ORTHOPAEDIC TISSUE ENGINEERING: NOVEL APPROACHES AND CLINICAL APPLICATION

GLENN DICKSON[1], Fraser Buchanan, David Marsh, Mervyn McCaigue, Eileen Harkin-Jones

[1] Department of Trauma & Orthopaedic Surgery Musgrave Park Hospital Stockman's Lane Belfast, BT9 7JB Northern Ireland

Tissue engineering combines the application of scaffold materials and cells. It has been defined as the science of persuading the body to reconstitute or repair tissues that have failed to regenerate or heal spontaneously. In the case of bone regeneration 3-D scaffolds are used as a framework to guide tissue regeneration. Mesenchymal cells obtained from the patient *via* biopsy are grown on scaffold materials, *in vitro*, and then implanted at the desired site in the patient's body. Medical implants that encourage natural tissue regeneration are generally considered more desirable than permanent metallic implants that need to be removed by subsequent intervention. Numerous polymeric materials, from natural and artificial sources, are under investigation as substitutes for skeletal elements such as cartilage and bone. For bone regeneration, cells (mainly obtained from bone marrow aspirate or as primary cell outgrowths from bone biopsies) are often combined with ceramics and/or absorbed growth factors so that osteoinduction is facilitiated together with osteoconduction; bioactive rather than bioinert materials. A newer class of medical materials termed 'biodegradable' polymers have included the application of homopolymers of for example polylactic acid (PLA), polyglycolic acid (PGA) and polycaprolactone (PCL) and co-polymers such as polylactic-polyglycolic acid (PLG) and L- and DL- lactide (PLDLA). An advantage of these aliphatic polyesters is that they can biodegrade within weeks or months to carbon dioxide and water, enabling natural tissue to fill the space occupied previously by the implant. However polymers in current use loose strength well before they loose mass. Novel strategies are addressing this problem. Early ingrowth of natural tissue is inhibited and the subsequent rapid loss of mass can produce inflammation resulting from the production of acidic degradation products. There is general appreciation of the properties required of an ideal polymeric scaffold but little agreement regarding the most critical scaffold requirements for successful tissue regeneration. Scaffold architecture informs properties such as stiffness, permeability and conductivity while the efficacy of tissue regeneration is related to scaffold porosity, pore diameter, interconnectivity and permeability. Surface roughness and surface chemistry (hydrophobic or hydrophilic) properties also impact on the effectiveness of cell behaviour, these can influence gene expression products and cell attachment. Cell signalling pathways are critical to product development with numerous genes, proteins and secreted molecules influencing the scaffold environment for cell attachment, growth, differentiation, extracellular matrix production and hence the attainment of the desired skeletal element. Effective quantitative evaluation of the resultant performance of 3-D polymeric scaffolds, in effecting bone regeneration, is enabled through use of novel imaging modalities (μCT). Pilot clinical investigation utilising autologous osteoblast cell therapy combined with digital radiographic analysis has facilitated assessment of bone repair in conditions such as fracture non-union.

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