CELL IMMOBILIZATION SYSTEMS FOR BONE TISSUE REGENERATION

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The potential of cell therapies to produce functional substitutes capable of restoring, maintaining or improving bone function is being widely investigated, in combination with novel and more efficient scaffold structures. Progenitor and stem cells provide improved possibilities for *in situ* tissue regeneration. New material structures are required not only to provide the physical and mechanical support to cells, but also to play the role of insoluble and soluble components of the extracellular matrix, thus assuring their signalling properties to promote cell growth and restore differentiated function.

Our research efforts are currently focused on: i) the functionalization of natural polymers, namely polysaccharides, to promote their interaction with biological systems, namely cell adhesion and migration through matrix degradation; ii) investigating the intercellular crosstalking between progenitor bone cells with other cells influencing their differentiation; and iii) stem cell–mediated gene therapy for bone tissue regeneration.

Cell immobilization, or encapsulation, has been extensively investigated with the purpose of to providing immunoisolation but few attempts have been made to use this strategy for tissue regeneration. Cells were immobilized within microspheres of alginate conjugated with oligopeptides including the Arg-Gly-Asp (RGD) sequence. Polymers were further modified to improve their biodegradability. After immobilization and under dynamic cell culture conditions, immobilized cells were viable, expressed bone phenotypic markers, synthesized new extracellular matrix, and were further able to degrade the artificial matrix, which indicates the capability of this approach to promote the regeneration of bone tissue (Evangelista 2007, Bidarra 2010).

Endothelial cells are known to influence the behavior of bone cells, and namely their differentiation through growth factor exchange and through direct contact. We have investigated the interaction between these cell types with a view to use their cocultures in therapeutically relevant settings. Mature and progenitor endothelial cells were shown to significantly enhance the differentiation of mesenchymal stem cells into the osteogenic pathway. Furthermore, immobilized cocultures promoted mineralization of bone defects *in vivo* (Grellier 2009). We have also been investigating non-viral systems to deliver osteogenic genes to mesenchymal stem cells, which, although resulting in low transfection levels, were able to induce differentiation towards the osteoblastic lineage (Santos 2009).

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