

NEW BONES FOR OLD - MESENCHYMAL STEM CELLS AND BIOMIMETIC SCAFFOLDS

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OVERVIEW: The requirement for new bone to replace or restore the function of traumatised or degenerated bone, or for the replacement of lost mineralised tissue as a consequence of increasing age is a major clinical and socio-economic need. To date, bone formation stimulation regimes, although attractive, have yet to demonstrate clinical efficacy. Bone is unique with a vast potential for regeneration from cells with stem cell characteristics. Mesenchymal stem cells or human bone marrow stromal stem cells are defined as pluripotent progenitor cells with the ability to generate cartilage, bone, muscle, tendon, ligament and fat.

These primitive progenitors exist postnatally and exhibit stem cell characteristics, namely low incidence and extensive renewal potential. These properties in combination with their developmental plasticity has generated tremendous interest in the potential use of mesenchymal stem cells to replace damaged tissues. In essence mesenchymal stem cells could be cultured to expand their numbers then transplanted to the injured site or after seeding in/on shaped biomimetic scaffold to generate appropriate tissue constructs. Thus, an alternative approach for skeletal repair is the selection, expansion and modulation of osteoprogenitor cells in combination with a conductive or inductive scaffolds to support and guide regeneration together with judicious selection of osteotropic growth factors. Furthermore, these biomimetic structures, when coupled with appropriate osteoinductive factors, can provide positional and environmental information to drive osteogenesis. These approaches, often referred to as bone tissue engineering or regeneration may provide alternative solutions for skeletal tissue reconstruction.

Current concepts, approaches and challenges to be presented from work in our group include: i)

the use of isolated and selected human osteoprogenitor cell populations with selected osteotropic agents in an attempt to modulate the phenotype of the mesenchymal stem cell to generate mineralised bone tissue, ii) Manipulation of the developmental potential of these osteoprogenitors on modified PLA / PLGA polymer structures and biomimetic structures with bone morphogenetic factors, and iii) the potential to combine gene delivery with tissue engineering to generate bone *in vivo*. While our knowledge of the processes of bone cell differentiation has increased, the mechanisms involved in many of these processes and how the architecture of bone can be developed in these new model systems are still unclear.

Although clinical efficacy has yet to be achieved, development of protocols, new tools and above all multidisciplinary approaches for *de novo* bone formation that utilise mesenchymal stem cells with biomimetic scaffolds offer significant rewards for an increasing aged population both in terms of healthcare costs and, more importantly, improved quality of life.

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