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Review Article

A Narrative Review of Intercellular Signaling Role in Dental Tissue Function

Kacper Nijakowski[1*], Martyna Ortarzewska[1], Jakub Jankowski[2], Anna Lehmann[1], Anna Surdacka[1]

[1]Department of Conservative Dentistry and Endodontics, Poznan University of Medical Sciences, 60-812 Poznan, Poland.
[2]Student's Scientific Group in the Department of Conservative Dentistry and Endodontics, Poznan University of Medical Sciences, 60-812 Poznan, Poland.

***E-mail** ✉ kacpernijakowski@ump.edu.pl

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ABSTRACT

This review examines the different types of cellular interactions in dental tissues, emphasizing both direct communication through structures like gap junctions and tight junctions, as well as indirect signaling involving soluble molecules such as growth factors, cytokines, and neurotransmitters. This review highlights the importance of these communication pathways in essential dental processes like tooth eruption, development, and periodontal tissue remodeling. It also addresses how the disruption of these signaling mechanisms is associated with a variety of dental conditions, such as craniofacial abnormalities, cavities, and gum diseases. Understanding the molecular details of cell communication is key to better comprehending the origins of these issues and exploring potential therapeutic options. Ultimately, a deeper knowledge of how cells communicate in dental tissues offers new insights into normal biological functions and paves the way for developing targeted treatments in dental medicine. This article summarizes the current understanding of cell communication processes, emphasizing their importance in dental biology and their implications for both clinical applications and future research.

Keywords: Dental tissue, Signaling pathway, Cell-to-cell communication, Craniofacial abnormalities

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Introduction

Cellular communication refers to the exchange of signals between cells, which can occur either through direct contact or via chemical messengers such as neurotransmitters and hormones. This exchange of information is essential for understanding the latest developments in signaling mechanisms and pathways that regulate cellular activities [1]. For an organism to develop and adapt, communication between its cells is vital. The growth of an organism is governed by its genetic code, which relies heavily on intracellular or intercellular signaling networks [2]. Effective integration and coordination among these signals are essential for the various physiological functions across the body's systems [3].

Mechanisms of cell communication

Cellular interactions can occur either directly or indirectly, with signals being transmitted over a distance through chemical messengers. These intricate mechanisms are crucial for maintaining homeostasis and ensuring the smooth execution of biological processes **(Figure 1)**. A method involves the secretion and detection the neurotransmitters, which act as messengers to transfer information between cells [4, 5]. When a neurotransmitter binds to its corresponding receptor on the surface of a target cell, it initiates a cascade of intracellular events that ultimately lead to a cellular response [6]. This process is essential for regulating cellular functions such as differentiation, proliferation, and survival. Another important form of

intercellular communication occurs through direct physical contact between cells. These interactions, including the release of neurotransmitters and direct cell-to-cell contact, allow cells to exchange information, coordinate their activities, and ensure the proper functioning of tissues and organs **(Figure 2)** [7]. This review examines the different types of cellular interactions within dental tissues, emphasizing both direct communication through structures like gap junctions and tight junctions, as well as indirect signaling involving soluble molecules such as growth factors, cytokines, and neurotransmitters. The review highlights the importance of these communication pathways in essential dental processes like tooth eruption, development, and periodontal tissue remodeling. It also addresses how the disruption of these signaling mechanisms is associated with a variety of dental conditions, such as craniofacial abnormalities, cavities, and gum diseases.

Materials and Methods

A thorough literature search was conducted using several academic databases, including Medline, PubMed, and ScienceDirect [8, 9]. The search utilized key terms such as “dental tissue” “cell-to-cell communication,” [10], “craniofacial abnormalities” “signaling,” and to identify relevant studies.

The inclusion criteria for selecting studies were as follows: case-control studies, randomized controlled trials, systematic reviews, meta-analyses, and expert opinions. Only studies published in English were considered, and the research had to be conducted in vivo, specifically involving human subjects.

Studies were excluded from the review if they were narrative reviews, survey-based studies, published in other languages, not English, or involved in vitro research. This ensured that the review focused on high-quality studies directly related to the topic.

Results and Discussion

Cell-to-cell communication is fundamental in regulating various biological processes, including those involved in dental procedures. For example, the release of cytokines by platelets plays a key role in maintaining homeostasis by attracting mesenchymal stem cells, which then differentiate into osteoblasts, essential for bone formation [11]. After a tooth extraction, the socket is filled with blood, providing a medium for the formation of new bone tissue, which typically takes about six months to fully regenerate. This ongoing communication between cells is crucial for the body's proper function [12].

One important example of cellular response during dental procedures involves periodontal ligament (PDL) fibroblasts [13]. These cells are responsible for securing the tooth in place by linking the tooth root to the surrounding bone [14]. When dental work is performed, PDL fibroblasts are activated, playing a critical role in tissue healing. Additionally, osteoblasts, another cell type in the oral cavity, contribute to the healing process. Dental pulp stem cells, found within the tooth’s pulp, also react to signals during dental interventions [15, 16].

Understanding how these oral cells—osteoblasts, periodontal ligament fibroblasts, and dental pulp stem cells—respond to various signals is crucial for optimizing healing and regeneration during dental treatments. This insight helps enhance the effectiveness of dental procedures by supporting tissue repair and regeneration [17, 18].

The role of cell communication in clinical dentistry

Cellular signaling plays a vital role in various physiological processes, including those critical to dental treatments. For instance, the cytokines produced by platelets are involved in regulating homeostasis by attracting mesenchymal stem cells, which then differentiate into osteoblasts responsible for bone regeneration [11]. After a tooth extraction, the socket is initially filled with blood, and over the next few months, bone cells begin the process of rebuilding the lost tissue. This repair process typically takes about six months, emphasizing the importance of continuous cell-to-cell communication for proper bodily function [12].

A notable example of oral cells responding to signals during dental procedures are the fibroblasts of the periodontal ligament (PDL) [13]. These cells play a pivotal role in ensuring the tooth remains stable within the socket by attaching the tooth root to the surrounding bone [14]. During dental procedures, PDL fibroblasts are activated and contribute significantly to the healing process. Osteoblasts, another type of cell, are also essential in the repair and regeneration of bone tissue. Additionally, dental pulp stem cells, located within the pulp tissue of the tooth [16], also respond to signaling during dental treatments [15].

For optimal healing and tissue regeneration following dental procedures, understanding the response of oral cells—such as PDL fibroblasts, osteoblasts, and dental pulp stem cells—is crucial. Recognizing how these cells react to signaling molecules and stimuli can help ensure successful dental treatments and promote effective tissue repair [17, 18].

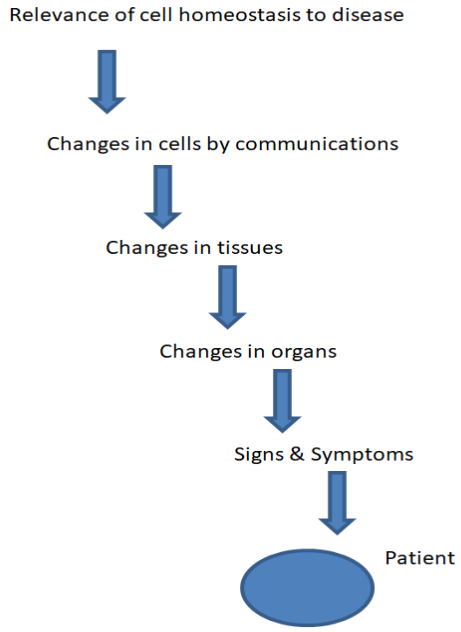

Figure 1. Stages of cell communication and changes occurring in the cell homeostasis process explain the signs and symptoms of how it appears on the patient.

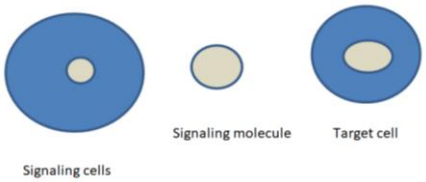

Figure 2. Cell communication through signaling molecules.

Pulp injury

The dental pulp is frequently subjected to trauma or exposure during procedures such as the preparation of teeth for bridge abutments, restorations, or the treatment of cavities [19]. When the pulp is exposed due to damage to the odontoblast layer, the formation of a dentin bridge can assist in the healing process. This healing requires the activation of progenitor cells capable of differentiating into odontoblasts. If no infection is present, the body may naturally initiate reparative dentinogenesis. Several materials have been explored to stimulate the production of reparative dentin **(Figure 3)**.

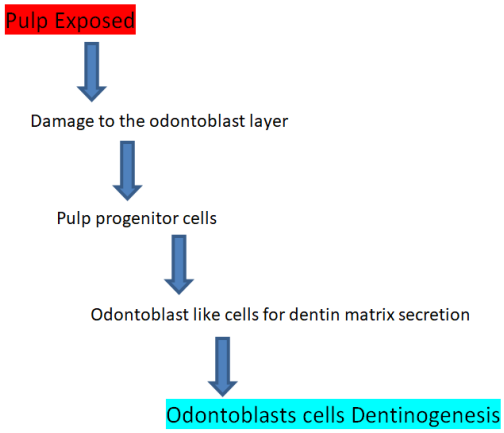

Figure 3. Process showing the odontoblasts cells the form (dentinogenesis process)

Tooth movement in orthodontics

When mechanical forces are applied during orthodontic treatment, pro-inflammatory signaling, involving cytokines, triggers bone-lining cells, known as passive osteoblasts, to respond. This mechanical strain prompts osteoclast precursors to differentiate into osteoclasts, which are responsible for resorbing bone. The "pressure-tension theory," which links the application of "physiologic" forces to changes in the periodontal ligament (PDL), including compression and tension, alongside the activation of mesenchymal stem cells (MSCs), was pivotal in advancing the understanding of cell involvement in orthodontic tooth movement (OTM) [20].

The inflammatory signaling caused by cytokines leads to the retreat of osteoblasts from the bone surface under mechanical stress, while osteoclast precursors are recruited and transformed into osteoclasts that resorb bone. These osteoclasts attach to exposed ligands, for example, osteopontin, on the bone matrix surface via specific receptors [8, 21-24]. This process results in the creation of Howship's lacuna, a distinct sign of bone resorption. Following this, bone formation occurs during the phase, with osteoblasts depositing new bone matrix once osteoclasts vacate the area [25-32]. The processes of bone resorption and apposition are intricately connected **(Figure 4)**. As noted by Bonewald [33], osteoclasts play a critical role in regulating bone remodeling. Additionally, sclerostin (SOST), a molecule that inhibits bone growth, is produced in response to mechanical forces, further demonstrating the role of cell-to-cell communication in the periodontium [34].

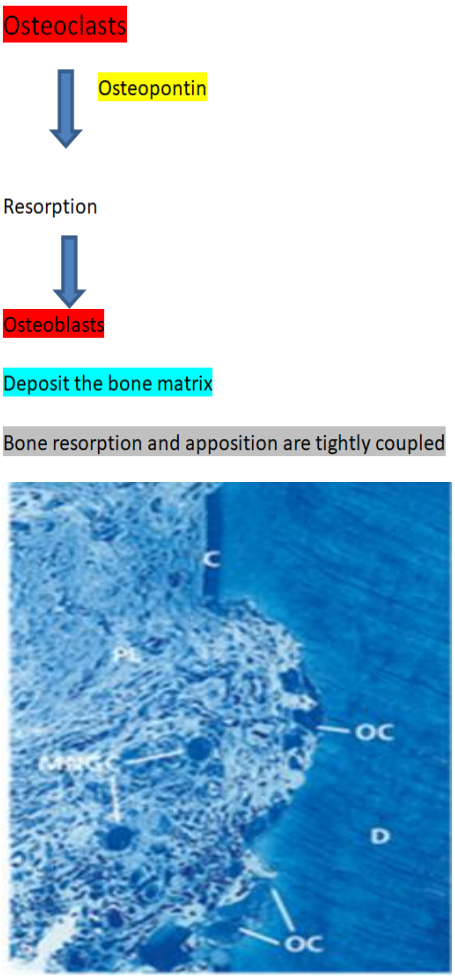

Figure 4. Bone resorption and apposition.

Cells rely on various channels to receive information and process it from both external sources and neighboring cells, with different cellular components facilitating communication with their environment [35].

In indirect communication methods, cells can also engage in direct physical interactions. This form of communication is especially critical in the immune system, the place where cells must cooperate to recognize and eliminate pathogens. Immune cells can form structures known as immunological synapses, which enable the exchange of signals and coordination of immune responses. Another means of communication is through the uptake and release of extracellular vesicles, which are integral to cellular signaling [36]. These signaling pathways are essential in all clinical dental practices aimed at promoting restoration, healing, and function, such as the repair of damaged tissues (oral mucosa, teeth) and the improvement of functions (jaw movements, tooth alignment, and occlusion).

In the context of oral tissue development, signaling pathways play a crucial role in embryology. Dental pulp stem cells (DPSCs) are unique in their ability to differentiate into various cell types, including odontoblasts, which contribute to dentin formation and can aid in dental regeneration. During dental procedures, the response of oral cells like osteoblasts, periodontal ligament fibroblasts, and dental pulp stem cells is vital for promoting effective healing and tissue regeneration [16].

The nature and severity of damage, whether from trauma or decay, significantly influence the pulp's response. In cases of reparative dentin formation, progenitor cells must be recruited from the pulp and differentiated into odontoblast-like cells to secrete additional dentin matrix. Conversely, moderate pulp injuries that involve reactive dentin require less intervention, as existing odontoblast cells are simply stimulated to produce dentin. If the injury is not severe enough to damage the odontoblast layer, tertiary dentin is produced to protect the pulp. The activation of these processes is heavily reliant on cell signaling [18].

Dental pulp regeneration is supported by DPSCs, which include progenitor stem cells capable of regenerating dentin by developing into odontoblast-like cells. Additionally, periodontal ligament stem cells (PDLSCs) with a specific phenotype serve as an important source of autologous stem cells that enhance dental regeneration. Studies have shown that coculturing endothelial cells with DPSCs can improve their odontogenic potential and promote the formation of blood vessel-like structures by the endothelial cells. However, the interactions between extrinsic signals and intrinsic factors in these systems remain unclear. In one coculture experiment, PDLCs exhibited significantly more elevated gene expression compared to DPSCs, suggesting that additional genes are involved in maintaining the pluripotent and nonmineralized states of PDLCs. This could be due to PDLCs' ability to maintain the necessary balance for cementum and bone formation while remaining nonmineralized. Identifying the exact signaling mechanisms that govern cell-to-cell communication in these systems is essential, as the culture environment can significantly influence cell properties [37-39].

In a study by Peng *et al*. [39], it was noted that after 3 and 5 days of coculture, the rate of apoptosis in cells was reduced, and they entered a halt in the G0/G1 phase of the cell cycle. Additionally, there was a marked rise in the expression of Oct-4, Sox2, and c-Myc after 3 and 5 days of coculture. These observations are consistent with findings from our previous research. Our earlier studies explored the molecular interactions between pluripotency, cell reprogramming, and the cell cycle. It was discovered

that Oct-4 and Sox2 play a role in regulating the cell cycle through the expression of miRNA. The Myc family, known for its involvement in cell cycle regulation, can impact Cdk activity to control cell growth and trigger the S-phase in cells. Our results revealed that apoptosis, cell proliferation, and cell cycle regulation in DPSCs and PDLCs—whether cocultured or cultured separately—followed similar expression patterns. These results regarding the relationship between pluripotency, reprogramming, and the cell cycle were unexpected and require additional analysis. Another study indicated that inhibiting the proliferation of somatic cells might improve the generation of induced pluripotent stem cells.

Conclusion

The process of cell communication is fundamental to regulating a wide range of functions within the human body.

Dentists should possess a deep understanding of the biological cellular mechanisms that underlie clinical procedures to ensure effective and successful treatment outcomes.

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