light elements partition between the core's solid and liquid portions at its temperature and pressure conditions. This is necessary to explain the compositional differences between the solid and liquid parts of the core. A theoretical study[12] addressing this question suggests that oxygen — not sulphur — may have the right partitioning behaviour, in conflict with Huang and colleagues' experimental results[3]. The extreme conditions of the core make a laboratory test of this partitioning behaviour highly challenging, but experimental capabilities are making rapid advances on several fronts in high-pressure–temperature science. The past few decades have seen remarkable progress in uncovering the state and structure of many features of the deep Earth, with the light elements of the core remaining a stubborn puzzle. The work reported here suggests that a solution to the problem may finally be at hand. ■

Thomas S. Duffy *is in the Department of Geosciences, Princeton University, Princeton, New Jersey 08544, USA.*
e-mail: duffy@princeton.edu

1. Birch, F. *J. Geophys. Res.* **57,** 227–286 (1952).
2. McQueen, R. G. & Marsh, S. P. *J. Geophys. Res.* **71,** 1751–1756 (1966).
3. Huang, H. *et al. Nature* **479,** 513–516 (2011).
4. Buffett, B. A. *et al. J. Geophys. Res.* **101,** 7989–8006 (1996).
5. Poirier, J.-P. *Phys. Earth Planet. Inter.* **85,** 319–337 (1994).
6. Wood, B. J., Walter, M. J. & Wade, J. *Nature* **441,** 825–833 (2006).
7. Kennett, B. L. N., Engdahl, E. R. & Buland, R. *Geophys. J. Int.* **122,** 108–124 (1995).
8. Jephcoat, A. & Olson, P. *Nature* **325,** 332–335 (1987).
9. Brown, J. M. & McQueen, R. G. *J. Geophys. Res.* **91,** 7485–7494 (1986).
10. Huang, H. *et al. J. Geophys. Res.* **115,** B05207 (2010).
11. Dreibus, G. & Palme, H. *Geochim. Cosmochim. Acta* **60,** 1125–1130 (1996).
12. Alfè, D., Gillan, M. J. & Price, G. D. *Earth Planet. Sci. Lett.* **195,** 91–98 (2002).

CANCER

Final act of senescence

Damaged cells can initiate cancer. To avert this, faulty cells disable their own propagation by undergoing senescence. But for full protection against liver cancer, the senescent cells must be cleared by the immune system. **See Letter p.547**

MANUEL SERRANO

Cellular damage is unavoidable and intrinsic to life, and it is often aggravated by pathogens or exposure to toxic agents. In long-lived multicellular organisms, however, damaged cells pose a problem not because of their loss of function, but mainly because their proliferation can escalate a minor local problem into a deadly cancer. Fortunately, cells can detect their own level of damage and eventually dismiss themselves in a final act of altruism for the benefit of the organism. Self-dismissal comes in two forms, apoptosis (self-destruction) and senescence (self-disabling), with the latter being at least as prominent as the former in providing protection against cancer[1,2]. On page 547 of this issue, Kang *et al.*[3] explore how the immune system targets senescent cells to limit the development of liver cancer.

The fate of senescent cells within tissues has long been uncertain. Some show extremely lengthy residency times *in vivo*. For instance, moles formed by senescent melanocyte cells can reside in human skin for decades[4]. Until recently, therefore, the possibility that senescent cells could be selectively targeted for elimination was generally overlooked. This changed with the discovery that such cells secrete signalling molecules that contribute to the establishment of senescence[5,6] and promote tissue repair by inducing proliferation of neighbouring cells and attracting cells of the immune system[7].

Rapid clearance of senescent cells was first observed in mouse liver cancers. In this work[8], reactivation of a silent *p53* gene (a major inducer of senescence) made cancer cells 'aware' of their own damage, triggering a strong senescence response. The cancer then became a senescent mass and was swiftly and selectively eliminated by immune cells — a fate delivered mainly by the innate arm of the immune system (macrophages, neutrophils and natural killer cells) (Fig. 1).

Subsequent work[9] reached similar conclusions. Disabling the driving oncogenes in mouse lymphoma and leukaemia resulted in tumour regression that was associated with apoptosis and senescence. In these cancer models, the immune system was necessary for the induction of senescence — but not apoptosis — and for complete and long-term tumour remission. The essential immune cells were $CD4^+$ T cells[9], which are part of the adaptive immune system and can recognize cancer cells. In the absence of $CD4^+$ T cells, senescence was not induced and tumour remission was incomplete, being rapidly followed by tumour relapse.

These studies[8,9] offered insight into how cancers respond to therapies. But understanding the role of the immune system in preventing the emergence of cancer is equally important. Kang *et al.*[3] set out to do just that. The authors introduced the $Nras^{G12V}$ oncogene into some 15% of liver cells in mice. Six days later, these 'transduced' — but otherwise normal — cells naturally became senescent and were progressively cleared during the following weeks, becoming undetectable after 2 months.

In a veritable tour de force, Kang and colleagues demonstrate that clearance depended on $CD4^+$ T cells — which showed specificity towards the $Nras^{G12V}$ mutation — and that it required senescence. Mouse liver cells that had been transduced with a non-oncogenic *Nras* gene ($Nras^{G12V/D38A}$) did not undergo senescence or clearance 2 months later. Moreover, transduction of $Nras^{G12V}$ into mice lacking the crucial senescence mediator Arf did not trigger a specific immune response against the $Nras^{G12V}$ mutation. These observations imply that the T-cell-mediated immune response to oncogenic mutations requires senescence. Although $CD4^+$ T cells were necessary for clearance of senescent cells, they instigated recruitment of macrophages, which directly executed the clearance.

What is most exciting about this work is

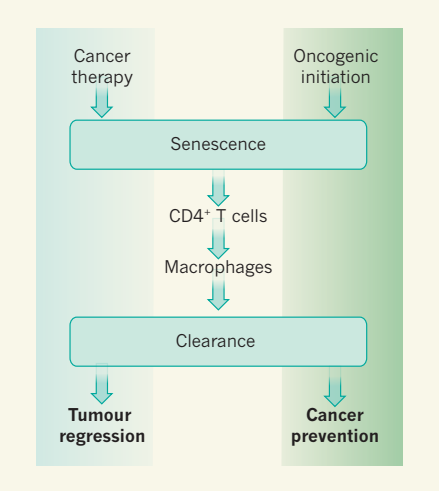

Figure 1 | Clearance of senescent cells. When damaged, cells may undergo senescence to disable their own proliferation and may even trigger their own clearance. In the case of cancer, treatments that lead to senescence and clearance by immune cells — $CD4^+$ T cells and macrophages — cause tumour regression[8,9]. Kang *et al.*[3] find that mouse liver cells that carry the hyperactive $Nras^{G12V}$ oncogene, but are otherwise normal, also trigger senescence and clearance by the immune system, and that these processes are essential for complete protection from cancer. $CD4^+$ T cells are essential for instigating clearance in some[3,9], but not all[8], cases, whereas macrophages are the final common executors of clearance.

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that the clearance of senescent cells leads to protection against cancer. In fact, when *Nras*^{G12V}-expressing senescent cells were not cleared (for example, in mice lacking CD4$^+$ T cells), numerous tumours appeared, whereas clearance of senescent cells robustly prevented tumour development.

The authors[3] also studied mouse models of liver inflammation and toxicity — known risk factors for liver cancer in humans. Again, in the absence of the adaptive immune system, cells that had undergone senescence following inflammation and liver toxicity were not cleared, and this was associated with increased tumorigenesis.

Kang *et al.* further extrapolated their findings to human disease, by analysing the livers of patients infected with hepatitis C virus (HCV) whose immune systems were either intact or compromised owing to concomitant infection with HIV. In agreement with their mouse data, the authors found that senescent cells were cleared in patients infected with HCV alone but not in those infected with both HCV and HIV. Similarly, HCV-infected patients with cirrhosis who were being treated with immunosuppressants had senescent cells in their livers, but this was not the case in untreated patients. As the authors note, HIV infection and immunosuppressant therapy are associated with increased risk of liver cancer.

It has been shown[10] that clearance of senescent cells by the immune system is also important for the resolution of fibrotic scars in liver. Together with Kang and co-workers' data, this suggests that the clearance of these cells could indeed prove generally beneficial for tissue repair, as previously proposed[7].

This paper[3] clearly shows that cell clearance is essential for the maximum tumour-suppressive effects of senescence. But this brings us to a conundrum: why do senescent cells, which cannot proliferate, pose a cancer risk? Two possible answers come to mind. First, it is conceivable that rare senescent cells exist at an intermediate — still undefined — state that has the potential to resume proliferation and initiate cancer. Second, the proliferative factors secreted by senescent cells for their tissue-repair function may be usurped by neighbouring cancerous cells to enhance their proliferation. Future work will undoubtedly resolve this issue and will continue to enrich the fascinating link between senescence and cancer. ■

Manuel Serrano *is at the Spanish National Cancer Research Centre (CNIO), Madrid E28029, Spain.*
e-mail: mserrano@cnio.es

1. Collado, M. & Serrano, M. *Nature Rev. Cancer* **10,** 51–57 (2010).
2. Hanahan, D. & Weinberg, R. A. *Cell* **144,** 646–674 (2011).
3. Kang, T.-W. *et al. Nature* **479,** 547–551 (2011).
4. Michaloglou, C. *et al. Nature* **436,** 720–724 (2005).
5. Acosta, J. C. & Gil, J. *Cancer Res.* **69,** 2167–2170 (2009).
6. Kuilman, T. & Peeper, D. S. *Nature Rev. Cancer* **9,** 81–94 (2009).
7. Campisi, J. *Curr. Opin. Genet. Dev.* **21,** 107–112 (2011).
8. Xue, W. *et al. Nature* **445,** 656–660 (2007).
9. Rakhra, K. *et al. Cancer Cell* **18,** 485–498 (2010).
10. Krizhanovsky, V. *et al. Cell* **134,** 657–667 (2008).

INTERFACIAL CHEMISTRY

Gold's enigmatic surface

Gold is not as inert as was believed — it can promote molecular synthesis. A study uses scanning tunnelling microscopy to catch gold in the act as it guides the formation of one-dimensional polymers from saturated hydrocarbons.

ROBERT J. MADIX & CYNTHIA M. FRIEND

Carbon–carbon bond-forming reactions are used to make molecules that have specific structures and properties, such as polymers. Particularly challenging is the use of saturated hydrocarbons (alkanes) as starting materials for these reactions, because strong carbon–hydrogen (C–H) bonds in the molecules must first be broken. Harsh reaction conditions are often required to do this, but in general such conditions make it difficult to break a specific C–H bond and thereby selectively control where in the molecule carbon–carbon bond formation occurs. Writing in *Science*, Zhong *et al.*[1] report that the adsorption of alkanes on a gold surface changes the structure of one-dimensional channels in the metal. These channels direct the polymerization of the alkanes, so that carbon–carbon bonds form only at, or close to, the ends of the molecules.

This result might sound surprising, because gold has traditionally been believed to be chemically inert. However, research has shown that the metal's surface is not inert, and it is now used as a supporting surface for self-assembled monolayers of molecules[2]. Furthermore, special reaction centres can be created on gold, for example by binding oxygen atoms to it, and this has facilitated the development of gold-catalysed reactions for making carbon–oxygen and carbon–nitrogen bonds[3–5]. Such reactions have been used to selectively catalyse the formation of low-molecular-weight compounds that are important in the chemical industry[6]. The advantage of using gold to promote reactions is that, where the reaction centres are not present, it is less able to break chemical bonds than are other commonly used catalytic metals. This means that, if a primary reaction can be initiated on the surface, the intermediate chemical species created will be unlikely to take part in side reactions, thus providing excellent control over which products form.

Zhong and colleagues' reaction[1] illustrates the use of such effects to make compounds of high molecular weight. The authors predicated their experiments on two principles. The first was that high-molecular-weight alkanes remain bound to gold surfaces at temperatures that are high enough to break C–H bonds. The second principle was that, once C–H bonds of an alkane have ruptured to form alkyl intermediates on a gold surface, recombination of neighbouring alkyl groups will occur, yielding polymer chains.

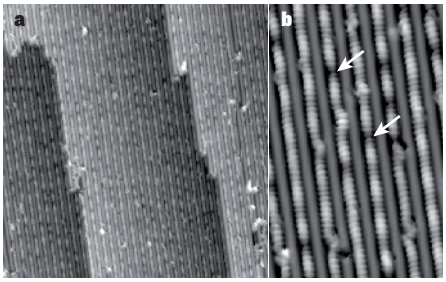

Figure 1 | Polymerization on gold. Zhong *et al.*[1] report that alkane monomers on a gold surface react selectively at their chain ends to form polymers. **a**, In this micrograph, the polymer chains (bright lines) line up in parallel along troughs in the gold surface. The area shown is 50 nm × 50 nm. **b**, This inset shows the chains at higher magnification. The arrows indicate gaps in the rows of gold atoms that underlie the polymers. These gaps form during the polymerization reaction, but the role of the missing atoms in the reaction, if any, is unknown. The area shown is 9 nm × 13 nm.

The rupture of C–H bonds by metallic gold is well documented: for instance, butyl groups ($CH_3CH_2CH_2CH_2$) attached to gold surfaces undergo C–H bond cleavage at 280 kelvin to form butene[7] ($CH_3CH_2CH{=}CH_2$); and terminal C–H bonds in *t*-butyl thiol bound to gold break at 490 K (ref. 8; *t*-butyl thiol is $(CH_3)_3CSH$). Furthermore, alkanes bind to the surfaces of precious metals primarily by van der Waals interactions, which means that the strength of binding increases with the number of carbon atoms in the alkane chain (and so with

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