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RESEARCH ARTICLE

Graft vascularization is a critical rate-limiting step in skeletal stem cell-mediated posterolateral spinal fusion

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Abstract

The ability of skeletal stem cells (SSCs) to direct spinal fusion (SF) upon transplantation in conjunction with osteoconductive biomaterials was investigated in a rabbit model. When tested in a mouse heterotopic transplantation assay, rabbit SSCs and Pro-Osteon 500R™ was osteoconductive and supported osteogenesis. When used in a SF model, the same constructs induced bone formation in periapophyseal regions (PARs). In this respect, they proved to be superior to grafts of cell-free carrier or total uncultured bone marrow–carrier constructs, used as controls. However, interapophyseal regions (IARs) remained devoid of new bone, such that true bony bridging of adjacent transverse apophyses (true SF) could not be achieved. Interestingly, this could not be predicted from high-resolution radiography. A systematic histological survey of the entire graft harvested at 6 months was essential for proper assessment of the transplantation procedure outcome. Immunohistochemical analysis of microvessel density revealed that IARs remained undervascularized, as compared to PARs, suggesting that differential vascularization could account for the absence or presence of new bone formation in the same regions. SF is an extreme model of stem cell-directed bone regeneration, requiring a combination of orthotopic (PAR) and heterotopic (IAR) bone formation. Our data show that, in this setting, graft size can be critical with respect to the necessary neovascularization, a crucial variable independent of proper osteogenic and osteoconductive competence of the cells and materials employed. Furthermore, stringent histological studies are mandatory for proper assessment of outcomes in SF studies, in which the use of mineralized materials can make radiographic assessment misleading. Copyright © 2009 John Wiley & Sons, Ltd.

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1. Introduction

Posterolateral spinal fusion (PLSF) is commonly performed in patients with developmental or degenerative spinal disorders unresponsive to conservative therapy. Autologous bone graft is the gold therapeutic standard, even though various problems, including donor site morbidity, the need for blood transfusion, prolonged operating times and non-union rates up to 35% have been associated with the procedure (Fernyhough *et al.*, 1992; Steinmann and Herkowitz, 1992). For these reasons, development of alternative strategies is desired.

Bone substitutes have gained large popularity in recent years as an alternative to autogenous bone graft in skeletal reconstructive surgery. Ideally, they should provide an

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