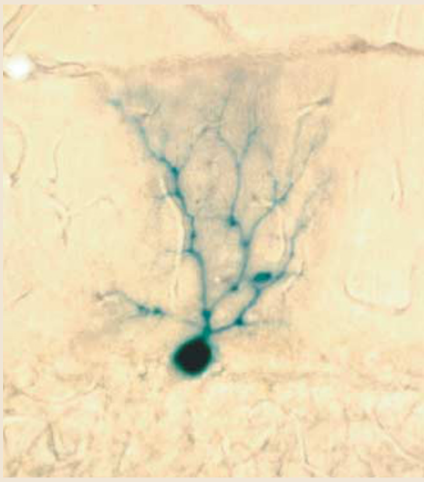
STEM CELLS

State of the union

Early reports that bone marrow stem cells could colonize the brain and differentiate into neurons raised hopes of an abundant and accessible supply of cells for brain repair. However, a different explanation has since been offered for these observations: instead of undergoing transdifferentiation to generate new neurons, the bone marrow-derived cells (BMDCs) fuse with pre-existing neurons. Previously, this fusion phenomenon was only seen *in vitro*, but two new reports confirm that it occurs in the living brain.



A *LacZ*-expressing Purkinje cell in the cerebellum of an R26R mouse transplanted with Cre recombinase-expressing bone marrow cells. Reproduced, with permission, from *Nature* © Macmillan Magazines Ltd.

In one study, Alvarez-Dolado *et al.* used a Cre/loxP-based cell-marking technique to detect cell fusion. They used a mouse line called R26R, which carries a *LacZ* reporter gene that contains a 'stop' cassette flanked by loxP sequences. They irradiated the mice, then reconstituted their bone marrow with a BMDC line that expressed green fluorescent protein (GFP) and Cre recombinase. When BMDCs fused with R26R cells, the Cre recombinase excised the stop cassette between the loxP sites, thereby permitting *LacZ* expression.

The authors found *LacZ*-expressing cells in the liver and heart, and also in the Purkinje cell layer of the cerebellum. Each *LacZ*-expressing Purkinje cell contained two nuclei, only one of which had a typical Purkinje cell nuclear morphology. To see whether any transdifferention events had taken place, the authors also screened the recipient mouse tissues for non-haematopoietic cells that expressed GFP but not *LacZ*. No such cells were found.

In the other study, Weimann *et al.* transplanted GFP-expressing BMDCs from male mice into irradiated female mice, and they also detected binucleate Purkinje cells. Only one nucleus in each cell contained the Y chromosome, confirming that the two nuclei came from different mice. The binucleate state could be maintained for at least 1.5 years, and the donor nucleus eventually acquired the morphology of a Purkinje cell nucleus. Moreover, the donor nucleus seemed to activate Purkinje cell-specific genes, implying that it had become reprogrammed.

So, do these findings quash the idea of turning bone marrow stem cells into neurons? It certainly seems that BMDCs are unlikely to provide a significant source of new neurons, but perhaps cell fusion could be harnessed in other ways for therapeutic purposes. For example, Alvarez-Dolado *et al.* hint that it might provide a mechanism for repairing damaged cells, and this tantalizing possibility should provide the impetus for further investigations.

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References and links

ORIGINAL RESEARCH PAPERS Alvarez-Dolado, M. *et al.* Fusion of bone-marrow-derived cells with Purkinje neurons, cardiomyocytes and hepatocytes. *Nature* **425**, 968–972 (2003) | Weimann, J. M. *et al.* Stable reprogrammed heterokaryons form spontaneously in Purkinje neurons after bone marrow transplant. *Nature Cell Biol.* 15 October 2003 (doi:10.1038/ncb1053)

COGNITIVE NEUROSCIENCE

I see what you mean

How does the brain process concepts such as 'peaceful' or 'diurnal'? As concepts have been regarded to be propositional in nature, their neural representation has been difficult to grasp. But some authors have argued that concepts are grounded in motor and sensory processes, leading to the prediction that the neural processing of concepts might activate specific motor and sensory areas. In support of this idea, a recent paper reports that auditory and action-related conceptual features that have been linked to specific visual stimuli lead to the activation of brain areas that respond to auditory and action-related sensory stimuli, respectively.

James and Gauthier trained people to associate a visual stimulus with words of a given knowledge type that could not be linked to the stimulus on the basis of its pure static appearance. For example, one visual stimulus might be associated with auditory features (squeals, howls, sings), and another one with action-related features (digs, climbs, walks). As auditory and motion-related features activate specific regions of the brain (the superior temporal gyrus and the posterior superior temporal sulcus, respectively), the key question was whether these regions were activated during a visual task that did not require the explicit retrieval of the associations. Indeed, the authors found this to be the case, supporting the idea that concepts are grounded in perception. But in addition, the data of James and Gauthier indicate that semantic knowledge might be stored in sensory- and motor-specific brain systems, instead of in a global, amodal system, as previously proposed.

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Examples of the visual stimuli used by James and Gauthier. Images courtesy of M. J. Tarr (Brown University, Providence, Rhode Island).

References and links

ORIGINAL RESEARCH PAPER James, T. W. & Gauthier, I. Auditory and action semantic features activate sensory-specific perceptual brain regions. *Curr. Biol.* **13**, 1792–1796 (2003)
FURTHER READING Kan, I. P. *et al.* Role of mental imagery in a property verification task: fMRI evidence for perceptual representations of perceptual knowledge. *Cogn. Neuropsychol.* **20**, 525–540 (2003) | Barsalou, L. W. *et al.* Grounding conceptual knowledge in modality-specific systems. *Trends Cogn. Sci.* **7**, 84–91 (2003)