Dental Surgeons as Gene Therapist
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Abstract
Gene therapy is a particular method by which defective gene is replaced or repaired by therapeutic gene. Vectors are vehicles which deliver the therapeutic gene into the host. Gene therapy can be used to treat wide range of diseases ranging from single gene disorder to multi-gene disorder. In dentistry the application of gene therapy includes bone repair, for treating auto immune disease, pain, DNA vaccination (for caries and periodontal disease) and cancer. Minor salivary glands and keratinocytes present in the oral mucosa are the excellent target sites for gene therapy since it can be readily accomplished with minimal invasive manner. This makes dentists as suitable candidate for gene therapy.

Keywords: Therapy;Gene;DNA;Somatic;Genetic Services;Biological Therapy;Vaccination;Immunotherapy;Oral Cancer;Vector.

Introduction
Rapid progress in molecular biological technology has made researchers to manipulate gene easier. A gene is a linear sequence of DNA that codes for a particular protein. Gene therapy is a technique in which defective genes that are responsible for disease development are corrected. The applications of gene therapy are based on the principle that a normal gene is inserted to compensate for a non functional gene and abnormal gene that can be repaired through selective reverse mutation. Scientists began gene therapy with bacteria in 1980 and first gene therapy in human (1990) was performed for treating severe combined immunodeficiency which worked for only few months. 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, pain, DNA vaccination, dermatological disorder and cancer 1.

Principles of Gene Therapy
Gene therapy is a technique in which normal gene is inserted in to host for a non-functional and abnormal gene, which are repaired through selective reverse mutation. The procedure involved in gene therapy includes
a. Pinpoint gene of interest,
b. Acquiring a normal copy of gene (therapeutic gene) by restrictive endonuclease enzyme (cutting and splicing) and

Requirements for Vector

Vector delivers the therapeutic gene into patient’s target. The target cells become infective with therapeutic gene through vector. Functional proteins are created from the therapeutic gene causing the cell to return to a normal stage 2.

Requirements for Vector

The ideal requirements for vectors are
a) It should not be identified by immune system (non-immunologic)
b) Should be stable and easy to reproduce and
c) Should have longevity of expression.

Types of Vector

Vectors can be either Viral or Non-Viral.
1. Commonly used viral vectors are Adeno virus, Adeno associated virus, Retro virus and Herpes virus. Among these, adenovirus is commonly used, as it can be cultured easily and because of its lower pathogenicity.
2. Non-Viral options include,
a. Direct introduction of therapeutic DNA - Disadvantage being it can be used only with certain tissue and requires a lot of DNA,
b. Creation of artificial lipid sphere with aqueous core, liposome - Carries therapeutic DNA through membrane,
c. Chemically linking DNA to molecules that will bind to special cell receptors - Less effective and
d. Trying to introduce a 47th chromosome; could carry a lot of information.

Types of Gene Therapy
1. Germ line gene therapy: Repair or replace defective gene in germ line cell. Modified gene would be inherited.
2. Somatic gene therapy: Repair or replace defective gene in some or all body cells of an individual.

Types of delivery
a) In vivo: delivery of gene takes place in the body.
b) Ex vivo: delivery takes place outside the body and the cells are placed back in to the body.

Applications in Dentistry
- Bone repair: Bone defects in the oral and maxillofacial region can be repaired by transferring genes encoding BMP’s (Bone morphogenic Protein). It will be possible to directly deliver the BMP-2 gene in vivo to tissues via an adenoviral vector to heal bone defects. Michigan research group has found non osteogenic fibroblasts (gingiva, dental pulp), which can express BMP-7 gene after being infected with an adenoviral vector.
- Pain: Managing or eliminating pain is a major part of dental practice. The use of gene transfer technology offers a potentially novel approach to manipulate specific, localized biochemical pathways involved in pain generation. Gene transfer may be particularly useful for managing chronic and intractable pain.
- DNA Vaccination: Dental scientists have tried to use classical vaccination technology to eradicate dental caries or periodontal diseases, thus far achieving mixed success. Applications of DNA vaccination are in the earliest stages of its use with oropharyngeal tissues. DNA vaccination will play a role in future strategies for preventing periodontal diseases and dental caries.
- Keratinocyte: Keratinocyte are the cells which are present in oral mucosa. Several features make epidermal and mucosal keratinocytes, attractive for treating local tissue disorders and as systemic gene therapeutics. Expression of therapeutic genes can be achieved with use of topically applied agents. Gene therapy can be used to treat keratinocytes disorder like ichthyosis and epidermolysis bullosa. In future it can be used to treat most of dermatologic disorders.
- Oral Cancer: The general strategy in cancer treatment is to express a gene product that will result in cancer cell death. It can be achieved by
  1. Addition of a tumor-suppressor gene (gene addition therapy);
  2. Deletion of a defective tumor gene (gene excision therapy);
  3. Down-regulation of the expression of genes that stimulate tumor growth;
  4. Enhancement of immune surveillance (immunotherapy);
  5. Activation of pro-drugs that have a chemotherapeutic effect (“suicide” gene therapy);
  6. Introduction of genes to inhibit tumor angiogenesis.

Dental surgeon as Gene Therapist
To conclude, the role of dental surgeon in gene therapy is tenable. Dental surgeon has got easy approach to areas like salivary glands and keratinocytes (oral epithelium). Salivary glands are excellent target sites for gene transfer, readily accomplished in minimal invasive manner. There are about 500-1000 minor salivary gland in oral cavity. Salivary gland produce large amount of proteins and it is a site where gene transfer can be readily accomplished in minimal invasive manner. Salivary glands could be used for gene therapeutic applications with single protein deficiencies. Irreversible salivary gland dysfunction due to autoimmune diseases and irradiation can also be corrected using GT. Keratinocyte are the cells which are present in oral mucosa. Several features make epidermal and mucosal keratinocytes, attractive for treating local tissue disorders and as systemic gene therapeutics. Expression of therapeutic genes can be achieved with use of topically applied agents. Gene therapy can be used to treat disorders of keratinocytes like ichthyosis and epidermolysis bullosa. In future it can be used to treat most of dermatologic disorders.

Dental surgeon can be the best fitting professional to administer gene therapy in the oral cavity which bears minor salivary glands and keratinocytes. Patient with intractable pain in any part of the body can
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walk in to dental clinic to get his/her pain relieved through gene therapy. In future dentist will have inseparable role in the field of gene therapy.

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