Figure 2 Balancing cancer and aging. a, Increases in p53 activity reduce the incidence of cancer but increase the aging rate. Counteracting decreases in p53 activity increase cancer incidence but decrease the rate of aging. b, As a consequence, the turnover of p53 on lifespan time result from a delicate balance between its anti-tumour and pro-aging effects, such that too small or too high p53 increases morbidity from cancer whereas too much p53 increases the fragility from aging.

mutations and promotes premature aging in mice.13 Tytel et al's results add an interesting twist to this hypothesis—they suggest that aging may be due to part to cellular responses to damage, and not damage per se (Fig. 1b). These responses protect vast people from cancer during their reproductive years but they may come at a price.

All of these models can be broadly linked to p53. The SBR2 protein can express p53 activity in mammalian cells.14 Cellular responses to telomere malfunction involve p53 (or p73), and a lack of p53 can counteract some of the effects of a lack of telomerase.15 Cells that proliferate without telomeres in vitro, a process that also involves p53 and was initially linked to human cancer, are called telomeric and fibroblast cells.15 Senescent cells remain metabolically active but cannot proliferate; they also show changes in gene expression that could produce alterations at the tissue level.16 "Reproductive" senescence is triggered by telomere erosion and can be prevented by telomerase. But the same events can also be involved in reproductive aging, for example, DNA damage, oxidative stress and suboptimal cell-cell, cell-tissue and tissue-tissue interactions.17 When telomeres are lost, the replicative 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 data, suggest that tissue aging to vivo results from many factors, not just telomere attrition but p53 has been suggested. It might seem paradoxical that overactive p53 suppresses cancer but promotes aging, 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 aging 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 aging. So p53 activity must be tightly controlled to balance a predisposition to cancer (too little p53) and premature aging (too much p53).2,7

Finally, Ters et al's work1 could have ramifications for understanding and treating human diseases. For example, p53 might contribute to premature aging 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.

Cosmology

A baryonic 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.

D o we live in a "vanishing Universe that will expand forever", or in a closed Universe whose expansion will eventually reverse? Part of the answer is found by accurately estimating the amount of ordinary matter, called baryonic matter, in the Universe. One way of reaching such an estimate arises from one of the predictions of Big Bang theory: that production of light nuclei (deuterium, helium-3, helium-4 and lithium-7) in the early Universe, in a process known as Big Bang nucleosynthesis. A precise measurement of the abundance of baryonic matter is required for modelization of the primordial abundances of light nuclei, and for those estimates to be consistent with the observations made so far.

On page 54 of this issue, Binns, Road and Hepburn report the first reliable assessment of the primordial abundance of He. Their result is based on two samples 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 the expectations from the primordial abundances. Almost everywhere, the chemical composition of the Universe has been modified by processes such as solar 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, high-mass stars such as our Sun should be producing large amounts of He. One dying star, the planetary nebula NGC3462, does indeed show the CSCG242, which is slightly more massive than our Sun, previously synthesized fresh elements in its interior, and is ejecting them into the interstellar medium. Among those elements is He, and it is being produced in the amounts predicted. In consequence, the expectation has been that the amount of He in the Galaxy would increase over time. Helium-3 can be observed only in relatively young stars in the Milky Way, such as the Sun, the local interstellar cloud, a
The planetary nebulae, and H II regions. The H II regions, which have just formed out of matter that has undergone 12 billion years of chemical evolution, should be particularly rich in He. But when Banis and collaborators started to look at them in 1984, the He problem emerged: there was no evidence of He enrichment having occurred. In consequence, the usefulness of He as an indicator of barium density — as a 'cosmological baryometer' — was thrown into doubt.

But ways have been found out of this quandary, both through theory and now observations. The lack of increase in He abundance can be accounted for if most low-mass stars consume most of their He before it can be emitted into the interstellar medium. This requires physical processes which the classical theory of stellar evolution did not take into account, but which have been revealed by anomalous carbon isotopic ratios observed at the surface of old stars. These anomalies can be explained by stellar rotation: by inducing internal mixing, rotation simultaneously leads to the destruction of He inside stars, so it is not emitted into the interstellar medium. About 10% of stars would be unaffected, however, NCG 3324 is one of them. This alternative view results in a much reduced He contribution from low-mass stars compared with that in the classical scheme of events.

Banis and collaborators now report progress on the observational side of things. They have tenaciously continued to sample H II regions, increasing the number covered and so probing a large part of the Galactic disk. Obtaining these data is quite a feat, as it has involved accumulating measurements of extremely weak spectral lines of He at centimeter wavelengths with the National Radio Astronomy Observatory's 140-foot telescope. Deriving an estimate of He abundance from the resulting spectra is also no easy job, as it requires technical demanding modelling of the complex structure of the sources. One of

The auditory system transforms information from one frame of reference into another to create a map of space in the brain. The source of a visual signal that guides this transformation in barn owls has now been found.

When a barn owl hears a noise, it can pinpoint where the sound came from because its brain has a mental map of how the noises it hears fit into the space around it. Various auditory cues are used to construct this 'auditory space map' but it must also be guided by visual inputs, because — assuming reasonable eyesight — vision provides more reliable, topographically organized information. But what part of the brain transmits this information to the auditory map, and what form does the information take? On page 7 of this issue Hyde and Kauflin provide an answer. They suggest that a signal from the optic tectum region of the barn owl's brain provides topographic, point-to-point instructions about the correct representation of auditory spatial cues.

For a hungry barn owl, it is vital to be able to use sounds to locate potential prey — hence the importance of the mental map of these sounds in space. This map is found in the midbrain, specifically the optic tectum. But it is initially produced nearby, in the inferior collicular, using auditory localization cues to tune individual neurons. Such cues include differences in the time it takes for sounds to reach each of the ears, and differences in the level of sounds that arrive at each ear. The map is then relayed to the overlying optic tectum, where it is aligned

sound signals, and signals maps and space Catherine Carr

Figure 1. Big Bang nucleosynthesis predictions for the primordial model. The boxes indicate the observational estimates for the primordial abundances of He (observed in plasmas H II regions), deuterium (derived from the absorption spectra of quasars and DII redshifted from the surface of the oldest stars in our Galaxy). For He the horizontal arrow points to the upper limit of the abundance, relative to hydrogen. The vertical arrow points down to the lower limit of the abundance. Data inferred from the upper limit and deuterium, assuming a He abundance of 65 km s^-1 Mpc^-1. The horizontal lines of the black box over the dotted line (the theoretical band) indicate the range of abundances derived from the upper limit and deuterium. The vertical lines show the allowed range of barium densities, which agree with the range of densities determined from deuterium abundances as shown by the vertical blue box. Modified from ref. 9.

The authors' refinements was to select for their sample H I regions with a relatively simple structure, for which it was easier to achieve accurate determinations of He abundances. Banais and colleagues find that, where H I regions are in the Galaxy, they all have a similarly low He content. Taken together with the theory that rotating stars will emit negligible He into the interstellar medium, this implies that the value of He in H II regions provides an upper limit to its primordial abundance, and a lower limit to the barium density.

The upbeat of Banais et al.'s 20 years of hard labor, then, is that they have rehabilitated He as a reliable cosmological baryometer. Their estimate of primordial barium density is in excellent agreement with that derived from the low abundance of deuterium measured in the absorption spectra of high-redshift quasars, and from the high content of He in H II regions in metal-poor dwarf galaxies. As they point out, it has been depleted by about a factor of two in the oldest stars in our Galaxy. The estimate also signifies in the He density observed in the cosmic microwave background radiation by the MAXIMA and Boomerang experiments. That estimate, however, is low — only about 4% of the amount required to close the Universe, assuming a value for the He abundance consistent with 65 km s^-1 Mpc^-1. So the answer to the question we started with — that the Universe cannot be closed with baryonic matter alone, but other evidence implies the existence of 'dark matter', or 'missing mass, the search for which now constitutes one of the most exciting areas of research at the interface between particle physics and cosmology.

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Neuroscience

Sounds, signals and maps space Catherine Carr

The auditory system transforms information from one frame of reference into another to create a map of space in the brain. The source of a visual signal that guides this transformation in barn owls has now been found.

When a barn owl hears a noise, it can pinpoint where the sound came from because its brain has a mental map of how the noises it hears fit into the space around it. Various auditory cues are used to construct this 'auditory space map' but it must also be guided by visual inputs, because — assuming reasonable eyesight — vision provides more reliable, topographically organized information. But what part of the brain transmits this information to the auditory map, and what form does the information take? On page 7 of this issue Hyde and Kauflin provide an answer. They suggest that a signal from the optic tectum region of the barn owl's brain provides topographic, point-to-point instructions about the correct representation of auditory spatial cues.

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