Review Article

ENAMEL REGENERATION WITHOUT THE USE OF STEM CELLS?

Rishika,[1] Garg N,[2] Lumbini P,[3] Yeluri R [4]

1. *Post Graduate Student, Department of Pedodontics & Preventive Dentistry, Teerthanker Mahaveer Dental College & Research Centre, Moradabad, Uttar Pradesh.*
2. *Reader, Department of Pedodontics & Preventive Dentistry, Teerthanker Mahaveer Dental College & Research Centre, Moradabad, Uttar Pradesh.*
3. *Senior Lecturer, Department of Pedodontics & Preventive Dentistry, Teerthanker Mahaveer Dental College & Research Centre, Moradabad, Uttar Pradesh*
4. *Professor & Head, Department of Pedodontics & Preventive Dentistry, Teerthanker Mahaveer Dental College & Research Centre, Moradabad, Uttar Pradesh*

Abstract

Enamel formation takes place before the tooth erupts in a confined extracellular environment between dentin and ameloblast cells. In the formation of enamel a series of physiological and chemical events are involved that includes gene expression, protein secretion and folding, mineral growth and protein degradation. After the eruption of tooth, mature enamel does not contain cells and does not remodel, so synthetic enamel is necessary for regeneration of enamel. Synthetic enamel can be regenerated by using tissue engineering technology in which stem cells are used along with growth factors and scaffolds to regenerate the tissue. The objective of this paper is to review various strategies available in the literature regarding regeneration of enamel without the use of stem cells in the management of early carious lesions and cavitated lesions as well.

Key words: Biomimetics, Enamel regeneration, Nano – hydroxyapatite, Self – assembling peptides, Stem cells.

Introduction

Regenerative procedures can be defined as biologically based procedures designed to replace damaged, diseased or missing structures.[1] The regeneration of oral tissues that are affected by inherited disorders, neoplastic diseases and trauma is anticipated to solve many dental problems. Within the next twenty five years, unparalleled advances in dentistry are set to take place with the availability of artificial teeth, bone and oral tissues.[2, 3] Regenerative dental procedures have a long history, emerging around 1952, when Dr. B.W. Hermann reported on the application of calcium hydroxide in a case report of vital pulp amputation.[4] Research on the regenerative dentistry has gained impetus only in the recent past and eluded the dramatic yet scientific advancements in the field of molecular biology.

Despite many benefits that are promised by the recent progress in stem cell research, a number of risks and disadvantages remains both in the theoretical as well as in scientific fields that includes In-vitro culture and other manipulation stages, that is, the mode of processing of cells as it requires biomaterial scaffolds to promote engraftment, dosage of stem cells used as these are difficult to obtain in large quantities, their storage in laboratory requires specific environmental conditions, the sourcing of embryonic stem cells is controversial and is surrounded by ethical and legal issues, it is a costly procedure and to date, the research is only confined to animal models and more human research trials are needed to determine the therapeutic utility of stem cells.

So as to overcome all these intricacies certain newer approaches have gained momentum in the field of enamel regeneration in which stem cells are not required to regenerate the lost enamel.

Newer Approaches in Enamel Regeneration

Biomimetic Approach

In biomimetic synthesis biomaterials are prepared in the laboratory under conditions close to those of the physiological microenvironment.[5] Understanding the timing and pattern of the ameloblast gene products – amelogenin, enamelin, and ameloblastin – as well as the nature of the mineral phase allows scientists to develop techniques for preparing enamel like material in the laboratory in a cell – free system.[6] The main challenge is to control the appropriate conditions (ie, pH) and the timing of protein addition to the system. In this a device with a special membrane that allows only calcium ions to enter the system in a unidirectional manner is used that mimics the ameloblast cell membrane when synthetic amelogenin protein is trapped between the two layers of membranes is used as the organic matrix to initiate mineralization.[7] Such a device has been used victoriously to grow apatite crystals with similar organization as that of enamel within the prisms. The formation of this material is one of the first key steps towards the formation of synthetic enamel in a cell – free system.

Self-Assembling Peptides

Scientists from the University of Leeds found a way to mimic the enamel matrix within enamel lesions and thus enabling regeneration via de novo biomineralisation by using Self – Assembling Peptides. In nature self – assembly is widespread and the best known examples are the spontaneous folding of proteins or genesis of the double helix from two strands of DNA. Self-assembling peptides can accomplish various biological functions and substitute for three – dimensional matrices. In initial caries defect, the hypermineralized plate covers the initial defect. Monomeric P 11-4 is applied onto the lesion and diffuses through the pores of the hypermineralized plate into the subsurface lesion body this is followed by the peptide monomers to spontaneously form a three – dimensional matrix via hydrogen bonds. After that, crystallisation around the matrix starts and calcium phosphate from saliva crystallises around the matrix, forming new enamel.[8]

Chemical Approach

Yin Y *et al*[9] in 2009 conducted a study in which the surface of a non-carious enamel slice, cut from disinfected human molars was polished lightly and then etched with 85% phosphoric acid for 30 seconds.

The treated enamel was immersed in a calcium phosphate solution with N-(2-hydroxyethyl) ethylene-diamine-triacetic acid (HEDTA) for 3 minutes, and then potassium fluoride solution was added to it. The resulting suspension contains 0.10 M HEDTA-Ca, 0.06 M KH_2PO_4, and 0.02 M KF. After keeping the enamel slice in this solution it was put into a water bath at 37°C with ambient pressure of 8 d. The final enamel with a newly-grown layer was achieved which was rinsed with distilled water and dried in the air.[9]

Regeneration of Enamel Using Nano-Hydroxyapatite

If a piece of tooth is submerged in a concentrated suspension of nanohydroxyapatite followed by drying of it, we can observe under an electronic microscope a transparent boundary that is formed between the part submerged in the hydroxyapatite and the intact part. In the reference part we can observe the damages caused by tooth brushing under normal conditions, but in the submerged part, differences are significant and it is because the tooth surface is covered completely by hydroxyapatite, which has a high concentration of dispersion. This layer shows that how much adsorption of nanoapatite is there on the surface of tooth enamel. Therefore, it is logical to expect that the more diluted the formulation is, the more adsorption rate will be. To study this issue in a more practical level, the nanohydroxyapatite was used in toothpaste with 5 percent concentration. The related toothpaste was diluted in proportion of 1 to 10, and was rubbed through a fabric on the tooth, and the tooth was washed. The tooth was studied under electronic microscope, and it was observed clearly that a sticky film was covering the defective areas of enamel.[10]

Future Directions

In the past two decades our understanding of the mechanisms of enamel formation has advanced greatly. The knowledge we now have of the genetics and biochemistry of enamel provides a valuable foundation for the development of cell-free strategies for enamel reconstruction. Efforts to regenerate enamel are on-going but remain at the level of laboratory investigation. The main challenge in cell-free fabrication of synthetic enamel is the creation of enamel's complex hierarchical prism and interprismatic structures. However, it is only a matter of time before an artificial material with enamel-like optical, mechanical, and esthetic properties will be available to replace the conventional restorative materials. In the dental operatory, this leads to patients receiving a dental device (a night guard for example) that contains the appropriate organic and inorganic materials for release into the oral cavity that will help enamel to regrow overnight. Eventually, nothing will be better than enamel—except enamel itself.

Concluding Remarks

- Stem cells are considered to be the most valuable cells for regenerative medicine. Research on stem cells provides advanced knowledge about how a tissue/organ develops from a single cell.
- Despite the many benefits promised by the recent progress in stem cell research, a number of disadvantages and risks remain. To overcome these risks, recently various regenerative strategies have been introduced that do not require stem cells for regeneration of tooth enamel.
- The modern strategies of enamel regeneration including self-assembling peptides, nano – hydroxyapatite, biomimetic approach and chemical approach have shown encouraging results.
- By applying these methods, the defective parts of tooth enamel can be regenerated and the degeneration of tooth enamel can be repaired.

References

1. Murray PE, Garcia – Godoy F, Hargreaves KM. A review of current status and a call for action. J Endod 2007;33(4):377 – 390.
2. Baum BJ, Mooney DJ. The impact of tissue engineering on dentistry. J Am Dent Assoc 2000; 131(3):309 – 318.
3. Baum BJ. Biomedical research, oral medicine, and the future. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94(2):141 – 142.
4. Hermann BW. On the reaction of the dental pulp to vital amputation and calxyl capping. Dtsch Zahnarztl Z. 1952;7(24):1446 – 1447.
5. Moradian - Oldak J. The regeneration of tooth enamel. Dimens Dent Hyg 2009;7(8):12 – 15.
6. Iijima M, Moradian – Oldak J. Control of apatite crystal growth in a fluoride containing amelogenin rich matrix. Biomaterials 2005;26(13):1595 – 1603.
7. Fan Y, Sun Z, Wang R, Abbott C, Moradian – Oldak J. Enamel inspired nano composite fabrication through amelogenin supra molecular assembly. Biomaterials 2007;28(19):3034 – 3042.
8. Kirkham J, Firth A, Vernals D, Boden N, Robinson C, Shore RC *et al*. Self – assembling peptide scaffolds promote enamel remineralization. J Dent Res 2007;86(5):426 – 430.
9. Yin Y, Yun S, Fang J, Chen H. Chemical regeneration of human tooth enamel under near – physiological conditions. Chem Commun 2009;21(39):5892-4.
10. Jayasudha, Baswaraj, Navin HK, Prasanna KB. Enamel Regeneration – Current Progress and Challenges. J Clin Diagn Res 2014;8(9):6-9.

Corresponding Author

Dr. Rishika
Post Graduate Student,
Department of Pedodontics & Preventive Dentistry,
Teerthanker Mahaveer Dental College & Research Centre, Moradabad, Uttar Pradesh, INDIA
Email id: rishika.choudharygill@gmail.com