growth of a cell population consisting solely of malignant glioma cells, but administering Adam10 inhibitors to mice containing tumour xenografts inhibited the growth and progression of their cancers. This finding is consistent with a model in which a positive therapeutic outcome can result from interrupting an interaction between malignant glioma and its microenvironment.

Inhibitors of the human ADAM family of enzymes have been used in clinical trials to prevent cleavage of other protein targets of these enzymes that have been linked to cancers such as lymphoma[8] and breast cancer[9]. These inhibitors could potentially be repurposed to treat individuals with malignant glioma. This approach would not have been immediately obvious from results using existing tools that identify potential biological targets for therapy, such as *in vitro* high-throughput drug screening. These tools are normally used to test whether drugs can limit the growth of cancer cells *in vitro* rather than whether they can inhibit interactions between cancer cells and their non-cancerous neighbours. However, some malignant gliomas treated with ADAM10 inhibitors *in vivo* in this study in mice showed a reduction in tumour growth, but not complete tumour destruction, suggesting that this type of therapy will probably need to be combined with other approaches.

In considering the unique physiology of the brain microenvironment, Venkatesh and colleagues offer a new approach to treating malignant gliomas by focusing on the surrounding cells. Most of the current targeted therapies for malignant gliomas are applicable to only a small subset of patients, but the idea of interrupting the molecular support that the glioma receives from its normal microenvironment raises the possibility of targeting a diverse range of glioma subtypes and patient ages. Rather than approaching the daunting glioma 'monster' head-on, clinicians might instead consider an indirect approach of 'draining the swamp' around the malignant cells (Fig. 1).

Such an environmental-blockade strategy might, in addition to the approach outlined by Venkatesh and colleagues, also include the inhibition of other microenvironmental factors that promote tumour growth. For example, combination therapies might also target the immunosuppressive environment of tumour cells that blunts the body's immune response targeting the tumour, or they might inhibit factors that aid the formation of tumour blood vessels. Such combinations could lead to improved outcomes that are urgently needed for these patients. ■

Michael D. Taylor *is in the Division of Neurosurgery and* **Vijay Ramaswamy** *is in the Division of Haematology/Oncology and the Department of Paediatrics, Hospital for Sick Children, Toronto, Ontario M5G 1X8, Canada.*
e-mail: mdtaylor@sickkids.ca

1. Ostrom, Q. T. *et al. Neuro-Oncology* **18,** Suppl. 5 (2016).
2. Venkatesh, H. S. *et al. Nature* **549,** 533–537 (2017).
3. Stupp, R. *et al. J. Am. Med. Assoc.* **314,** 2535–2543 (2015).
4. Stupp, R. *et al. N. Engl. J. Med.* **352,** 987–996 (2005).
5. Vredenburgh, J. J. *et al. J. Clin. Oncol.* **25,** 4722–4729 (2007).
6. Gibson, E. M. *et al. Science* **344,** 1252304 (2014).
7. Venkatesh, H. S. *et al. Cell* **161,** 803–816 (2015).
8. https://clinicaltrials.gov/ct2/show/NCT02141451
9. Witters, L. *et al. Cancer Res.* **68,** 7083–7089 (2008).

This article was published online on 20 September 2017.

GEOCHEMISTRY

Evaporating planetesimals

Two studies show that evaporation of molten rock was intrinsic to the formation of Earth and other rocky bodies in the Solar System, suggesting that violent collisions played a key part in the formation process. SEE LETTERS P.507 & P.511

EDWARD D. YOUNG

The concentrations of elements in meteorites called chondrites are thought to reflect the chemistry of the early Solar System — an idea reinforced by the fact that chondrites have a similar composition to that of the Sun. However, Earth and comparable bodies in the Solar System are depleted in some of the more volatile rock-forming elements relative to chondrites[1]. In general, the more volatile the element, the greater its affinity for gas rather than rock, and the more depleted it is in these bodies. The origin of the volatility trend is hotly debated[2–4], but two studies now suggest an answer to this abiding geochemical question.

On page 511, Hin *et al.*[5] demonstrate that isotope ratios of magnesium in Earth, Mars and some asteroids provide evidence for extensive evaporation of molten rock. On page 507, Norris and Wood[6] report experiments showing that Earth's concentrations of several chalcophile (sulfur-loving) elements are also best explained by the partial melting and evaporation of rock. Both studies propose energetic collisions between planetesimals — the asteroid-sized rocky precursors to planets — as the likely cause of rock melting and evaporation.

During their formation, Earth and many

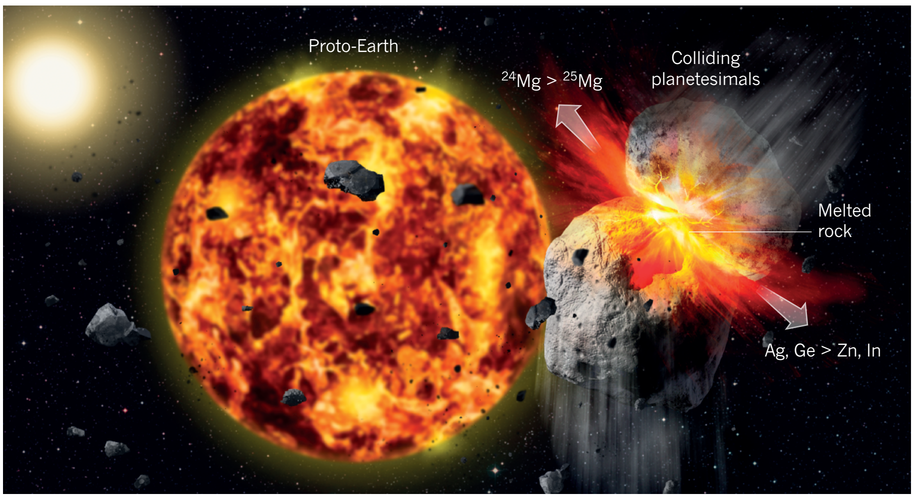

Figure 1 | Evaporation of colliding planetesimals. The early Earth (proto-Earth) grew by collisions of countless asteroid-sized rocky bodies called planetesimals. Particularly violent collisions could have melted rock and triggered the escape of vapour produced by evaporation of the molten rock. Hin *et al.*[5] report evidence for this process by measuring an enrichment of a heavy isotope of magnesium (^{25}Mg) compared with a lighter isotope (^{24}Mg) in Earth, Mars and melted asteroids. Norris and Wood[6] find further evidence by comparing the abundances of chalcophiles — sulfur-loving elements, including silver (Ag), germanium (Ge), zinc (Zn) and indium (In) — in Earth with laboratory experiments that simulate the evaporation process. The relative volatilities of the escaping magnesium isotopes and of the chalcophile elements are indicated next to the arrows.

NIK SPENCER/NATURE; ASTEROID IMAGE: NASA/JPL-CALTECH

© 2017 Macmillan Publishers Limited, part of Springer Nature. All rights reserved.

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. ■

Edward D. Young *is in the Department of Earth, Planetary, and Space Sciences, University of California, Los Angeles, Los Angeles, California 90095-1567, USA.*
e-mail: eyoung@epss.ucla.edu

1. McDonough, W. F. & Sun, S. *Chem. Geol.* **120,** 223–253 (1995).
2. Allègre, C., Manhès, G. & Lewin, E. *Earth Planet. Sci. Lett.* **185,** 49–69 (2001).
3. Young, E. D. *Earth Planet. Sci. Lett.* **183,** 321–333 (2000).
4. Day, J. M. D. & Moynier, F. *Phil. Trans. R. Soc. A* **372,** 20130259 (2014).
5. Hin, R. C. *et al. Nature* **549,** 511–515 (2017).
6. Norris, C. A. & Wood, B. J. *Nature* **549,** 507–510 (2017).
7. Davis, A. M., Hashimoto, A., Clayton, R. N. & Mayeda, T. K. *Nature* **347,** 655–658 (1990).
8. Young, E. D., Tonui, E., Manning, C. E., Schauble, E. & Macris, C. A. *Earth Planet. Sci. Lett.* **288,** 524–533 (2009).
9. Pringle, E. A., Moynier, F., Savage, P. S., Badro, J. & Barrat, J.-A. *Proc. Natl Acad. Sci. USA* **111,** 17029–17032 (2014).
10. Sossi, P. A., Nebel, O., Anand, M. & Poitrasson, F. *Earth Planet. Sci. Lett.* **449,** 360–371 (2016).
11. Polyakov, V. B. *Science* **323,** 912–914 (2009).
12. Georg, R. B., Halliday, A. N., Schauble, E. A. & Reynolds, B. C. *Nature* **447,** 1102–1106 (2007).
13. Shahar, A. *et al. Science* **352,** 580–582 (2016).
14. Palme, H. & O'Neil, H. St. C. in *Treatise on Geochemistry* 2nd edn, Vol. 3 (eds Holland, H. D. & Turekian, K. K.) 1–39 (Elsevier, 2014).
15. Pecaut, M. J. & Mamajek, E. E. *Mon. Not. R. Astron. Soc.* **461,** 794–815 (2016).
16. Lock, S. J. & Stewart, S. T. *J. Geophys. Res. Planets* **122,** 950–982 (2017).
17. Poitrasson, F., Halliday, A. N., Lee, D.-C., Levasseur, S. & Teutsch, N. *Earth Planet. Sci. Lett.* **223,** 253–266 (2004).

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,

© 2017 Macmillan Publishers Limited, part of Springer Nature. All rights reserved.