Matrix Reloaded: Devitalized Cartilage as a Functional Extracellular Niche to Promote Osteogenesis and Angiogenesis

Jaselle M Perry, Donna M Poscablo, Brandon T Gaston, Diane P Hu, Theodore Miclau, Karen L Christman, Ralph S Marcucio and Chelsea S Bahney

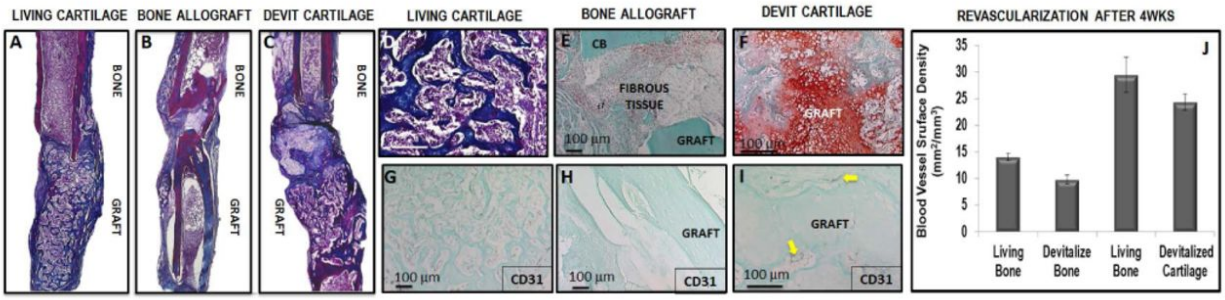
Published Online:1 Apr 2016**Abstract Number:**9.2

Abstract

There remains an unmet clinical need to develop improved therapeutic strategies to promote vascularized bone regeneration. Transplantation of living bone autograft remains the clinical gold standard, but clear drawbacks are associated with limited availability of donor tissue and pain at the harvest site. Devitalized bone allograft and bone grafting substitutes have been developed as alternative approaches. However, this technique suffers from limited revascularization leading to failure of the graft to integrate and remodel. In previous work we have demonstrated that cartilage primed to undergo endochondral ossification can repair a bone defect by transformation of chondrocytes into osteoblasts/cytes. In this study we test the hypothesis that the cartilage matrix alone is sufficient to promote bone regeneration through endochondral ossification. Our results demonstrate that devitalized cartilage retains sufficient bioactivity to promote osteogenesis and angiogenesis when grafted into a critical sized segmental defect in a murine tibia. Devitalized cartilage remodeled more slowly than living cartilage grafts, but demonstrated significantly better vascular invasion compared to devitalized bone, suggesting it has the potential to improve clinical outcomes (FIGURE 1). Using fourier transform infrared spectroscopy (FTIR), cell-based reporter assays, and ELISA we are characterizing a spectra of cartilage sources to understand the attributes of the matrix that contribute to its ability to promote or resist endochondral ossification. This endochondral cartilage matrix is being processed to develop a tissue engineering approach for therapeutic applications in bone regeneration.

Support or Funding Information

This project was supported by the National Center for AdvancingTranslational Sciences, National Institutes of Health, through UCSF-CTSI Grant Number UL1TR000004 and the UCSF Core Center for Muskuloskeletal Biology and Medicine Grant Number P30AR066262. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. Additional support was provided by the AO Foundation, Grant # S-14-114B.



Bone regeneration after 4 weeks in a murine segmental defect.

(A–C) Trichrome histology demonstrates devitalized cartilage converts to a trabeculated bone at ~50% the rate living cartilage. **(D–F)** Integration between the graft and host shows robust healing in cartilage grafts, but not bone allograft. (**G–I**) PECAM IHC of tissue regenerates shows vascular invasion of cartilage grafts, but not bone allograft. **(J)** Quantification of blood vessel surface density from PECAM stained sections.