DNA DAMAGE

Stem cells hide from the sun

Adult stem cells reside in niches that maintain, regulate and protect them. Fresh light has now been shed on how the need for protection has driven changes in the locations of these niches during evolution. SEE LETTER P.445

ISABEL BEERMAN

Tissue-specific stem cells have the crucial role of maintaining and replenishing all the specialized cells that make up a given tissue or system, so it is essential that their functions are preserved throughout an organism's life. These adult stem cells therefore reside in dedicated microenvironments called stem-cell niches, which help to regulate and protect the stem cells. On page 445, Kapp *et al.*[1] investigate factors that affect the locations of niches for haematopoietic stem and progenitor cells (HSPCs), which give rise to all blood-cell lineages. Their findings provide insights into the evolutionary drivers of niche location.

Stem-cell niches have several commonalities, regardless of the type of tissue stem cell they sustain. They provide structural support, enable access to molecular signals from either local or remote sources, produce proteins that help tether stem cells to the location and help to regulate stem-cell metabolism[2]. Cues from the niche also restrict unnecessary stem-cell divisions, presumably both to prevent stem-cell exhaustion (in which stem cells lose the ability to regenerate cell lineages) and to minimize the number of genetic mutations that arise during DNA replication, maintaining the fidelity of the genome.

Most information that researchers have about the HSPC niche has been gained from mouse studies. These analyses have revealed that, during development, there are several different sites at which blood lineages are generated[3]: in mice, HSPCs and their niches move, depending on the developmental stage. Moreover, studies of adult HSPC populations in flies[4,5], and in zebrafish[6,7] and other vertebrates[3], have revealed different niche locations in different species — the bone marrow in birds and mammals, the kidney in fish, and the liver in frogs[8], for example.

A theory published almost 40 years ago states that HSPC niches in terrestrial animals evolved at sites that minimize damage from ionizing radiation[9], with the assumption that water would have provided aquatic organisms with protection from damaging ultraviolet light. Kapp *et al.* set out to examine whether the need to minimize damage might influence HSPC-niche location in the model organism zebrafish, which tends to inhabit clear bodies of water that offer little UV protection. During embryonic stages, zebrafish are largely transparent, making them well suited to live imaging using fluorescently labelled cells. However, the authors found that visualization of the HSPC population was consistently obscured by pigmented cells called melanocytes.

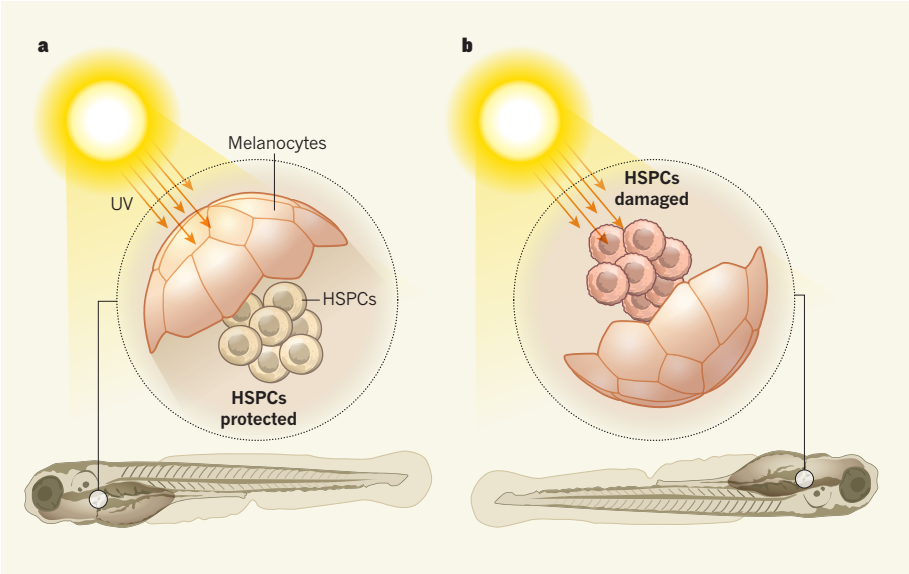

Figure 1 | Stem cells under an umbrella. Haematopoietic stem and progenitor cells (HSPCs), which give rise to blood-cell lineages, reside in specialized microenvironments called niches that help to protect them from DNA damage. **a**, Kapp *et al.*[1] have described a population of pigmented cells called melanocytes close to the HSPC niche in zebrafish. The cells act as an opaque umbrella, protecting HSPCs from ultraviolet irradiation. **b**, The authors anaesthetized the fish, causing them to flip on to their backs. The melanocytes no longer protected the HSPCs from UV damage, demonstrating that the pigmented cells provide a physical shield, rather than acting through signalling mechanisms.

The researchers used genetic engineering to generate zebrafish lacking melanocytes, and found that HSPCs developed normally, indicating that the pigmented cells are not essential for HSPC maintenance. However, this finding raised the question of what (if any) role the melanocyte population has in relation to HSPCs. Kapp and colleagues performed a series of clever experiments to investigate. They genetically engineered fish to lack melanocyte pigmentation, and showed that UV radiation caused higher levels of DNA damage in these fish than in controls, as well as an increase in HSPC death. Next, they anaesthetized pigmented fish, causing them to flip onto their backs. This removed the protection provided by the physical location of the melanocytes — again, the HSPCs were rapidly damaged by UV. Thus, melanocytes protect HSPCs by generating a physical opaque shield against UV irradiation (Fig. 1).

Kapp *et al.* next showed that this melanocyte 'umbrella' is present in other species of fish, as well as in frogs, in which melanocytes shield the HSPC niche in tadpoles before the cells migrate to the bone marrow during development. Fish without melanocytes in this location might have had a selective disadvantage during evolution, because their HSPCs would not have been protected by the umbrella and would have been exposed to UV damage. This would have led to decreased numbers of HSPCs, and daily exposure to UV would probably have been lethal.

These findings raise the question of whether aquatic organisms have evolved so that other crucial, vulnerable cells are also physically shielded — either by melanocytes or by other carefully positioned cells — to prevent UV-induced damage. It will be interesting to determine how many other tissue-specific

stem cells have appropriated this type of physical protection in fish.

It remains to be seen whether HSPCs home to locations protected by melanocytes, or whether melanocytes can be recruited or stimulated to proliferate by signals from blood stem-cell niches. Another question is why HSPCs seek out a different niche in terrestrial vertebrates. HSPCs regularly leave their niches and circulate in the blood, whereas other adult stem cells, although capable of movement, tend to be more static. Indeed, Kapp *et al.* highlighted this mobility in adult *Rana* frogs, in which the location of HSPCs switches depending on the season — perhaps driven by changing exposure to UV. This mobility could give HSPCs an increased capacity to seek out alternative sites that can better protect them from damage. Bone would completely encapsulate the stem cells, providing a shield from all angles. There might also be other benefits to a niche in the bone marrow, such as lower oxygen levels, which could provide protection from other forms of DNA damage.

Fish have evolved the ability to mitigate UV-induced DNA damage through light-dependent DNA repair[10]. The fact that, despite this ability, HSPCs seem to be under evolutionary pressure to seek additional protection highlights the importance of maintaining the fidelity of tissue stem cells. Physical protection might be of particular value in the haematopoietic system, because blood cells have a high turnover rate. If HSPCs are unable to re-establish blood-cell populations, the organism would be likely to die from anaemia or infection.

Finally, it might be predicted that other tissue-specific stem cells that have less migratory potential than HSPCs would be more prone to damage, because they would be less able to move to protective niches. By gaining insight into the evolutionary steps taken to protect haematopoietic stem cells, we might be able to develop strategies to protect these cell types, refining their current niches to better maintain stem-cell potential in longer-lived organisms, including humans. ■

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ASTRONOMY

Missing matter found in the cosmic web

The location of nearly half of the ordinary matter in the Universe is unknown. X-ray observations suggest that this elusive 'baryonic' matter is hidden in the filamentary structure of the cosmic web. SEE LETTER P.406

TAOTAO FANG

We live in a dark Universe: just 5% of it consists of ordinary matter such as that found in atoms, whereas the rest is 'dark' matter and energy that cannot currently be detected directly[1]. However, observations of the nearby Universe suggest that up to 40% of this ordinary matter — which is made up primarily of particles known as baryons — is missing[2–5]. Baryonic matter is thought to be distributed through the Universe like a cosmic web, and the missing baryons are predicted to be located in the filamentary structures that connect the web, and in intergalactic space[4]. On page 406, Nicastro *et al.*[6] report the detection of the X-ray absorption signatures of baryons in the spectra of a bright background object. The findings might finally reveal a major reservoir for baryonic matter.

Why have the missing baryons been so difficult to detect? One reason is that the density of the baryonic matter in the filaments is extremely low. The other reason is that the high temperature in the filaments causes the most abundant element (hydrogen) to be almost completely ionized — which means that it has no electrons to produce spectral features that could be used to detect it. However, there might be trace amounts of heavier elements such as oxygen, in which a few electrons are bound. These ions can produce detectable (but extremely weak) spectral features, typically in the X-ray and/or ultraviolet regions of the electromagnetic spectrum.

Nicastro *et al.* observed the X-rays emitted by a special type of astronomical object known as a BL Lacertae (BL Lac) object. These are typically extremely bright, and have no (or very few) intrinsic spectral features — which makes it easy to detect any absorption of their emissions by other objects between them and Earth, such as filaments in the cosmic web.

The BL Lac object studied by the authors is called 1ES 1553+113, and is more than 2,200 megaparsecs away. Nicastro and colleagues observed this target with the European Space Agency's XMM-Newton X-ray Space Telescope over several periods, for a total observation time of about 1.75 million seconds (about 20 days). They thus obtained a spectrum with an extremely high signal-to-noise ratio, which allowed them to perform high-resolution spectroscopy of very weak spectral features (Fig. 1).

The authors discovered two highly statistically significant systems of absorption lines produced by helium-like oxygen (oxygen ions that have only two bound electrons) at redshifts of 0.43 and 0.36. Redshift measures the change in wavelength that occurs when light travels over astronomical distances, and is approximately proportional to the distance of the light-emitting object from Earth. The researchers also performed an optical survey of galaxies along the sight line towards

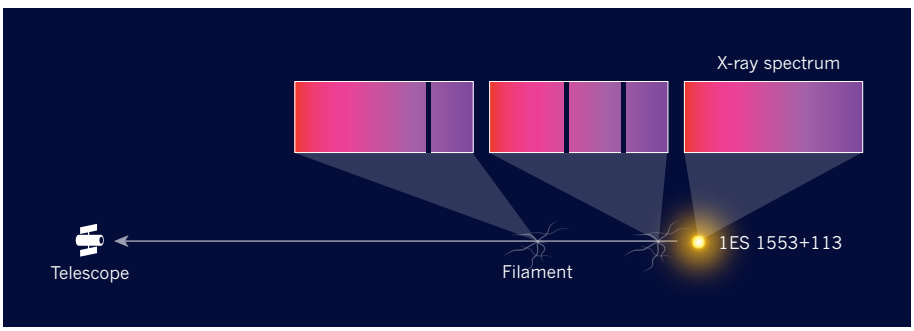

Figure 1 | The search for baryonic matter. Nicastro *et al.*[6] used the XMM-Newton X-ray Space Telescope to detect the emission spectrum of a bright astronomical object called 1ES 1553+113. They observed lines superimposed on the spectrum, which they attribute to X-ray absorption by helium-like oxygen (oxygen ions that have just two bound electrons, not shown) in two filaments of the cosmic web located between the telescope and the emitter. The cosmic web is a massive structure composed of ordinary (baryonic) matter, such as that found in all atoms. If the authors' attribution is correct, then the finding reveals the location of a major reservoir of baryonic matter. Distances and sizes of objects not shown to scale.