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Gene therapy a new approach in dentistry: human or microbial gene modification

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ABSTRACT

Introduction: This review provides an update on transfer techniques and clinical implications of gene therapy in dentistry. Gene therapy is a new biomedicine emerging field that manipulates genes to achieve gain function in patient cells. Gene therapy essentially consists of introducing specific genetic material into target cells to compensate for abnormal genes or to make a beneficial protein without producing toxic effects on surrounding tissue.

Gene therapy can be used to treat wide range of diseases ranging from single gene disorder to multi gene disorder. It has variety of applications in the field of dentistry like in periodontal disease, cancerous and precancerous condition, salivary gland disorders, autoimmune diseases, bone repair, DNA vaccination, etc. Minor salivary glands and keratinocytes present in the oral mucosa are excellent target sites for gene therapy since it can be readily accomplished with minimal invasive manner. As a new aspect scientists investigating for tooth regrown using shark gene network activation in human cells. Applications of gene therapy to dental and oral problems illustrate the potential impact of this technology on dentistry. Aim of this article is to description in brief on the application, limitation and disadvantage of gene therapy in dentistry.

Key words: Gene therapy, Dentistry, Viral vector, Stem cell.

Introduction

Gene therapy means altering or editing a gene in the cell by delivering a vector construct carrying right gene and handling of its expression for compensating incorrect gene expression [1]. The efficient transfer of transgenes into somatic cells for therapeutic purposes is very important. Using viral vectors for gene transfer is a basic method. Several kinds of viruses, including retrovirus, adenovirus, adeno-associated virus, and herpes simplex virus, have been manipulated for use in gene transfer and gene therapy applications [2]. Gene therapy in recent days has grown by leaps and bounds and its application in dentistry includes bone repair, treatment of salivary gland diseases, auto immune diseases, cancerous and precancerous lesions, pain, DNA vaccination (periodontal diseases, caries) and dermatological disorders [4]. It is used to replace a faulty gene or to introduce a new gene whose function is to cure or to favorably modify the clinical course of the condition. Transferred genes can be used for either reparative or pharmacological purposes [4]. The tissue engineering is other aspect of gene therapy for reconstruction of damaged periodontium including cementum, gingival, periodontal ligament and bone [5].

In tissue regeneration for example in periodontal tissue, many factors should be considered such as progenitor cell population, matrix scaffold and signaling molecules. Signaling molecules like BMP2 can modify by introducing a novel mutation for increasing efficacy or releasing from scaffold [6]. Progenitor cell population like precementoblast, prefibroblast and preosteoblast can carry main signaling molecules that they require for differentiation or orderly signal transduction for tissue development can make better formation of new functional attachment, formation of cementum, periodontal ligament and alveolar bone. By gene switch on/off molecules like siRNA/miRNA can control specific differentiation of dental pulp or ligament stem cells. Dental pulp stem cell and periodontal ligament stem cell are committed progenitors that mature to dentin/fibrous pulp and cementum/ligament [7].

periodontal disease is chronic, nagging, and requires meticulous attention by the clinician, dental hygienist, and great efforts by the patients in the form of compliance. Various treatment options are available in the armory of a periodontist including surgical and non-surgical therapy, regeneration techniques, tissue engineering etc. Gene therapy and use of stem cells are new approach to treatment of periodontal disease. Gene therapy and use of stem cells are new approach to treatment of periodontal disease [8].

The newer approaches may be listed as follows:

Gene therapy in human cells

Regeneration of periodontal tissue using PDGF is an applicable gene transfer strategies to tissue engineering originally to improve healing in soft tissue wounds [9]. Early studies in dental applications using recombinant adenoviral vectors that encode PDGF demonstrated the ability of these vectors constructs to transduce potently the cells isolated from the periodontium (eg osteoblasts, cementoblats, PDL cells, and gingival fibroblasts) [10]. continuous exogenous delivery of PDGF-α may delay mineral formation induced by cementoblasts, whereas PDGF clearly is required for mineral neogenesis [11].

Jin et al., demonstrated in their study that direct in vivo gene transfer of PDGF-B stimulated tissue regeneration in large periodontal defects [12]. reported that in an ex vivo investigation, the expression of PDGF genes was prolonged for up to 10 days in gingival wounds , investigated in vitro and in vivo Ad gene transfer of BMP-7 for bone formation and demonstrated that in case of direct in vivo gene delivery of Ad/BMP-7 in a collagen gel carrier promoted successful regeneration of alveolar bone defects around dental implants [13,14].

Gene therapy in microbial cells

As sharma and his colleagues reported periodontal vaccination using modification of porphyromonas gingivalis fimbrial gene resulted in production of several salivary and serum antibodies in mouse. Immunoglobulin thus secreted could neutralize P. gingivalis and limit its pathogenic ability. Immunization with genetically engineered s. gordoni vector expressing P. gingivalis fimbrial antigen acted as a vaccine against P. gingivalis induced periodontitis in rats [15]. Recombinant hemagglutinin, which is an important virulence factor of P gingivalis, when injected into rats, gave protection against P gingivalis induced bone loss [16].

In other aspect that Mah TF 2003 report biofilm bacteria show great resistance to antibiotics. Gene ndvB, which protects a wild form of Pseudomonas aeuroginosa strain, has been rendered ineffective by isolation of a ndvB mutant strain, which makes it susceptible to antibiotic therapy [17].

Tsuchiya S and their colleagues reports remodeling of alveolar by electric impulse (electroporation) is one such stimuli mediated through a gene transfer into periodontium and using plasmid as a vector [18].

For minimizing colonization of actinobacillus actinomycetemcomitans and control or alter periodontal disease progression, Schreiner HC and hiscolleaguesuse mutant tight adherence gene (TAG) that is essential for adherence and virulence of actinobacillus actinomycetemcomitans. Mutant strains lacking TAG and the consequent lack of aggressiveness have been developed [19].

Huang GT has showed that host defense can be enhanced by transfecting host cells with an antimicrobial peptide/protein–encoding gene. Host cells infected with β defensin-2 (HBD-2) gene via retroviral vector showed enhanced antimicrobial activity and improved host defense [13].

To suppressing inflammatory and harmful substances, gene delivery of TNF alpha is investigating. The process is complicated and still in the animal model stage only. Stem cells, tissue engineering, and proteomics have made great inroads into periodontics. Stem cell based therapies such as mesenchymal stem

cells therapy, are not far from being launched in the periodontium. Seo BM and his colleagues have reported periodontal ligament stem cells transplanted into immune compromised mice differentiated into cementoblast-like cells, adipocytes and collagen forming cells, and it was suggested that periodontal ligament (PDL) stem cells have the potential to generate cementum/PDL like tissue in vivo [5,6].

Gene therapy for regrown tooth

As of now, the only options for a missing tooth include implants, or if all teeth are missing, dentures. However, these two methods cause serious dental health problems. Health issues associated with dental implants include infection at the implant site, injury or damage to the surrounding structures, nerve damage, and sinus problems. Human teeth could eventually be made to regrow just like those of sharks as we still possess the same genes that allow regrowth, scientists have found. Sharks and other fish regrow their teeth repeatedly through their lives while humans have the capacity to regrow their teeth just once [11]. But now scientists at the University of Sheffield have discovered that the same network of genes like PAX9 clusterthat allow sharks to regrow teeth is present in humans [15]. According to this report, seems scientists investigating for gene modify of human to regrow of his loosed teeth. In another approach by using tissue engineering and autologous stem cells being tried to regrow a new tooth. growth factor-infused, three-dimensional scaffold with the potential to regenerate an anatomically correct tooth in just nine weeks from implantation [18]. By using a procedure developed in the Laboratory, Once the stem cells have colonized the scaffold, a tooth can grow in the socket and then merge with the surrounding tissue. it is may be a less expensive process. However, one thing that is known for sure is that it is far less invasive [20].

Conflict of Interest

There is no conflict of interest to declare.

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