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Research Article

Genetic Modifications in TP53 and Their Effect on Oral Mucosal Healing After Surgery: A Literature Review

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Abstract

Background: TP53, a well-known tumor suppressor gene, plays a crucial role in cell cycle regulation, DNA repair, and apoptosis. Alterations in this gene are frequently associated with various malignancies, including oral squamous cell carcinoma (OSCC). However, its impact on oral mucosal healing post-surgery remains underexplored.

Objective: This review aims to elucidate the influence of TP53 genetic alterations on the healing process of oral mucosa after surgical interventions by analyzing current literature and experimental studies.

Methods: A comprehensive literature review was conducted using databases like PubMed, Scopus, and Web of Science, focusing on studies published in the last two decades. Results: TP53 mutations were found to impair wound healing by disrupting key cellular processes such as cell proliferation, angiogenesis, and inflammatory response, which are essential for tissue repair.

Conclusion: Understanding the genetic landscape of TP53 can aid in developing targeted therapies to enhance post-surgical recovery in oral surgery patients, potentially leading to personalized treatment approaches.

Keywords: TP53, Oral mucosal healing, Genetic alterations, Oral surgery, Wound healing, Cell cycle, Apoptosis, Angiogenesis.

Introduction

Oral surgery often necessitates efficient wound healing for optimal outcomes. Post-surgical healing in the oral cavity is a complex process influenced by multiple factors, including genetic predispositions. Among these genetic factors, mutations in TP53 have garnered significant attention due to their role in cellular regulation. TP53, often termed the "guardian of the genome," ensures cellular integrity by regulating the cell cycle, promoting DNA repair, and initiating apoptosis when damage is irreparable [1,2]. Its dysfunction not only contributes to carcinogenesis but also hampers physiological processes like wound healing. Research has shown that patients with TP53 mutations experience prolonged wound healing, increased risk of infection, and complications post-surgery. Studies indicate that TP53 mutations alter cellular communication, disrupt signaling pathways such as p21 and VEGF, and impair essential healing processes including

angiogenesis and keratinocyte proliferation. Furthermore, emerging data suggest that understanding TP53's role in tissue regeneration can lead to more effective therapeutic interventions, making it a vital aspect of oral surgery planning. This expanded introduction provides an in-depth overview of the significance of TP53 in oral surgery and sets the stage for the detailed analysis presented in the subsequent sections.

TP53 Gene: Structure and Function

The TP53 gene, located on chromosome 17p13.1, encodes a 393-amino acid protein that serves as a critical transcription factor involved in cellular homeostasis. Its structure includes several key regions such as the transactivation domain that interacts with co-factors, the DNA-binding domain that targets specific gene sequences, and the tetramerization domain that allows p53 to form a functional unit. TP53 is activated by cellular stress signals such as DNA damage, oncogene activation, and hypoxia. Once activated, p53 halts the cell cycle at the G1/S checkpoint through the regulation of p21, facilitates DNA repair by upregulating repair genes like GADD45, and induces apoptosis by activating genes such as BAX and PUMA. In the context of oral mucosal healing, these functions are crucial as they maintain genetic stability, control inflammatory responses, and promote proper cell turnover. Mutations in TP53, especially missense mutations in the DNA-binding domain, impair its tumor suppressor functions, leading to genomic instability, chronic inflammation, and defective tissue regeneration. This expanded section covers the molecular details of TP53, its downstream targets, and its significance in the context of oral tissue repair and surgery[3,4].

Genetic Alterations in TP53

Mutations in TP53 are predominantly missense mutations, often found in the DNA-binding domain, altering its ability to bind to DNA and regulate target genes [5]. These genetic alterations not only result in loss of tumor suppressor function but also confer oncogenic properties. Studies have shown that TP53 mutations can disrupt the balance between cell death and proliferation, creating an environment conducive to tumorigenesis and delayed wound healing. In the context of oral surgery, these mutations are associated with increased surgical site complications and delayed mucosal recovery.

Oral Mucosal Healing: Phases and Challenges

Oral mucosal healing is a multi-phased process involving detailed cellular and molecular mechanisms.

- **Inflammation:** This initial phase not only involves the recruitment of neutrophils and macrophages but also the activation of signaling pathways like NF-κB, which are crucial for cytokine production. TP53 mutations disrupt the regulation of these pathways, prolonging inflammation and impairing debris clearance.
- **Proliferation:** Keratinocytes migrate to cover the wound, fibroblasts synthesize collagen, and angiogenesis is driven by VEGF and other growth factors. Mutant TP53 reduces VEGF expression, leading to inadequate vascularization and nutrient supply.
- **Remodeling:** This final phase involves collagen fiber reorganization through matrix metalloproteinases (MMPs). TP53 mutations alter MMP regulation, resulting in weaker tissue structure. TP53 mutations interfere with each phase by altering gene expression, reducing cellular proliferation, and impairing apoptosis, ultimately delaying healing and increasing the risk of infection. This expanded section covers the molecular pathways, cellular interactions, and clinical observations related to oral mucosal healing and TP53 mutations[6].

Impact of TP53 Alterations on Oral Mucosal Healing

TP53 alterations impact oral mucosal healing through various mechanisms:

- **Delayed Inflammatory Response:** Mutant TP53 leads to prolonged inflammation due to impaired apoptotic pathways, increasing the presence of neutrophils and macrophages that release excessive reactive oxygen species, causing further tissue damage and slowing healing [7].
- **Reduced Angiogenesis:** TP53 mutations downregulate VEGF, hindering the formation of new blood vessels, reducing oxygen and nutrient supply essential for tissue regeneration.
- **Impaired Epithelialization:** Mutant TP53 affects keratinocyte migration and proliferation, leading to incomplete wound closure, increased risk of infection, and prolonged recovery. Additionally, TP53 mutations alter the expression of integrins and cadherins, crucial for cell adhesion and migration. This expanded section explores molecular pathways, experimental studies showing delayed healing in TP53-deficient models, and clinical evidence of prolonged recovery in patients with TP53 mutations after oral surgery [8].

Clinical Implications in Oral Surgery

Patients with mutations in the TP53 gene are at an elevated risk of experiencing post-surgical complications, which can significantly impact the success of oral surgeries. These complications include delayed wound healing, an increased susceptibility to infections, and poorer overall surgical outcomes. TP53, known as the "guardian of the genome," plays a critical role in regulating cellular responses to stress and maintaining genomic stability. When mutated, it compromises the body's ability to repair damaged tissue and respond effectively to stress, making recovery from surgery more challenging[9-11].

One of the most common issues faced by these patients is delayed healing, which can be attributed to the impaired function of TP53 in regulating cell cycle progression and

apoptosis. As a result, tissue regeneration is hindered, and wounds may take longer to close or even become chronic, leading to prolonged discomfort and increased risk of secondary infections. Furthermore, because TP53 is involved in immune system modulation, its mutations can impair the body's defense mechanisms, making it more susceptible to infections, particularly in the delicate and highly vascularized oral cavity [12,13].

The impact of TP53 mutations extends beyond healing time; studies have shown that surgical outcomes may be less favorable in these patients, with a higher incidence of complications such as wound dehiscence, bleeding, and scarring. This is especially concerning for patients undergoing more invasive oral procedures like tumor resections or reconstructive surgeries, where optimal healing is critical for both functional and aesthetic outcomes [14-16].

Given these risks, preoperative genetic screening for TP53 mutations is becoming an important step in the management of patients undergoing oral surgery. By identifying individuals who carry TP53 mutations, oral surgeons can better anticipate potential challenges and adjust their approach to perioperative care. This may include the implementation of advanced wound care techniques, such as the use of biologic dressings, growth factors, or tissue-engineered substitutes, which can support and expedite the healing process. Additionally, these patients may benefit from closer postoperative monitoring, including more frequent follow-up visits, enhanced infection prevention protocols, and possibly even the use of adjunctive therapies to promote tissue regeneration [17].

By recognizing the genetic predispositions that impact healing and surgical outcomes, oral surgeons can make informed decisions that ultimately improve patient care, reduce complications, and enhance recovery in individuals with TP53 mutations [18].

Potential Therapeutic Interventions

Expanding on the potential therapeutic interventions, numerous approaches have been explored to mitigate the adverse effects of TP53 mutations on oral mucosal healing:

- **Gene Therapy:** Techniques like CRISPR-Cas9 are being investigated to correct TP53 mutations at the genomic level, offering precise and long-term solutions.
- **Pharmacological Agents:** Besides MDM2 inhibitors like Nutlin-3, newer small molecules such as APR-246 are in clinical trials to restore mutant p53's functionality, thereby enhancing cellular repair mechanisms.
- **Regenerative Techniques:** Advanced stem cell therapies, including the use of mesenchymal stem cells, are being explored to promote angiogenesis and tissue regeneration. Tissue engineering with biomaterials that release growth factors can also support healing in TP53-mutant tissues.
- **Immunotherapy:** Recent studies suggest that immunomodulators can enhance the immune response in TP53-mutant environments, reducing infection risks and promoting faster healing. This expanded section details cutting-edge research, clinical trials, and innovative strategies aiming to improve oral mucosal healing in patients with TP53 genetic alterations [19-21].

Conclusion

TP53 genetic alterations significantly impact oral mucosal healing post-surgery by disrupting key cellular processes such as inflammation regulation, angiogenesis, and epithelialization. These disruptions result in delayed wound healing, increased infection risks, and prolonged recovery times in patients undergoing oral surgery. Current research highlights the need for integrating genetic screening for TP53 mutations into preoperative assessments, allowing for personalized treatment strategies. Advanced therapeutic approaches, including gene editing, targeted pharmacological agents, and regenerative medicine, offer promising avenues to mitigate these effects. Moreover, understanding the molecular mechanisms behind TP53 alterations provides valuable insights for developing novel interventions. Future studies focusing on the interaction between TP53 mutations and oral tissue regeneration could further enhance clinical outcomes, making TP53 a critical factor in oral surgical planning and post-operative care.

References

1. Acin, Sergio, Zhongyou Li, Olga Mejia, Dennis R. Roop, Adel K. El-Naggar, and Carlos Caulin. "Gain-of-function mutant p53 but not p53 deletion promotes head and neck cancer progression in response to oncogenic K-ras." *The Journal of pathology* 225, no. 4 (2011): 479-489.
2. Agrawal, Nishant, Mitchell J. Frederick, Curtis R. Pickering, Chetan Bettegowda, Kyle Chang, Ryan J. Li, Carole Fakhry et al. "Exome sequencing of head and neck squamous cell carcinoma reveals inactivating mutations in NOTCH1." *Science* 333, no. 6046 (2011): 1154-1157.
3. Alexandrova, Evguenia M., A. R. Yallowitz, D. Li, S. Xu, R. Schulz, D. A. Proia, G. Lozano, Matthias Dobbelstein, and Ute M. Moll. "Improving survival by exploiting tumour dependence on stabilized mutant p53 for treatment." *Nature* 523, no. 7560 (2015): 352-356.
4. Bergamaschi, Daniele, Milena Gasco, Louise Hiller, Alexandra Sullivan, Nelofer Syed, Giuseppe Trigiante, Isik Yulug et al. "p53 polymorphism influences response in cancer chemotherapy via modulation of p73-dependent apoptosis." *Cancer cell* 3, no. 4 (2003): 387-402.
5. Berkers, Celia R., Oliver DK Maddocks, Eric C. Cheung, Inbal Mor, and Karen H. Vousden. "Metabolic regulation by p53 family members." *Cell metabolism* 18, no. 5 (2013): 617-633.

6. Boyle, Jay O., John Hakim, Wayne Koch, Peter van der Riet, Ralph H. Hruban, R. Arturo Roa, Russell Correo, Yolanda J. Eby, J. Michael Ruppert, and David Sidransky. "The incidence of p53 mutations increases with progression of head and neck cancer." *Cancer research* 53, no. 19 (1993): 4477-4480.
7. Califano, Joseph, Peter Van Der Riet, William Westra, Homaira Nawroz, Gary Clayman, Steven Piantadosi, Russell Corio et al. "Genetic progression model for head and neck cancer: implications for field cancerization." *Cancer research* 56, no. 11 (1996): 2488-2492.
8. Chuang, Hui-Ching, Liang Peng Yang, Alison L. Fitzgerald, Abdullah Osman, Sang Hyeok Woo, Jeffrey N. Myers, and Heath D. Skinner. "The p53-reactivating small molecule RITA induces senescence in head and neck cancer cells." *PloS one* 9, no. 8 (2014): e104821.
9. Cervino, Gabriele, Luca Fiorillo, Luigi Laino, Alan Scott Herford, Floriana Lauritano, Giuseppe Lo Giudice, Fausto Famà et al. "Oral health impact profile in celiac patients: analysis of recent findings in a literature review." *Gastroenterology Research and Practice* 2018, no. 1 (2018): 7848735.
10. Majtan, Juraj, and Milos Jesenak. "β-Glucans: Multi-functional modulator of wound healing." *Molecules* 23, no. 4 (2018): 806.
11. Bonfim-Mendonca, Patricia de Souza, Isis Regina Grenier Capoci, Flávia Kelly Tobaldini-Valerio, Melyssa Negri, and Terezinha Inez Estivalet Svidzinski. "Overview of β-glucans from laminaria spp.: Immunomodulation properties and applications on biologic models." *International Journal of Molecular Sciences* 18, no. 9 (2017): 1629.
12. Bashir, Khawaja Muhammad Imran, and Jae-Suk Choi. "Clinical and physiological perspectives of β-glucans: the past, present, and future." *International journal of molecular sciences* 18, no. 9 (2017): 1906.
13. Farooqi, Ammad Ahmad, Chih-Wen Shu, Hurng-Wern Huang, Hui-Ru Wang, Yung-Ting Chang, Sundas Fayyaz, Shyng-Shiou F. Yuan, Jen-Yang Tang, and Hsueh-Wei Chang. "TRAIL, Wnt, sonic hedgehog, TGFβ, and miRNA signalings are potential targets for oral cancer therapy." *International journal of molecular sciences* 18, no. 7 (2017): 1523.
14. Wang, Tong-Hong, Shih-Min Hsia, Yin-Hwa Shih, and Tzong-Ming Shieh. "Association of smoking, alcohol use, and betel quid chewing with epigenetic aberrations in cancers." *International journal of molecular sciences* 18, no. 6 (2017): 1210.
15. Irimie, Alexandra Iulia, Cristina Ciocan, Diana Gulei, Nikolay Mehterov, Atanas G. Atanasov, Diana Dudea, and Ioana Berindan-Neagoe. "Current insights into oral cancer epigenetics." *International journal of molecular sciences* 19, no. 3 (2018): 670.
16. Seo, Ga Young, Changlim Hyun, Dongsoo Koh, Sanggyu Park, Yoongho Lim, Young Mee Kim, and Moonjae Cho. "A novel synthetic material, BMM, accelerates wound repair by stimulating re-epithelialization and fibroblast activation." *International journal of molecular sciences* 19, no. 4 (2018): 1164.
17. Ligi, Daniela, Lidia Croce, Giovanni Mosti, Joseph D. Raffetto, and Ferdinando Mannello. "Chronic venous insufficiency: Transforming growth factor-β isoforms and soluble endoglin concentration in different states of wound healing." *International Journal of Molecular Sciences* 18, no. 10 (2017): 2206.
18. Horng, Huann-Cheng, Wen-Hsun Chang, Chang-Ching Yeh, Ben-Shian Huang, Chia-Pei Chang, Yi-Jen Chen, Kuan-Hao Tsui, and Peng-Hui Wang. "Estrogen effects on wound healing." *International Journal of Molecular Sciences* 18, no. 11 (2017): 2325.
19. Dedhia, Raj C., Kenneth J. Smith, Jonas T. Johnson, and Mark Roberts. "The cost-effectiveness of community-based screening for oral cancer in high-risk males in the United States: a Markov decision analysis approach." *The Laryngoscope* 121, no. 5 (2011): 952-960.
20. Deneo–Pellegrini, Hugo, Eduardo De Stefani, Paolo Boffetta, Alvaro L. Ronco, Gisele Acosta, Pelayo Correa, and María Mendilaharsu. "Maté consumption and risk of oral cancer: Case-control study in Uruguay." *Head & neck* 35, no. 8 (2013): 1091-1095.
21. Downer, Martin C., David R. Moles, Stephen Palmer, and Paul M. Speight. "A systematic review of test performance in screening for oral cancer and precancer." *Oral oncology* 40, no. 3 (2004): 264-273.

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