Production of Bioengineered Oriented 3D-PLGA/aCaP Scaffolds for Improving the Treatment of a Critical Size Defects

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Purpose: Healing of large bone defects remains a challenge in orthopeadic surgery and is often associated with poor outcomes and complications. A major issue with bioengineered constructs is the achievement of a continuous interface between host bone and graft to enhance both biological processes and mechanical stability. Many efforts have been made in the past decade to develop biomimetic materials that functionally augment the native bone tissue, spanning from metals to ceramics and polymers. However, often formation of fibrous tissue occurs at the biomaterial-tissue interface, resulting in osseointegration failure.

Methods: In this study, we have developed a new bioengineering strategy to produce oriented biocompatible 3-dimensional (3D) PLGA/aCaP (poly-lactic-co-glycolic acid and amorphous calcium phosphate) nanocomposites with enhanced osseointegration. Decellularized scaffolds, containing only extracellular matrix (ECM), or scaffolds seeded with adipose-derived mesenchymal stromal cells (AD-MSCs) were tested in a mouse model for critical size bone defects. Micro-CT analysis, SAXS (small-angle x-ray scattering) tensor tomography and 2D scanning SAXS were employed to determine the 3D arrangement and nanostructure within the critical sized bone defect 7 weeks after surgery.

Results: Analysis of the quantity of bone formed inside the scaffold and the bone quality parameters, such as alignment of collagen, alignment, and size of the hydroxyapatite minerals, indicated that aligned PLGA/aCaP nanocomposites seeded with AD-MSCs or loaded with AD-MSC-generated ECM are superior to random PLGA/aCaP scaffolds. Even though both types of scaffolds possess similar cytocompatibility and osteogenicity in vitro, they show in vivo strong differences in osseointegration and bone regeneration capacity.

Conclusion: The similar properties observed in vivo between aligned scaffolds containing either cells or only ECM highlights the possible advantage of using only the ECM for the preparation of bioengineered bone scaffolds. Decellularized matrices as scaffolds have not only the advantage to mimic the tissue to be replaced but they also trigger scaffold repopulation with patient's own cells. The use of ECM would be therefore of particular interest for the preparation of off-the-shelf grafts for bone regeneration. Re-cellularization of the ECM with autologous cells could help prevent host rejection, fibrosis, and eliminating the need of long-term immunosuppression.