Biomaterials - The Changing *face* of Bone Tissue Engineering

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The worldwide incidence of bone disorders and conditions continues to steadily increase and bone transplantation is a commonly required surgical procedure. Due to the nature and complexity in some cases, their treatment presents a significant challenge to clinicians and surgeons, often requiring specialist intervention involving an interdisciplinary team approach.

Biomaterials are used to restore both structure and function and, in most cases, provide a replacement for the lost bone. Depending on the location of the bone defect and the nature and extent of bone loss, the properties of biomaterials that are used may vary considerably. An ideal biomaterial would serve the purpose of 'bridging the gap' and acting as a template and as a delivery vehicle, to address the causative disease of the bone loss.

Engineered bone tissue has been viewed as a potential alternative to the conventional use of bone grafts, due to their limitless supply and no disease transmission. However, despite significant progress in the field associated with the synergistic combination of biomaterials, cells, and stimulatory factors a major challenge that still remains is that of obtaining adequate vascularization for the successful integration of *in vitro*-generated tissues *in vivo*. Furthermore, numerous bioengineered scaffolds have been proposed as substitutes for regeneration of critical size bone defects, however, synthetic scaffolds often result in a fibrotic rather than osteogenic response.

The group is focussed primarily on bioengineering bone grafts and over the years have adopted various strategies to facilitate the remodelling and regeneration of the native tissue. These include, biomaterial scaffolds comprising incorporation of biomimetic properties and/or growth factors and various cellular approaches, including the use of mesenchymal stem cells (MSCs), embryonic stem cells (ESCs), adult stem cells and induced pluripotent stem cells (iPSCs), investigated for their potential clinical application strengths and limitation. More specifically this approach has been adopted for the reconstruction of maxillofacial and cranial bone tissue, where the major challenge is size and the lack of vascularization at the defect site.

This lecture will present an overview of the changing face of bone tissue engineering, advances of biomaterial and cell-based research, as well as approaches used to enhance bone regeneration. Various strategies being exploited by the group include maxillofacial reconstruction using 3D customised scaffolds, with tissue-like self assembly properties, comprising endothelial cells and MSCs/osteoblasts tailored to attain the formation of capillary- like network *ex-vivo*.

Self-assembling ionic complementary peptides have been receiving much interest due to their ability to mimic the extracellular matrix, offering three-dimensional support for cell growth, and being usable as delivery systems for cells and drugs. We have demonstrated the angiogenic potential of the self-assembling peptide DAR 16-II to support the adhesion of both human umbilical vein endothelial cells (HUVEC) and human mesenchymal stem cell and promote endothelial cell activation toward an angiogenic phenotype. These scaffolds function not only as space maintainers, but are also able to promote cell colonization, angiogenesis and favour bone regeneration rather than fibrous substitution in a pre-clinical in vivo model.

Our strategy paves the way toward a simple and effective method to enhance the biological activity of tailor made scaffolds for bone tissue engineering, thus facilitating rapid clinical translation.