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Review

Mechano-regulation of collagen biosynthesis in periodontal ligament

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ABSTRACT

Periodontal ligament (PDL) plays critical roles in the development and maintenance of periodontium such as tooth eruption and dissipation of masticatory force. The mechanical properties of PDL are mainly derived from fibrillar type I collagen, the most abundant extracellular component. The biosynthesis of type I collagen is a long, complex process including a number of intra- and extracellular post-translational modifications. The final modification step is the formation of covalent intra- and intermolecular cross-links that provide collagen fibrils with stability and connectivity. It is now clear that collagen post-translational modifications are regulated by groups of specific enzymes and associated molecules in a tissue-specific manner; and these modifications appear to change in response to mechanical force. This review focuses on the effect of mechanical loading on collagen biosynthesis and fibrillogenesis in PDL with emphasis on the post-translational modifications of collagens, which is an important molecular aspect to understand in the field of prosthetic dentistry.

Contents

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Abbreviations: PDL, periodontal ligament; ECM, extracellular matrix; Pro, proline; P4H, prolyl-4-hydroxylase; P3H, prolyl-3-hydroxylase; Lys, lysine; LH, lysyl hydroxylase; GGT, galactosylhydroxylysine-glucosyl transferase; GT, hydroxylysyl galactosyl transferase; LOX, lysyl oxidase; FACIT, fibril-associated collagens with interrupted triple helices; SLRPs, small leucine-rich proteoglycans; HPLC, high performance liquid chromatography; LC/MC, liquid chromatography–tandem mass spectrometry; FTIR, Fourier transform infrared.

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1. Introduction

Periodontal ligament (PDL) is a specialized soft connective tissue that attaches the tooth to the alveolar bone socket. This fibrous tissue is very dynamic with high cellularity and vascularity, and plays critical roles in the development and maintenance of periodontium. These include tooth support, regulation of tooth eruption, dissipation of masticatory forces, neurological feedback and orthodontic tooth movement. The mechanical properties of PDL are, thus, very important for these functions and they are mainly derived from the primary extracellular matrix protein; fibrillar type I collagen. One of the major characteristics of PDL collagen is its exceptionally high rate of turnover [1], which could be critical for tooth eruption and orthodontic tooth movement. One of the intriguing features of PDL is its ability to maintain the tissue without being mineralized despite the fact that it is connecting two specialized mineralized tissues, alveolar bone and cementum. Although this tissue is highly adaptive to external forces by temporarily changing the tissue space [2], the width remains relatively constant throughout its lifetime.

In daily prosthodontic practice, occlusion needs to be adjusted when a dental prosthesis is installed. The acceptable range of occlusal adjustment in natural teeth is generally considered to be ~30 μm because of the pressure displacement of PDL [3]. If the occlusal adjustment is performed inappropriately, it could cause widening of PDL space and increment of tooth mobility [4]. This clinical observation underscores the significance of optimum mechanical loading in the tissue maintenance of PDL. The expansion of PDL space and subsequent increase in tooth mobility are not only due to the expansion of PDL fibers, but also to the accelerated tissue turnover in response to mechanical loading [5]. Since fibrillar collagen is the predominant extracellular matrix (ECM) component of this tissue, it is important to understand how mechanical loading affects cells, subsequent collagen biosynthesis and tissue construction. Owing to recent advances in molecular and cellular biology and analytical technologies, it is now clear that collagen post-translational modifications are highly regulated by groups of specific enzymes, these modifications change in response to mechanical forces and ultimately affects collagen fibrillogenesis, stability and tissue mineralization [6–12]. This review focuses on the effects of mechanical loading on collagen biosynthesis and fibrillogenesis in PDL with emphasis on the post-translational modification of collagens.

2. Mechanical loading in PDL

The PDL is subject to various mode of mechanical loading in different clinical circumstances. For instance, occlusal loading is the intermittent jiggling force and orthodontic tooth movement is the continuous static force. Thus, when the effect of mechanical loading on PDL is investigated, it is utmost important to carefully consider the loading conditions (e.g. mode, magnitude and duration) and interpret the data. Kang et al. reported that 2D and 3D cultured PDL-derived cells showed different gene expression profiles in response to similar mechanical loading [13]. This indicates that the culture environment could also influence on cellular response. To analyze the effect of mechanical loading on PDL-derived cells in vitro, a number of investigators have used commercially available loading apparatus, such as Flexcell (Flexcell International Co., Hillsborough, NC) [14–19], Strex (STREX Inc., Okayama, Japan) [20,21] and general laboratory centrifuge [17,22,23], while others fabricated their own loading devices [24–27]. Since optimal mechanical loading varies depending on cell type, culture condition and loading mode, it is important to use well defined loading regimen with a thoroughly characterized loading apparatus. However, unfortunately, such characterization of loading apparatus has been often overlooked [28].

In animal studies, models such as excessive occlusal loading and orthodontic tooth movement are frequently used to analyze the effect of mechanical loading in PDL at the tissue level. Excessive occlusal loading condition can be created by bite-raising as reported by many groups [29–32]. However, with this model, loading conditions such as magnitude, frequency and profile of wave cannot be controlled. To overcome this limitation, a motor-controlled device has recently been developed [33]. Using this device, the recruitment of TRAP-positive osteoclasts and the increment of RANKL/OPG ratio, which illustrates the osteoblast-mediated osteoclast recruitment, were confirmed in a magnitude- and time-dependent manner. The orthodontic tooth movements have been simulated by inserting elastic rubber band between molars (Waldo method) [34] or by installing coil spring between incisor and molar [35]. In these models, the loading condition can be manipulated in a relatively well-controlled manner. Histological studies demonstrated that compression side of PDL showed destructive changes, while tension side revealed additive changes [35].