SEMS: RESEARCH PROJECT DESCRIPTION

1. Project Background and Description

Optimising scaffold porosity for delivery of autologous cells for enhanced bone grafting

In order to develop synthetic bone graft substitute (SBG) materials optimised for cell delivery, the aim of this studentship is to investigate the capacity of 3D porous scaffolds with micron and nano-scale strut porosity to enhance bone grafting outcomes with autologous cells.

Administration of surpra-physiological doses of growth factors (GF) to biologically enhance bone regeneration poses the risk of untargeted tissue formation. There is increasing interest in pre-seeding orthobiologic SBGs with autologous cells, harvested during the operative procedure, to boost the rate and quality of bone regeneration. The efficacy of this approach has been demonstrated in vivo, where a SBG, Actifuse (AF), a silicate substituted hydroxyapatite (Si-HA) SBG with micron-scale strut-porosity, supported osteoinductive bone formation in a murine model when inoculated with freshly harvested adipose tissue derived stromal vascular fraction (SVF) cells and a physiological dose of a GF, rhBMP-2.

Our recent in vitro studies indicate that AF SBG and Inductigraft (IG), a Si-HA SBG with elevated levels of strut porosity, both stimulate osteogenic differentiation of bone marrow derived human mesenchymal stem (hMSC), both in the absence and presence of physiological doses of rhBMP-2. Moreover, in vivo, in the absence of any additional GF, the osteogenic capacity of Si-HA SBGs increased with increased levels of strut-porosity in an ovine model. Furthermore, in an in vitro perfusion bioreactor model there was enhanced upregulation of pro-osteogenic genes by hMSC cells incubated on IG as compared to AF.

In collaboration with Baxter Inc., we have recently developed porous scaffolds with nano-scale strut-porosity structures, the aim of this PhD is to correlate osteogenic differentiation with strut-porosity characteristics for bone marrow and adipose derived hMSC cells – the latter being more relevant to optimisation of these scaffolds for autologous cell delivery.

2. Project Scope

1) Characterise and compare the pro-osteogenic response of bone marrow and adipose derived human mesenchymal stem cells to manipulation of perfusion flow rate profiles in a 3D perfusion culture on Inductigraft synthetic bone graft substitute scaffolds.

2) Correlate the relationship between structural morphology of Si-HA BGS with pro-osteogenic responses through a staged series of tests to quantify:

i) The differences in the magnitude of pro-osteogenic responses of adipose derived hMCSs and bone marrow derived hMSCs to incubation with nano-scale vs micron-scale strut porosity, Si-HA BGS materials in 3D perfusion culture.

ii) The effect of varying porosity levels on the osteogenic capacity of the most promising Si-HA BGS material in 3D perfusion culture.

3) Quantify the differences in pro-osteogenic responses of hMSC cells obtained from donors with histories of impaired bone biology to the structurally optimised Si-HA BGS with the view to extending the clinical relevance/screening capability and understanding of a synthetic grafts capacity to encourage bone regeneration.

3. Desired Skills from the Student

A first degree (BEng/BSc Hons 2:1 or First) in either Materials Science and Engineering, Biomedical Materials Science, Biology, Biomedical sciences or a closely allied discipline such as Biomedical Engineering.

Some expertise in in vitro cell testing techniques.

Some exposure to the field of materials science.

Excellent communication (written and oral), inter-personal and organisational skills.

4. Supervisory Team

Primary: Dr Karin Hing

Secondary: Dr Simon Rawlinson (SMD)

Additional: Mr Dan Johnson (Baxter)