

Human Fetal & Adult Osteoprogenitors - Isolation, Lineage Modulation and Potential for Skeletal Regeneration

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OVERVIEW:

Human bone marrow stromal stem cells or mesenchymal stem cells are multipotent 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. Their developmental plasticity has generated tremendous interest in the potential use of these cells to replace damaged tissues.

Strategies to isolate homogenous mesenchymal stem cell populations remain elusive and the phenotypic characteristics of mesenchymal stem cells *as opposed* to marrow stromal cells as well as direct *in vivo* confirmation of the lineage potential and plasticity or interconversion potential remain unclear. Thus critical in the development of this field will be an understanding of the phenotype, plasticity, and potentiality of these cells and the tempering of patients' expectations driven by commercial and media hype to match current laboratory and clinical observations. Nevertheless, strategies harnessing tissue engineering approaches offer much promise for skeletal regeneration using mesenchymal populations.

Upon isolation of an appropriate progenitor population, repair and reconstruction of bone defects present additional challenges to the orthopaedic, reconstructive and maxillo-facial surgeon including an ability to generate a functional microvascular network within engineered constructs to provide oxygen and nutrients that facilitates growth, differentiation, and tissue. The development of a functional vasculature is critical in respect to bone defects which can be extensive. The proximity of this vascular supply will become critical when this technique is combined with mesenchymal stem cells to help regenerate the bone.

Our work is centered on isolation, expansion and translational studies of humans fetal and adult mesenchymal populations for skeletal repair. Three areas of work will be reviewed using data from the group including: i) isolation, expansion and characterisation of the plasticity of fetal and

adult mesenchymal populations, ii) combination of progenitor cells with tailored growth factor containing biomimetic polymer scaffolds in an attempt to modulate the phenotype of the mesenchymal populations to generate mineralised bone tissue and iii) translational studies to examine the efficacy of mesenchymal populations using impaction bone grafting as an exemplar.

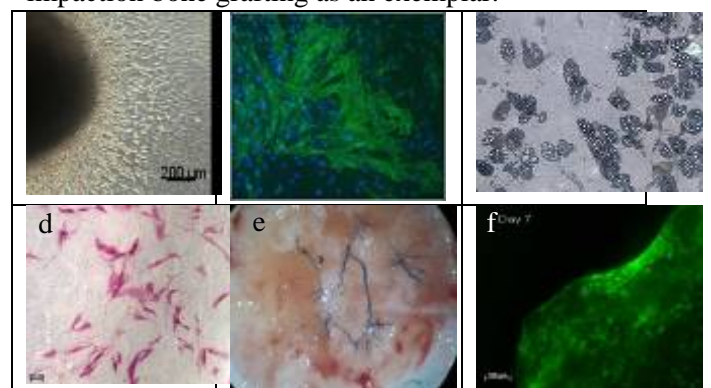


Fig. 1: Human skeletal progenitor cells in culture (a), expressing STRO-1 (b) and differentiated along adipogenic (c) and osteogenic lineages (d). Panel e shows human osteoprogenitors after in vivo implantation for augmentation of bone in impaction bone grafting and viable cells on impacted bone (f).

The development of protocols, tools and above all multidisciplinary approaches for de novo bone formation that utilise marrow stromal cells and enriched mesenchymal populations containing mesenchymal stem cells may improve the quality of life for many as a result of strategies to augment skeletal regeneration.

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