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Pioneering Ligaplants: The Future of Biofunctional Tooth Implants – A Systematic Literature Review

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The Ligaplants concept represents a game-changing development in implant dentistry, blending the proven benefits of osseointegration with the dynamic, biologically active features of the periodontal ligament (PDL). Unlike traditional implants, which rely solely on the connection between bone and implant, Ligaplants integrate a functional PDL, offering the potential for enhanced biological integration, faster healing, and more natural tooth function. Traditional dental implants are rigid, lacking the flexibility and shock-absorbing properties of natural teeth. This lack of mobility can lead to complications such as bone loss, inflammation, and discomfort. In contrast, Ligaplants mimic the natural tooth roots movement, proprioception, and cushioning effect, helping to preserve surrounding bone and tissue health. This innovative design could revolutionize tooth restoration by providing a solution that better mirrors the biomechanics of natural teeth. Although early animal studies have shown promise in generating periodontal-like tissue around Ligaplants, further clinical trials, especially in humans, are essential to determine their long-term stability and success. There are still challenges, such as the complexity, cost, and time required for tissue-engineered implants, but rapid advancements in tissue engineering are bringing the possibility of biologically integrated, off-the-shelf tooth replacements closer to reality. If successful, Ligaplants could reshape the future of prosthodontics, offering more durable, natural, and functional solutions for tooth restoration. As research and technology continue to advance, Ligaplants hold the potential to redefine dental implantology, providing a future where tooth restoration not only replaces lost teeth but also restores the natural biological function of the human dentition.

Keywords: Dental implants, Periodontal tissue regeneration, Ligaplants, Osseointegration, Tooth transplantation, Implant surface modifications, Cell culture techniques.

1. Introduction

In modern dentistry, dental implants have become the preferred method for replacing missing teeth, increasingly superseding traditional fixed and removable partial dentures (1). The success of implants is influenced by several factors, including sufficient jawbone volume, the patient's overall health, the type of implant used, and the skill of the surgeon (2) [Figure 1].

However, significant challenges persist, particularly due to the lack of a periodontal ligament (PDL) attachment (3). The PDL, a vital soft, vascular connective tissue, plays a key role in the function of natural teeth, helping to distribute chewing forces, providing proprioception, and maintaining the dynamic relationship between the tooth and surrounding bone (4). Unlike natural teeth, dental implants are ankylosed to the bone, meaning they are rigidly fused and lack the mobility and shock-absorbing properties of the PDL. This absence can lead to inflammation and accelerated bone loss around the implant compared to natural teeth (5). This limitation has spurred extensive research into replicating or regenerating the PDL to enhance implant functionality (6). A landmark study by Buser et al. in 1990 demonstrated that titanium implants placed in contact with retained root tips could utilize the PDL cells from these roots to promote healing around the implant. This concept laid the foundation for tissue engineering, which has since seen considerable advancements (7). For example, Lin et al. successfully used autologous rat PDL cells to regenerate PDL tissue on titanium implants, incorporating a three-dimensional scaffold known as Matrigel. Their findings showed the formation of cementum-like tissue and PDL fibers, highlighting the potential for improved healing and integration (8). Despite the success of osseointegrated implants, which remain the most widely, used and have high long-term success rates, they still face challenges due to the lack of a functional PDL. The development of ligaplants, or periodontio-integratedtissue-engineered implants, offers a promising solution. These implants aim to recreate the natural PDL structure by combining PDL cells with implant biomaterials, potentially improving both bone integration and soft tissue attachment (9). The rising popularity of dental implants can be attributed to several factors, including increasing life expectancy, limitations of traditional prosthetics, and the proven effectiveness of implants in replacing lost teeth. However, many patients require bone reconstruction prior to implant placement due to local defects or insufficient bone quality (10). Additionally, localized bone loss and gingival recession remain clinical challenges that may necessitate further surgical intervention. The loss of natural teeth also results in the loss of PDL cells, which are critical for optimal healing around implants (11). As a result, osseointegration—the direct contact between the implant and bone—remains the primary goal. While this method ensures high success rates, the lack of a functional PDL remains a significant limitation (12). To address these challenges, researchers are exploring shock-absorbing systems and developing ligaplants, which integrate functional PDL tissue into the implant (13). These innovations hold promise for improving the healing process and ensuring better long-term outcomes. By closely mimicking the natural tooth attachment system, ligaplants could dramatically enhance implant functionality, offering superior shock absorption, better proprioception, and a more dynamic interface with the surrounding bone and soft tissue (14). This could reduce the risk of long-term bone loss, inflammation, and implant failure, positioning ligaplants as a transformative development in the future of dental implantology. While osseointegrated implants remain the gold standard in tooth replacement, the development of ligaplants—implants with integrated PDL tissue—could revolutionize the field. By replicating the natural tooth structure more closely, ligaplants offer significant advantages in terms of function, comfort, and long-term stability, making them a promising breakthrough in implant dentistry.This review highlights that ligaplants replicate natural tooth attachment, improving bone integration, soft tissue attachment, and implant longevity (15).

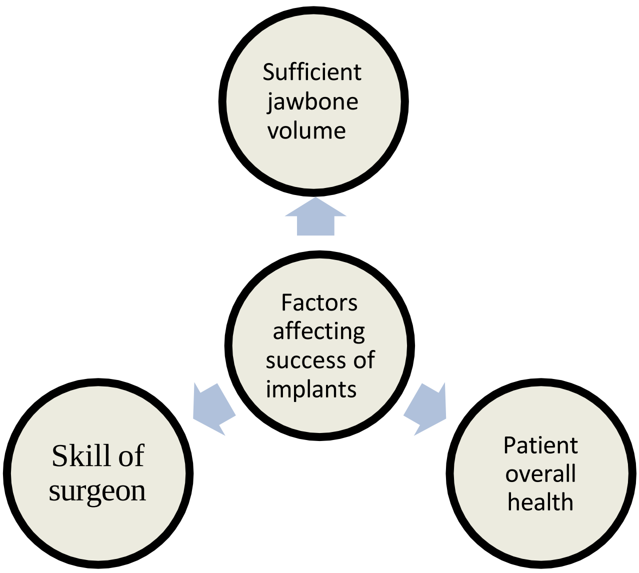

Figure 1: Factors influencing implant success and outcomes

2. Methodology

Search Strategy

This study employed a systematic search strategy to comprehensively explore the development, properties, and clinical potential of Ligaplants in dental implantology. The search aimed to identify relevant studies, clinical trials, and advancements in periodontal ligament (PDL) regeneration and implant technology. The strategy was designed to ensure an inclusive and thorough review of existing literature while focusing on quality and relevance.

Searches were conducted across multiple reputable databases, including PubMed, Scopus, Google Scholar, Web of Science, and the Cochrane Library. These databases were chosen for their comprehensive indexing of biomedical and dental research articles. To retrieve relevant studies, the search incorporated a combination of specific keywords and phrases such as “Ligaplants,” “osseointegration,” “periodontal ligament regeneration,” “tissue-engineered implants,” “implant surface modifications,” “shock absorption in implants,” and “proprioception in dental implants.” Boolean operators (AND, OR, NOT) were employed to refine and combine search terms for broader or more specific result coverage as needed.

Inclusion and Exclusion Criteria

The inclusion criteria were meticulously defined to ensure the relevance and quality of the selected studies. Peer-reviewed articles, clinical trials, systematic reviews, and meta-analyses focusing on dental implants with an emphasis on PDL regeneration or Ligaplant development were included. The date range was limited to the last 20 years, prioritizing recent advancements, and publications in English were considered. Both animal studies and human clinical trials were included to provide a comprehensive understanding of experimental and clinical findings. Conversely, studies unrelated to dental implants or periodontal ligament regeneration, anecdotal reports, and those with insufficient data or unclear methodologies were excluded.

The search process involved a multi-step screening approach. Titles and abstracts of retrieved articles were first reviewed to assess relevance. Subsequently, full texts of the shortlisted studies were comprehensively analyzed to ensure alignment with the research objectives. A manual search of the references cited in the selected studies was also conducted to identify additional relevant articles. Data from the included studies were extracted systematically, recording variables such as study objectives, methodology, implant material properties, PDL regeneration outcomes, and biomechanical testing results. These findings were organized in a tabular format for comparison and synthesis.

Quality Assessment

To ensure the reliability of the results, the quality of the included studies was assessed using standardized tools. The Cochrane Risk of Bias tool was employed for clinical trials, while the ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines were applied to animal studies. For systematic reviews, the AMSTAR (A Measurement Tool to Assess Systematic Reviews) criteria were used. The data synthesis process categorized findings under key themes, including tissue engineering approaches, clinical outcomes, and the biomechanical advantages of Ligaplants, providing a holistic understanding of their potential.

By employing this rigorous and structured approach, the methodology ensured a thorough and high-quality review of the literature, facilitating a detailed exploration of Ligaplants and their transformative role in dental implantology.

Prisma Flowchart of the Study is shown in [Figure 2].

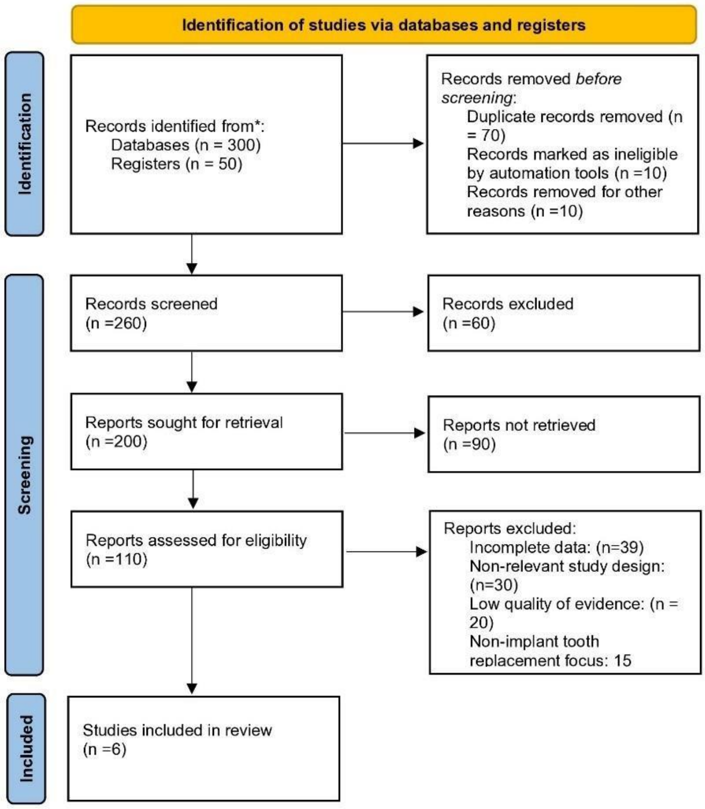

Figure 2: Prisma Flowchart of the Study

3. Review

The boom in implant dentistry can be attributed to several factors: the prolonged lifespan of aging individuals, failures associated with removable and fixed prostheses, and the advantages and predictable outcomes of implants (16). Dental implants have become ideal replacements for missing teeth, largely due to the process of osseointegration. Initially described by Brånemark et al., osseointegration was later defined by Albrektsson et al. as the direct contact between the implant and bone, ensuring stable fixation (17). For implants to be successful, factors such as sufficient bone height and width are crucial. However, local bone defects and poor bone quality often necessitate bone reconstruction prior to implant placement (18).Despite the success of conventional implants, challenges remain. One of the most significant clinical issues is localized bone loss around the implant, particularly in the case of gingival recession, which may require further surgical interventions. Furthermore, traditional implants lack the PDL, meaning any inflammation around the implant can cause more severe bone loss compared to inflammation around natural teeth (19). Additionally, because these implants are ankylosed, they do not have the same mobility as natural teeth, and the focus of implant placement is typically on osseointegration, rather than the regeneration of the periodontium around the implant (20).Ligaplants represent a groundbreaking advancement in implant dentistry. Ongoing ethical applications of Ligaplants are being tested both in vitro and in vivo, with animal studies showing promising results (21). These studies have demonstrated the feasibility of developing "periodontium-supported implants" that preserve the form, function, and proprioceptive responses similar to those of a natural tooth (22). The results from these experiments provide strong evidence that ligaplants have the potential to revolutionize implant dentistry. While in vivo results still require further validation, the clinical application of these implants holds great promise, offering a future solution that could be highly favored by patients due to their biological advantages and natural integration (23).

Properties of ligaplants

The PDL functions as a shock absorber, allowing slight tooth movement within the socket and providing proprioception[Figure 3]. It also plays a crucial role in the interaction with adjacent bone, acting as the periosteum on the bone side facing the root (24).

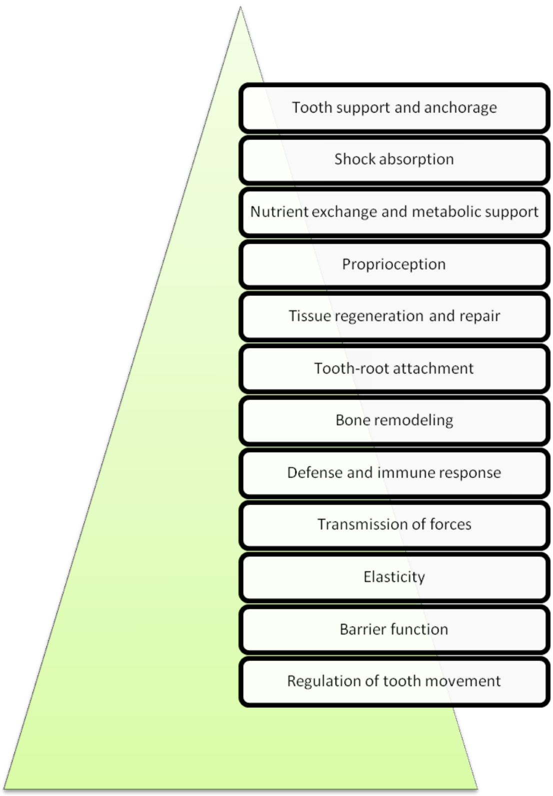

Figure 3: Functions of PDL

The PDL contains vital cells, including osteoclasts, osteoblasts, fibroblasts, cementoblasts, cementoclasts, and undifferentiated mesenchymal stem cells. These cells are essential for maintaining the dynamic relationship between the tooth and bone, facilitating both structural stability and tissue regeneration (25).

Procedure of making Ligaplants

Tooth transplantation with dual PDL stimulation is a promising technique demonstrating the healing potential of the periodontal tissues. In this process, the donor tooth is extracted and immediately replanted into its original socket, typically after being stored for 14 days (26). This deliberate trauma triggers a healing response within the PDL, leading to cellular proliferation and differentiation around the root. By the 14th day, the cellular activity peaks, and millions of cells, now attached to the root surface, contribute to the formation of new Sharpey's fibers. These fibers integrate with the surrounding tissues, facilitating healing and regeneration. This process can be performed biologically and clinically, using tissue engineering techniques to mimic the natural periodontal tissue formation around the root (27).

Studies supporting periodontium-integrated implants:

Buser et al. in 1990 demonstrated that titanium dental implants, when placed in contact with retained root tips, allow the PDL cells of the root to populate the implant surface during healing, aiding in the integration process (28). This finding has opened new avenues for periodontal regeneration, particularly in dental implant treatments, where various scaffolds and matrices have been effective in regenerating the entire periodontium (29). Further studies, such as Gault et al. in 2010, have explored ligaplants—combinations of PDL cells and implant biomaterials—for tooth replacement (30). In animal studies on mice and canine models, and human clinical investigations, ligaplants have shown promising results (31). For instance, in the canine model, PDL formation and a cementum-like tissue layer were observed on the ligaplant surface (32). In humans, radiographs indicated the formation of a desmodontal gap around a ligaplant, resembling the PDL space of a natural tooth (33). In the realm of periodontal regeneration, debates persist regarding which cell types are responsible for cementum formation on exposed root surfaces (34). Some studies suggest that cells residing in the alveolar bone contribute to cementum production, while others argue that only PDL cells can produce cementum. This underscores the critical role of PDL cells in the healing process, particularly around dental implants (35). Kiong and Arunkumar in 2014 highlighted the advantages of ligaplants over traditional osseointegration implants, noting that ligaplants promote periodontal tissue regeneration (36). The ligaplant procedure is less invasive as it doesn't require a tight fit in the socket, reducing the need for bone grafting and minimizing patient discomfort during placement (37). In summary, tooth transplantation with dual PDL stimulation is an innovative approach to periodontal regeneration, offering a promising alternative to conventional implant methods (38). It encourages natural tissue healing and integration around the implant surface.Ligaplants have shown promising results in both animal and human studies for tooth replacement and periodontal regeneration (39). [Table 1] provides a detailed comparison of the findings from each study, contrasting animal versus human model results, materials used, and key observationsThese studies collectively underscore the growing potential for Ligaplants and PDL regeneration in implant dentistry, offering new avenues for improving implant integration and restoring natural tooth function (30, 40-44)

Table 1: Studies onLigaplant and PDLregeneration

Author	**Animal Model**	**Human Model**	**Materials Used**	**Key Findings**
Gault et al. (30)	-	Yes	Ligaplants	Observed PDL formation around new ligaplants resembling tissue repair. Radiographs showed Ligaplants moved within bone. Desmodontal gap and normal PDL width maintained.
Nyman et al. (40)	-	Yes	Dental Implants	Confirmed the regenerative potential of PDL-derived cells. Formation of cementum-like tissue and PDL observed around dental implants.
Nunez et al. (41)	-	Yes	Dental Implants	PDL-derived cells showed potential to regenerate PDL. Cementum-like tissue and PDL formed near implants.
Takata et al. (42)	Animal Study	-	Bioglass, Hydroxyapatite	Bioactive materials promoted connective tissue attachment. Bioinert materials like titanium alloy showed poor connective tissue attachment.
Choi (43)	Canine	-	Cultured PDL Cells	Successful formation of cementum-like tissue and collagen fibers around implants using cultured PDL cells.
Kano et al. (44)	Canine	-	Hydroxyapatite-coated Titanium Implants	Tooth-shaped implants maintained PDL-like tissue when placed immediately after extraction, preventing osseointegration by preserving PDL-like tissue.

Preparation of temperature-responsive culture dishes

The polystyrene culture dishes are used and N-isopropylacylamide monomer in 2-propanaol solution is spread onto them. Then, the dishes are subjected to electron beam irradiation using an area beam electron processing system. The temperature-responsive polymer-grafted (poly nisopropylacrylamide) dishes are then rinsed with cold water, and ungrafted monomer is removed and then they are sterilized with ethylene oxide (45).

Cells and Cell Culture

The human PDL cells are isolated from an extracted tooth by scraping the periodontal tissue from middle third of the root with a scalpel blade. The harvested tissue was then placed into culture dishes containing Dulbecco's modified Eagle's minimal essential medium, supplemented with 10% fetal bovine serum, and 100 units/mL of penicillin streptomycin (46). Then, those outgrowth cells are cultured in a humidified atmosphere of 5% CO_2 at 37°C for 48 h to allow attachment of the cells to the dishes. The dishes are then washed to eliminate debris, and the medium is changed three times per week (47). To harvest the cell sheet, human periodontal ligament (PDL) cells are plated on temperature-responsive culture dishes (35 mm in diameter) at a density of 1×10^5 cells and cultured at 37°C, supplemented with 50 mg/mL ascorbic acid 2-phosphate, 10 nM dexamethasone, and 10 nM β-glycerophosphate, which function as an osteo differentiation medium (48).

Culture of Pdl Cells in a bioreactor

In this innovative bioreactor setup, a titanium pin coated with hydroxyapatite is placed within a hollow plastic cylinder, creating a 3 mm gap around the pin. Culture medium is continuously pumped through this gap, facilitating optimal nutrient exchange. Human-derived single cell suspensions are first seeded into plastic vessels and cultured under a flow of growth medium for 18 days. This system provides an effective environment for the growth and development of PDL cells, advancing the potential for tissue engineering applications (49).

Precautions taken during the preparation of ligaplants

To ensure the successful development of Ligaplants, it is crucial to maintain a cushion of sufficient thickness to support PDL formation, while avoiding prolonged cell culturing that could lead to non-PDL cell types. The bioreactor must be designed to mimic the natural PDL environment, with cells positioned in the narrow gap between the Ligaplant and the surrounding hollow cylinder, promoting tight cell attachment to the implant and favoring the PDL phenotype. Key guidelines for preparing Ligaplants include minimizing mechanical disturbances in the medium flow, optimizing the space between the implant and culture, and carefully controlling the duration of surface treatment. These measures collectively contribute to the successful integration of Ligaplants, offering significant advancements over traditional implant systems (50).

4. Discussion

Advantages of Ligaplants: Ligaplants offer significant advantages over conventional implants by addressing issues like gingival recession and bone defects at the site of the missing tooth. Unlike traditional implants, which cannot be used in cases of periodontal bone defects, Ligaplants can be successfully applied in these challenging situations (51). They mimic the natural insertion of tooth roots into the alveolar bone, allowing for integration without direct bone contact or interlocking, which preserves the PDL cushion. Despite an initial loose fit, Ligaplants facilitate bone formation and exhibit movement within the bone, indicating healthy tissue communication between the implant surfaces and surrounding bone. This design enhances implant stability while maintaining natural tooth function, offering a more biologically favorable alternative to traditional implants (52).

Disadvantages of Ligaplants:

Culturing ligaplants requires precise control over several factors, including temperature, cell selection, and culturing duration. Any disruption in these conditions can lead to the development of non-periodontal cells, which may compromise the success of the implant. Additionally, limited research facilities and resources contribute to the high cost of ligaplants. The unpredictability of the host's acceptance of the implant and the successful growth of the PDL in the socket further heightens the risk of implant failure (53).

Interphase of Implant and Periodontal Ligament Tissue:

Following implantation, tissue-specific characteristics are observed, including the formation of a cementum-like layer and proper orientation of cells and fibers across the nonmineralized peri-implant space. This organization of the PDL facilitates the integration of surrounding tissues, while bone formation indicates the osteogenic potential of the newly formed PDL (54). The regeneration of the PDL is guided by site-specific signaling, mediated by an anatomical code expressed through homeogene-coded transcription factors. These homeoproteins influence the synthesis of cell surface components and signaling molecules, with feedback mechanisms that modulate homeogene expression, determining cell identities according to the tissue type and anatomical site. For example, the homeogeneMs × 2 plays a role in segregating mineralized bone from nonmineralized PDL. Asporin, a small leucine-rich proteoglycan (SLRP) in the extracellular matrix, helps inhibit PDL mineralization (55).

Clinical Importance of Ligaplants:

Ligaplant represents an exciting new area of development in implant dentistry, aiming to improve the biological performance of implants by incorporating a tissue-engineered PDL around them (56). This approach offers significant advantages over traditional osseointegrated implants, including mimicking natural tooth mobility and shock absorption, and potentially reducing the need for bone grafting. The success of ligaplants depends on several critical elements [Figure 4] (57):

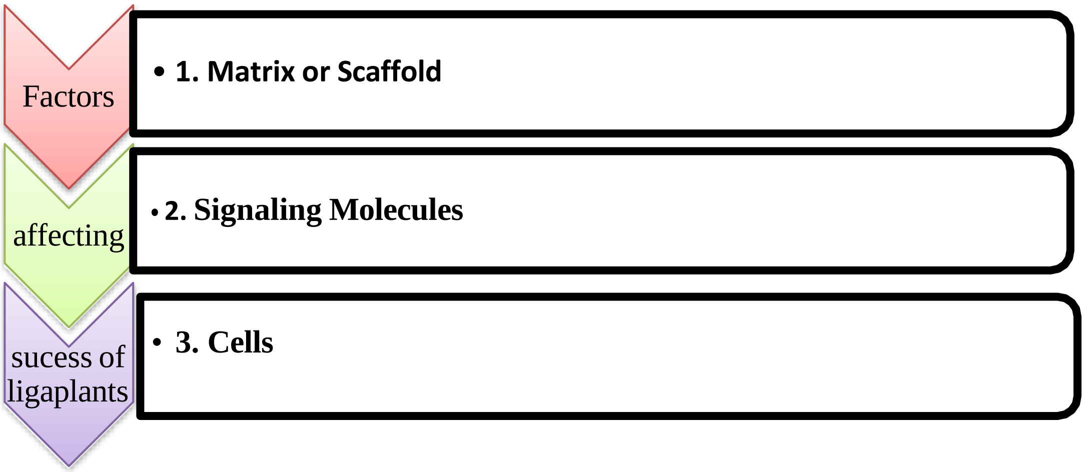

Figure 4: Critical Elements for Ligaplant Success

In vitro techniques involve cultivating cells on biodegradable scaffolds with signaling molecules, which are then transplanted into the body. In vivo techniques place cultivated tissues directly into a defect site, where they undergo natural healing and regeneration. The primary goal of both methods is to induce intrinsic healing activity at the tissue defect site. However, factors affecting host acceptance and PDL growth in the socket are unpredictable, and prolonged cell culturing may favor the appearance of non-PDL cell types, which may compromise implant success (58).

Risk Factors and Challenges:

While ligaplants show promise, their development is not without challenges. The growth of PDL around implants depends heavily on site-specific signaling, which is influenced by homeogene-coded transcription factors. These factors are essential for the synthesis of signaling components and cell surface molecules. However, the growth of PDL is often unpredictable, making it a significant risk factor for the success of the implant (59).

Success and Future Prospects of Ligaplants:

Ligaplant implants hold significant potential to revolutionize implant dentistry by offering more natural and functional integration with surrounding tissues (60). Unlike traditional osseointegrated implants, which can lead to periodontal tissue degeneration and a lack of flexibility, ligaplants aim to restore the mobility and shock absorption characteristics of natural teeth. This could enhance both the comfort and long-term performance of implants. While much of the research to date has been conducted in animal models, further clinical studies, especially human trials, are essential to evaluate the long-term stability and success of this promising technology (61).

Future Prospects:

1. Enhanced Implant Functionality:

One of the most exciting aspects of ligaplants is their potential to incorporate periodontal ligament (PDL)-like tissue, which would restore the natural mobility and shock absorption of teeth. This would make ligaplants feel more like natural teeth, enhancing patient comfort while reducing the risks associated with long-term bone loss and inflammation seen with traditional implants.

2. Improved Long-Term Outcomes:

The regenerative capacity of ligaplants is a game-changer for dental implants. By using tissue engineering to recreate a PDL, ligaplants could mitigate the complications typically associated with implant failure, such as peri-implantitis and bone loss. This could lead to more stable, long-lasting implants compared to current osseointegrated solutions.

3. Advancements in Tissue Engineering:

As tissue engineering techniques advance, the processes for creating and culturing PDL cells will become more efficient and cost-effective. This could increase the availability of ligaplants and lower treatment costs. Additionally, breakthroughs in biomaterials may lead to the development of personalized implants tailored to individual patient needs, further improving clinical outcomes.

4. Biological Integration with Bone and Soft Tissue:

Ligaplants aim to promote integration with both bone and soft tissue, addressing aesthetic concerns while improving oral health. This would be particularly beneficial for patients with advanced bone loss or that requiring significant bone reconstruction prior to implant placement. Enhanced biological integration could lead to better aesthetic outcomes and overall oral health (62).

5. Customization and Personalization:

With continued advancements in biotechnology, ligaplants could become highly customizable. Personalized implants tailored to a patient's specific anatomy would provide better clinical outcomes and reduce complications, especially for patients with complex cases involving extensive bone loss or compromised tissue health.

6. Challenges to Overcome:

Despite their potential, ligaplants face significant challenges. The precise control required during cell culturing and ensuring successful PDL growth is critical. Additionally, overcoming the unpredictable host response to implants is another hurdle. The high costs of research and the limited facilities for tissue engineering also present obstacles to making ligaplants a mainstream solution in dental practice (63).

5. Conclusion

Ligaplants represent a groundbreaking development in implant dentistry, merging the benefits of traditional osseointegration with the biological dynamics of the PDL. They offer a more functional and stable solution for tooth replacement, promoting tissue regeneration and enhancing implant integration with both bone and soft tissue. With the ability to mimic natural tooth function and reduce complications, ligaplants are poised to transform dental implantology.While research has predominantly been conducted in animal models, with promising results in generating periodontal-like tissue around implants, more extensive human clinical trials are needed to evaluate long-term success. Despite challenges in tissue engineering, such as high costs and technical limitations, the development of periodontio- integrated implants like ligaplants presents exciting opportunities. These advancements could lead to the creation of hybrid implants that combine living tissue with synthetic materials, potentially revolutionizing the future of dental implantology with more natural, functional, and durable solutions for tooth replacement.

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