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Tissue engineering

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Tissue engineering applies the principles of engineering and life sciences towards the development of biologic substitutes that restore maintain or improve tissue function[1]. The aim of tissue engineering is to develop alternative methods of tissue replacement that eliminate the complications caused by damage to normal tissue traditionally harvested as graft or flaps. Tissue engineering has been made possible by the fusion of clinical surgery, engineering and biology.

The earliest examples of tissue engineering relate to the introduction of biomaterials such as silicone gel breast implants which have been clinically used since 1960s[2]. The second phase started in 1970s and saw the designing of glass and calcium ceramics for bone replacement. A number of biodegradable synthetic polymers that are used as absorbable suture materials came in to clinical usage and are another example of tissue engineering. Presently we have biodegradable materials that could serve as a temporary scaffold for cell attachment and guide tissue formation undergoing clinical trials[3].

In the domain of plastic surgery, tissue engineering represents a fundamental advance because it modifies tissues at the level of cells and molecules, thus allowing surgeons to alter tissues in a manner that is as sophisticated as their ability to transfer tissues. The clinical goals are timely healing, maximal functional and aesthetic restoration and minimal morbidity. Moreover tissue engineering allows tissue replacement to be as patient specific as possible.

Engineering tissues for anatomic defects in cancer patients pose special problems. The excision defects in such patients consist of a combination of several tissue types, each of which must be taken into consideration at the time of reconstruction. Adjuvant radiotherapy makes the local tissue unreliable and the risk of local recurrence should be kept in mind at the time of planning reconstruction.

The principles of tissue engineering can be well illustrated in the designing of a replacement for a segmental mandibular defect. The fundamental steps would consist of

1. Identification of missing tissue elements and precise dimensions of the defect
2. Fabrication of a computer assisted custom device of scaffolding material as per specifications of defect
3. The device would consist of a hollow chamber containing bioactive factors and a porous degradable tissue conducting scaffold.
4. Implantation of the device into the defect to guide three dimensional tissue and blood vessel in growth.
5. The bioactive factors within the device would consist of cells with osteogenic potential harvested from the patient along with recombinant growth factors.

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6. An alternative method could be to place the scaffold device at a distant site such as the inner table of ileum and allow the patient to grow a replacement part into the degradable scaffold prior to its implant into the mandible[4].

Making this mandibular substitution a possibility would require inputs form computer software specialists, biomaterial development and biotechnology.

Biomaterials

Several varieties of biomaterials are used in tissue engineering as implantable devices such as tissue molding chambers, tissue scaffolds and bioactive material delivery vehicles. Molds are used to guide tissue formation into predetermined shapes and help direct blood supply to facilitate surgical transfer. Titanium, silicone, rubber and polymethacrylate have been clinically used as tissue molds[5].

Another usage of biomaterials is as tissue scaffolds. For this purpose the material should be biocompatible, degradable and should have good tissue conductivity. Compounds used for this purpose are hyaluronin, glycosaminoglycans, collagen and fibrin. Synthetic polymers provide greater design flexibility. Degradable polymers have chemical bonds that undergo hydrolysis on exposure to aqueous body fluids, or undergo cellular digestion or enzymatic degradation. The rate of degradation is influenced by porosity, hydrophobicity, copolymer ratio and crystallinity. The commonly used synthetic scaffolds are made of biodegradable polymers and calcium ceramics. Bioactive molecules can be incorporated into the scaffold or mold which is released as the material disintegrates.

Biotechnology

Biotechnology aims to understand, alter or direct the function of organic cells. These include techniques of cell transplantation as well as in vivo cell recruitment. Cell harvesting involves harvesting cells, expanding and if required modifying them in culture and then transplanting them back to the donor to restore tissue function. Stem cells because of their pluripotential nature and ability to divide in culture are especially useful for cell transplantation. The differentiation of stem cells can be directed in to particular specialized cells by modifying culture conditions. A number of growth factors and hormones can be used during the tissue culture process to co-ordinate specialized tissue formation and angiogenesis. Genetic engineering can be combined with cell culture technology to produce tissue replacements with improved function. Natural tissues can be altered to produce increased quantities of growth factors and will function as implantable living protein secretory devices.

Tissue substitution

Skin, adiopose tissue, musculoskeletal and vascular tissues have all been replaced. The most successful skin substitute is cultured human keratinocytes on an acellular dermis or fibroblast bed. This has been use din burns, diabetic and venous foot ulcers. For adiopose tissue replacement, autologous preadiopocyte culture techniques are being tried in mastectomy patients[6]. Cartilage repair by autologous cultured chondrocyte implantation is clinically available. Chondrocytes have a low metabolic rate and therefore function well under low oxygen tension. Articular cartilage has been designed from polyglycolic acid, calcium alginate and polypropylene. Secure healing of the engineered cartilage to the underlying bone is obtained by a composite of porous calcium ceramic on one surface to obtain osseous integration and a chondrocyte seeded scaffold towards the joint surface[7]. Investigators are focusing on tissue substitution techniques for bone and musculoskeletal elements like tendons, ligaments and skeletal muscle fabrication.

The biggest limiting factor in tissue engineering is the development of a viable capillary network capable of maintaining tissue viability. Delivery of angiogenic growth factors has had only a limited success. Approaches to develop lengths of vascular conduits from smooth muscle and endothelial cells cultured under pulsatile conditions have been tried[8]. These conduits had good handling

and functioning including contractile response to pharmacological agents and showed patency 24 days after implantation in animals.

Developments in tissue engineering will depend on cooperation among engineers, biologic scientists and clinicians. Although laboratory experiments have been successful, ultimate progress will depend on the ability to develop marketable products. Acceptable safety and efficiency standards for tissue engineering products also need to be defined. Embryonic stem cells which can terminally differentiate into all types of somatic cells are considered a promising source of seed cells for tissue engineering.

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