals of a battery, electrons flow through the wire. This represents a charge current, because all electrons are charged, but not a spin current, despite the fact that all electrons have spin. The net spin of the electrons is zero on a macroscopic scale because the spin of each electron is randomly oriented. However, a net spin alignment is possible, thanks to Einstein's special theory of relativity, which tells us that an electric field is transformed into a magnetic field in the reference frame of electrons travelling at sufficiently high velocities (close to the speed of light). The spins will align with this magnetic field, in a direction that depends on both the motion of the electrons and the orientation of the electric field through which they propagate.

If the electric field is generated by protons in atoms, the resulting interaction is known as atomic spin–orbit coupling (SOC). The magnitude of this interaction grows with the number of protons and is therefore largest in materials composed of heavy elements. However, SOC alone does not produce a net spin alignment in materials because the average electric field that arises from a periodic arrangement of atoms is zero on a macroscopic scale. A second material property is needed: inversion-symmetry breaking (ISB), whereby opposite orientations of a material can be distinguished. The combination of SOC and ISB produces the spin–momentum coupling required for spintronics applications.

How is inversion symmetry broken? Some crystal structures are naturally inversion-asymmetric, and the resulting spin–momentum coupling is called the Dresselhaus effect[2]. More generally, inversion symmetry is always broken at a material's surface, producing a spin–momentum coupling known as the Rashba effect[3]. Because both of these effects require SOC, they should be pronounced in materials composed of heavy elements. Accordingly, the first direct experimental discovery of the Rashba effect was in electronic states near the surface of gold[4]. However, the necessity for heavy elements should not be overstated, because the magnitude of ISB is equally important[5,6].

This is the idea seized on by Sunko *et al.* to explain their discovery of a surprisingly large Rashba effect in the platinum cobalt oxide $PtCoO_2$. In this material, the heavy element platinum has a passive role, because conduction takes place through a cobalt-related pathway. This fact is backed up by the authors' observation that the spin–momentum coupling increases dramatically when cobalt is replaced

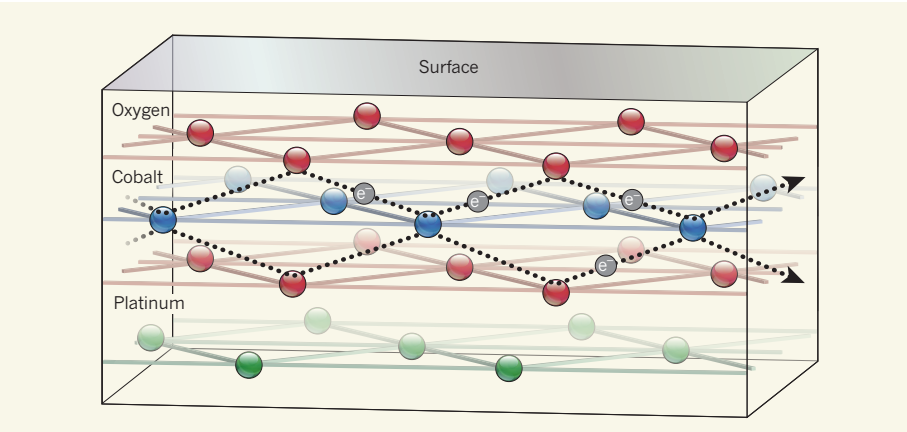

Figure 1 | Electron pathways that break inversion symmetry. The crystal structure of the platinum cobalt oxide $PtCoO_2$ comprises layers of platinum, cobalt and oxygen atoms. At the surface, the structure is terminated by a sandwich of oxygen–cobalt–oxygen layers. Conduction electrons (e^-) derive from the cobalt atoms, but cannot jump directly between these atoms because the interatomic distance is too large. Instead, they take one of two zigzagging routes (dotted arrows) between cobalt and oxygen layers. Although these two pathways look similar, they have different environments: the lower oxygen layer is directly above a platinum layer, and the upper oxygen layer has nothing but vacuum above it. Consequently, there is a pronounced difference in the electron occupation of the two conduction pathways, breaking what is known as inversion symmetry. Sunko *et al.*[1] suggest that this asymmetry generates strong coupling between the magnetic moment (spin) and the momentum of each electron that flows along the two pathways — a requirement for spin-based devices that offer improved performance over conventional electronics. Solid lines connect neighbouring atoms in the same layer.