A superelastic organic crystal such as that presented here could be used to make internal valves that both sense and control the pressure in these devices. Such superelastic materials could also act as fillers in shock absorbers designed to dampen shock and vibration. ■

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1. Ölander, A. *J. Am. Chem. Soc.* **54,** 3819–3833 (1932).
2. Takamizawa, S. & Miyamoto, Y. *Angew. Chem. Int. Edn* **53,** 6970–6973 (2014).
3. Otsuka, K. & Ren, X. *Prog. Mater. Sci.* **50,** 511–678 (2005).
4. Jani, J. M., Leary, M., Subic, A. & Gibson, M. A. *Mater. Design* **56,** 1078–1113 (2014).
5. Kato, T., Mizoshita, N. & Kishimoto, K. *Angew. Chem. Int. Edn* **45,** 38–68 (2006).
6. Prins, L. J., Reinhoudt, D. N. & Timmerman, P. *Angew. Chem. Int. Edn* **40,** 2382–2426 (2001).

STEM CELLS

Reprogramming finds its niche

Production of blood stem cells from reprogrammed adult cells is notoriously difficult. It emerges that a supportive microenvironment may be crucial for their efficient generation. SEE ARTICLE P.312

DANIEL LUCAS & PAUL S. FRENETTE

Bone-marrow transplants can be life-saving, but a large proportion of patients who are in need of a transplant — particularly those from ethnic minorities — lack suitable donors. Blood-cell precursors called haematopoietic stem cells are the basis of transplants because, when they are injected intravenously, they can migrate and engraft into the bone marrow, regenerating every blood-cell lineage. One way to combat the donor deficit, therefore, would be to generate patient-derived haematopoietic stem cells. However, this strategy has been hampered by problems with engrafting engineered stem cells, and by difficulties with maintaining haematopoietic 'stemness' in laboratory-cultured cells. On page 312 of this issue, Sandler *et al.*[1] describe an approach for generating haematopoietic stem cells that circumvents these problems.

In their seminal experiment[2], the stem-cell biologists Shinya Yamanaka and Kazutoshi Takahashi reprogrammed skin fibroblast cells into a 'reset' state. Starting with a series of candidate transcription factors, the researchers defined a combination of four factors that induce complete cellular dedifferentiation. The reprogrammed cells, called induced pluripotent stem (iPS) cells, can theoretically differentiate into any cell type in the body. However, differentiation of iPS cells into functional adult tissues has proved to be a challenge, owing to our lack of understanding about the complex cues required to program cells *in vitro*. As such, differentiation protocols for haematopoietic stem cells (HSCs) tend to yield embryonic-like blood cells that do not engraft efficiently into bone marrow[3].

An alternative strategy is the direct reprogramming of adult cells into another lineage, without going through a pluripotent-cell stage. Adult fibroblasts have been successfully reprogrammed into several cell types, including neurons, cardiomyocytes and hepatocytes[4]. Last year[5], four transcription factors (Gata2, cFos, Gfi1b and Etv6) were used to reprogram mouse fibroblasts into cells that expressed HSC surface markers and differentiated into blood-cell progenitors *in vitro* (Fig. 1). However, the reprogrammed cells could not robustly engraft into bone marrow after transplantation.

During embryonic development, HSCs arise from vascular cells that line the aorta, and the cells continue to require signals from the vascular bed, or niche, for their maintenance and function throughout their lives. Sandler *et al.* reasoned that they could enhance the efficiency of direct reprogramming and maintain the self-renewing abilities of the induced HSCs (iHSCs) by starting with a cell type with a similar developmental origin to HSCs, and growing the cells in a microenvironment comparable to their *in vivo* niche.

The authors isolated human umbilical-vein endothelial cells (HUVECs, readily available cells that line the umbilical vein), and forced them to express 26 transcription factors that are enriched in HSCs, but not in HUVECs. The researchers maintained the cultured cells in a medium that lacked serum, which can impair HSC maintenance (serum is normally included in culture media because it contains growth factors that promote cell proliferation). Sandler and colleagues kept the cells on a feeder-cell layer; this underlying

50 Years Ago

Some top-rank public schools and university colleges produce men of brilliant academic achievement who have poor judgement, no power of decision and no capacity to delegate work or to control men. These men can be the tragedies of industry because their deficiencies are not revealed in their academic record and are difficult to detect at a selection interview. They can get started on a promising career, but end in the wilderness of the unpromotable clever boys … some of the highest places in industry have been filled successfully by men whose education has been obtained the hard way. In these cases, the task of getting education and training the hard way has imposed personal disciplines which have probably led imperceptibly to the acquisition of those characteristics needed in industry. Sometimes, however, such a course produces an almost characterless 'swot'.
From *Nature* 18 July 1964

100 Years Ago

Everyone is familiar with the dramatic story of Bernard Palissy, the potter, and how he fired a kiln with his household furniture in order to produce sufficient heat to melt his glazes, but his scientific work is rarely mentioned … during the years 1575–84 he exercised great influence upon society in the city. He lectured in agriculture, chemistry, mineralogy, and geology, and illustrated his lectures with demonstrations of natural objects from his museum. "Into the faces of the learned of his time he thrust his facts; he urged the might of the verified fact, the tests of practical experience, the demonstration of the senses; and these in a keen and original way." … At the age of eighty Palissy was thrown into the Bastille as a dangerous heretic.
From *Nature* 16 July 1914