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Origins of endothelial and osteogenic cells in the subcutaneous collagen gel implant

I. Bilic-Curcic, Z. Kalajzic, L. Wang, D.W. Rowe*

Department of Genetics and Developmental Biology, University of Connecticut Health Center, Farmington, CT 06030, USA

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Abstract

The interdependent relationship between vascular endothelial cells and osteoblasts during bone formation and fracture healing has been long appreciated. This paper reports a heterotopic implant model using FGF-2-expanded bone marrow stromal cells (BMSC) derived from Tie2eGFP (endothelial marker) and pOBCol3.6GFPcyan or topaz (early osteoblast marker) transgenic mice to appreciate the host/donor relationships of cells participating in the process of heterotopic bone formation. The study included various combinations of Tie2eGFP and pOBCol3.6GFPcyan and topaz transgenics as BMSC or whole bone marrow (WBM) donors and also as recipients. Rat tail collagen was used as a carrier of donor cells and implantation was done in lethally irradiated mice rescued with WBM injection. Development of ossicles in the implants was followed weekly during the 4- to 5-week long post-implantation period. By 4–5 weeks after total body irradiation (TBI) and implantation, a well-formed bone spicule had developed that was invested with bone marrow. Experiments showed absolute dominance of donor-derived cells in the formation of endothelial-lined vessels inside the implants as well as the marrow stromal-derived osteogenic cells. Host-derived fibroblasts and osteogenic cells were confined to the fibrous capsule surrounding the implant. In addition, cells lining the endosteal surface of newly formed marrow space carrying a pOBCol3.6GFP marker were observed that were contributed by WBM donor cells and the host. Thus, FGF-2-expanded BMSC appear to be a source of endothelial and osteogenic progenitor cells capable of eliciting heterotopic bone formation independent of cells from the host. This model should be useful for understanding the interactions between these two cell types that control osteogenic differentiation in vivo.