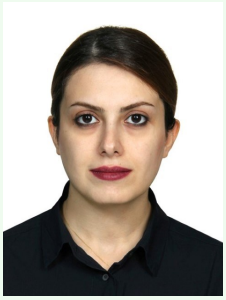
Life Sciences Student Journal
2025 Vol. 3 No. 4, pp : 60-67
10.22034/LSSJ.2025.198

Microenvironmental Control of Dental Implant Interface

Mahdis Nesabi[1], Sirus Safaee[2] and Mohammad Reza Nourani [3*]

1. .Department of Dental and Biomedical Materials Science, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan
2. Department of Prosthetic Dentistry, Graduate School of Biomedical Sciences, Nagasaki University, Japan
3. Tissue Engineering and Regenerative Medicine Research center, Baqiyatallah University of Medical Sciences. Tehran-Iran

*. Corresponding author: Mohammad Reza Nourani, r.nourani@yahoo.com



Mahdis Nesabi, PhD

Article type

Review

Received: 11 Nov. 2025
Revised: 12 Dec. 2025
Accepted: 20 Dec. 2025
ePublished: 25 Dec. 2025

Abstract

The dental implant interface (DII) constitutes a highly specialized and dynamic microenvironment that emerges immediately following implant placement and governs the biological success or failure of osseointegration. Distinct from native bone healing, the DII is shaped by the presence of a permanent foreign biomaterial, surgical trauma, host immune responses, and evolving mechanical stimuli. This review synthesizes contemporary evidence from periodontology, molecular biology, and biomaterials science to provide an integrated, phase-dependent framework of repair and osseointegration at the DII. We delineate the temporal progression of healing into hemostatic, inflammatory, proliferative, and remodeling phases, highlighting the molecular signaling networks, cellular dynamics, and mechanobiological cues that regulate each stage. Particular emphasis is placed on osteoimmunological mechanisms, including macrophage polarization and immune–bone crosstalk, as critical determinants of regenerative versus fibrotic healing outcomes. Additionally, the role of biochemical gradients, physicochemical conditions, and implant surface properties in directing protein adsorption, cell fate decisions, angiogenesis, and soft tissue integration is discussed. Translational implications for implant surface design, surgical protocols, and loading strategies are explored, underscoring the shift toward biologically intelligent and immunomodulatory implant systems. Finally, emerging approaches such as single-cell and spatial omics are presented as future tools to enable personalized implant therapy and improve long-term peri-implant tissue stability.

Keywords: dental implant interface; osseointegration; osteoimmunology; mechanobiology; peri-implant mucosa; implant surface.

Introduction

The dental implant interface (DII) represents a highly specialized microenvironment formed immediately after implant placement. Unlike native bone healing, this microenvironment is uniquely shaped by the presence of a foreign biomaterial, surgical trauma, and early mechanical stimuli. These factors collectively influence molecular signaling pathways that govern immune responses, angiogenesis, osteogenesis, and and peri-implant soft tissue integration. Understanding the DII as a dynamic, multi-factorial system provides insight into the mechanisms underlying successful osseointegration and offers avenues for biologically intelligent implant design. and informs strategies to prevent complications such as peri-implant mucositis and peri-implantitis.

Temporal Organization of Repair and Osseointegration at DII

Successful dental implant therapy relies on the establishment and long-term maintenance of osseointegration, a process that unfolds within the highly specialized microenvironment of the dental implant interface (DII). Unlike native bone healing, repair at the DII occurs in the presence of a permanent foreign biomaterial and is initiated by surgical trauma and early biomechanical conditions. Consequently, osseointegration represents a biologically regulated, time-dependent sequence of events involving coordinated cellular, molecular, and mechanical interactions rather than a passive bone–implant contact phenomenon(1–3).

Following implant placement, the DII undergoes a predictable but dynamic progression of repair that can be conceptually organized into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling. Each phase is characterized by distinct biological priorities and mechanobiological sensitivities that collectively determine the quality and stability of the hard and soft tissue implant interface. (2,4).

Hemostatic Phase (Minutes to Hours)

The initial hemostatic phase occurs within minutes to hours after implant insertion and is defined by blood clot formation and rapid protein adsorption onto the implant surface. This provisional fibrin matrix not only stabilizes the surgical site but also establishes the biological identity of the implant through selective adsorption of plasma proteins such as fibrinogen, fibronectin, and vitronectin(5,6). Platelet activation within the clot results in the localized release of growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and vascular endothelial growth factor (VEGF), which initiate chemotactic signaling and angiogenic responses(7). The mechanical stability of the implant during this phase is critical, as excessive micromotion can disrupt clot integrity and compromise subsequent cellular recruitment and interface maturation(8).

Inflammatory Phase (Days 1–7)

The hemostatic phase transitions into an inflammatory phase spanning approximately the first week after implantation. Parallel to osseous events, the early formation of a peri-implant mucosal seal begins, mediated by the adhesion and proliferation of gingival fibroblasts and epithelial cells, establishing a critical biological barrier against the oral microbiome. During this period, innate immune cells, primarily neutrophils and macrophages, dominate the DII microenvironment. While neutrophils contribute to early debridement, macrophages play a central regulatory role by orchestrating the balance between pro-inflammatory and pro-regenerative signaling (9). The polarization of macrophages from a classically activated (M1) phenotype toward a pro-healing (M2) phenotype is increasingly recognized as a decisive determinant of osseointegration versus fibrous encapsulation(10,11). Concurrently, angiogenic processes are initiated, enabling oxygen and nutrient delivery essential for subsequent osteogenesis. Implant surface chemistry and topography have been shown to modulate immune cell behavior during this phase, highlighting the emerging concept of osteoimmunomodulation at the DII (12).

Proliferative Phase (Weeks 2–8)

Between approximately two-eight weeks post-implantation, the proliferative phase is characterized by active osteogenesis and the formation of new bone at the implant interface. Concurrently, maturation of the supracrestal soft tissue complex occurs, with organization of a dense connective tissue zone and a well-adapted junctional epithelium, a process influenced by implant surface topography and emergence profile. Mesenchymal stem cells and osteoprogenitor cells migrate to the DII, differentiate into osteoblasts, and deposit osteoid matrix through both contact and distance osteogenesis (1,13). This process is driven by the activation of osteogenic signaling pathways, including bone morphogenetic protein (BMP), Wnt/β-catenin, and Runx2-dependent transcriptional programs(14,15). The newly formed bone is initially woven in nature and mechanically immature but establishes increasing bone, implant contact. During this phase, the interface remains highly sensitive to mechanical conditions, as excessive strain or micromotion may divert healing toward fibrous tissue formation rather than mineralized bone (8) (16)

Remodeling Phase (Months 2–12)

The final remodeling phase extends from approximately two months to one year after implantation and involves the gradual replacement of woven bone with organized lamellar bone adapted to functional loading. Osteoclast-mediated resorption and osteoblast-mediated bone formation occur in a tightly coupled manner, regulated by osteocyte-derived mechanosensory signals and the RANK–RANKL–OPG pathway (17,18). Functional loading during this phase plays a critical role in shaping peri-implant bone architecture, density, and long-term stability(19). Implant macrodesign and surface characteristics continue to influence stress distribution and bone maintenance, underscoring the long-term interaction between biomaterials and host tissue(20).

Within this complex microenvironment, repair and osseointegration do not occur as isolated events but rather as a temporally coordinated sequence of biological and mechanical processes. Conceptualizing DII healing as a time-dependent continuum provides a framework for understanding how early events dictate long-term implant stability. (Fig 1).

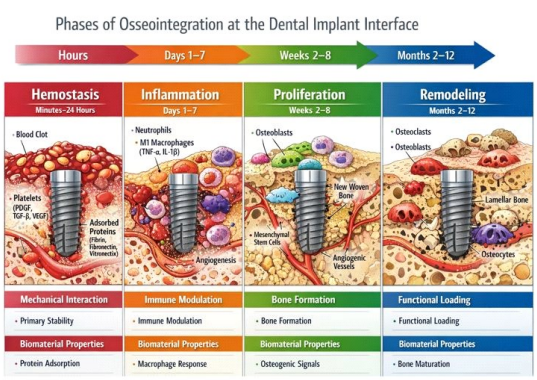


Figure 1. Temporal phases of osseointegration at the dental implant interface (DII).

Schematic representation of the phase-dependent repair process at the dental implant interface following implant placement. The hemostatic phase (minutes–hours) is characterized by blood clot formation, protein adsorption onto the implant surface, and platelet-derived growth factor release, establishing a provisional matrix under conditions of primary stability. The inflammatory phase (days 1–7) involves recruitment of innate immune cells, particularly macrophages, whose polarization and angiogenic signaling regulate the transition from inflammation to regeneration. During the proliferative phase (weeks 2–8), mesenchymal stem cells and osteoblasts drive woven bone formation through contact and distance osteogenesis in coordination with neovascularization. The remodeling phase (months 2–12) encompasses coupled osteoclast–osteoblast activity, leading to maturation of lamellar bone and functional adaptation under mechanical loading. Collectively, the figure illustrates osseointegration as a dynamic, mechanobiologically regulated process influenced by biomaterial properties and temporal biological cues.

Biochemical Microenvironment

The temporal progression of healing at the DII is underpinned by rapid and dynamic biochemical signaling, which establishes the molecular context for subsequent cellular recruitment, differentiation, and tissue integration. The initial biochemical milieu at the DII is dominated by blood-derived components, including fibrin clots enriched with growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and vascular endothelial growth factor (VEGF). These molecules regulate chemotaxis, angiogenesis, and osteoprogenitor recruitment through activation of PI3K/AKT, MAPK, and Smad signaling pathways. Spatial gradients of cytokines and growth factors evolve rapidly, determining the balance between osteogenesis and fibrous tissue formation(21–23).

Protein adsorption onto implant surfaces forms a biomolecular corona, which differs depending on surface chemistry and energy. This layer modulates integrin-mediated cell adhesion and downstream signaling, influencing early cell fate decisions. In the supracrestal region, adsorbed proteins also guide the attachment and proliferation of fibroblasts, influencing the quality of the peri-implant connective tissue attachment. (24).

Cellular Microenvironment

These biochemical gradients do not act in isolation but instead orchestrate the recruitment, activation, and phenotypic modulation of diverse cellular populations that collectively determine the regenerative outcome at the implant interface. The cellular composition of

the DII microenvironment changes dynamically during early healing. Neutrophils dominate the acute phase, followed by macrophages, mesenchymal stem cells (MSCs), endothelial cells, osteoblasts, fibroblasts, and epithelial cells. Crosstalk among these cells is mediated by cytokines, chemokines, and extracellular vesicles, including exosomes carrying microRNAs that regulate osteogenic and inflammatory gene expression(25,26)

Macrophages serve as central regulators. Their polarization state determines whether the interface favors regeneration or chronic inflammation. M2-polarized macrophages promote osteogenesis and angiogenesis via VEGF, BMP-2, and IL-10, whereas prolonged M1 dominance can impair osseointegration through sustained NF-κB activation and is also associated with the breakdown of soft tissue integration and initiation of peri-implant disease (23).

Soft Tissue Integration and the Peri-Implant Mucosa

Soft tissue healing and the establishment of a stable mucosal seal are critical for long-term peri-implant health. The peri-implant mucosa differs from the periodontal attachment in architecture and vascularity and is more susceptible to microbial ingress and inflammatory breakdown(27). Preservation of the early fibrin matrix and the pattern of protein adsorption onto transmucosal surfaces influence epithelial and connective tissue adhesion, guiding early soft tissue organization(6,28). Implant transmucosal design, surface wettability, and micro-/nanotopography modulate epithelial cell attachment and fibroblast orientation, thereby affecting the quality of the junctional epithelium and connective tissue cuff(12,29). Immune cells and resident osteal macrophages interact with soft tissue cells at the transmucosal interface; immunomodulatory surface properties can favor a pro-healing milieu that supports mucosal integrity and resists inflammatory breakdown(11,26). Atraumatic surgical handling, careful soft tissue management, and transmucosal designs that promote epithelial adhesion are therefore essential to maintain a robust mucosal seal that limits bacterial colonization and inflammatory penetration(12,27).

Mechanical Microenvironment

While cellular behavior is governed by molecular cues, it is simultaneously shaped by mechanical forces transmitted through the implant–bone interface, highlighting the inseparable nature of biological and biomechanical regulation during osseointegration. The mechanical microenvironment is defined by primary implant stability, interfacial strain, and micromotion. Mechanical cues are sensed by cells via integrins and cytoskeletal elements, activating mechanotransduction pathways such as focal adhesion kinase (FAK), RhoA/ROCK, and YAP/TAZ. These pathways influence osteogenic differentiation, matrix mineralization, and gene transcription (30,31). Emerging evidence suggests that these surface modifications may also enhance the sealing capability of peri-implant soft tissues by promoting fibroblast adhesion and collagen synthesis. Controlled mechanical stimulation enhances osteogenesis, whereas excessive micromotion (>100 μm) favors fibrous tissue encapsulation(32). Hence, mechanical and molecular signaling are tightly integrated to dictate healing trajectories.

Physicochemical Microenvironment

In parallel with mechanical stimuli, local physicochemical conditions further modulate cellular responses, influencing metabolic activity, inflammatory signaling, and mineralization processes at the DII. Physicochemical conditions at the DII include oxygen tension, pH, ionic composition, and surface charge. Early hypoxia activates hypoxia-inducible factor-1α (HIF-1α), promoting angiogenesis and coupling vascularization to osteogenesis. Local pH fluctuations influence osteoclast activity and mineral deposition.

Implant surfaces releasing bioactive ions such as Ca^{2+}, Mg^{2+}, and Sr^{2+} enhance osteogenic signaling and suppress inflammatory pathways. These ionic cues act synergistically with surface topography to regulate cell behavior at the molecular level(29,33) (Figure 2).

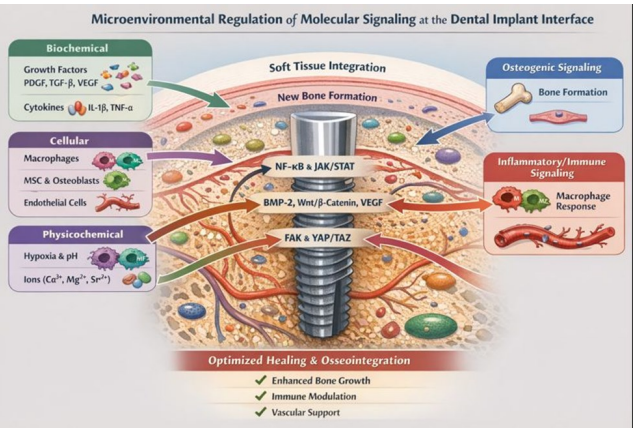


Figure 2. Microenvironmental Regulation of Molecular Signaling at the Dental Implant Interface (DII):

This conceptual illustration depicts the dynamic microenvironment surrounding a dental implant during early healing. The DII is regulated by coordinated biochemical, cellular, mechanical, and physicochemical cues, which collectively modulate molecular signaling pathways. Biochemical mediators, including PDGF, TGF-β, VEGF, IL-1β, and TNF-α, guide immune activation, angiogenesis, and osteogenic commitment. Cellular components—macrophages, MSCs, osteoblasts, and endothelial cells—sense surface properties and microenvironmental signals, promoting macrophage polarization, vascular ingrowth, and bone formation. Physicochemical factors, including hypoxia, pH fluctuations, and bioactive ions (Ca^{2+}, Mg^{2+}, Sr^{2+}), further regulate cellular behavior and matrix mineralization. Key intracellular pathways include NF-κB, JAK/STAT, BMP-2, Wnt/β-catenin, VEGF, FAK, and YAP/TAZ, ultimately promoting soft tissue integration, immune modulation, and stable new bone formation.

Immuno-Microenvironment and Osteoimmunology

Together, biochemical, mechanical, and physicochemical cues converge to shape the local immune landscape, positioning the DII as a quintessential example of osteoimmunological regulation. The DII exemplifies osteoimmunology, where immune responses and bone regeneration are tightly interconnected. Cytokines such as IL-17, TNF-α, and IL-6 influence osteoclastogenesis via the RANK/RANKL/OPG axis, while regulatory immune responses facilitate osteoblast activity. Implant surface modifications that promote a pro-healing immune microenvironment enhance early osseointegration (34).

Clinical and Translational Implications

A comprehensive understanding of the dental implant interface as a dynamic and phase-dependent microenvironment has important implications for contemporary implant therapy. Rather than viewing osseointegration as a binary outcome, clinicians must recognize that early biological and mechanical conditions critically shape long-term peri-implant bone stability and soft tissue integration.(4,35,36)

From a surgical perspective, optimization of primary stability and preservation of the early fibrin matrix are essential to support favorable biochemical and cellular signaling during the hemostatic and inflammatory phases [4,5]. Furthermore, meticulous soft tissue management to preserve keratinized mucosa and achieve primary wound closure is paramount to establish a healthy peri-implant mucosal barrier. Excessive compression, overheating, or early micromotion may disrupt immune polarization and angiogenic coupling, predisposing the interface to fibrous encapsulation rather than mineralized integration(8,37). These considerations are particularly relevant in compromised bone conditions, such as low-density posterior maxilla or immediate implant placement scenarios(38).

Implant surface design emerges as a key translational factor capable of actively modulating the DII microenvironment. These advanced surfaces may also play a preventive role against peri-implantitis by promoting a more resilient soft tissue seal and mitigating biofilm-induced inflammation. Surface topography, chemistry, and wettability influence protein adsorption, macrophage polarization, osteogenic differentiation, and mechanotransduction pathways (6,12,39). Immunomodulatory and ion-releasing surfaces represent promising strategies to enhance early osteogenesis while attenuating excessive inflammatory responses, especially in patients with systemic risk factors such as diabetes or smoking(11,40).

Loading protocols should be informed by the temporal sensitivity of the DII. Post-restoration, periodic

evaluation of occlusal forces remains a critical component of periodontal maintenance to prevent peri-implant biomechanical overload. While controlled mechanical stimulation during the proliferative and remodeling phases can enhance bone maturation and functional adaptation, premature or excessive loading during early healing may overwhelm the regenerative capacity of the interface(8,16). This reinforces the need for individualized loading strategies based on bone quality, implant design, and patient-specific biological factors(41).

Future translational advances integrating single-cell transcriptomics, spatial biology, and biomaterial engineering are expected to further elucidate microenvironmental heterogeneity at the DII (25,42). Understanding the DII microenvironment highlights the need for biologically intelligent implant designs that actively modulate local conditions. Furthermore, adjunctive therapies such as platelet-rich fibrin (PRF), growth factor applications, and local antimicrobial delivery systems are being investigated to positively steer the DII toward regeneration, particularly in complex or compromised cases. Strategies such as immunomodulatory surfaces, controlled ion release, and biofunctional coatings optimize the microenvironment during early healing. Future advances incorporating spatial transcriptomics and single-cell analyses will further elucidate microenvironmental heterogeneity, enabling personalized implant therapies(42).

Conclusion

Osseointegration at the dental implant interface is not a static phenomenon but a tightly regulated, phase-dependent biological process shaped by dynamic interactions among immune responses, cellular behavior, molecular signaling, and mechanical forces. Recognition of the DII as a specialized microenvironment underscores the importance of early biological events in determining long-term peri-implant bone stability and soft tissue integrity. Advances in osteoimmunology and mechanobiology reveal that immune modulation, particularly macrophage polarization, and controlled mechanical conditions are central to successful integration. Translational strategies that incorporate surface biofunctionalization, immunomodulatory design, and patient-specific loading protocols hold significant promise for improving clinical outcomes. Future integration of single-cell and spatial biological approaches will further refine our understanding of microenvironmental heterogeneity at the DII, enabling more personalized, biologically intelligent implant therapies aimed at long-term peri-implant health and disease prevention.

Achnowledgement

The conceptualization, research, analysis, and original writing were conducted by the author. The author utilized ChatGPT-4 (OpenAI) as a tool to assist in the following specific editorial and illustrative tasks: paraphrasing portions of the draft for clarity, restructuring certain sections for improved logical flow, and generating visual aids and schematic images. The final content, interpretations, and conclusions remain the sole responsibility of the author

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Author Contributions:

Nourani M.R. contributed to conceptualization, writing, original draft, and visualization. Sirus Safaei and Mahdis Nasabi are contributed to accumulated data, writing, review and editing. All authors have read and agreed to the published version of the manuscript.

References

1. P I Branemark BOHRAUBJLOHAO. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. 1977;16 (1):132.

2. Davies JE. Understanding peri-implant endosseous healing. J Dent Educ. 2003 Aug;67(8):932–49.

3. T. A, C. J. Osteoinduction, osteoconduction and osseointegration. European Spine Journal. 2001 Oct 1;10(0):S96–101.

4. Berglundh T, Abrahamsson I, Lang NP, Lindhe J. *De novo* alveolar bone formation adjacent to

endosseous implants. Clin Oral Implants Res. 2003 May 20;14(3):251–62.

5. Wilson CJ, Clegg RE, Leavesley DI, Pearcy MJ. Mediation of Biomaterial–Cell Interactions by Adsorbed Proteins: A Review. Tissue Eng. 2005 Jan;11(1–2):1–18.

6. Anselme K. Osteoblast adhesion on biomaterials. Biomaterials. 2000 Apr;21(7):667–81.

7. Marx RE. Platelet-rich plasma: evidence to support its use. Journal of Oral and Maxillofacial Surgery. 2004 Apr;62(4):489–96.

8. PILLIAR R. M. PH.D.; LEE JMPHD; MCDDS, MSc. Observations on the Effect of Movement on Bone Ingrowth into Porous-Surfaced Implants. Clin Orthop Relat Res. 1986;

9. Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. Semin Immunol. 2008 Apr;20(2):86–100.

10. Brown BN, Ratner BD, Goodman SB, Amar S, Badylak SF. Macrophage polarization: An opportunity for improved outcomes in biomaterials and regenerative medicine. Biomaterials. 2012 May;33(15):3792–802.

11. Miron RJ, Bosshardt DD. OsteoMacs: Key players around bone biomaterials. Biomaterials. 2016 Mar;82:1–19.

12. Hotchkiss KM, Reddy GB, Hyzy SL, Schwartz Z, Boyan BD, Olivares-Navarrete R. Titanium surface characteristics, including topography and wettability, alter macrophage activation. Acta Biomater. 2016 Feb;31:425–34.

13. Davies JE. Mechanisms of Endosseous Integration. International Journal of Prosthodontics. 1996;11(5):391.

14. Chen D, Zhao M, Mundy GR. Bone Morphogenetic Proteins. Growth Factors. 2004 Dec 7;22 (4):233–41.

15. Baron R, Kneissel M. WNT signaling in bone homeostasis and disease: from human mutations to treatments. Nat Med. 2013 Feb 6;19(2):179–92.

16. H M Frost 1. Wolff's Law and bone's structural adaptations to mechanical usage: an overview for clinicians. Angle Orthod . 1994;64(3):176–88.

17. Nakashima T, Hayashi M, Fukunaga T, Kurata K, Oh-hora M, Feng JQ, et al. Evidence for osteocyte regulation of bone homeostasis through RANKL expression. Nat Med. 2011 Oct 11;17(10):1231–4.

18. Robling AG, Turner CH. Mechanical Signaling for Bone Modeling and Remodeling. Crit Rev Eukaryot Gene Expr. 2009;19(4):319–38.

19. Isidor F. Influence of forces on peri-implant bone. Clin Oral Implants Res. 2006 Oct;17(S2):8–18.

20. Albrektsson T, Wennerberg A. Oral implant surfaces: Part 1--review focusing on topographic and chemical properties of different surfaces and in vivo responses to them. Int J Prosthodont. 2004;17(5):536–43.

21. Davies JE. Understanding Peri-Implant Endosseous Healing. J Dent Educ. 2003 Aug;67(8):932–49.

22. Davies JE. Understanding Peri-Implant Endosseous Healing. J Dent Educ. 2003 Aug;67(8):932–49.

23. Rupp F, Liang L, Geis-Gerstorfer J, Scheideler L, Hüttig F. Surface characteristics of dental implants: A review. Dental Materials. 2018 Jan;34(1):40–57.

24. Chen Z, Bachhuka A, Wei F, Wang X, Liu G, Vasilev K, et al. Nanotopography-based strategy for the precise manipulation of osteoimmunomodulation in bone regeneration. Nanoscale. 2017;9(46):18129–52.

25. Chen Z, Klein T, Murray RZ, Crawford R, Chang J, Wu C, et al. Osteoimmunomodulation for the development of advanced bone biomaterials. Materials Today. 2016 Jul;19(6):304–21.

26. Franz S, Rammelt S, Scharnweber D, Simon JC. Immune responses to implants – A review of the implications for the design of immunomodulatory biomaterials. Biomaterials. 2011 Oct;32(28):6692–709.

27. CAMERON J. WILSON BE. Mediation of Biomaterial–Cell Interactions by Adsorbed Proteins: A Review. Tissue Eng. 2005;11(1/2).

28. Berglundh T, Abrahamsson I, Lang NP, Lindhe J. *De novo* alveolar bone formation adjacent to endosseous implants. Clin Oral Implants Res. 2003 May 20;14(3):251–62.

29. Wilson CJ, Clegg RE, Leavesley DI, Pearcy MJ. Mediation of Biomaterial–Cell Interactions by Adsorbed Proteins: A Review. Tissue Eng. 2005 Jan;11(1–2):1–18.

30. Wennerberg A, Albrektsson T. Effects of titanium surface topography on bone integration: a systematic review. Clin Oral Implants Res. 2009 Sep 24;20(s4):172–84.

31. Li J, Jansen JA, Walboomers XF, van den Beucken JJJP. Mechanical aspects of dental implants and osseointegration: A narrative review. J Mech Behav Biomed Mater. 2020 Mar;103:103574.

32. Davies JE. Mechanisms of Endosseous Integration. International Journal of Prosthodontics. 1998;11(5):391.

33. Winter W, Klein D, Karl M. Micromotion of Dental Implants: Basic Mechanical Considerations. J Med Eng. 2013 Nov 20;2013:1–9.

34. Shayeb M AL, Elfadil S, Abutayyem H, Shqaidef A, Marrapodi MM, Cicciù M, et al. Bioactive surface modifications on dental implants: a systematic review and meta-analysis of osseointegration and longevity. Clin Oral Investig. 2024 Oct 11;28 (11):592.

35. Nakkala JR, Li Z, Ahmad W, Wang K, Gao C. Immunomodulatory biomaterials and their application in therapies for chronic inflammation-related diseases. Acta Biomater. 2021 Mar;123:1–30.

36. Davies JE. Understanding peri-implant endosseous healing. J Dent Educ. 2003 Aug;67(8):932–49.

37. T. A, C. J. Osteoinduction, osteoconduction and osseointegration. European Spine Journal. 2001 Oct 1;10(0):S96–101.

38. Isidor F. Influence of forces on peri-implant bone. Clin Oral Implants Res. 2006 Oct;17(S2):8–18.

39. Esposito M, Hirsch J, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants, (I). Success criteria and epidemiology. Eur J Oral Sci. 1998 Feb 28;106(1):527–51.

40. Wennerberg A, Albrektsson T. Effects of titanium surface topography on bone integration: a systematic review. Clin Oral Implants Res. 2009 Sep 24;20(s4):172–84.

41. Chen Z, Bachhuka A, Wei F, Wang X, Liu G, Vasilev K, et al. Nanotopography-based strategy for the precise manipulation of osteoimmunomodulation in bone regeneration. Nanoscale. 2017;9(46):18129–52.

42. Li J, Jansen JA, Walboomers XF, van den Beucken JJJP. Mechanical aspects of dental implants and osseointegration: A narrative review. J Mech Behav Biomed Mater. 2020 Mar;103:103574.

43. Li J, Ye LJ, Dai YW, Wang HW, Gao J, Shen YH, et al. Single-cell analysis reveals a unique microenvironment in peri-implantitis. J Clin Periodontol. 2024 Dec 2;51(12):1665–76.