was also predicted to occur for a quantum gas in an optical lattice by Jaksch *et al.*[5]. Their proposal has several advantages, as demonstrated by Greiner *et al.*, because there are no lattice imperfections (disorder) so the physics of the quantum phase transition occurs in its most ideal form. Another advantage of using a quantum gas in an optical lattice is that the height of the mountains in the energy landscape can easily be changed by varying the intensity of the laser fields. This makes it possible to switch back and forth between superfluid and insulating behaviour. For granular superconductors and Josephson-junction arrays it is essentially impossible to achieve the same control over the energy landscape because creating a new landscape requires a new sample. So one cannot actually see the superfluid–insulator transition taking place in a single system.

A tantalizing application for the ideal array of single atoms created in the insulating phase is quantum computing. Every rubidium atom has a magnetic moment and so has two internal states that may serve as the 0 and 1 of a quantum bit. Because there are a large number of rubidium atoms in the optical lattice, they can act as a memory for a quantum computer. Moreover, if there are two such memories that can be moved relative to each other, we can even make use of the interactions between the atoms to perform a quantum computation[6]. The first step towards this exciting goal has now been taken. ■

Henk T. C. Stoof is in the Institute of Theoretical Physics, Utrecht University, Leuvenlaan 4, 3584 CE Utrecht, The Netherlands.
e-mail: h.t.c.stoof@phys.uu.nl

1. Greiner, M., Mandel, O., Esslinger, T., Hänsch, T. W. & Bloch, I. *Nature* **415,** 39–44 (2002).
2. Anderson, M. H., Ensher, J. R., Matthews, M. R., Wieman, C. E. & Cornell, E. A. *Science* **269,** 198–201 (1995).
3. Sachdev, S. *Quantum Phase Transitions* (Cambridge Univ. Press, 2001).
4. Fisher, M. P. A., Weichman, P. B., Grinstein, G. & Fisher, D. S. *Phys. Rev. B* **40,** 546–570 (1989).
5. Jaksch, D., Bruder, C., Cirac, J. I., Gardiner, C. W. & Zoller, P. *Phys. Rev. Lett.* **81,** 3108–3111 (1998).
6. Jaksch, D., Briegel, H.-J., Cirac, J. I., Gardiner, C. W. & Zoller, P. *Phys. Rev. Lett.* **82,** 1975–1978 (1999).

Ageing

The price of tumour suppression?

Gerardo Ferbeyre and Scott W. Lowe

The p53 protein works to suppress cancer, so one might think that bumping up the levels of this protein would be a good idea. But this isn't so — mice with too much p53 age prematurely.

The p53 gene is often touted as 'the most frequently mutated gene in human cancer'. As a result, a great deal is known about it. When fully functional, p53 works to suppress the development of tumours, and current thinking suggests that it does so by affecting how cells respond to damage[1]. p53 can be activated by many stresses, such as breaks in DNA, and in turn induces responses that keep cell numbers down, including cell death (apoptosis) and permanent cell-division arrest (senescence; Fig. 1a). When p53 is mutated, cells cannot respond correctly to stress and are predisposed to becoming cancerous.

Indeed, mice that lack p53 develop normally but rapidly succumb to cancers[2], implying that, at the whole-organism level, p53 acts purely as a tumour suppressor (Fig. 1b). But on page 45 of this issue, Tyner *et al.*[3] identify an unexpected aspect of p53 biology. They show that mice engineered to have high p53 activity are resistant to tumours — but age prematurely. Their results raise the shocking possibility that ageing may be a side effect of the natural safeguards that protect us from cancer.

Tyner *et al.*'s findings[3] were serendipitous. They were trying to engineer mice with a particular mutation in p53, and instead produced animals in which a large portion at one end of the p53 gene (the 5′ end) was missing. The remaining portion, which they call the *m* version of the gene, is just the 3′ end and encodes a shortened protein. Mice with one normal copy of the p53 gene and one copy of the *m* version were resistant to tumour formation, but even relatively young animals resembled old normal mice. By contrast, mice with one non-functional p53 gene and the *m* gene were indistinguishable from mice that lack p53 altogether. So it seems that a normal p53 gene is needed for the *m* gene to have an effect, hinting that the protein encoded by the *m* gene steps up the activity of normal p53. This seems remarkable, yet is consistent with the observation[4] that short peptides encoded by the 3′ end of the p53 gene can activate normal p53.

It is not yet certain that the features of ageing are only due to the mutant p53 gene. The authors could not detect the truncated protein in the mutant mice, and at least one essential gene near the p53 gene was also deleted. Still, a second p53-mutant strain also shows signs of premature ageing[3]. Of course, the definitive experiment — showing that loss of p53 increases longevity — is impossible, because p53 and cancer are so intertwined.

Tyner *et al.*'s results might simply reflect a highly abnormal, diseased state. But they may also reveal a role for p53 in normal ageing. What might this role be? The evolutionary theory of ageing suggests that organisms invest resources to ensure reproductive success early in life, at the expense of longevity. It is not clear how this works at the molecular level. One model proposes that loss of the normal mechanisms for quelling gene expression leads to genes being expressed incorrectly and, ultimately, to ageing. So, enforced expression of the gene-silencer SIR2 extends lifespan in yeast and worms[5]. Another model holds that non-reproductive cells have a clock that monitors how often they have divided (based on the lengths of telomeres, protein–DNA complexes that cap chromosome ends and erode gradually with each cell division). Short telomeres eventually trigger senescence. Indeed, mice with critically short telomeres age prematurely[6].

In a third model, cellular damage leads to mutations or general cellular decline, ultimately producing the spectrum of age-related characteristics[7]. Support for this idea comes from the fact that radiation increases

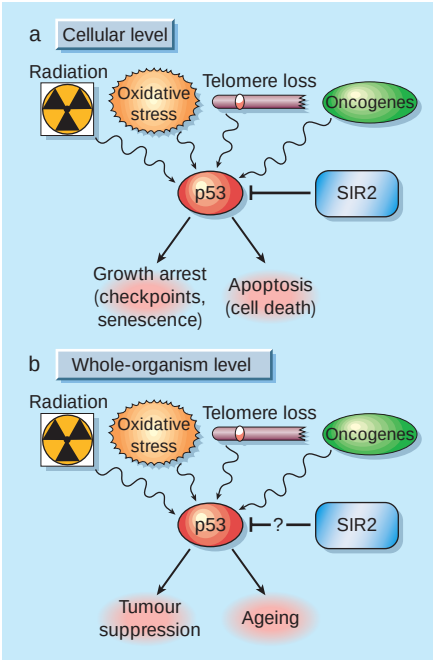

Figure 1 **The p53 system and ageing.** a, **At the cellular level several stresses can activate p53, inducing checkpoints in the cell-division cycle, permanent cell-division arrest (senescence) and cell death. Suppression of p53 activity prevents these responses, predisposing cells to becoming cancerous.** b, **At the whole-organism level, p53 activation results in a lower cancer incidence. But Tyner *et al.*[3] show that p53 can also promote ageing. The SIR2 protein, which increases longevity in experimental organisms such as yeast, can associate with p53 and suppress its activity in cultured cells (**a**). It is not known whether this process contributes to whole-organism ageing (**b**). Tyner *et al.*'s results suggest that aspects of ageing may arise as by-products of p53's tumour-suppressor activity.**

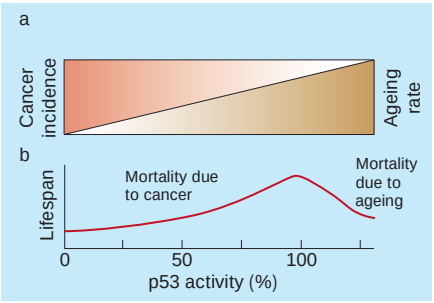

Figure 2 **Balancing cancer and ageing.** a, **Increases in p53 activity reduce the incidence of cancer but increase the ageing rate. Conversely, decreases in p53 activity increase cancer incidence but may decrease the rate of ageing.** b, **As a consequence, the influence of p53 on lifespan may result from a delicate balance between its antitumour and pro-ageing effects, such that too little p53 increases mortality from cancer whereas too much p53 increases mortality from ageing.**

mutations and promotes premature ageing in mice[8]. Tyner *et al.*'s results add an interesting twist to this hypothesis — they suggest that ageing may be due in part to cellular responses to damage, and not damage per se (Fig. 1b). These responses protect most people from cancer during their reproductive years, but they may come at a price.

All of these models can be loosely linked to p53. The SIR2 protein can suppress p53 activity in mammalian cells[9,10]. Cellular responses to telomere malfunction involve p53 (ref. 11), and a lack of p53 can counteract some of the effects of a lack of telomerase (an enzyme that regenerates telomeres) in mice[12]. Finally, doses of radiation that promote premature ageing in mice activate p53 efficiently[13]. Despite these connections, p53 has been on the periphery of ageing research — until now.

The new work[3] also has other implications. The ageing of whole organisms has been linked to cellular senescence *in vitro*, a process that also involves p53 and was initially linked to the finite lifespan of cultured human fibroblast cells[14]. Senescent cells remain metabolically active but cannot proliferate; they also show changes in gene expression that could produce alterations at the tissue level[15]. 'Replicative' senescence is triggered by telomere erosion and can be prevented by telomerase. But the same events can also be produced in response to, for example, DNA damage, oxidative stress and suboptimal cell-culture conditions[14]; telomerase has no effect here. Confusion over the exact process has led to a semantic debate, but it is clear that senescence parallels apoptosis as a cellular response to stress. These facts, coupled with the new results[3], suggest that tissue ageing *in vivo* results from many factors, not just telomere attrition as has been suggested.

It might seem paradoxical that overactive p53 suppresses cancer but promotes ageing, given that the incidence of cancer usually increases with age. But the problem can be resolved by the fact that cancer results from the malfunctioning of p53 in single cells, whereas ageing involves a tissue-wide process. So, cells with inactive p53 ultimately shorten lifespan because cancer develops. Conversely, cells with abnormally high p53 activity do not contribute to cancer, but instead undergo cell death or senescence. With time, these changes may compromise tissue physiology, shortening lifespan through ageing. So p53 activity must be tightly controlled to balance a predisposition to cancer (too little p53) and premature ageing (too much p53; Fig. 2).

Finally, Tyner *et al.*'s work[3] could have ramifications for understanding and treating human diseases. For example, p53 might contribute to premature ageing syndromes or age-related disorders in humans. And although longevity is complex and involves many p53-independent factors, it is conceivable that variation in lifespan is influenced by variation in p53's response to cellular damage. The results also raise the disturbing possibility that the DNA-damaging drugs used to treat cancer in young people might prompt p53 into action and accelerate age-related disorders later on. This is a testable hypothesis, and the prospect alone underscores the need for less toxic anticancer drugs. But perhaps the most provocative implication is that, if p53 is involved in ageing, then drug-related approaches to interfere with this process may come at a price — the disruption of our natural mechanisms for keeping cancer at bay. ■

Gerardo Ferbeyre is in the Department of Biochemistry, Université de Montréal, Montréal, Quebec, Canada, H3C 3J7.
e-mail: g.ferbeyre@umontreal.ca
Scott W. Lowe is at the Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 11724, USA.
e-mail: lowe@cshl.edu

1. Vogelstein, B., Lane, D. & Levine, A. J. *Nature* **408,** 307–310 (2000).
2. Donehower, L. A. *et al. Nature* **356,** 215–221 (1992).
3. Tyner, S. D. *et al. Nature* **415,** 45–53 (2002).
4. Hupp, T. R., Sparks, A. & Lane, D. P. *Cell* **83,** 237–245 (1995).
5. Guarente, L. & Kenyon, C. *Nature* **408,** 255–262 (2000).
6. Rudolph, K. L. *et al. Cell* **96,** 701–712 (1999).
7. Szilard, L. *Proc. Natl Acad. Sci. USA* **45,** 30–45 (1959).
8. Curtis, H. J. *Science* **141,** 686–694 (1963).
9. Luo, J. *et al. Cell* **107,** 137–148 (2001).
10. Vaziri, H. *et al. Cell* **107,** 149–159 (2001).
11. Karlseder, J., Broccoli, D., Dai, Y., Hardy, S. & de Lange, T. *Science* **283,** 1321–1325 (1999).
12. Chin, L. *et al. Cell* **97,** 527–538 (1999).
13. Komarov, P. G. *et al. Science* **285,** 1733–1737 (1999).
14. Campisi, J. *Trends Cell Biol.* **11,** S27–S31 (2001).
15. Shelton, D. N., Chang, E., Whittier, P. S., Choi, D. & Funk, W. D. *Curr. Biol.* **9,** 939–945 (1999).

Cosmology

A baryometer is back

Corinne Charbonnel

The usefulness of helium-3 as a probe of the early Universe has been in doubt. A rethink of stellar theory and new observational data put those doubts to rest.

Do we live in an open Universe that will expand forever, or in a closed Universe whose expansion will eventually reverse? Part of the answer can be found by accurately estimating the amount of ordinary — baryonic — matter in the Universe. One way of reaching such an estimate stems from one of the predictions of Big Bang theory: that production of light nuclei (deuterium, helium-3, helium-4 and lithium-7) occurred within the first seconds of the Universe, in a process known as Big Bang nucleosynthesis. A precise measurement of cosmological baryon density requires determination of the primordial abundances of light nuclei, and for those estimates to be consistent with each other[1].

On page 54 of this issue[2], Bania, Rood and Balser report the first reliable assessment of the primordial abundance of ^{3}He. Their result is based on two decades of radio observations of star-forming H II regions and planetary nebulae in our Galaxy, the Milky Way, and on theoretical developments in the field of stellar evolution. Beyond the observational challenges, which in themselves are considerable, the main difficulty in using Big Bang nucleosynthesis as a cosmological probe lies in departures from the primordial abundances. Almost everywhere, the chemical composition of the Universe has been modified by processes such as stellar nucleosynthesis and cosmic-ray collisions. To infer the primordial abundances of the light elements from those measured, this chemical evolution has to be understood and quantified.

According to the classical theory of stellar evolution, formulated in the early 1970s, low-mass stars such as our Sun should be producing large amounts of ^{3}He. One dying star, the planetary nebula NGC3242, does indeed do this. NGC3242, which is slightly more massive than the Sun, previously synthesized fresh elements in its interior, and is ejecting them into the interstellar medium. Among those elements is ^{3}He, and it is being produced in the amounts predicted. In consequence, the expectation has been that the amount of ^{3}He in the Galaxy would increase over time[3].

Helium-3 can be observed only in relatively young objects in the Milky Way, such as the Sun, the local interstellar cloud[4], a