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GLIMPSE ON APPLICATIONS OF BIOTECHNOLOGY IN DENTISTRY – ARE DENTISTS READY TO USE?

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ABSTRACT

The molecular biology and its application in the study of cancer have significantly advanced the field of human cancer research. It is another change at this time with the help of nanotechnology combined with Nanomaterials, Biotechnology and Nanorobotics. Biopharmaceuticals, Biomaterials, Biomechanics, Biomedical Engineering, Bimolecular Materials, Bioprocessing, Biomotors, Biopolymers, Bioinformatics, Biomimetics are the various fields of bio-technology. Probiotics are dietary supplements which contain beneficial bacteria or yeasts. Tissue engineering is a novel and exciting field that aims to re-create functional, healthy tissues and organs in order to replace diseased, dying, or dead tissues. Biomimetics is the study of natural structural processes to try to mimic or replicate it artificially in an attempt to restore the same aesthetics or function.

INTRODUCTION

Biotechnology is any technological application that uses biological process living organisms or derivatives thereof to make or modify products or process for specific use. Biomedical science and technology are lead of the medical and dental research in the field. Biotechnology has important role in developments, innovations, advances & research in the field of dentistry. Biomedical science and technologies refers to the application of biologic knowledge and techniques to enhance human health. Evaluation of the genome [genomics], the messenger RNA transcribed from active genes [transcriptomics], and the proteins coded for by this mRNA [proteomics] and the metabolites which are the end products of gene expression [metabolomics] all utilize techniques which outcome in great amounts of data. Even saliva contains 300 proteins [3000 m-RNA]. Out of which 180 m-RNA are common in healthy individuals [1]. In the general population, oral cancer is the sixth most usual cancer for both gender and the third most usual cancer in developing nations.

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In India, due to this disease, cancer popularity is determined to be around 2.5 million, with over 8, 00, 000 new cases and 5, 50,000 deaths obtaining each year. Telomerase is a ribonucliоprotein complex which protects the end of chromosome by preventing chromosomal end to end fusion. Telomerase is composed of 2 constituents. [1] RNA template [2] two associated proteins, TP1 & HTRT. Levels of HTRT are detected by m-RNA reverse Transcriptase PCR. It is correlated with diagnosis of oral malignancy, clinically as well as pathologically. So detection of telomerase activity in oral rinses is a diagnostic marker for oral cancer. Telomerase activity is detected in cancer cells whereas normal cells do not show Telomerase activity. Telomerase activity is detected in oral SCC, Adenoid cystic carcinoma, Malignant melanoma, Leiomyosarcoma, Malignant rhomboid tumor, Metastatic leukemia. Telomerase Activity is not detected in Benign & Precancerous lesions such as ameloblastoma, dysplastic lesions, hyperplastic lesions, cyst wall of radicular& follicular cyst, benign lesions-pleomorphic adenoma, irritation fibroma, giant cell tumor and normal tissues of oral cavity such as gingiva, buccal mucosa, tongue, salivary gland & muscle. Genes such as IL-8, IL-1B, Ornithine decarbonase, spermidine acetyl transferase,

are higher in saliva of patients suffering from oral squamous cell carcinoma and IL-6, TNF-α in patients with precancerous lesions. i.e. Leukoplakia. Oral fluid nanosensor test is used for the detection of multiple salivary proteins & nucleic acid. Thioredoxin, IL-8 & 4 can detect oral cancer with high sensitivity & specificity. In early oral cancer, gene is knocked out. So, cancer cell contains a deleted region in chromosome 9p-21, 22. This is detected by DNA image cytometry multinucleated cell analysis. Especially useful for doubtful or suspicious [dysplastic cells].

Dielectrophoresis technique detects electrophysiological parameters like conductivity & permeability of cellular cytoplasm & membranes. Abnormal cells show different parameters [2]. "The word nano is obtained from Greek word "dwarf". Nanomaterials are the substances with constituent less than 100 nm in at least one dimension, including clusters of atoms, grains less than 100 nm in size, fibres less than 100 nm diameter, films less than 100 nm in thickness, nanoholes and composites that are integration of these. Nanotechnology is a manipulation of matter, atom by atom. Nanorobots assemble things from atomic & molecular building blocks. It is useful in diagnosis & treatment of oral cancer, diagnosis of other diseases, oral anesthesia induction, dentinal hypersensitivity and tooth repair. Nano-biotechnology is examined to be special fusion of biotechnology and nanotechnology by which classical micro-technology can be integrated to a molecular biological approach in real. Collins in 1954 and Southam and Selwyn in 1970, opposed and refused the idea of bone to implant contact without formation of a fibrous layer, since there had been an opinion of development of fibrous layer around implant, reduce integrity with bone. Per-Ingvar Branemark and his colleagues in 1950s and 1960s, while considering microcirculation of bone and wound healing that means of vital microscopy accidentally found the process of Osseo integration. [3].

Optical coherence tomography (OCT) imaging of hard & soft tissues differentiates keratinized & nonkeratinised mucosa, normal & abnormal tooth structure such as difference between carious & non carious teeth. Use of Optics in oral medicine reveals detection of initial occlusal dental caries by near IR light at 1310nm, LASER ablation of dental tissues, optical path length spectroscopy, use of evanescent wave fiber optic spectroscopy for detection of bacterial activity, cancellation of coherent artifacts in OCT to improve image contrast, sharpen the air enamel & enamel dentin interface.

With the use of Electromagnetic energy such as Ultraviolet or Infrared vibrations to eliminate resistant bacteria and to eliminate odor produce by them. Biopharmaceuticals, Biomaterials, Biomechanics, Biomedical Engineering, Bimolecular Materials, Bioprocessing, Biomotors, Biopolymers, Bioinformatics, Biomimetics are the various fields of bio-technology [4].

APPLICATIONS

Chemiluminiscent light: 1 minute mouth rinse with diluted acetic acid to remove glycoprotein barrier & then mucosa is dried & then bluish white chemiluminiscent light is applied. By the application of chemiluminiscent light, normal cells absorb light & appear blue. Abnormal cells reflect light & appears acetowhite with distinguish border [5].

Fluorescence light: Normal oral mucosa emits green auto fluorescence whereas abnormal areas absorb fluorescence appear dark. Computer-aided design [CAD] and computer-aided manufacturing [CAM] technology systems use computers to accumulate information, design, and manufacture an extensive range of products [6]. A biofilm is an efficient, collaborating community of organisms. Biofilm appear such as formation of conditioning layer, bacterial adhesion, bacterial growth and biofilm expansion. The field of tissue engineering has advanced over the previous decade to re-create functional, healthy tissues and organs in order to replace diseased, dying, or dead tissues. Current procedure used for treatment of lost tissues which involve the utilization of autogenous grafts, allografts, and synthetic materials [alloplasts].Tissue engineering induced biomimetics involves therapies for the patients suffering from xerostomia & dental diseases. The research on bioactive material and molecules are area of growth of novel bioactive material and molecules which have extensive application in dentistry and biomedical field. There are various types of bioactive materials like osteogenic, osteoconductive, osteoinductive. Biomaterials are native or synthetic polymers that achieve extensive importance in root canal therapy, tooth repair, pulp therapy and dental surgery in the field of dentistry and drug delivery [7]. Mastication is a necessary part of the digestive process. The capability of the masticatory organ to grind and process food is directly associated with the individual purpose and general state of health. Dental plaque is an adherent deposit of bacteria and their products, which forms as a white greenish or even yellow film on all tooth surfaces. Due to many epidemiological, experimental and animal studies that Mutans streptococci [Streptococcus mutans and Streptococcus sobrinus] are the most major bacteria in the pathogenesis of dental caries [8].

GENE THERAPY –BIOGENETICS Branch of biotechnology associated with the genetics & gene therapy is known as biogenetics. Introduction of growth factor protein is used in bone around implants.

RECOMBINENT DNA

Replacement therapy is developed by Dr. Hillman for the prevention of tooth decay.

S.Mutans produces tooth decay. Whereas new strains of S.Mutans are incapable to produce acid & produces anti-bacterial substances which is toxic to naturally occurring

cariogenic organisms & thereby prevention of tooth decay [9].

Major Advances in Biomedical Science and Technologies

A timeline of significant achievements in biotechnology:

- **1990** Human Genome Project commenced
- **1995** First complete genome sequence Haemophilus influenza. First use of microarray for gene expression profiling
- **1996** Affymetrix produced the first commercial gene chip. BRC Analysis diagnostic test for breast cancer predisposition to detect *BRCA1* and *BRCA2*
- **1997** Dolly – first cloned mammal [from DNA of adult sheep]. Poly–cloned using nuclear transfer technology [sheep DNA with some human genes]. IL-1 polymorphism associated with periodontal disease
- **1998** Embryonic stem cells first grown
- **2001** Draft human genome sequence published
- **2002** Genomes of 125 organisms sequenced
- **2003** Human Genome Project completed
- **2007 S**alivary proteome completed

Use of Affymetrix chips to detect susceptibility to periodontal disease

- **2017?** Replace missing tooth with cloned tooth. [10]

Molecular Basis and Biology of Human Oral Cancer

Carcinogenesis is a complex, multi-step process in which genetic events within signal transduction pathways governing normal cellular physiology are quantitatively or qualitatively altered. There are two mechanisms by which proto-oncogenes can be converted to cellular oncogenes:

Quantitative: Tumor formation influenced by increase in the absolute number of proto-oncogene products or by its production in inappropriate cell types.

Qualitative: Conversion from proto-oncogene to transforming gene involves changes in the nucleotide sequence and obtained of the new properties. [11]

Nano Tissue Engineering By utilizing cellular and mineral components occur when we will be able to generate whole new tooth with the principles of genetic engineering, tissue engineering and tissue regeneration at nanoscale. Chen et al by using nanorods like calcium hydroxyapatite crystals which were aligned roughly parallel to each other, were able to create hardest tissue in human body, i.e., dental enamel and pretend the natural bio mineralization process. [12]

Nanomaterials Siegel has arranged nanomaterials as zero dimensional, one dimensional, two dimensional and three dimensional nanostructures. Various nanostructures involve: Nanoparticles, Nanopores, Nanotubes, Nanorods, Nanospheres, Nanofibres, Nanoshells, Dendrimers & dendritic copolymers.

Nanodentistry and Its Applications Nanodentistry will make possible the continuity of comprehensive oral health by utilizing nanomaterials, biotechnology, including tissue engineering, and ultimately, dental nanorobotics.

Nanodentistry involves:

- Nanorobotics
- Nanodiagnostics
- Nanomaterials

NANOROBOTICS

Local Anaesthesia In dental practice, it is the most common method, to make oral anesthesia in which dental professionals will generate a colloidal suspension containing millions of active analgesic micron-sized dental nanorobot 'particles' on the patient's gingivae.

Hypersensitivity Cure Dentin hypersensitivity may be induced by changes in pressure transmitted hydro dynamically to the pulp teeth.

Dental Biomimetics The most exciting venue for opinion on the nanorestoration of tooth structures is that of nanotechnology resemble processes that occur in nature [biomimetics], such as the formation of dental enamel.

Dental Durability and Cosmetics Artificial materials such as sapphire or diamond are used to raise the durability and appearance of tooth which have 20 to 100 times the hardness and failure strength of natural enamel or contemporary ceramic veneers, as well as good biocompatibility.

Renaturalization Procedures Through esthetic dentistry, the dentition renaturalization approach may become a popular addition to the future dental practice. This can be mostly used in patients who determine old dental amalgams excavated and their teeth remanufactured with native biological materials [13].

NANODIAGNOSTICS

Nanoscale Cantilevers These are flexible beams similar a row of diving boards that can be arranged to bind to molecules related with cancer.

Nanopores These are minute holes that enable DNA to pass through one strand at a time. They will make DNA sequencing better organized.

Nanotubes These are carbon rods that half the diameter of a molecule of DNA and not only can identify the manifestation of altered genes but may also help researchers the exact location of those changes.

Quantum Dots These are nanomaterials that glow very brightly when enhanced by ultraviolet light. Quantum dots are attaching themselves to proteins special to cancer cells and show tumors to light.

Nano Electromechanical Systems [NEMS] Nanotechnology based NEMS biosensors that demonstrate perfect sensitivity and specificity for analyte detection and down to single molecule level are being developed [14].

NANOMATERIALS IN DENTISTRY

Nanocomposites Non agglomerated distinct nanoparticles are homogeneously spread in resins or coatings to produce nanocomposites. The nanofiller involve an aluminosilicate powder having a mean particle size of 80 mm and a 1:4 M ratio of alumina to silica and a refractive index of 1.508.

Nanosolution produces individual and dispersible nanoparticles, which can be added to various solvents, paints & polymers in which they are dispersed homogenously.

Nano-optimised Mouldable Ceramics
Nanofillers
Nanopigments
Nanomodifiers

Nanoneedles Suture needles integrating nano-sized stainless steel crystals have been developed.

Implants Nanotechnologies are used for surface variation of dental implants as surfaces properties such as chemistry and roughness play a determinant role in attaining and sustaining their long-term stability in bone tissue [15].

Nanomedicine It is the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and improving human health, using nanoscale structured materials, biotechnology and genetic engineering and ultimately complex machine systems and nanorobots. Tiny machines, known as nano assemblers, could be managed by computer through dentists to perform specialized jobs. Nanocomputers would suppose the major task of activation, controlling and deactivating such nano-mechanical devices.

Future prospects of Nanobiotechnology It could show indication of a choice of various new materials and devices that is useful in the field of medicine, electronics, biomaterials and energy production. It may show to alter by playing a major role in various biomedical applications ranging from drug delivery and gene therapy to molecular imaging, biomarkers and biosensors.

Ozone therapy Studies have shown that 99% of all the bacteria causing tooth decay have been obliterated after 10 s of ozone exposure and even 99.9% bacteria after 20 s exposure. Ozone can now be organized in several treatments like bleaching of discolored teeth, root canal treatment, desensitization and treatment of some soft tissue infections [16].

Genomics In 1990, the ambitious Human Genome Project [HGP] commenced. A draft of the human genome was published in 2001 and the project was completed in 2003, with 99% decoded. Mapping the genome was only the first step.

Proteomics It is the study of the products of the 2% or less of the human genome which is transcribed - that is, protein coding. These proteins experience significant post-translational modification [proteolysis, glycosylation etc.] resulting in a number of different products from a single gene; 30000 human genes code for 400000 or more proteins [17].

Biomaterials

Biomaterials research is changing from testing of "synthetic biomaterials" to evolving and testing "biological biomaterials". In this context, two research directions will decide future education and clinical procedures.
[i] Characterization of the structure-property events within synthetic and biological restorative materials, and
[ii] The interactions at their interfaces with oral tissues and vice versa [18].

Genetic damage in oral cancer cells can be divided into two categories:-
1. Dominant changes: Those occur in proto-oncogenes and certain tumor suppressor genes [TSGs] developing in gain of function.
2. Recessive changes- Those occur in growth inhibitory pathway genes or commonly in tumor suppressor genes causing loss of function [19].

Biomimetics in Restorative Dentistry: The physiological performance of intact teeth is the result of intimate and balanced relationships between mechanical, biological, functional and esthetic parameters.

Biomimetics Endodontics: By application of tissue engineering, biomimetic approach to restore tooth structure is established on regenerative endodontic procedures [20].

Prebiotics and Symbiotic
Prebiotics are dietary substances that take care of a selected group of microorganisms living in the gut.

Mechanisms of Probiotic in Oral Cavity
[a] Normalization of intestinal micro biota
[b] Modulation of immune response
[c] Metabolic effects

In oral cavity, probiotics act as a preventive lining for oral tissues against oral diseases by producing a biofilm. Such a biofilm keeps bacterial pathogens off oral tissues by lining a space pathogens would perfuse in the absence of the biofilm and engaging with cariogenic bacteria and periodontal pathogens growth [21].

Role of probiotics in dental caries Dental caries is a disease where bacterial process effect damage to the hard structure of tooth, characterized by acid demineralization of the tooth enamel. When changes occur in the micro flora in oral cavity resulting in an overgrowth of several bacteria involving Streptococcus sorbinus, Streptococcus mutans and Porphyromonas gingivalis which are identified as the primary cause of the dental caries.

Role of Probiotics in Halitosis

Halitosis is caused by a number of volatiles and most of its etiologic factors are present in the oropharynx [gingivitis, periodontitis, tongue coating and tonsillitis]. F. nucleatum, P. intermedia, P. gingivalis, and T. denticola are produce "Volatile Sulphur Compounds" [VSC‟s] are responsible for halitosis.

Probiotics in infections and oral diseases When a test group of older people consumed cheese containing Propionibacterium freudenreichii, Shermanii JS and L. rhamnosus strains GG and LC705 for 16 weeks, the number of high oral yeast counts decreased but no changes were observed in mucosal lesions [22].

Probiotic delivery

Probiotic bacteria are normal commensals of the intestines. Probiotics can be given in the form of lozenges, sucking tablets and chewing gums in replacement therapy. Probiotics can be provided in food by four basic ways:

1. Beverages
2. Prebiotic fibers
3. Dietary supplements
4. Milk and milk products

RECENT TRENDS IN PROBIOTICS: PATHO-BIOTECHNOLOGY

Patho-biotechnology techniques are being used to manufacture new modified probiotics which is a major biological goal for probiotic which have raised stress profile tolerance and ability to overcome the physiochemical defense of the host. Lactic acid bacteria [LAB] have been altered to produce new varieties by traditional and genetic engineering methods [23].

SAFETY ASPECTS OF PROBIOTICS

When probiotics are applied orally can communicate with a patients systemic health and at least a part of them will be ingested. When ingested orally, probiotics are generally safe and well allowed with bloating and flatulence occurring normally [24].

FUTURE PERSPECTIVES

The following future applications of probiotics may be identified:

1. Genetic engineering of already identified probiotics.
2. Biotherapy using antibiotic-sensitive bacteria to displace resistant strains.
3. Micro biota removal
4. Passive immunization
5. Interference with signaling mechanisms involving Competence Stimulating Peptide [CSP] as the signaling molecule. Probiotics can be used as passive local immunization against dental caries. Primarily probiotic Lactobacillus and Bifido-bacterium strains have been used along with few more strains [25].

APPLICATIONS OF BIOACTIVE MATERIALS AND MOLECULES DENTISTRY

Root Canal Therapy Portland cement or Mineral trioxide aggregate [MTA] is a bioactive material used for preserving pulp and periodontal tissue vitality as part of pulp capping and perforation repair procedures.

Tooth Repair and Regeneration Growth factors which can develop tooth healing and pulp regeneration by dentin extracellular matrix proteins [ECMPs]. ECMPs can stimulate dental pulp stem cell proliferation, differentiation and migration to sites of injury.

Coating of Implants When metals have good physical and mechanical properties such as low density and mechanical resistance then they can be used in dental and medical devices. Dental implants are made from titanium alloys and have a coating of hydroxyapatite to help in osteogenesis and bone healing [18].

CONCLUSION

Currently, molecular biosciences and technologies are appearing fields in dentistry. Nanodentistry still faces many important challenges in recognizing its enormous potential. Probiotics play a major role in preventing issues with overuse of antibiotics and antimicrobial resistance. CAD/CAM systems have raised dentistry by providing high-quality restorations. Genetic engineering, nanotechnology and ozone therapy will change dentistry, healthcare, and human life more extremely than other developments of the past. Osseointegration is a very complex method then there are many micro and macro molecular aspects of bone-implant interface that need to be understood and illuminated.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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