stress response (for instance, apoptosis or senescence). Accordingly, three groups[1–3] provide evidence that one key p53 effector in the process is the cell-cycle inhibitor p21. Indeed, Gil and colleagues[10] suggest that senescence represents the primary barrier to reprogramming. It is well established that cells with an intact p53 network are prone to senescence in culture[11], and perhaps this alone explains why normal cells are more difficult to reprogram. Accordingly, Utikal *et al.*[4] show that spontaneously immortalized cells exhibiting unrestricted growth in culture, with or without obvious p53 impairment, are readily reprogrammed into iPS cells.

At face value, the results of these studies are reminiscent of work[12], published 25 years ago, showing that loss of p53 facilitates cellular immortalization — a state of endless self-renewal that is one of the first steps towards cancer. And more recently, p53 has been implicated as a factor that limits the self-renewal capacity of certain stem cells[13,14]. Even in the iPS field, previous work had shown that the SV40 T antigen — an immortalizing oncogenic protein that disables p53 — or transient inhibition of p53 using small interfering RNAs, enhance reprogramming efficiency[15,16]. The current studies substantially extend and expand on these findings, and provide new platforms for more effectively studying reprogramming.

Just as the race to find new reprogramming factors is reminiscent of the hunt for cooperating oncogenes, the remarkable similarities between the reprogramming processes and oncogenic transformation may provide insights into cancer (Fig. 1). Indeed, both processes require specific combinations of collaborating genes that can produce a less differentiated cell able to proliferate and self-renew indefinitely. All four factors initially shown to reprogram cells are overexpressed in at least some types of tumour, and at least two of them — *c-myc* and *Klf4* — are established oncogenes. Now we find that p53 — a tumour suppressor whose loss greatly increases the efficiency of oncogene cooperation in transforming normal cells to tumour cells[17] — affects reprogramming similarly. Notably, a gold-standard assay for the formation of iPS cells is in fact a tumorigenesis assay that measures their ability to form germ-cell tumours following transplantation into mice.

If the processes that lead to the production of iPS cells and tumours overlap, one wonders whether so-called cancer stem cells — cells capable of self-renewal that are considered essential for the propagation of some tumour types — might initially arise through a reprogramming-like mechanism. Moreover, not all of the factors required to trigger reprogramming of cells to iPS cells are necessary for their maintenance[8,9]. If cancer arises through reprogramming-like processes, then perhaps many of the oncogenes that initiate tumour formation might be dispensable for tumour progression and, hence, be poor targets for new cancer therapies. If this proves to be the case, further studies into reprogramming might eventually point towards new treatments for cancers as well. ■

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EXTRASOLAR PLANETS

Secrets that only tides will tell

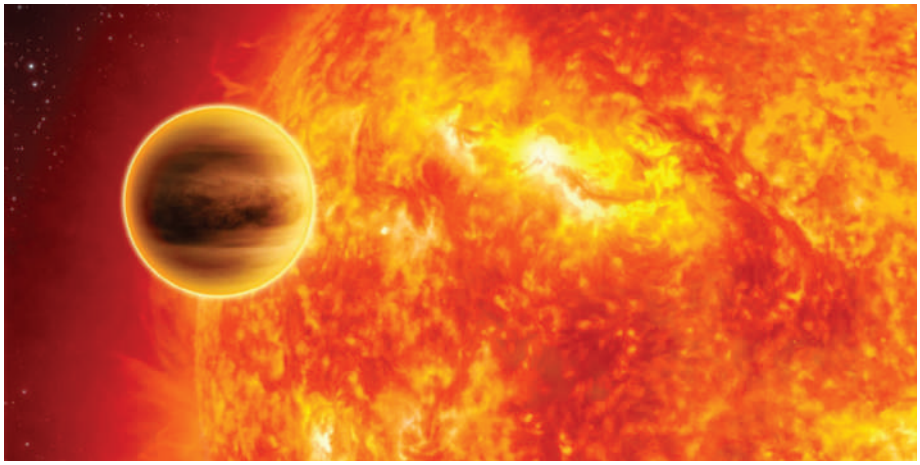
Douglas P. Hamilton

Evidence that the most recently discovered extrasolar planet is virtually at the end of its life is a surprise. The odds of that are very low — similar to drawing two consecutive red aces from a well-shuffled deck of cards.

When it was first discovered in 1995, the planet 51 Pegasi b astounded scientists with its 4.3-day orbital period. This placed the Jupiter-sized planet at around 5% of the Earth–Sun distance from its host star (0.05 AU), a sweltering location where no planet had been expected to exist. But now with almost 375 extrasolar planets discovered to date, and nearly 20% of them located within 0.05 AU of their parent stars, a discovery of another 'hot Jupiter' is no longer as exciting as it once was. On page 1098 of this issue, however, Hellier *et al.*[1] report the discovery of WASP-18b, a hot Jupiter (Fig. 1) that is sure to generate some buzz: the predicted remaining lifetime of the planet is less than a thousandth of the age of its host star, far shorter than that for any other known planet.

WASP-18b, the eighteenth planet discovered by Britain's Wide Angle Search for Planets project[2], is only the second planet found with an orbital period of less than a day. Proximity to the host star, as well as the planet's large mass (10.3 times that of Jupiter), lead to strong tidal interactions between the two bodies, which elongate both of them along the line joining their centres. If the bodies spin as well, the tidal bulges can misalign, causing torques that couple their spins to their orbital angular momentum.

For a planet orbiting a star, the tides raised on the smaller object act swiftly to reduce its spin until one face is locked towards the star. The planet's initially elongated orbit also rapidly becomes circularized by these tides. By contrast, tides raised on the star usually act more slowly, and can either pull the planetary orbit inward (if the planet orbits faster than the star spins) or push it outward (if the stellar spin is faster). WASP-18b should be spiralling inward towards the star, and it is so close and



C. CARREAU/ESA

Figure 1 | The ultimate in global warming. This artist's impression depicts an exoplanet similar to the newly discovered[1] WASP-18b. As seen from the planet, the host star spans an angle of more than 30° and hovers menacingly at a fixed position in the sky. WASP-18b completes an orbit in 0.94 days, buzzing just 2.5 stellar radii above the star's surface. That distance may be shrinking surprisingly rapidly.

so massive that the infall timescale is predicted to be well under a million years.

That stings. Planets and stars form together, and Hellier and colleagues[1] find the star to be about a billion years old. So it seems that WASP-18b has lived a billion years and has just a million years left before its fiery demise. The odds of finding a planet so close to the end of its life are low — only about 1 in 1,000. Did Hellier *et al.* really draw the two red aces from the deck? How can this be?

There are a number of possibilities, but none of them is entirely satisfactory. First, 1-in-1,000 odds may not be so bad, considering the roughly 320 planetary systems discovered to date[3]; effectively, astronomers have had multiple tries at drawing two red aces. Formally, the likelihood of getting a positive result in 320 chances is a respectable 27%. But have we really had 320 chances? The hidden assumption here is that all 320 systems once had a massive planet that was lost to its star. When corrected for the fact that most systems may not have had such a planet, the odds go down considerably. Even more problematic is the fact that there are only three other known planets located within 0.06 AU of their host stars with masses as large as that of WASP-18b. We would probably expect to see many more such objects if this interpretation were correct.

Second, as suggested by Hellier *et al.*, the star may be particularly poor at dissipating tidal energy, which would dramatically increase the planet's lifetime. The tidal-dissipation rate may be loosely parametrized by Q, the quality factor, which depends on properties of the stellar interior. More properly, the dissipation rate is proportional to Q/k_2, where k_2 is a measure of the star's response to a tidal perturbation. The quantity Q/k_2 is often assumed to be about 10^6 for stars, but is relatively well determined only for colder balls of gas: for example, the values for Uranus[4] ($Q/k_2 = 2\times10^5$) and Neptune[5] ($Q/k_2 = 4.5\times10^4$) are uncertain by about a factor of 2. For Jupiter[6], the nominal value of Q/k_2 is 8×10^5, although it could be up to six times higher or lower. Hellier *et al.* show that a Q/k_2 value as high as 10^9 would be required to increase the planet's remaining lifetime towards a billion years; longer-lived planets are much easier to find. If the star's Q/k_2 really is thousands of times above what is measured for either gaseous planets or binary stars, it would be a spectacular finding.

Third, perhaps we are forced to abandon the assumption that the planet has been tidally evolving throughout the billion-year age of its host star. Hot Jupiters are thought to have formed much farther from their stars than where they are found today. A more distant origin gives a planet a far greater supply of raw materials early in its lifetime, allowing growth to Jupiter mass and beyond. After reaching its full size, however, another process, such as interactions with a second planet, must place one planet close to the star, where tidal forces take over. Perhaps such an event occurred recently in the WASP-18 system. It is impossible to rule this out, and extremely difficult to assess the odds.

Finally, maybe something is holding the planet up against the inward drag of tides. Some poorly understood aspect of stellar convection? An unappreciated subtlety of tides? Another planet? Although these may seem unlikely possibilities, given the existence of the unusual WASP-18 system they should be examined more closely. It is useful here to draw an analogy with the similar situation faced by Mars's largest moon Phobos. Like WASP-18b, Phobos is close to its host, skimming just 1.73 Mars radii above the surface, and its orbit is predicted to decay inward in about 30 million years, a timescale more than 150 times shorter than the age of the Solar System. The past history of Phobos, like that of WASP-18b, is not understood, and possibilities similar to those discussed above are equally unpalatable. Perhaps we really are missing some key bit of physics.

Relief, however, is on the way. Hellier *et al.*[1] emphasize that if the orbit of WASP-18b is really decaying inward rapidly, the effects will become visible within a decade. Continuous monitoring of this system — as well as others that are predicted to undergo slower, albeit still rapid, tidal evolution[7] — would be well worth the effort. Only then will tides begin to reveal the secrets of these unusual systems. ■

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DEVELOPMENTAL BIOLOGY

Jumping-gene roulette

Sandra L. Martin

Jumping genes, which make DNA copies of themselves through an RNA middleman, provide a stochastic process for generating brain diversity among humans. The effect of their random insertion, however, is a bit of a gamble.

The enormous complexity of the human nervous system is generated by the combined actions of incompletely understood genetic and environmental factors. Coufal *et al.*[1] (page 1127 of this issue) now reveal one remarkable genetic contribution to individual variation in the nervous system. The authors show that normally quiescent 'jumping genes' can be activated in neural progenitor cells. Each hop generates genetic diversity in the nervous system that may or may not affect function or health.

LINE-1 (L1) retrotransposons are the most dynamic force operating in the human genome. These elements are regions of mobile DNA that make copies of themselves by converting their RNA transcript into DNA, which then reinserts into the genome — a process known as retrotransposition. Cleverly, the proteins that convert the L1 RNA transcript into a DNA copy are encoded by the L1 sequence itself. Depending on where the new L1 inserts, its effect on a neighbouring gene can range from nil to destruction[2].

As selfish mobile elements whose goal it is to make copies of themselves, L1s must be able to retrotranspose in egg and sperm, or in the early embryo, ensuring that new L1 copies are passed on to future generations. That more than 600,000 copies of L1 retrotransposons pepper our genome is proof of the evolutionary success of this strategy. Meanwhile, the human genome has evolved elaborate mechanisms for repressing L1 retrotransposition[3], particularly by blocking transcription, a compulsory first step in the process leading to insertion of a new L1 copy. Methylation of DNA in regulatory regions of genes is a widespread and effective method of transcriptional repression. However, during gamete formation, and in the early embryo, short waves of demethylation in a region of L1 that serves as a promoter of transcription allow the mobile element to temporarily escape transcriptional silencing.

In the body's non-gametes (somatic cells), where new copies of L1 would not be passed on to the next generation but transposition could be harmful, the L1 promoter is methylated and transcription is repressed. Thus, it was surprising to find[4] that L1 transcription seemed to be increased during the differentiation of neuronal progenitor cells isolated from the hippocampus of adult rat brains. Human L1 also retrotransposed when introduced into these same cells and when expressed in the brain cells of transgenic mice[4]. These results raised the possibility that the genome of individual brain cells could harbour different insertion sites and numbers of L1s (so-called somatic mosaicism), and fuelled speculation that L1 retrotransposition might lead to unique neuronal properties among humans[4].

Coufal *et al.*[1] provide data to support this suggestion. They show that human neural progenitor cells, whether derived from fetal brains