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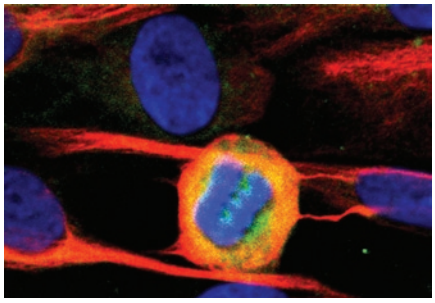
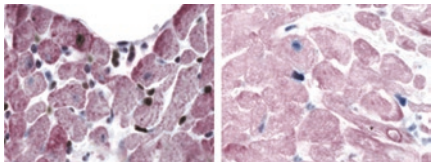
Imaging of human embryonic stem cell–derived neural stem cell grafts



Real-time imaging of transplanted stem cells is essential for tracking cell fate and function and for successful delivery and safety monitoring in the clinical setting. In this issue, Daadi *et al.* used bioluminescence and magnetic resonance imaging to visualize the fate of grafted human embryonic stem cell–derived human neural stem cells (hNSCs) in stroke-damaged rat brain. The hNSCs were genetically engineered with a lentiviral vector carrying a reporter gene that expressed enhanced green fluorescence protein and firefly luciferase. Grafted hNSCs were observed to differentiate into neurons, into oligodendrocytes in stroke regions undergoing remyelination, and into astrocytes extending processes toward stroke-damaged vasculatures. *See page 1282.*

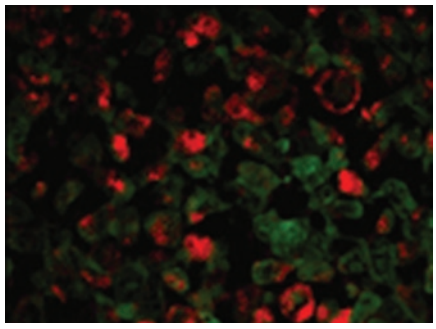
Getting to the heart of cell therapy

Cell therapy using cells derived from bone marrow following myocardial infarction (MI) has shown promise in animal models in reducing the size of the infarct and improving cardiac function. However, the mechanism of action of such cell therapies remains highly controversial. Yeghiazarians *et al.* compared the therapeutic benefits of intramyocardial injection of unfractionated bone marrow cells (BMCs) versus BMC extract as treatments for MI. By day 6, BMCs increased the number of cycling cardiomyocytes (CMs) versus control, whereas extract therapy resulted in significant reduction in the number of apoptotic CMs at the border zone of the infarct. Overall, the results suggest that intact cells are not necessary and that the death of implanted cells may be a major component of the benefit. *See page 1250.*



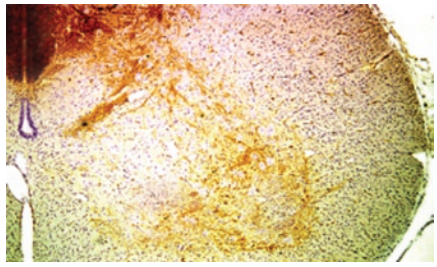
Engineered bone marrow stromal cells prevent the growth of liver metastases

Liver metastases respond poorly to current therapy and remain a frequent cause of cancer-related mortality. Tumor cells expressing a soluble form of the insulin-like growth factor-I receptor (sIGFIR) lose the ability to metastasize to the liver. Wang *et al.* present a therapeutic approach for prevention of hepatic metastasis based on sustained *in vivo* delivery of the soluble receptor by genetically engineered autologous bone marrow stromal cells. The results show that the soluble receptor acted as a decoy to abort IGFIR functions during the early stages of metastasis and identify sustained sIGFIR delivery by cell-based vehicles as a potential approach for prevention of hepatic metastasis. *See page 1241.*



Intravenous self-complementary AAV9 delivers transgenes to motor neurons

Therapeutic gene delivery to the whole spinal cord is a major challenge for the treatment of motor neuron diseases. Systemic administration of therapeutic molecules from blood to the spinal cord is hindered by the presence of the blood–brain barrier (BBB). Duque *et al.* describe motor neuron transduction in adult animals following intravenous delivery of self-complementary adeno-associated virus serotype 9 (scAAV9) vectors. Intravenous motor neuron transduction was achieved in adults without pharmacological disruption of the BBB, and transgene expression lasted at least 5 months. Importantly, this finding was successfully translated to large animals, with the demonstration of efficient systemic scAAV9 gene delivery to the neonatal and adult cat spinal cord. *See page 1187.*



Sleeping Beauty transposition from nonintegrating lentivirus

Lentiviral vectors enter cells with high efficiency and deliver stable transduction through integration into host chromosomes, but their preference for integration within actively transcribing genes raises concern for insertional mutagenesis. Vink *et al.* combine the efficient cell and nuclear entry properties of HIV-1-derived lentiviral vectors with the integration-profile benefits of *Sleeping Beauty* transposase. Integration-site analysis revealed redirection away from integration within transcriptionally active genes favored by integrase-proficient lentiviral vectors. In a related article, Staunstrup *et al.* describe a similar hybrid vector. These authors also demonstrate that the *Sleeping Beauty* transposase overrides the natural lentiviral integration pathway and directs vector integration less frequently toward transcriptional units, resulting in a random genomic integration profile. *See pages 1197 and 1205.*