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COMMENTARY

Dental & Craniofacial Research

Enamel once formed can never be replaced

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Such is the complexity of human body that although being one of the hardest substances in nature, enamel still has its existence dependent on constant demineralization and remineralization within the oral cavity and in spite of years and years of research, its replacement is still an issue.

Enamel regeneration is not possible because ameloblasts that form it are lost after the tooth eruption. Various treatment protocols till date use the synthetic materials are unable to mimic the natural enamel. The thorough understanding of amelogenesis along with recent research in material science has shown a way for formation of synthetic enamel. The understanding of enamel formation and knowledge of protein interactions and their gene products function makes possibility for biological based enamel regeneration.

Amelogenesis is a highly regulated process where a complex protein mixture is synthesized into the extracellular space, along with protein-protein interactions, protein mineral interactions and interactions involving the cell membrane. Amelogeninis the most abundant protein and acts as a key factor in controlling the orientation and elongated growth of enamel rods during the mineralization process. Ameloblastin, is a non-amelogenin enamel-specific glycoprotein, and it, functions as a cell adhesion molecule for ameloblasts. Enamelin and tuftelin proteins are thought to control apatite nucleation and growth in conjunction with amelogenin. Amelogenin and other enamel proteins are eventually degraded by the action of proteinases such as enamelysin (MMP-20) and kallikrein 4 (KLK4) at different stages of amelogenesis.

Various notable efforts in synthesis of enamel happening round the globe are like; Chen et al. fabricated fluoapatitenanorods that resembled enamel prism like structures from a supersaturated chemical solution under physiological condition. These nanorods have similar characteristics to those of natural enamel crystals isolated from rat incisor enamel. Then Yin et al., regenerated enamel like microstructures using a simple chemical approach, which may be a potential clinical application to repair enamel damage in dental clinics. Also Zhang et al. have achieved an ordered dental enamel-like structure of hydroxyapatite (HAP) through a solution mediated solid-state conversion process with organic phosphate surfactant and gelatin as the mediating agent.

Stephen Mann and colleagues prepared electrospun hydrogel mats of amorphous calcium phosphate and polymer nano and micro fibres. These mats generated HAP crystals as an immediate layer, which covered the enamel surface. Hence, it could be used for regrowing the lost enamel. Ying et al. used an agarose hydrogel method, which mimics the natural enamel at secretory or matrix formation stage. This biomimetic mineralization model regenerates enamel like prismatic structure with hardness similar to natural enamel.

Recently scientists from the University of Leeds found a way to mimic enamel matrix within enamel lesions and thus enabling regeneration. They have patented their technology for enamel regeneration. The monomers of peptide p11-4 (curodont) forms a matrix that enables denovo enamel crystal formation from saliva in constant equilibrium with demineralization. In vivo studies revealed that the peptides were shown to decrease demineralization and show a strong trend toward increasing remineralization.

New strategies have been emerging based on the finding that amelogenin's ability to function in critical phases of biomineralization. Marinet proposed a cation selective membrane system to synthesize amelogenin-based composite under biomimetic conditions.

Presently investigators are interested in developing cell-based strategies to regenerate enamel. Regenerative treatment requires a stem cells, scaffold and growth factors.

Huang et al. studied the possibility of using synthetic and bioactive nanostructures that are known to self-assemble in physiologic environments into nanofibers network, in order to mimic the extracellular matrix that surrounds the ameloblasts.

Further study was done to elucidate the coupling response of integrin receptors to the biomaterial and gene expression profiles. Thus an insight into molecular mechanisms involved in enamel formation is there, which helps in designing synthetic regenerative approaches and to manipulate pathways to control enamel regeneration.

Honda et al. examined the enamel-forming capability of subcultured EOE cells, by transplanting cells onto a biodegradable scaffold in vivo and amelogenin immune-reactivity was detected

in tall columnar epithelial cells on the surface of the dentin or enamel, indicating that the tissue-engineered enamel contains well-developed ameloblasts. Together, these results indicate that the subcultured EOE cells have the potential to generate enamel.

This culture model provides a promising step towards a new therapy for reforming enamel. As EOE cells disappear in adult teeth after tooth eruption. Alternative cell source for enamel forming cells are epithelial cell rest of malassez, bone marrow cells, human embryonic stem cell derived epithelial cells, oral keratinocytes and skin epithelial cells.

Janet Moradian-Oldak, a professor at the Herman Ostrow School of Dentistry of USC and her team engineered a string of amino acids that contained only the parts needed for enamel crystal creation. Over seven days, the shorter peptide grew synthetic aprismatic enamel that was two times harder than the softened control enamel.

The shorter peptide developed have a few benefits over a longer one: It's economical, and would be easier to be approved from the U.S. Food and Drug Administration. The study was a proof of concept, but eventually the peptides could be incorporated into a gel. This could be painted on teeth with lost enamel and effectively replacing it.

Researchers at King's College London have been studying the effects of stem cells, specifically how to renew in order to facilitate dentine production, as reported in science daily. In their paper, "Promotion of natural tooth repair by small molecule GSK3 antagonists" published in Scientific Reports, they found that a drug currently in clinical trials to treat neurological disorders like Alzheimer's disease, Tideglusib, was effective in stimulating stem cells in the pulp to create dentine.

All these researches promise that the day is not far where treatment of caries would be more natural than use of synthetic materials and yes, "Enamel will be regenerated."

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