

The Clinical Application of Human Connective Tissue Progenitor Biology to Bone Tissue Engineering

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Regardless of the tissue of interest, tissue engineering strategies are fundamentally all based in cell therapy. Preservation, repair, augmentation and regeneration of all tissue is based on the processes that are entirely dependent upon living cells. These can be grouped into four basic cell therapy strategies: local targeting of cells in native tissues (targeting), homing of cells to a site via systemic circulation (homing), physical processing and transplantation of cells into a site (transplantation), and biological modification *ex vivo* prior to transplantation (biological modification). Each of these can be used alone or in combination, but each has the requirement that one or more populations of stem cells or progenitor cells that are capable of forming the tissue of interest are present, and present in sufficient numbers to allow their response to achieve the desired outcome. The most readily available clinical source of stem cells and progenitors are autogenous cells that are resident tissues of the individual being treated. However, a variety of cell source options can be considered as opportunities for optimization. The functions of stem cells and progenitors that represent targeting opportunities for tissue engineering strategies include: activation, attachment, migration, proliferation, differentiation and survival. Each of which are modulated by the balance of chemical, endocrine, mechanical and biophysical stimuli in the milieu around a given cell.

Transplantation represents perhaps the least elegant but most powerful tissue engineering strategy. Transplantation provides the opportunity to select the cell type(s), concentration, distribution, as well as signaling, mass transport environment and tissue development of the cells within a given anatomic site. However each of these opportunities brings with it a host of challenges and potential variables that are only beginning to be refined to an acceptable clinical standard. Control of cell type, concentration and distribution requires means of harvest, isolation, characterization, concentration and selection (i.e. selection of desired cells and exclusion of undesired or competing cells). Control of signaling, mass transport and tissue development requires biological or synthetic scaffolds offering features or surface chemistry, topography and micro and macro architecture and delivery of bioactive agents that induce desired activation, attachment, migration, proliferation, differentiation and survival of cells throughout the grafted volume.

This presentation will provide an overview of selected examples to demonstrate the evolution and evolving accessibility of tools enabling the enhancement of clinical bone tissue engineering procedures (i.e. Bone Grafting) through improved methods for harvest, isolation, assay, selection and concentration and transplantation of osteoblastic connective tissue progenitors (CTPs). Provide evidence of the capacity for surface modification to modulate the performance of human osteogenic CTPs, with respect to attachment, migration, differentiation and survival.