Review Article

CELL TO CELL COMMUNICATION AND RELEVANCE TO DENTAL TISSUE; A NARRATIVE REVIEW

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ABSTRACT

This review explores the diverse modes of cell communication in dental tissues, encompassing direct cell-to-cell interactions through gap junctions and tight junctions and indirect signaling mediated by soluble factors like cytokines, growth factors, and neurotransmitters. Particular emphasis is placed on the role of cell communication in key dental processes, including odontogenesis, tooth eruption, and periodontal tissue remodeling. Furthermore, the dysregulation of cell communication pathways is implicated in various dental disorders, including caries, periodontal diseases, and craniofacial abnormalities. Understanding the molecular intricacies of cell-to-cell communication provides valuable insights into the etiology and potential therapeutic interventions for these conditions. In conclusion, deciphering the complexities of cell-to-cell communication in dental tissues enhances our understanding of normal physiological processes and offers promising avenues for targeted therapies in dental medicine. This review consolidates current knowledge on cell communication mechanisms, shedding light on their relevance to dental tissue biology and their potential implications for clinical practice and future research endeavors.

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

Introduction

Cell communication

The process by which an organism's living cells exchange messages directly or by using neurotransmitter chemicals like hormones. The context of specific cell types and activities is used to consolidate and provide the most recent findings on cell signals and signal pathways [1]. For an organism to differentiate and evolve, cellular communication is crucial. An organism's genetic programming, always based on intercellular and intracellular signaling pathways, drives its growth [2]. Integration and coordination are necessary for the body's systems to engage in various activities [3].

How cell communication occurs

Cells may interact with one another directly or indirectly by chemical signals at a distance. Through many complicated mechanisms, cells interact with one another to maintain homeostasis and coordinate various biological activities **(Figure 1)**. One such mechanism is releasing and detecting chemical signals called neurotransmitters. These neurotransmitters act as messengers, carrying information from one cell to another [4, 5]. When a cell receives a neurotransmitter, it binds to specific receptors on its surface, triggering a series of events inside the cell that ultimately lead to a response [6]. Cell communication is crucial for coordinating cell proliferation, differentiation, and survival functions. Another crucial mode of intercellular communication involves direct physical contact between cells. Cells communicate with each other through a variety of mechanisms, including the release and detection of neurotransmitters and direct physical contact. Through these processes, cells can exchange information, coordinate their actions, and maintain the proper functioning of tissues and organs **(Figure 2)** [7].

Materials and Methods

A literature review was performed using PubMed, Medline, and ScienceDirect databases [8, 9]. The keywords used were cell-to-cell communication, dental tissue [10], signaling, and craniofacial abnormalities.

Inclusion criteria

- Case-control and randomized control studies, Systematic reviews, meta-analyses, or expert opinions.
- English language of publication
- In vivo (humans)

Exclusion criteria

- Narrative reviews
- Survey-based studies
- Language other than English
- In vitro

Results and Discussion

Clinical relevance of cell communication (signaling) in clinical dental practice

Cell-to-cell transmission causes development factors. For example, the homeostasis processes of the cytokines generated by platelets are used to attract mesenchymal stem cells and drive them to develop into osteogenic cells [11]. After the extraction, the socket will be mostly filled with blood, and then the bone cells start to form new bone; reconstructing it takes six months. Only because cells are in continual communication with one another can the body operate correctly [12].

One example of an oral cell that responds to signals during dental procedures is the periodontal ligament fibroblasts [13]. These cells are responsible for maintaining the stability of the tooth within the socket by attaching the tooth root to the surrounding bone [14]. PDL fibroblasts are activated during dental procedures and play a crucial role in the healing process. Another essential cell involved in dental procedures is the osteoblast. Another oral cell that responds

to signals is the dental pulp stem cells [15]. These cells are found within the dental pulp, the tissue inside the tooth [16]. To promote proper healing and tissue regeneration during dental procedures, it is essential to consider the response of oral cells, such as periodontal ligament fibroblasts, osteoblasts, and dental pulp stem cells [17]. To promote successful dental procedures and tissue regeneration, it is crucial to understand the response of different oral cells, such as periodontal ligament fibroblasts, osteoblasts, and dental pulp stem cells, to signals and stimuli [18].

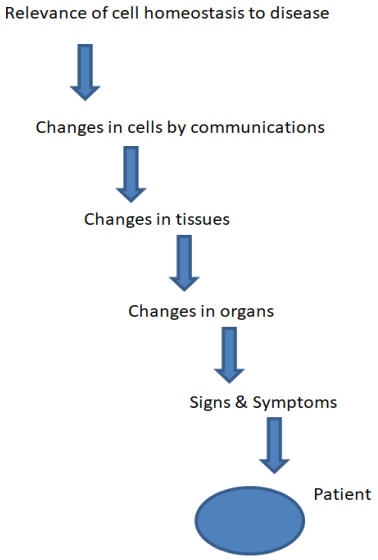

Figure 1. Stages of cell communication and changes occurring in the cell Homeostasis process explain the signs and symptoms of how it appears on the patient.

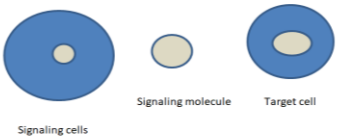

Figure 2. Cell communication through signaling molecules.

Pulp injury

The pulp of teeth is often traumatized or exposed while preparing them for bridge abutments, dental restorations, or caries treatment [19]. A dentin bridge may aid in the healing process when the pulp becomes exposed due to damage to the odontoblast layer. However, doing so requires the recruitment of progenitor cells with the ability to develop into odontoblasts. In the absence of microorganisms, reparative dentinogenesis may occur naturally. Various substances have been used to promote the production of reparative dentin **(Figure 3)**.

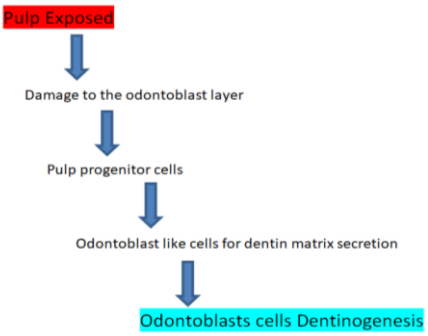

Figure 3. Process showing the odontoblasts cells the form (Dentinogenesis Process)

Tooth movement in orthodontics

The bone-lining cells (passive osteoblasts) are induced by pro-inflammatory signaling that involves cytokines when subjected to mechanical strain. Osteoclast precursors give rise to osteoclasts that may resorb bone. The "pressure-tension theory," which connected the application of "physiologic" force to PDL compressional and tensional changes and the consequent activation of Mesenchymal stem cells (MSCs), made the majority of orthodontists aware of the function of cells in orthodontic tooth movement (OTM) [20].

Pro-inflammatory signaling involving cytokines causes the passive osteoblasts that line the bone to retreat in response to mechanical pressure, and osteoclast precursors are attracted and develop into bone-resorbing osteoclasts. Osteoclasts attach themselves to exposed ligands (such as osteopontin) on the surface of the denuded bone matrix via receptors [8, 21-24]. On the bone surface, they dig a convex resorption cavity known as the Howship's lacuna, a clear morphological and physiological indicator of resorption. Bone apposition occurs after bone resorption during the reversal phase [25-32]. Osteoblasts deposit the bone matrix after osteoclasts have left the area. Apposition and bone resorption are closely related processes **(Figure 4)**. According to Bonewald (2011) [33], osteoclasts are crucial to the control of bone remodeling. Sclerostin (SOST), a negative regulator of bone growth, is produced in response to mechanical stimulation [34]. This is yet another excellent illustration of periodontium cell-to-cell communication.

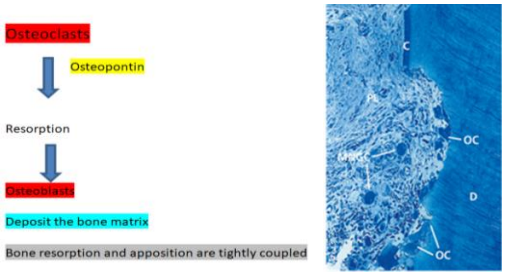

Figure 4. Bone resorption and apposition.

Many channels receive and process information from the outside world, from other cells in the body, and various parts of the cell serve as how cells communicate with their surroundings [35].

Another way cells communicate is through direct physical contact. This is particularly important in the immune system, where cells must work together to identify and destroy pathogens. Immune cells can form adhesive connections called immunological synapses, which allow them to exchange signals and coordinate their immune response directly. In addition to these direct communication mechanisms, cells can communicate through the release and uptake of extracellular vesicles [36]. These signaling pathways are crucial in all clinical Dental Procedures that aim for good practices, restoration, or healing of damaged tissue/organ (oral mucosa, tooth) or function (tooth alignment, jaw movements, and occlusion). Role of Signaling Pathways in Oral Tissue's Embryology.

The capacity to develop into multiple cell types, such as odontoblast cells, which form dentin and may aid in dental repair and regeneration, is a unique quality of dental pulp stem cells (DPSCs). To facilitate appropriate healing and tissue regeneration, it is crucial to consider the reaction of oral cells during dental operations, including osteoblasts, periodontal ligament fibroblasts, and dental pulp stem cells [16].

The extent and duration of dental damage, whether caused by trauma or caries, greatly affects the following pulp response. Whereas the reparative dentin has to recruit pulp progenitor cells and differentiate them into odontoblast-like cells to secrete more dentin matrix, the reactive dentin in moderate pulp injuries merely needs to stimulate the already-existing odontoblastic cells [32, 37, 38]. To shield the recovering pulp from more damage, the cells are triggered to create tertiary dentin if the lesion is mild enough and does not destroy the odontoblast layer. Cell signaling is necessary to initiate each of these activities [18].

Because Dental Pulp Stem Cells (DPSCs) include progenitor stem cells, dental pulp can regenerate. Through the development of odontoblast-like cells, these cells are attracted and participate in the dentin regeneration process. Periodontal ligament stem cells (PDLSC) with a particular phenotypic profile serve as an invaluable source of autologous stem cells that promote dental regeneration. According to a publication, coculturing endothelial cells with (DPSCs) may improve the DPSCs' odontogenic qualities and encourage the endothelial cells' creation of blood vessel-like structures. However, the methods by which extrinsic signals and intrinsically active variables interact are still unclear. In the current coculture system, PDLCs had significantly more elevated genes than DPSCs. This suggested that more genes may be involved in preserving the pluripotent and nonmineralized states of PDLCs compared to DPCs. This finding might be explained by the fact that PDLCs can maintain the equilibrium required to form cementum and bone while remaining nonmineralized. It is necessary to identify the precise signals that control cell-cell communication since the culture environment may significantly impact cell properties [39].

After three and five days of coculture, Peng *et al*. (2021) cells underwent apoptosis at a downregulated rate and were stopped in their G0/G1 phase [39]. After three and five days of coculture, there was a significant increase in the expression levels of Oct-4, Sox2, and c-Myc. These findings closely matched those of our earlier investigation. A comprehensive examination of the molecular connections among pluripotency, reprogramming, and the cell cycle was covered in an earlier study. It has been shown that Oct-4 and Sox2 regulate the cell cycle via expressing miRNA. It has been shown that the Myc family includes distinct cell cycle progression regulators and may influence Cdk activity to control cell growth and induce S-phase in cells. According to our findings, the apoptosis rate in DPSCs and Periodontal ligament stem cells (PDLCs) with direct or indirect coculture exhibited a comparable expression pattern with proliferation. These results concerning the connections between pluripotency, reprogramming, and the cell cycle were surprising and needed further explanation. According to a different study, inhibiting the proliferation of somatic cells may enhance the production of induced pluripotent stem cells.

Conclusion

- *Cell communication* is a mechanism that regulates the various *functional* processes in the human body.
- The *practicing dentist* should have adequate knowledge of and pay great attention to the *biological cellular processes* that underpin clinical procedures.

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