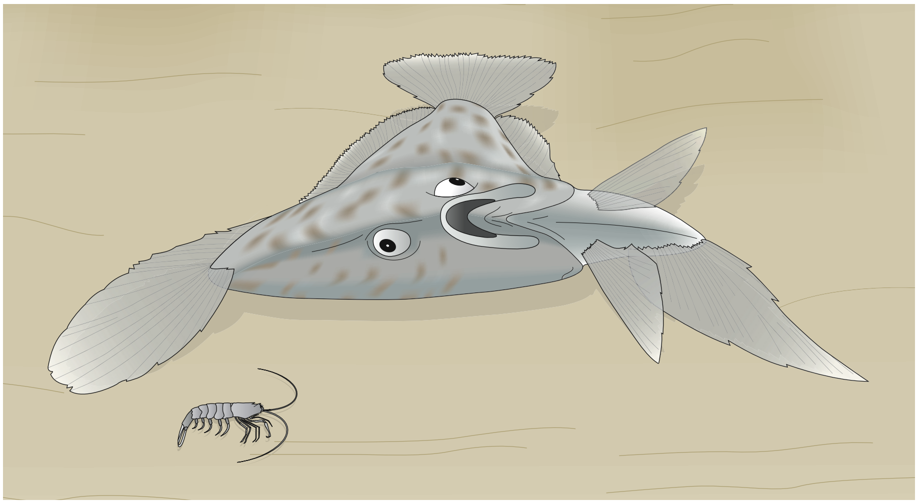

Figure 2 | The benefit of squinting? **Living flatfishes sometimes raise their head above the sea bottom by bending down their fin rays. Ancestral flatfishes, such as the 45-million- year-old *Amphistium* depicted here, already possessed an asymmetrical skull but — as Friedman[1] describes — retained eyes on either side of the head. As shown in this drawing, they may have used the strategy of lifting their head to look for prey with one eye and for predators with the other. For ease of visual orientation, rotate the image by 90° clockwise. (From a sketch by P. Janvier.)**

down would have been useless. Lamarck[5] invoked the need for flatfish precursors to survive in very shallow water. In the same vein, Malm[6] cited the propensity of the symmetrical larval flatfishes to rest on one side, but this was later dismissed. Darwin[7] pointed out the correlation between eye migration and jaw asymmetry, which brought the prey within closer reach of the mouth[5]. More recent scenarios also invoke internal asymmetry, which generates a lateral tilt at rest in many deep-bodied fishes, including batfishes.

Friedman[1] himself points out that some modern flatfishes, when lying in ambush, tend to lift up their head from the ground by bending down their dorsal- and anal-fin rays. Similar behaviour in the flatfish ancestors described here may have been the rule, thereby allowing both eyes to be functional even though they lay on either side of the head. Perhaps one eye was used to watch for predators and the other to search for prey (Fig. 2). Squinting may have had a selective advantage for a while, but regaining binocular vision — albeit on one side — ensured the lasting success of flatfishes.

One of the informative properties of fossils is that they may display character combinations that no longer exist in the living world, and so provide 'intermediate' or 'transitory' forms or organs that support some evolutionary scenario or other. On occasion, this property has been pooh-poohed, even by palaeontologists who have considered that fossils can help in refining relationships already inferred from living species, but tell us little about the process of evolutionary character transformation[8]. In the case of the fossils described by Friedman, however, one cannot but admire the vindication of a prediction, made by Darwin, of a gradual eye migration during flatfish evolution that mirrors the metamorphosis of the living forms. ■

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PLANETARY SCIENCE

The early Moon was rich in water

Marc Chaussidon

Analyses of lunar volcanic glasses show that they are rich in volatile elements and water. If parts of the lunar mantle contain as much water as Earth's, does this imply that the water has a common origin?

The Moon's chemical composition differs from Earth's. It is enriched by a factor of two to three in refractory elements (those that condense first from a high-temperature gas) such as aluminium, calcium and titanium; most easily vaporized (that is, volatile) elements, such as sodium and potassium, are rare; and it is considered to be almost devoid of water[1]. The partial loss of all but the least volatile elements is generally thought to be a signature of the lunar forming event. High temperatures were reached in the debris ejected when a Mars-sized body hit the 30-million-year-old proto-Earth. On page 192 of this issue, Saal *et al.*[2] present data counter to this classic image of lunar geochemistry. They show that some parts of the lunar mantle may contain a few hundred or even a few thousand parts per million (p.p.m.) of water.

The water content of Earth's upper mantle can be estimated from the analysis of mid-ocean-ridge basalt (MORB) glasses — more precisely, from the analysis of micrometre-sized melt inclusions that were trapped within crystals of the mineral olivine when these crystals grew deep in their parent mantle melts[3]. Water is concentrated in melts during mantle melting, so calculating the composition of the original solid source material requires corrections for, among other things, the distribution coefficient of water in the melt and the amount of melting undergone. From the concentration ratios of water to the element cerium[4], and the absolute water contents of MORB glasses and their melt inclusions (400–1,600 p.p.m.[3,4]), the water content of Earth's upper mantle has been calculated to be about 150 p.p.m. The water content of the bulk Earth (mantle plus surface) is estimated to be 350 ± 50 p.p.m.[5].

Saal *et al.*[2] have taken a similar approach using samples of lunar soils collected during the Apollo missions (Fig. 1). The soils contain glasses that colour the soils green (collected by Apollo 15) or orange (collected by Apollos 11 and 17), and are probably of volcanic origin. These glasses have peculiar compositions: the green glasses are rich in magnesium, the orange ones rich in titanium. Most glasses found on the Moon were produced by the melting of lunar rocks during meteorite impacts. But the green and orange glasses lack the typical characteristics of impact glasses[6], such as high levels of nickel derived from the incoming meteorite, or fragments from the impacted rocks. In addition, the ages of the green and orange glasses are similar to those of the surrounding lunar basaltic rocks, which links them to the geological evolution of the Moon. These green and orange glasses, (spherules 0.1–0.4 mm in size) are believed to be the products of volcanic eruptions on the surface of the Moon — 'fire fountaining' events that are well known for terrestrial volcanoes.

Coating the surfaces of the green and orange glasses are a variety of volatile elements[1]. These

NASA

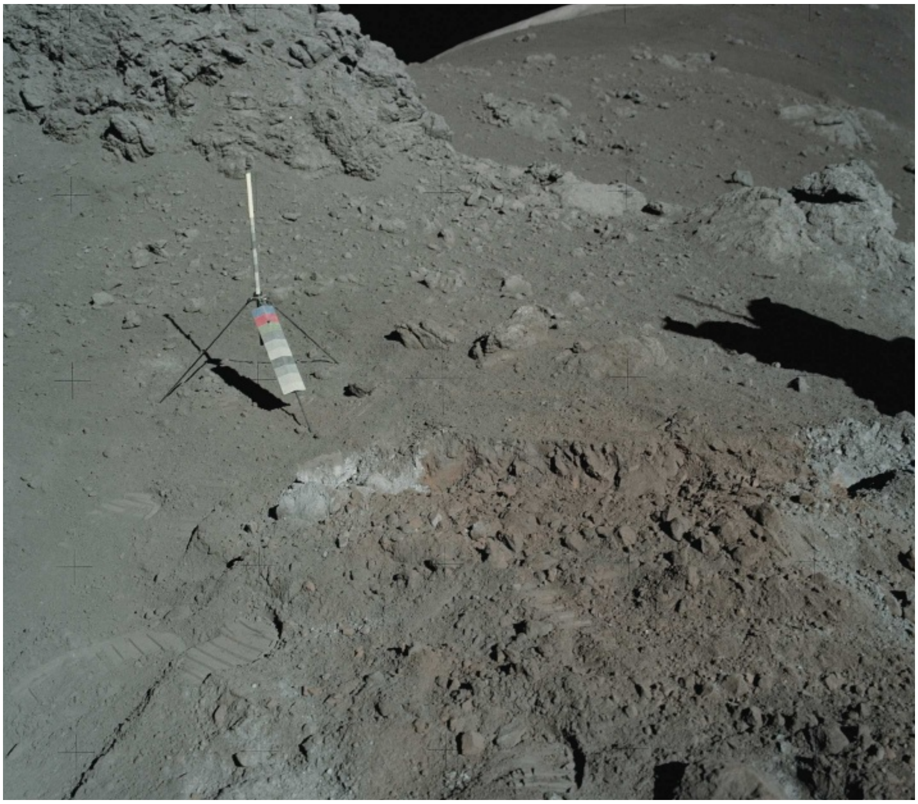

Figure 1 | Glass bead game. Orange soil discovered by the Apollo 17 astronauts on the rim of the Shorty crater on the Moon. The colour is due to the presence of numerous glassy spherules, 0.1–0.4 mm in diameter, which are orange because of their high titanium content. The glasses are thought to be products of volcanic fire fountains. They were buried in the soil after eruption and exposed during the impact responsible for the crater. The high concentrations of water found within the glasses by Saal *et al.*[2] suggest that the Moon may have had a damper origin than previously thought.

volatiles are assumed to have condensed onto the glasses from hot, transient plumes of gas associated either with lunar volcanism or meteorite impacts. However, Saal *et al.*[2] have looked for the presence of indigenous volatiles deep within the glasses. Using a technique known as secondary ion mass spectrometry (ion microprobe), the authors found significant amounts of chlorine, fluorine, sulphur and water, with the highest concentrations at the cores of the glass beads. This relationship is the opposite to that which would be seen if the volatiles had been added to the glass by any process, including contamination back on Earth, after its formation. The volatiles are present at depths of between 18 and 140 μm (and presumably deeper in large enough fragments). This also precludes a significant contribution of solar wind, because solar ions penetrate to a depth of only about 0.1 μm, even if hydrogen from the solar wind can diffuse to greater depths after its implantation[7].

The simplest explanation is that these volatiles were present in the molten glass when it formed. Their distribution profile would then be a result of volatile loss by diffusion from the surface of the glasses during the short period when solidifying droplets were exposed to the lunar vacuum.

Modelling the initial water content before such degassing depends on the size of the droplets, the diffusion coefficient of the water in the molten glass, and the temperature path encountered between eruption and quenching (the period during which volatiles could be lost). Saal *et al.*[2] calculate that the observed concentration profiles result from high initial levels of volatiles, although the precise concentrations are uncertain. Initial water contents could have been as low as 260 p.p.m. or as high as several thousand parts per million, with best fits to the data around 750 p.p.m., values similar to those in the MORB glasses. Most of the variations between samples probably resulted from variations in the degassing process.

These results raise many questions. Are the volatile contents of the melts that formed the green and orange glasses typical for the Moon? Can the general scarcity of most volatile elements on the Moon be reconciled with the apparent abundance of sulphur, chlorine, fluorine and especially water in the lunar glasses? What happened to all the water during the Moon's formation? And if the Moon is not bone dry, where did the water come from?

Another mystery in lunar geochemistry is that the relative abundance of the various oxygen isotopes on the Moon is the same as that on Earth to within 0.0005% (ref. 8). Different explanations have been proposed for this puzzling observation (Earth, Mars and all meteorites have different oxygen isotopic

NATURE

50 & 100 YEARS AGO

50 YEARS AGO

In the past ten years the number of television licences in Britain has grown from less than 15,000 to nearly eight million, and the estimated number of adults aged sixteen or more in homes with television sets from 80,000 (all in the London region), which was 0.2 per cent of the total adults, to 21,850,000 or 57.9 per cent. For every person who had a television set in 1947 there are five hundred to-day, and six out of ten adults can see television in their own homes ... The United Kingdom now ranks third with Canada in its ratio of persons to television receivers (6); only the United States (4) and Hawaii (5) exceed it ... Published evidence as to the effect of television on social habits and hobbies does not indicate a wide difference between the habits of those owning television sets and those without, in many activities such as sport, gardening, theatre-going and card-playing: the most significant differences appear in reading, attendance at the cinema, church-going and dancing.

From *Nature* 12 July 1958.

100 YEARS AGO

Count Zeppelin last week made a remarkably successful flight in his new airship ... The distance covered is estimated at 250 miles, and the journey lasted twelve hours. The greatest height reached by the airship's own engine-power is stated to be some 750 metres, and the highest speed 15.3 metres per second ... We notice that Count Zeppelin has received a telegram of congratulation from the German Emperor.

ALSO:

The prize of 10,000 francs (400*l*.) offered by M. Armengaud to the first aëroplane to remain in the air for a quarter of an hour was won by Mr. Farman on Monday ... Mr. Farman made a flight with his apparatus which lasted 20m. 20s. according to official timing. He covered a distance of about eleven miles.

From *Nature* 9 July 1908.

compositions). One theory is that turbulent exchange of volatile material between Earth and a slowly coalescing Moon, for a few hundred years after the impact that formed it, caused oxygen isotopic equilibration between the two bodies[9]. Such a process could also have transferred volatiles such as water from Earth to the Moon.

This might be one explanation for the high water contents found in the green and orange glasses, but it is not the only one. The ratio of deuterium to hydrogen found on Earth is consistent with that expected if all terrestrial water has been delivered by chondritic meteorites after the cataclysm that formed the Moon had driven off most of the hydrogen present previously[5]. Is a late arrival of volatiles also possible for the Moon? Clearly, the next step is to measure the deuterium to hydrogen ratios in the green and orange glasses, not least because the only such data currently available for an orange soil[10] are probably marred by contamination with water after the samples were brought to Earth. ■

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CANCER

An unexpected addiction

John D. Shaughnessy

Both oncogenes and normal genes can mediate the development and progress of cancer. What used to separate their effects was cancer's dependence on, or 'addiction' to, oncogenes but not normal genes. Not any more.

A central tenet of cancer is that it arises from a single cell through progressive acquisition of genetic mutations that lead to the activation of oncogenes (cancer-promoting genes) and/or inactivation of tumour-suppressor genes. Cancer's 'addiction' to oncogenes is sometimes so strong that even brief inactivation of a single oncogene can cause remission in model systems[1,2], implying that oncogenes are the 'Achilles' heel' of cancers[3]. On page 226 of this issue, Shaffer and colleagues[4] reveal that the cancer multiple myeloma is similarly addicted to a non-oncogene, the product of which — the IRF4 transcription factor — has a central role in health.

Myeloma is a cancer of immune cells, specifically of antibody-secreting plasma cells in bone marrow. These cells arise from B cells, which, when stimulated by antigens, show increased activity of IRF4, leading to their differentiation into plasma cells[5] (Fig. 1a). Multiple myeloma covers a spectrum of distinct molecular subtypes, and the disease is driven by several oncogenes[6,7]. Chromosomal abnormalities such as translocations are common in multiple myeloma, and the bone-marrow microenvironment provides support for tumour-cell survival, mainly through growth factors secreted by bone-marrow stromal cells. These cells, and the bone-marrow microenvironment in general, can also protect myeloma cells from being killed by chemotherapy or cytokine deprivation.

Shaffer *et al.*[4] wanted to know what genes are crucial for the proliferation and/or survival of myeloma cells. They screened about 10% of all known genes, reducing their expression by the technique of RNA interference (RNAi) using small hairpin RNAs (shRNAs). Several oncogenes, such as *FGFR3*, *MMSET*, *MAF*, *MAFB* and the three *cyclin D* genes, are activated by chromosomal translocations associated with myeloma, to initiate myeloma formation[8]. But Shaffer and colleagues' screen did not identify an effect of suppressing these oncogenes, suggesting that the survival of myeloma cells does not depend on them. Instead, they found that, although the *IRF4* gene is not mutated in myeloma, depletion of IRF4 protein rapidly kills all myeloma cells, but has little effect on cells of another type of blood cancer, lymphoma.

That the inappropriate activation of a normal protein can mediate cancer-cell proliferation and survival is well documented. Also, previous studies[6,9] have found that IRF4 is highly active in both normal plasma cells and primary myeloma. What is surprising about Schaffer and colleagues' observations is that, despite its battery of oncogenic mutations, myeloma is addicted to a normal gene.

What is the effect of IRF4 malfunction in myeloma? Gene-expression profiling studies[10] have shown that a subset of myeloma exhibits features both of normal plasma cells and of their precursors — antigen-stimulated mature B cells. Shaffer *et al.* propose that IRF4 might direct the gene-expression program that results in this abnormal feature of myeloma cells. One of their main findings is that, in myeloma, the *MYC* gene (which when mutated can potentially become an oncogene) is a direct target of IRF4 (Fig. 1b).

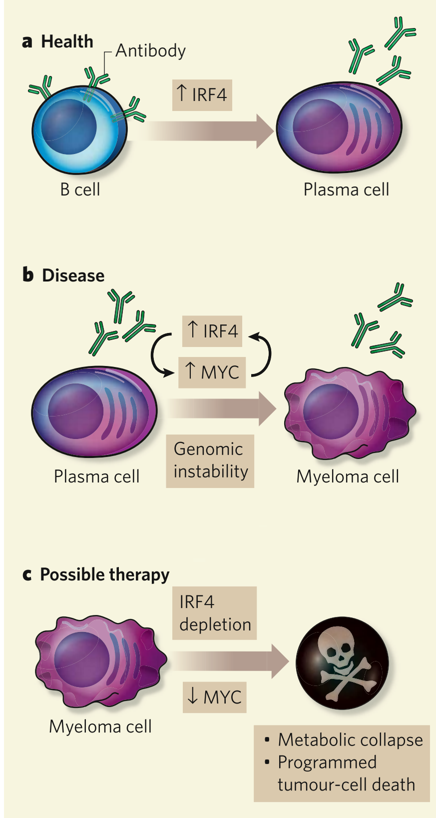

Figure 1 | IRF4 in health and disease. a, Normally, antigen-stimulated B cells differentiate into antibody-secreting plasma cells, a process that is partly driven by increased expression of the transcription factor IRF4. **b,** Like their normal counterparts, myeloma cells also express IRF4. Schaffer *et al.*[4] find that, although *IRF4* is not an oncogene, it has a unique transcriptional repertoire of target genes in myeloma cells related to both its targets in plasma cells and in antigen-stimulated B cells. IRF4 also regulates the expression of the MYC protein, which itself regulates IRF4 through an autoregulatory loop. Apart from these IRF4-mediated effects in myeloma cells, genomic instability and both oncogenic mutations that initiate tumorigenesis (primary mutations) and secondary oncogenic mutations also contribute to myeloma. **c,** Despite myeloma cells harbouring oncogenic mutations, depleting IRF4 in these cells causes decreased expression of numerous genes including the *MYC* oncogene, as well as metabolic collapse and programmed cell death. These results suggest that inhibiting IRF4 might represent a new treatment for myeloma.

Expression of *IRF4* increases in both plasma cells and myeloma cells, but that of *MYC* is higher only in myeloma cells[9]. MYC has a central role in the formation of both myeloma and two other plasma-cell tumours,