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Review Article

Regenerative Dental Medicine- A Boon in New Era

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***ABSTRACT*:**
With the widespread advances in all details of science over the past decade, the regenerative dentistry has also come up with the breakthrough innovations. The tooth regeneration offers innovative approaches to the common problems encountered in the oral and dental sciences. The strategies based upon the regenerative medicine that facilitates the repair or replacement of the damaged teeth may hold particular promise as a means in order to reduce the cost of the dental care. The tooth is also a compelling candidate as a template for the organogenesis which could have the far-reaching implications in the field of regenerative medicine.

Key words: Gene therapy, regenerative dental medicine, tissue engineering

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INTRODUCTION:

Tooth is a complex biological organ which consists of multiple tissues including enamel, dentin, cementum and pulp, which has been encased in a biological socket comprised of the periodontium. The periodontium includes periodontal ligament (PDL), bone as well as the gingiva which is continuous with the oral mucous membrane. The dental caries is one of the most common disorders in humans and tooth loss is the most common organ failure, which affects a vast majority of population.[1] The conventional dental treatment modalities range from a simple restoration of decayed tooth, tooth devitalization and also disinfection (root canal therapy), extractions as well as the replacement by an implant supported prosthesis. Magnitude of the clinical success of the concepts of regenerative medicine is debatable because of the fact that the clinical studies conducted either in a controlled environment or lacks the long-term observations. [2]Due to its inherent scarcity of the number of cases and its practicality, it might also be difficult to estimate the general outcome as well as the usefulness of the procedure. In spite of these limitations, the regenerative dentistry has witnessed its genuine share of successful innovative technologies by a combined multidisciplinary effort which offers a wealth of the opportunities and also leading a path for superior treatment techniques which are closer to the natural.[3]

Regenerative Medicine & Tissue Engineering: Tissue engineering is the field of functional restoration of tissue structure and also the physiology for the impaired or damaged tissues due to any disease, cancer and trauma.[4]The aspects of tissue engineering promises a wide range of solutions to the challenging clinical problems in the field of dentistry that have not been adequately addressed because of the use of conventional techniques. Tissue engineering generally has three constituents:

Stem cells/progenitor cells- A stem cell can commonly be defined as a cell that has the ability to continuously divide and produce the progeny cells that differentiate into the various other types of cells or tissues.

Scaffolds or extra cellular matrix-In order to create a more practical tissue engineering therapy, stem cells must be organized into a 3D structure that can support the cell organization as well as the vascularization. Thus, this can only be accomplished by using a scaffold seeded with stem cells. A scaffold should contain the growth factors in order to aid in the proliferation and differentiation of stem cell, leading to an improved and faster tissue development.

Morphogens (i.e., signaling molecules) or growth factors-the growth factors are biological modulators which are capable to promote the cell proliferation and differentiation.[20]The growth factors are the extracellular matrix molecules that are involved in the signaling and regulating the odontogenic events during the tooth development, thereby, application of these exogenous signaling factors has been recommended for the regenerative therapies. However, before they are to be used in the regular clinical practice**,**a number of challenges in the methods of delivery should be addressed.

Clinical Applications: In the field of regenerative medicine, the dental stem cells are also made into use in order to facilitate the repair of tissues such as the nerves and bone.[5]

The tissue engineering in the regenerative endodontic represents a new treatment modality that focuses on the re-establishment of the pulp vitality and also continued root development. In dentistry, the tissue engineering can be utilized for *de novo* pulp replacement, *in situ* partial pulp regeneration, regeneration or replacement of the mineralized tissues like enamel, dentin, cementum and bone as well as the regeneration of periodontium. The repair or regeneration of the pulp tissue recapitulates the tooth development and also points to the brighter possibilities in the coming future.

De novo synthesis of pulp replacement- Before the creation of an entire pulp tissue; the prime objective or goal of the tissue engineering effort for pulp regeneration is to harness the pulp's own capacity in order to regenerate a functionally active pulp tissue that can physiologically respond to the metabolic cues. [6]There should be complete de novo synthesis of pulp in order to entirely regeneration the tissue in the cases when entire pulp tissue is lost. The generation of a well-vascularized pulp-like tissue by making the use of a tooth slice model that has been reported recently by several groups with the help of dental stem cells.

In situ partial pulp regeneration – It has been suggested by various **c**urrent evidences that under certain conditions, the remaining healthy portion of pulp could be recoverable before the final stages as well as may also have the potential to regenerate the lost portion. Thereby, in order to enhance this regeneration, an inductive medical devices or engineered pulp constructs based on the stem cells can be inserted into the pulp space for facilitating the total regaining of the pulp tissue and thus generation of new dentin.[6]

Micro scale and Nano scale Technologies for Dental Tissue Engineering and Regeneration: With the advent in the field of tissue engineering over the past decade, there have been many challenges that remain in the aspect of tooth regeneration and tissue engineering. Thereby, for this purpose, various micro-scale approaches that spatially pattern and also support the development of the different cell types in the close proximity can be used in order to regulate the micro environment of the cell as well as they are promising approaches for the tooth development. Application of these micro scale and nano scale technologies will likely to help in the advancement of the technology and also the knowledge associated with the regeneration of the dental tissue. [6, 7] Moreover, these technologies are likely to enhance the development of the scaffold and also increase the sources of stem cell sources for the regeneration of the dental tissue. Along with the controlled properties as well as the architecture, the micro scale scaffolds may facilitate the generation of cell-laden, complex, load-bearing and vascularized scaffolds for the regeneration of the hard tissue and also the neo-vascularization which is essential for the *in vitro* tooth development.[7]

GENE THERAPY- Year 2003 has been marked as a major milestone in the world of genetics and also molecular biology. The genetic sequence i.e., genes are contained in the DNA which control the cell activity as well as the cellular function. Various new techniques involving the viral or non-viral vectors can deliver the genes for the morphogens, growth factors, extracellular

matrix molecules and transcription factors into the target cell populations.[8] In the field of endocontics, one use of gene delivery in could be to deliver the mineralizing genes into the pulp tissue in order to promote the tissue mineralization. The gene therapy is a relatively new field, and thereby it lacks the evidences which are very much required to demonstrate that this therapy has the potential to rescue the necrotic pulp. The potential benefits as well as the disadvantages are highly theoretical at this point of time. [7, 8]

The barriers and future directions of Regenerative Dentistry: It is a highly meritorious approach to regenerate the tooth by cell transplantation. However, there are hurdles in the translation of cell-delivery-based tooth regeneration into the therapeutics. The most important one of these difficulties is inaccessibility of the autologous embryonic tooth germ cells for the human applications. Irrespective of the cell source, the cell-delivery approaches for the tooth regeneration encounter the similar translational barrier as that of the cell-based therapies for other tissues. [8, 9]The costs for commercialization process and the difficulties in the regulatory approval in regard with the *ex vivo* cell manipulation have also precluded any significant clinical translation effort upto the date in the field of tooth regeneration. As with the tissue engineering of other biological structures, the regeneration of various teeth or an entire tooth and also associated structures such as enamel, dentin, cementum, dental pulp, periodontium, by the cell transplantation faces a number of translational, scientific as well as the regulatory difficulties.[9]

The near future- The technology of restoring a lost tooth tissue will be studied for many years to come. Although the tooth transplantation as well as the dental implants have existed for many years, but they were never been full satisfactory. With an innovative focus, the regenerative endodontics is going to have a significant effect on clinical practices of the dentistry and also in the field of regenerative medicine. [9] These technologies which may be practical for the clinical application in the near future are: establishment of the stem cell banks which are readily accessible and can increase the clinical probability of stem cell therapy, also the procedures which involve the biological pulp implants and respective implant storage banks, moreover, the mainstream of the tissue engineering which will be specifically related to the tissue regeneration in the dentistry. [10]This also may involve the cell printing as well as the assembly on biological templates, an advanced and practical scaffold as well as the growth factor delivery techniques. In addition to this, amenable advances in the biological microscale and nanoscale technologies will also gain its popularity over time.

The distant future-The synthesis and assembly of bio proteins by the nanorobots is the next generation of regenerative treatment techniques, in which these entities would be injected to a desired location and they would weave up the entire collagen framework upon which the proteins will be assembled and also are the possibilities where the dental tissues are grown to a particular requirement and then transplanted on a routine basis.[9, 10] The possibilities are coveting and infinite. Thereby these ground breaking strategies can provide a novel and innovative biology-based new generation of the clinical treatments for various dental diseases.[10]

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