Geomorphology

A bigger Hockney

PHOTO: RICHARD SCHMIDT

For some weeks London tube-travellers were treated to posters of this David Hockney painting, "A Closer Grand Canyon, 1998", advertising the annual summer exhibition of the Royal Academy of Arts at Burlington House, Piccadilly, in central London. The posters, let alone this picture, scarcely do justice to the scale of the work, which is painted in oils on 96 canvases, with an overall dimension of about 11 by 24 feet. A room at the exhibition is devoted to six such vivid depictions of the canyon.

According to Hockney, it is the space rather than geology of the canyon he has tried to capture in this and similar studies: "the sense of the eye meandering through a vast landscape". Photography failed to do so. So pastel drawings were used as the basis for the final works in oils, which have come to London after being on display at the Centre Georges Pompidou in Paris.

The summer exhibition includes art of various forms, including architectural models, both by academicians such as Hockney and non-academicians, and runs until 15 August. Hockney's Grand Canyon pastels and other drawings can be seen at Annely Juda Fine Art, 23 Dering Street, London W1, in a separate showing which starts on 30 June and ends on 18 September.

Tim Lincoln

mantle, so why do these heterogeneities not get smeared out instead of coming back into the uppermost mantle with roughly the same dimensions as originally formed on the ocean floor? Furthermore, why do the incompatible trace-element ratios of Hawaiian magmas not look more like those of altered oceanic basalt? If the Hawaiian magmas are re-melting well-preserved ancient ocean floor in a plume, why are the trace elements not highly variable as in modern altered oceanic crust? Some of these more mobile elements may be partially removed in the subduction zone, but there should be some trace of these processes in the Nb/U and Ce/Pb ratios for example.

Some of these issues are addressed by Putirka[2], who uses trace-element compositions of lavas combined with melting models to 'retrieve' the original composition of the mantle beneath Hawaii. He argues that the degree of variability in mineralogy and chemical composition in the source is in fact very small. Subducted slabs should be highly heterogeneous in major and trace elements, and in mineralogy, not just because they have been altered by seawater but because the upper portion of the slab is metamorphosed basaltic rocks with high levels of sodium, calcium and aluminium (very distinct from the more magnesium-rich and Al-depleted peridotite that makes up the bulk of the mantle). The exact mineralogy would depend on the pressure, but rocks called garnet pyroxenite and eclogite are the most likely types. The mineralogy also affects the partitioning of certain trace elements. Furthermore, even if the mineralogy remains the same, the degree to which key trace elements partition between melt and silicate minerals is pressure dependent.

Putirka constructs models of partitioning between peridotite and melt as a function of temperature and pressure (depth). The sodium/titanium ratio is particularly sensitive to pressure during melting, and from such data Putirka argues that the Hawaiian mantle does not vary greatly in major-element composition. If recycled ocean floor was involved, a reasonably efficient homogenization of any such chemical heterogeneity must have occurred. Furthermore, Putirka claims that the isotopic heterogeneities, such as those used by Lassiter and Hauri[1], are related to the depth of melting of the mantle and are not simply lateral variations in a plume.

Putirka's arguments run counter to those of Hauri[12], who demonstrated correlations between the isotopic and major-element compositions of Hawaiian lavas that he interpreted to reflect the incorporation of up to 20% of silica-rich 'dacitic' melts from recycled oceanic crust (now converted to garnet pyroxenite). Putirka's arguments are based more on trace elements and their partitioning, and he admits that not all of the variability in Hawaii can be explained by a homogeneous source. Nonetheless, he disputes Hauri's claim that a garnet pyroxenite (recycled slab) component is so important.

Where does all this leave us? We know that subduction occurs and that ultimately subducted slabs must contribute to mantle heterogeneity as evident in OIB. But which isotopic features are the product of re-melting of ancient subducted components? One might get cynical about mantle geochemistry because basic questions such as these keep recurring. Particularly with integrated chemical and isotopic studies, however, they look more tractable than they ever have been. We must keep going. □

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Cancer

DNA damage enables p73

Eileen White and Carol Prives

The *p53* gene product is a critical human tumour suppressor. In response to cellular stresses such as DNA damage and oxygen starvation, p53, a sequence-specific transcriptional activator, induces cell-cycle arrest or programmed cell death (apoptosis)[1].

Until 1997, scientists working on *p53* assumed that this gene was unique. So, the discovery of two *p53*-related genes — *p73* and *p63*, each of which is comprised of several isoforms — was a big surprise[2]. As might be predicted, both genes encode proteins with transactivation, DNA-binding and tetramerization domains, and they share considerable homology with *p53*. Some isoforms of p63 and p73 can transactivate many of p53's targets (albeit to differing extents), and some forms also induce cell-cycle arrest and apoptosis. Hence the idea that certain cellular responses previously assumed to be 'p53 independent' might, in fact, be attributable to these relatives of p53.

One small comfort for p53 researchers was the possibility that only p53 can be induced when cells are exposed to stress signals such as DNA damage. Now, this assumption has been challenged too. Papers by Gong *et al.*[3], Agami *et al.*[4] and Yuan *et al.*[5] (pages 806, 809 and 814 of this issue) together provide evidence that p73 is a target of the non-receptor tyrosine kinase c-Abl in response to

DNA damage. Thus another functional parallel emerges between p53 and p73.

The c-Abl tyrosine kinase is the cellular homologue of v-Abl — the product of the oncogene carried by Abelson murine leukaemia virus[6]. Expression of v-*abl* induces lymphomas in mice, and activation of c-*abl* by chromosomal translocation is associated with chronic myelogenous leukaemia and some forms of acute lymphoma in humans. Furthermore, c-Abl deficiency causes diverse developmental effects in the mouse. So, c-Abl gain-of-function promotes cancer, whereas c-Abl loss-of-function has profound developmental consequences.

Insight into how c-Abl acts came from the identification of its upstream regulatory signals and downstream targets. DNA damage (from ionizing radiation and alkylating agents) activates c-Abl's kinase activity (Fig. 1), providing a connection between c-Abl and the response to DNA damage[7]. The absence of c-Abl disrupts the G_1–S checkpoint in response to DNA damage. In cells that receive DNA damage, the c-Abl protein is phosphorylated, suggesting that there is another protein kinase upstream in the signalling pathway. Indeed, the ataxia-telangiectasia-mutated (ATM) gene product, a component of the DNA-damage checkpoint[8], interacts with and phosphorylates c-Abl[9–11]. The ATM protein is a widely expressed member of the family of protein kinases with similarities to phosphatidylinositol 3-kinases. It is activated by DNA damage, and loss of ATM function in human and mouse cells causes defects in DNA repair and cell-cycle checkpoint control. The result is radioresistant DNA synthesis and, not surprisingly, humans and mice with compromised ATM function are prone to cancer.

There is strong evidence that a key downstream target of ATM is p53, which is phosphorylated and stabilized by ATM in response to DNA damage[12–14]. Although functional interactions between c-Abl and p53 have been observed, they are likely to be indirect because p53 is not phosphorylated on tyrosine. Activation of c-Abl and p53 by ATM probably implements distinct pathways, and we now have an indication that p73 may be a downstream effector of c-Abl.

The three groups report that p73 is affected by some forms of DNA damage. Gong *et al.*[3] demonstrate that levels of p73 protein are increased after cells are treated with cisplatin. Agami *et al.*[4] and Yuan *et al.*[5] show that p73 is phosphorylated after γ-irradiation of cells and by c-Abl. Activation of p73 requires functional c-Abl — neither phosphorylation nor stabilization occur in c-Abl-deficient cells[3–5]. It is not clear why p73 stabilization is seen with cisplatin, but not with γ-irradiation or ultraviolet light, nor why tyrosine phosphorylation of p73 is observed with γ-irradiation but not with cisplatin. Nonetheless, the effect of c-Abl on p73 is likely to be direct, because Agami *et al.* and Yuan *et al.* provide evidence that c-Abl's Src-homology-3 (SH3) domain interacts with p73's carboxy-terminal PXXP motif. All three groups observe that the pro-apoptotic activity of p73 is potentiated by c-Abl, and diminished in c-Abl null cells, consistent with a model in which specific DNA-damage signals are channelled through c-Abl and thence to p73 (Fig. 1). If this is correct, p73-deficient cells should have defective DNA-damage checkpoint control.

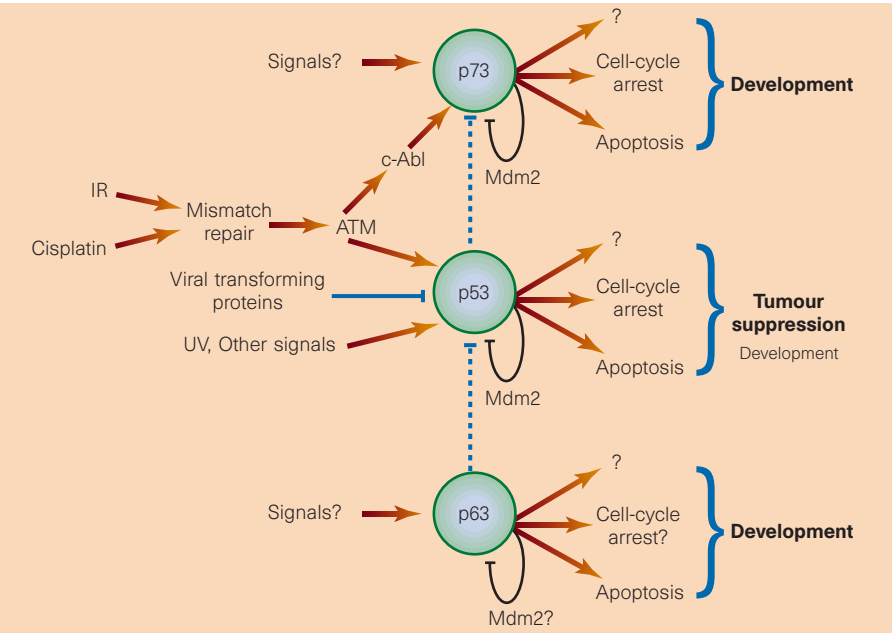

Figure 1 **Regulatory targets and downstream signals affecting p53 and the related proteins p63 and p73. Gong *et al.*[3], Agami *et al.*[4] and Yuan *et al.*[5] have shown that, like p53, the p73 protein is induced in response to DNA damage, via the non-receptor tyrosine kinase c-Abl. Dotted lines indicate inhibition of p73 by mutant forms of p53, and inhibition of p53 by alternately spliced forms of p63. IR, ionizing radiation; ATM, ataxia-telangiectasia-mutated protein; UV, ultraviolet light.**

100 YEARS AGO

Prof. Arrhenius contributes to the *Revue Générale des Sciences* an interesting account of his investigations into the causes of secular variations of temperature at the earth's surface. It is shown that widespread changes of mean temperature are more likely to be due to variations in the proportion of terrestrial rays absorbed by the atmosphere than to any variation connected with the solar rays, and that the absorption of terrestrial rays is most likely to be affected by changes in the amount of carbonic acid present in the atmosphere. Using Langley's data, it is calculated that if the amount of carbonic acid were diminished by a little more than half, the temperature would be lowered by about 4°·5 C., while an increase to two and half or three times the present amount would raise the temperature about 8°·5C., corresponding to the conditions of Glacial and Eocene times respectively.

From *Nature* 22 June 1899.

50 YEARS AGO

During the Academy celebrations in 1945, I had asked to see Lysenko and his results, but had been told that he was too busy. However, after repeated requests, it was suddenly announced that he would lecture next day, and I went to listen, accompanied by Prof. Ashby, and by an excellent interpreter who was also a biologist. Her running translation was at one moment drowned by a burst of laughter from the audience. On my asking her afterwards what had provoked this, it appeared that Lysenko was discussing Mendelian dominance and segregation, which his opponents sometimes brought up against him. Dominance, he said, was easy to explain on his own theories; it was the 'assimilation' ... of one heredity by a second, after a cross. But segregation (of recessive characters in F_2)? That also was easy. 'We know in our persons,' he said, 'that assimilation (or digestion) is not always complete. When that is so, what happens? We belch. *Segregation is Nature's belching*; unassimilated hereditary material is belched out' (presumably in a 1 : 3 ratio!). I cite this remark as further evidence of the fact that, scientifically, Lysenko can only be described as illiterate. Julian Huxley

From *Nature* 25 June 1949.

As the boundaries continue to blur between p53 and its relatives, compelling differences remain. For example, despite their similarities, the three genes seem to have very different functions. Whereas deletion of *p63*[15,16] and *p73* (F. McKeon, personal communication) has dramatic developmental consequences in mice, *p53* null mice develop normally[1] (with some interesting exceptions). But p53 null mice are highly prone to tumours. That p53 is unique in serving as a tumour suppressor is supported by the fact that, in human cancers, loss or mutation of *p73* or *p63* seems to be infrequent[2]. Additionally, only p53 is susceptible to inactivation by the SV40 T antigen, the adenovirus E1B 55K protein and the human papillomavirus E6 protein. Finally, although Mdm2 binds to p53 and p73 (Fig. 1), only p53 is degraded as a result of this interaction[2].

Why might p53 alone be a tumour suppressor? There are several possible answers, all supported by published reports[2]. First, the tissue distribution of p63 and p73 is more restricted than that of p53. Second, the downstream targets of p53 and its relatives may differ, and perhaps p53 is more effective in inducing key apoptosis-related targets under some circumstances. Third, there may be a broader range of upstream regulators that can signal to p53. And fourth, interactions between some forms of p53 and its relatives have been documented. For instance, tumour-derived p53 mutants can repress transactivation and apoptosis induced by p73, and amino-terminally-truncated forms of p63 can repress wild-type p53 (ref. 2). So, cross-talk between p53 and its relatives may contribute to their different roles in tumorigenesis.

It has been suggested that p53 is the most recently evolved member of this family. We might speculate that, with the development of more complex multicellular organisms, a need arose for a more versatile stress-response factor — one that can respond to and transmit a more diverse set of signals to a more complex set of targets. Whatever the explanation for the differences among p53 family members, there is much work to be done to find out how these genes regulate important processes in cells, and why only p53 suppresses tumour formation. □

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Evolutionary genetics

No sex please, we're fungi

Ian R. Sanders

According to evolutionary theory, the advantage of sex is that recombination shuffles together new combinations of genes, thereby producing genetic variation and allowing deleterious mutations to be purged[1–3]. But some extremely successful organisms are both asexual and ancient[4]: the very existence of such 'scandalous' asexuals[5] flies in the face of theory. Among them are counted the arbuscular mycorrhizal fungi, the Glomales, studies of the genome structure and organization of which now reveal some remarkable phenomena. The papers concerned appear in *Fungal Genetics and Biology*[6] and *Gene*[7]. Most notably, they identify a striking degree of divergence in the ribosomal sequences of individuals among the Glomales.

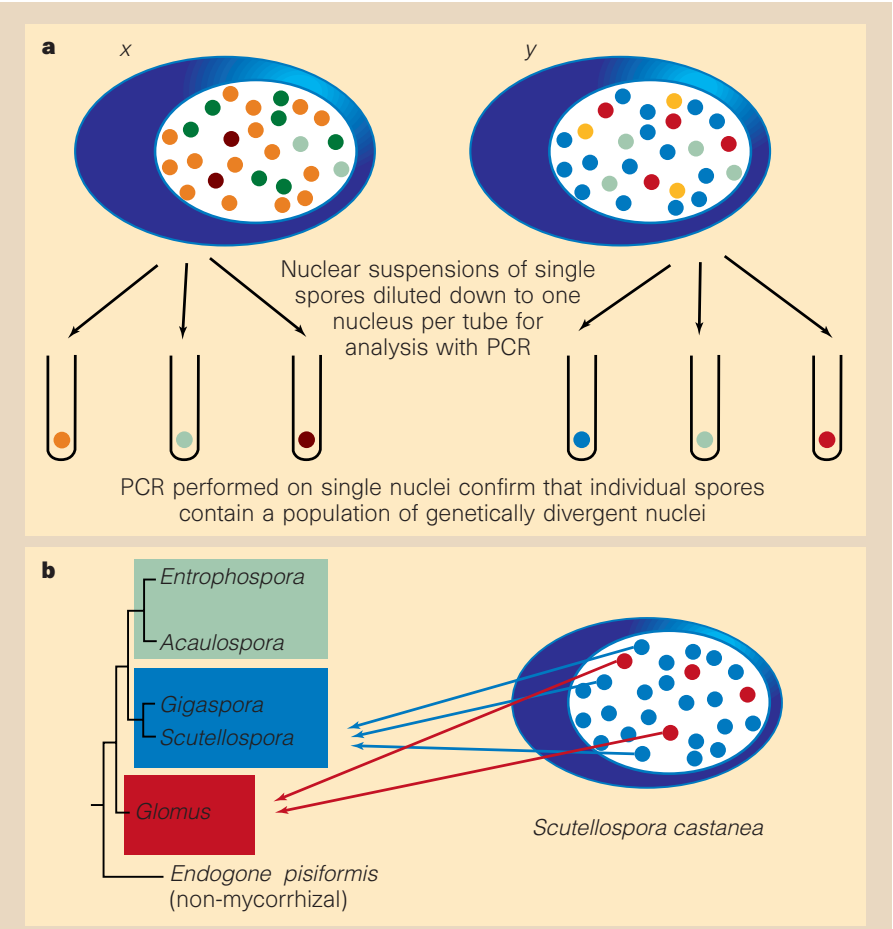

Figure 1 **Genetics of asexual mycorrhizal fungi of the order Glomales.** a, **Hijri *et al.*[6] demonstrate that different spores of *Scutellospora castanea* (*x* and *y*) contain different sequences of ribosomal DNA, but that each spore does not have the same complement of sequences. Further, they show that rDNA differs between nuclei from the same fungal individual, which may be because lack of recombination has allowed the multiple copies of rDNA to diverge.** b, **Hosny *et al.*[7] find that different sequences of the 18S gene from an isolate of *S. castanea* group into two different Glomales genera, *Scutellospora* and *Glomus*. The Glomales consists of three different families: Glomaceae (red), Gigasporaceae (light blue) and Acaulosporaceae (green), and the first two are thought to have diverged 353–367 million years ago[15]. The discovery of rDNA sequences in *S. castanea* that match genera in two different families suggests that genetic diversity in these fungi may have been increased by acquisition of DNA from their ancestors.**