this suggests that a different CXCL12-producing cell regulates the mobilization of HSCs. It has been shown[4] that HSCs in the bone marrow are affected by a type of CXCL12-producing reticular cell (a cell that contributes to the stroma), although the specific nature of these cells is unclear.

The authors find that, downstream of the β_3 receptor, the stability of the gene transcription factor Sp-1 is reduced by the removal of a phosphate group. Such dephosphorylation might contribute to the decreased expression of the *Cxcl12* gene. With reduced CXCL12 to anchor HSCs to the bone marrow, these cells would be able to transiently enter the circulation.

The task ahead is to discern the physiological significance of the cyclic changes in stem-cell circulation. On noting circadian variation in a stem-cell circulation, the authors of a previous study[5] proposed that it could be used to harvest stem cells for transplantation. This clinical application would certainly be good. But from an evolutionary perspective, the advantage for the organism of circadian variation in the circulating levels of HSCs, or indeed HSC circulation at all, is unclear.

A clue to why HSC circulation is advantageous might lie in its circadian nature. Perhaps bone and bone marrow function as an integrated system. Bone formation occurs in a diurnal manner in rodents, with the greatest remodelling occurring during periods of light[6]. Many hormones affecting skeletal mass, including parathyroid hormone and leptin, undergo circadian cycling[7]. Also, clock genes, such as *Per1*, *Per2* and *Cry*, in osteoblasts inhibit bone formation and, in their absence, leptin-driven adrenergic stimulation has a proliferative effect on osteoblasts[8]. Circadian bone-modifying events might occur in synchrony with adrenergic stimulation of the β_3 receptors on stromal cells, causing Sp1 degradation, decreased CXCL12 production and increased HSCs in the blood (Fig. 1).

Because modifications to bone would also be expected to modify both bone marrow and the niches it provides for blood-cell production, it could be that it is the remodelling of their 'home' that sends HSC residents packing. If remodelling or making new bone creates bone-marrow niches, filling them with stem cells rather than with 'foreign' cell types such as more mature or even mutant cells may be advantageous. In invertebrate animal models, foreign cells occupying niches can undergo dedifferentiation and other events inducing cell division[9,10]. This might be problematic considering the risk of malignancy in longer-lived organisms.

During embryonic development, blood-cell production in the bone marrow requires circulating HSCs to migrate to and engraft in the niche[11]. Perhaps the same is true for the constantly remodelling adult bone and bone-marrow niches, in that they require a circulating cell to undergo migration and engraftment as a selection process for the fittest stem cells. Circadian oscillations in stem-cell location might contribute to synchronized generation of niches and their rapid occupancy by the best-suited stem cells. Perhaps a good breakup can ultimately ensure 'domestic tranquillity'. ■

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1. Méndez-Ferrer, S., Lucas, D., Battista, M. & Frenette, P. S. *Nature* **452,** 442–447 (2008).
2. Shepherd, B. E. *et al. Exp. Hematol.* **32,** 1040–1050 (2004).
3. Katayama, Y. *et al. Cell* **124,** 407–421 (2006).
4. Sugiyama, T. *et al. Immunity* **25,** 977–988 (2006).
5. D'Hondt, L. *et al. J. Cell. Physiol.* **200,** 63–70 (2004).
6. Simmons, D. J. & Nichols, G. Jr *Am. J. Physiol.* **210,** 411–418 (1966).
7. Fraser, W. D., Ahmad, A. M. & Vora, J. P. *Curr. Opin. Nephrol. Hypertension* **13,** 437–444 (2004).
8. Fu, L. *et al. Cell* **122,** 803–815 (2005).
9. Kai, T. & Spradling, A. *Proc. Natl Acad. Sci. USA* **100,** 4633–4638 (2003).
10. Kai, T. & Spradling, A. *Nature* **428,** 564–569 (2004).
11. Laird, D. J. *et al. Cell* **132,** 612–630 (2008).

ASTRONOMY

Starbursts near and far

Yu Gao

Observations of intensely bright star-forming galaxies both close by and in the far Universe seem to emphasize their similarities. But look a little closer, and telling differences emerge.

In a recent issue of the *Astrophysical Journal*, two papers[1,2] present the latest measurements of 'starburst' galaxies — galaxies whose extreme brightness is thought to indicate short, intense bursts of star formation. This latest work is a fine example of the instruments and methods that are providing ever deeper insight into these spectacular objects. But equally, it exposes gaps in our knowledge that cannot be filled by using current instrumentation, and that must wait for the next generation of more powerful telescopes.

The first of the papers, by Mangum *et al.*[1], provides perhaps the most accurate measurements so far of the density of star-forming molecular gas in nearby starburst galaxies. The authors used the National Radio Astronomy Observatory's 100-metre-aperture Green

50 YEARS AGO

Handbuch der Physik. Herausgegeben von S. Flügge. Band 14: Kältephysik I. Band 15: Kältephysik II. — To find, in an encyclopædia of physics running to fifty volumes, that two should be devoted specifically to low-temperature physics raises the question whether nowadays it is a sufficiently distinct branch to justify separate treatment ... Indeed, so much labour has gone into these exhaustive compilations of facts that it may seem ungrateful to complain that the total effect is one of deplorable dullness. Yet there is indeed only one article, that by J. Bardeen on the theory of superconductivity, which can be said to be exciting; and this is distinguished from the rest chiefly because the author is not content to act as an impassive recorder of what is known, but is eager to explore those regions where the meaning of the observations is obscure.
From *Nature* 29 March 1958.

100 YEARS AGO

An interesting lecture was given by Sir William Preece at the Institution of Electrical Engineers on March 12 on his recent visit to America, and the various improvements in constructional and engineering works since his previous visits were dealt with. The sky-scraper buildings appear to afford a considerable day load, in that they employ numerous lifts which are constantly in use ... On the telephone question, America seems to have gone ahead of us on this side. In most of the hotels telephones are installed in every bedroom, so that business may be transacted with any part of the country. This applies also to the restaurants, where telephones may be plugged on to your table if desired. The Telephone Tariff question has also been thoroughly considered in America, and the message rate has been adopted in preference to the simple annual rental.
From *Nature* 26 March 1908.

50 & 100 YEARS AGO