lithium-poor. Although lithium-deficient stars are not unknown in the Galaxy's halo, which contains the oldest and more iron-poor stars in the system and in which the lithium deficiency is driven perhaps by their being members of binary systems[8], they comprise only about 5% of the Galaxy's halo stars. The absence of lithium in the most iron-poor stars discussed here is an exciting and potentially fundamental result. What has happened to the lithium created at the birth of the Universe?

The caveat to the above discussion is, of course, the small number of currently known iron-poor stars that have less than $10^{-4.5}$ the solar iron abundance. Caffau *et al.*[1] comment that they expect 5–50 stars of similar (or lower) iron content to that of SDSS J102915+172927 to be found in the Sloan Digital Sky Survey, in which they discovered this star. If they, and other currently planned surveys for the most metal-poor stars, are successful, the long-standing tyranny of small numbers will indeed have been overcome. ■

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ECOLOGY

Nitrogen from the deep

Ecosystems acquire nitrogen from the atmosphere, but this source can't account for the large nitrogen capital of some systems. The finding that bedrock can also act as a nitrogen source may help solve the riddle. SEE LETTER P.78

EDWARD A. G. SCHUUR

In many parts of the world, the rates at which plants grow are controlled by the availability of nitrogen, an essential element for all life[1]. Forest growth is fuelled by the nitrogen capital contained in soils and biomass. Like money in a bank account, this capital increases slowly within ecosystems over hundreds to thousands of years from the accumulation of tiny deposits of nitrogen that arrive each year from the atmosphere[2]. But on page 78 of this issue, Morford *et al.*[3] report that nitrogen-rich bedrock can double nitrogen input rates to forest ecosystems, which flourish as a result.

Nitrogen is the fourth most abundant element in living organisms, and is used as a building block for critically important biological molecules such as amino acids and nucleic acids. In many ecosystems worldwide, nitrogen is the element whose supply rate from the environment is most limited. Because competition is fierce for this resource, nitrogen supply controls the behaviour of many organisms and shapes the structure and function of whole ecosystems.

Most of the nitrogen needed by organisms to grow is supplied by recycling, in which decomposing organic matter releases nitrogen in forms that can be acquired by plants and microorganisms. Recycling, in turn, is dependent on the nitrogen capital that has accumulated over time in an ecosystem. New inorganic nitrogen is deposited into ecosystems abiotically in rainfall, or with the assistance of certain microbes that, individually or in close relationships with plants or fungi, convert inert atmospheric nitrogen gas into a form that organisms can use.

The new deposits of nitrogen are small relative to the quantities of the element that are recycled. But they are vital, not only as a source of nitrogen for newly forming ecosystems, but also because they sustain growth over centuries of ecosystem development by balancing natural nitrogen loss out of ecosystems into streams or back to the atmosphere. Scientists have made detailed measurements of atmospheric nitrogen inputs in many places, but have sometimes encountered a puzzling phenomenon: the nitrogen capital within some ecosystems is larger than can be accounted for by known atmospheric sources[4].

Morford and colleagues' discovery[3] that bedrock can provide substantial quantities of nitrogen to organisms provides a new piece of the puzzle, and in doing so helps reshape our view of ecosystem nitrogen budgets. The authors compared plants and soils from forest ecosystems in California that are similar in terms of their stand age, climate and soil type, but which grow on two different types of bedrock. They found that tree species common to both sites were enriched in nitrogen in forests growing on soils derived from mica-schist (a type of marine sedimentary rock) compared with those in forests growing on soils derived from gabbro-diorite (a type of igneous rock). Tellingly, the sedimentary rock contained roughly ten times the levels of nitrogen found in the igneous rock.

The authors found that the trees growing on the sedimentary rock not only had higher nitrogen levels, but also had more leaves than did trees growing on the igneous rock (Fig. 1). This presumably enables them to grow faster and results in a more productive forest. The elevated nitrogen levels in these trees corresponded to the measured nitrogen capital of the underlying soils, which are the direct source of the nitrogen to the forest — that is, the nitrogen capital in these soils was twice that of conifer-forest soils overlying igneous rock.

Nitrogen levels vary across forest stands for many reasons, and so Morford *et al.* needed more evidence to show that bedrock was responsible for the observed variations. The authors therefore took advantage of the fact that plants, soils and bedrock all

S. MORFORD

Figure 1 | Flourishing forests. Morford *et al.*[3] report that conifer forests at South Fork Mountain, California, are enriched in nitrogen supplied by the underlying sedimentary rock. This nitrogen boost increases the above-ground biomass of the forest.

contain measurably different amounts of ^{15}N in their nitrogen pools. They found that, in the forest growing on nitrogen-rich sedimentary rock, the ^{15}N-content in both plants and soils matched that of the bedrock; this was not true for forests growing on the nitrogen-poor igneous rock, ruling out the possibility of significant nitrogen contribution from this rock.

Although the nitrogen-isotope measurements helped build the case for sedimentary bedrock as a nitrogen source for forests, they alone were not a smoking gun. To extend the findings beyond the carefully matched forest stands, the authors carried out a regional analysis of similar conifer forests in California. Sure enough, they found that the above-ground biomass of forests growing on nitrogen-rich sedimentary bedrock was almost 50% bigger by mass than that of forests on igneous bedrock, after accounting for differing ages of tree stands.

The 'imprint' of nitrogen from bedrock on streams[5] and soils[6] has previously been reported for isolated sites in the same general region as the current study[3], and so Morford and colleagues' analysis makes the case for this as a regional pattern. But less than 2% of conifer-forest soils in that same region have a nitrogen capital as high as the sedimentary-bedrock forest that has been intensively studied by the authors (see Supplementary Information for ref. 3). This means that the high input of nitrogen from bedrock beneath that forest — which is equivalent to atmospheric nitrogen inputs — probably represents an upper estimate for the extent of this phenomenon. With 75% of Earth covered by sedimentary and related rock types[7], there is a real need to explore the phenomenon beyond this region to determine what more common levels of bedrock-nitrogen inputs are for ecosystems elsewhere. ■

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CANCER

Tumour-fighting virus homes in

An early clinical trial demonstrates the delivery and replication of a cancer-killing virus in metastasized tumour tissue. These promising results could provide a foundation for systemic virotherapy for patients with cancer. SEE LETTER P.99

EVANTHIA GALANIS

Clinical advances in cancer research are often slow to materialize, in part because the efficacy of a treatment has to be balanced against its potential toxicity to normal tissues. Infection of tumours with oncolytic (cancer-killing) viruses has been explored as a new type of treatment that is not cross-resistant with approved cancer therapies and, being target-specific, may have fewer toxic side effects. On page 99 of this issue, Breitbach *et al.*[1] describe a phase I clinical trial in which an intravenously delivered oncolytic poxvirus was capable of replicating selectively in metastasized tumours. This is a milestone in the development of an effective oncolytic agent for systemic administration.

Oncolytic viruses became a focus of attention for cancer therapy following observations that natural viral infection or vaccination can lead to spontaneous regression of malignancies[2]. Unhindered by interferon-mediated antiviral defence, which is compromised in many tumours[3], these viruses specifically attack cancer cells by gaining entry through receptors that are overexpressed in these cells and/or by exploiting molecular pathways associated with malignant transformation for their replication[4,5]. As the virus starts to replicate at the tumour site, its destructive effect increases. Strategies are being devised to make this process even more efficient by deploying genetically engineered oncolytic viruses that carry therapeutic or immunomodulatory transgenes.

In advanced cancer, systemic dissemination of solid tumours is linked with a poor prognosis. Before oncolytic viruses can be used to treat such metastases, they must be able to reach and replicate in metastatic sites following intravenous administration. But there are obstacles to be overcome, including the antiviral immune response, and the uptake and destruction of the virus by the endothelial reticulum system in the liver and spleen.

Breitbach *et al.*[1] take up the challenge using a genetically engineered oncolytic poxvirus known as JX-594. This is a smallpox-vaccine derivative of Wyeth-strain vaccinia virus carrying an inactivated thymidine kinase gene to increase tumour specificity, and expressing two transgenes: one encoding human granulocyte–macrophage colony-stimulating factor (GM-CSF) to stimulate anti-tumour immunity and the other β-galactosidase, a surrogate marker for detecting viral gene expression.

The authors tracked the virus in 23 cancer patients, all with advanced solid tumours that were resistant to other treatments. Patients were each given one dose of JX-594 at one of six different dosage levels by intravenous injection; these were all well tolerated. The maximum feasible dose was 3×10^7 plaque-forming units (PFU) per kilogram of body weight (corresponding to a total dose of about 2×10^9 PFU). This dosage is in line with doses of other oncolytic viruses that can safely be given intravenously, including adenovirus, reovirus, paramyxovirus (Newcastle disease virus and measles) and Seneca Valley virus.

Breitbach *et al.* demonstrated such dose-dependent delivery of the virus (at 8–10 days after intravenous administration) to metastatic tumour deposits from a variety of tumour types, including leiomyosarcoma, mesothelioma, and lung, ovarian and colorectal cancers. In eight patients who had received 10^9 PFU or more per dose, delivery and replication were confirmed by quantitative polymerase chain reaction in five patients and by immunohistochemistry using a polyclonal anti-vaccinia antibody in six patients: granular cytoplasmic staining evident in tumour tissue was indicative of replicating virus (viral factories; Fig. 1).

Although JX-594 administration seemed to result in disease control in a dose-dependent way, with patients treated with the higher doses benefitting the most, viral infection and replication in metastatic deposits did not consistently affect clinical outcome. Some patients experienced clinical benefit — defined as disease stabilization for more than ten weeks — even when there was no evidence of viral replication in their tumour biopsies. By contrast, two out of six patients who were JX-594-positive by immunohistochemistry had progressive disease at first evaluation, even though replicating virus was detected in their metastatic tumours.

The explanation for these discrepancies may be down to several factors. For example, patients were allowed only one viral dose and treatment cycle: as with other cancer therapies, it is unlikely that a single round of treatment would be enough to stop tumour growth. Sampling variability in patients, whether