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Review Article

Tissue Engineering: A New Era in the Medical and Dental Field

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Abstract

Tissue engineering has been introduced as the latest modality to manage the medical and dental problems which indirectly affect the physical health, esthetics and wellbeing of patients. This technique has shown the appreciable reconstruction of the innate organisation and function of organs or whole teeth as well as their periodontal structures and in near future, is going to benefit the human beings in many more ways.

Keywords: Phosphorene; Wheat; Bio Fertilizers; Varieties; Packages; Yield

Introduction

Millions of patients are in serious need for Medical and Dental treatment for loss of tissue or end-stage organ failure worldwide each year. Over the past decade, the field of tissue engineering has gained a considerable importance to regenerate healthy tissues and organs to replace the diseased or dead tissues and to recover the function and esthetics.

The objectives behind the current clinical approaches to tissue replacement and reconstruction were to alleviate pain in case of injuries to the oral-maxillofacial apparatus, hard and soft tissue defects secondary to trauma, and to restore mechanical stability and function as in congenital defects like cleft palate and acquired diseases like cancer and periodontal diseases. Till now, different types of grafts like autogenous grafts, allografts, and synthetic materials (alloplasts) were being used for treatment of lost tissues. All these treatment approaches have been major advances in medicine, but they have some limitations as well. The human body does not have significant stores of excess tissue for transplantation which is one of the major shortcomings with autografts, as well as allografts. The other problems associated with replacing lost bone include donor site morbidity, anatomic and structural problems, and increased levels of resorption during healing [1].

In the case of allografts, there always exists the possibility of eliciting an immunologic response due to genetic differences, as well as inducing transmissible diseases [2]. On the other side, we have synthetic material replacements (e.g., dental implants).

The human body has a natural tendency to encapsulate foreign materials in a thin, fibrous membrane as a part of natural defence mechanism. In case of dental implants, this fibrous capsule can prevent the implant from achieving true osseointegration, [3,4] leading to the failure.

Furthermore, if implants do achieve initial osseointegration, the changing needs of the body often will lead to failure over time. With the advent of viable tissue engineering, this problem has been overcome upto a large extent.

Different types of Approaches

Conductive Approach: The common examples of a conductive or passive approach to tissue engineering are dental implants and guided tissue regeneration. Now a day, use of dental Implants is quite common in conjunction with prosthetic rehabilitation, for replacing multiple and single teeth. Guided tissue regeneration is used to regenerate the periodontal supporting structures and uses a material barrier to create a protected compartment for selective wound healing [5].

Tissue Induction: This approach uses activation of certain cells which are situated close to the damaged or deficient tissue with specific signals. After implantation of powdered bone, new bone could be formed at a non-mineralizing site. It led to the isolation of the active ingredients from the bone powder, the cloning of the genes encoding these proteins, and their now large-scale production by a number of companies [6,7]. These proteins have been termed as bone morphogenetic proteins or BMPS and have been used in many clinical trials. The identification of proteins that promote new blood vessel formation, and their clinical application, followed closely the identification and use of the BMPS. There are certain specific molecules that regulate new blood vessel forma-

tion and the other ones either promote or inhibit this process [8]. These have found several applications, including in the induction of new vessel formation to bypass blocked arteries.

An alternative tissue-inductive approach involves placing specific extracellular matrix molecules on a scaffold support at the tissue site. These molecules direct the function of cells already present at that site and promote the formation of a desired tissue or structure. For example, a preparation of enamel proteins derived from pigs is used to promote new bone formation in periodontal defects [9]. For tissue induction to be successful clinically, it is critical to deliver the appropriate biologically active factors to the desired site at the appropriate dose and for the necessary time. Typically, many of these proteins have short half lives in the body, yet they need to be present for an extended period to be effective. These concerns have been addressed by delivering extremely large doses of the protein at the sites of interest. Recently efforts are being put to develop controlled release systems [10]. A similar approach involves the delivery of a gene that encodes for the inductive factor, rather delivering the protein itself.

Cell Transplantation: This can be used when the inductive for a specific tissue factors are not known, when a large tissue mass or organ is needed, or when tissue replacement must be immediate. The greatest success in this area has been the development of a tissue-engineered skin equivalent. For example, 250,000 ft2 of skin tissue can be manufactured from a 1 in 2 sample of starting tissue [11]. A similar approach has also been developed for replacement of oral mucosa [12,13].

Now the investigators have engineered the new cartilaginous tissues in the animal models with precisely defined sizes and shapes (e.g., nasal septum and ear), which makes this method potentially useful for craniofacial reconstruction [14,15].

For the development of vasculature to support the metabolic needs of the organs and for the integration of the engineered organ with the host, two different approaches are being used.

The first involves transplantation of endothelial cells on the scaffold with the tissue cells type of interest. Transplanted endothelial cells can increase the vasculature in polymer scaffolds and integrate with growing host capillaries [16]. The second approach uses localized delivery of inductive angiogenic factors at the site of the engineered tissue [9].

Gene Therapy: TGene transfers to well differentiated cells can be viewed as one way of engineering a tissue. It was used in the treatment of two children suffering from a severe combined immunodeficiency resulting from an inherited reduced production of the enzyme adenosine deaminase (ADA) [17]. These patients were treated with a procedure termed ex vivo gene therapy. The ADA gene was transferred to their lymphocytes in the laboratory and these modified cells were then reinfused into the patients. Both patients are alive today.

A wide number of clinical research protocols have been approved worldwide for gene transfer in a wide range of conditions, including cystic fibrosis, muscular dystrophy, and numerous malignancies. The principal problem is the lack of adequate gene transfer vectors to deliver foreign genes to host cells. Most often modified viruses are used, but all common viruses have their drawbacks [18,19].

Ongoing research activity shows the development of new vectors, both non-viral and viral which are likely to offer many advantages over current gene delivery systems.

Safety Measures in Gene Therapy

There has been a controversy regarding the hazards of gene therapy techniques. An overview of the international regulatory mechanisms shows clearly that, despite widely varying legislative approaches, the emphasis in (legislative) efforts everywhere is on patient safety and biological safety [20]. Strict test criteria have been put forward to limit the risks associated with gene therapy. Ethics commissions present in all the countries serve to ensure the maximum possible safety for the patient. In most of the countries, the opinion of the ethics commissions has to be obtained before approval is granted for conduct of gene therapy trials in humans.

Another important safeguard is the professional ethical regulations covering the clinical applications of gene therapy. Under French law, there is a separate act (the 'Loi Huriet') covering the duties and responsibilities of the ethics commissions. In German law, the ethics commission's powers are covered by section 40 I of the Drugs Act and, in Austria, by sections 30 et seq. of the Genetic Engineering Act. In Italy, on the other hand, there is no special regulation covering the responsibilities of the ethics commissions.

In the USA, the responsibilities of the local ethics commissions are limited to projects promoted by the National Institutes of Health. The licensing procedure in the UK operates at two levels:

Besides local ethics commissions, the central ethics commissions must also give its approval for every gene therapy project. With respect to the binding nature of their votes, some national ethics commissions have a purely advisory status, as for example in France. In other countries (e.g., USA, Austria, UK, and Denmark) the commission's vote is more important and can result in refusal of approval.

Tissue Engineering and Dentistry

It has a good scope in dentistry. However, reconstruction of complex tissue defects, has not yet been attempted in the craniofacial complex, as it would require multiple cell types. Such a goal will likely take many more years to realize.

Research activity is focused on applying the principles of tissue engineering to dental and craniofacial structures, because of the ease of access to these sites and the extent and nature of the clinical problems.

These biological therapies utilize mesenchymal stem cells, delivered or internally recruited, to generate craniofacial structures in temporary scaffolding biomaterials. Craniofacial tissue represents an opportunity that dentistry cannot afford to miss [21].

Gene therapy in the craniofacial area has been used in head and neck cancers [22-24]. In the next decade, gene transfer technologies will be commonly used as a part of the standard treatment of neoplasms.

There are many areas involving tissue loss that are non-life threatening yet that markedly affect quality of life, e.g., the loss of salivary gland parenchyma and the consequent inability to make saliva; without saliva, these patients experience dysphasia, rampant caries, mucosal infections, etc. For such patients, a program has been developed to create a 'blind end' tube that would be suitable for engrafting in the buccal mucosa.

The lumen of these tubes would be lined with compatible epithelial cells and be physiologically capable of unidirectional water movement. This system should be ready for clinical testing within 10 years. The major salivary glands are inviting targets for gene transfer, mainly because of the ease of access to the parenchymal cells. Gene transfer has been used to treat patients undergoing ionizing radiation and those with Sjogren syndrome who had some remaining non-secretory, ductal epithelial cells.

To make the surviving ductal cells secretory in nature and, thus, capable of fluid movement. The major impediment to fluid flow from non-secreting ductal cells was the absence of a pathway for water in their luminal membranes. So, the strategy was to transfer the gene coding for-the water channel aquaporin-1-into the radiation-surviving cells via a recombinant adenovirus. The virus, AdhAQP1, was tested in an irradiated rat model. Three days after being given AdhAQP1, these rats experienced an increase in fluid production to near normal levels [25].

Conclusion

Tissue engineering provides a new era for therapeutic medicine; it is progressing very rapidly and extends to involve all tissues in our body. Regenerating oral tissues, in particular, is very challenging and requires recapitulation of the biological development of several tissues and interfaces. Recent advances in tissue engineering suggest that significant changes in the more traditional areas of clinical dentistry are beginning to occur. As new technologies have always affected the Dental practice so tissue engineering has been proved to be a boon to medical sciences and dentistry as well. There has been a paradigm shift in dentistry, e.g., improved treatment for intraosseous periodontal defects; enhanced maxillary and mandibular grafting procedures, possibly even allowing lost teeth to be regrown; use of devices such as an artificial salivary gland and muscle (tongue) or mucosal grafts to replace tissues lost through surgery or trauma. The most recent advances in restorative dentistry involve the development, techniques and materials to regenerate the whole tooth complex in a biological manner. The future of these therapies involving more biological approaches and the use of dental tissue stem cells is promising and advancing.

As more and more information, and knowledge are acquired with respect to dental stem cells and tissues, there may well be a significant interest of their application and wider potential to treat disorders beyond the craniofacial region of the body.

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