JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 4 (2011) 829–840

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jmbbm

Research paper

Multiscale mechanobiology of *de novo* bone generation, remodeling and adaptation of autograft in a common ovine femur model

Melissa L. Knothe Tate[a,b,*], *Scott Dolejs*[b], *Sarah H. McBride*[b], *R. Matthew Miller*[b], *Ulf R. Knothe*[c]

[a] *Department of Mechanical & Aerospace Engineering, 10900 Euclid Avenue, Case Western Reserve University, Cleveland, OH 44106, United States*

[b] *Department of Biomedical Engineering, 10900 Euclid Avenue, Case Western Reserve University, Cleveland, OH 44106, United States*

[c] *Department of Orthopaedic Surgery, 5900 Euclid Avenue, Cleveland Clinic, Cleveland, OH 44195, United States*

ARTICLE INFO

Article history:
Published online 16 March 2011

Keywords:
Periosteum
Bone graft
Critical sized defect
Tissue generation and adaptation
Bone healing
Tissue engineering
Progenitor or stem cell
Multiscale mechanobiology

ABSTRACT

The link between mechanics and biology in the generation and the adaptation of bone has been studied for more than a century in the context of skeletal development and fracture healing. However, the interplay between mechanics and biology in *de novo* generation of bone in postnatal defects as well as healing of morcellized bone graft or massive cortical bone autografts is less well understood. To address this, here we integrate insights from our previously published studies describing the mechanobiology on both *de novo* bone generation and graft healing in a common ovine femoral defect model. Studying these effects in a common experimental model provides a unique opportunity to elucidate factors conducive to harnessing the regenerative power of the periosteum, and ultimately, to provide mechanistic insights into the multiscale mechanobiology of bone generation, remodeling and adaptation. Taken together, the studies indicate that, as long as adequate, directional transport of cells and molecules can be insured (*e.g.* with periosteum *in situ* or a delivery device), biological factors intrinsic to the periosteum suffice to bridge critical sized bone defects, even in the absence of a patent blood supply. Furthermore, mechanical stimuli are crucial for the success of periosteal bone generation and bone graft healing. Interestingly, areas of highest periosteal strain around defects correlate with greatest amounts albeit not greatest mineralization of newly generated bone. This may indicate a role for convection enhanced transport of cells and molecules in modulation of tissue generation by pluripotent cells that ingress into the defect center, away from the periosteum and toward the surface of the intramedullary nail that fills the medullary cavity. These insights bring us much closer to understanding the mechanobiological environment and stimuli that stimulate the proliferation and differentiation of periosteum-derived progenitor cells and ultimately drive the generation of new bone tissue. Furthermore, these insights provide a foundation to create virtual predictive computational models of bone mechanophysiology, to develop cell seeding protocols for scale up and manufacture of engineered tissues, to optimize surgical procedures, and to develop post-surgical therapies with the ultimate goal of achieving the best possible healing outcomes for treatment and/or reconstruction of postnatal bone defects.

* *Corresponding author at:* Department of Mechanical & Aerospace Engineering, 10900 Euclid Avenue, Case Western Reserve University, Cleveland, OH 44106, United States. Tel.: +1 216 368 5884; fax: +1 216 368 4969.
E-mail addresses: knothetate@case.edu, mkt4@case.edu (M.L. Knothe Tate).

1751-6161/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jmbbm.2011.03.009