Stem Cell Therapy for Tissue Repair: The Stem Cell-Host
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Introduction
Mesenchymal stem cells (MSCs) have generated a great deal of interest because of their potential use in regenerative medicine and tissue engineering. While the therapeutic testing of these cells has progressed well, there are still many questions to be addressed concerning the role of endogenous populations of stem cells in the adult and the function of various stem cell niches. The purpose of this study was to evaluate the nature of the transplanted stem cell-host interaction that underlies the therapeutic mechanism of action. Three animal models of human disease were used, each of which allows an assessment of aspects of the host response. The disease models were (1) osteoarthritis (OA) of the knee, (2) myocardial infarction (MI) and (3) human breast cancer xenografts.

Materials and Methods
MSCs were isolated from bone marrow aspirates and characterised by measurement of cell surface antigens. OA was induced by complete medial meniscectomy in goats and MSCs were delivered by intraarticular injection. MI was induced by irreversible ligation of the LAD coronary artery in Fischer rats and PKH26-labelled MSCs were delivered by intramyocardial injection. Female athymic nude mice received a subcutaneous injection of 2x10⁷ T47D cells. When tumors had reached a volume of ≥100 mm³ the mice received a subcutaneous injection of 1x10⁶ PKH26-labelled MSCs. Animals were sacrificed at several time points and the target tissue was sectioned for histological evaluation. In the case of the infarcted rats the hearts were harvested, digested and the resulting cell suspension was separated by high speed cell sorting. The retrieved labelled MSCs were analysed for expression of tissue-specific and cell-specific markers and for differentiation potential.

Results
In each disease model, labelled transplanted cells were observed at the site of injury (Fig. 1).

Engraftment levels appeared low in the OA joints and in the infarcted hearts and higher in the xenograft tumours, even when they cells were delivered by IV infusion. Cells retrieved from the infarcted hearts up to 7 days after delivery showed no evidence of cardiomycytic differentiation but appeared to retain the stem cell phenotype.

Discussion and Conclusions
MSCs delivered to the injured host have the capacity to migrate to the site of injury and engraft, although with low efficiency. Engrafted MSCs apparently do not differentiate in a tissue-specific manner, but certainly remain viable. It appears unlikely that the engrafted cells proliferate but this cannot be ruled out. These observations suggest that the therapeutic effect associated with MSC delivery is unrelated to their capacity to differentiate and more likely associated with their capacity to deliver soluble factors to the injured host. In conclusion, neither extensive engraftment nor cell differentiation are prerequisites for a therapeutic response.

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Disclosures
Authors have nothing to disclose.