A systematic review of the impact of amelogenin peptides on periodontal regeneration

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Background

- Periodontitis is a gum disease that damages the periodontium, which is composed of cementum and bone as mineralized tissue, and of gum and periodontal ligament as soft tissues. This can result in tooth loss and esthetic displeasure.¹
- Periodontal regenerative therapies consist of regenerating these tissues, as part of the attachment apparatus.²
- Enamel matrix derivative (EMD) is a heat-treated preparation derived from enamel matrix proteins (EMPs) of developing porcine teeth. Amelogenin makes up 55% of its protein content.³
- Certain amelogenin splicing variants have significant positive effects on wound healing, bone formation and root resorption, making it the subject of many periodontal regeneration studies.⁴
- Disadvantages of using EMDs during therapeutic procedures are (1) the use of animal-derived preparations & (2) the use of complex proteins, which carry risks of animal-to-human transmission and antigenicity.⁵

This systematic review will primarily focus on recombinant and synthetic amelogenin variants and analyze their effects on periodontal regeneration, in order to better understand the individual effects of the EMD components.

Methodology

Identification

Records identified through database searching: PubMed (n=28)

Additional records identified through other sources (n=64)

Records after duplicates removed (n=64)

Records screened (n=64)

Records excluded (n=24)

Full-text articles assessed for eligibility (n=40)

Studies included in qualitative synthesis (n=32)

Included

Studies included in quantitative synthesis (meta-analysis) (n=0)

Screening

Parameters based on the characteristics of periodontal regeneration:
- (A) cell adhesion (5 studies)
- (B) proliferation (18 studies)
- (C) migration (10 studies)
- (D) mineralization (9 studies)
- (E) wound healing (1 study)
- (F) angiogenesis (4 studies)
- (G) differentiation (14 studies)
- (H) gene expression (9 studies).

Cell types that were studied:
- (I) human gingival fibroblasts (HGF) (2 studies)
- (J) periodontal ligament cells (PDL) (18 studies)
- (K) cementoblasts (8 studies)
- (L) mesenchymal stem cells (MSC) (3 studies)
- (M) human umbilical vein endothelial cells (HUVEC) (2 studies)
- (N) other types of cells and/or extracellular components (11 studies)

Tyrosine-rich amelogenin peptide (TRAP)
- no sig effect on (B) of (K) and (I).
- ↑(C) for (M) and (I).
- no sig effect on (D); ↑(F); ↑(H)

Synthetic amelogenin peptide (WYQQMIR)
- ↑ (B) of (J) and (L).
- ↑ (C) of (J); ↑(G); ↑(H); ↑(D).

Leucine-rich amelogenin peptide (LRAP)
- Contradicting results for (B) and (C) for (J) and (K).
- ↑(G); ↑(D)

Human recombinant amelogenin
- ↑(B) of (K) and (J) and (L)
- ↑(G) and (H)
- ↑(D) and (F)

Murine recombinant amelogenin
- ↑ (A) and (B) and (C) of (J)
- ↑ (G) and (D)
- Porcine recombinant amelogenin
- ↑ (A) of (I); ↑ (B) for (I) and (J)
- ↓ (C) of (I)
- ↑ (D)

Discussion

• Amelogenin products showed varied responses on different cell types and different characteristics of periodontal regeneration.
• No specific peptide elicits a response in all aspects of regeneration studied.
• It is the mixture of amelogenin products that will ultimately allow for targeted regeneration of periodontal tissues.
• Most of the studies tested recombinant variants of amelogenin, with only a few that tested a synthetic amelogenin peptide (WYQQMIR) and synthetic TRAP.
• Using synthetic peptides that are short decreases the chance of eliciting an immunological response, which helps to solve the limitations of enamel matrix derivatives (EMD), such as the therapeutically used Emdogain™.
• A limitation of the review is grouping the effects of some of the recombinants together when there was not enough information provided in the article to make distinctions.
• I.e. some articles did not specify exact molecular weights of the peptides that were being tested, so the reviewers had to make categorizations based on the contexts given and combine the effects in that manner.

Conclusions & Future Directions

• This review systematically summarizes the results of the research that has been conducted to find new and improved techniques for periodontal tissue regeneration.
• It will allow for synthetic amelogenin peptide mixtures to be developed so that they will target certain cell types and elicit various responses to counteract the effects of periodontitis.
• Developing synthetic peptides will eliminate the immunological response problems of EMDs as well as the need for animal-based derivatives in a more cost and time-effective manner.

References


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