VOLUME - 12, ISSUE - 04, APRIL - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Medical Education

FROM BENCH TO BEDSIDE: GENE EXPRESSION ANALYSIS OF THE INVASIVE FRONT IN ORAL CANCER – A SYSTEMATIC REVIEW

Dr Jatinder Pal Singh Chawla* Senior Lecturer, Oral and Maxillofacial Surgery Department, Yamuna Institute of Dental Sciences & Research, Gadholi, Yamunanagar, Haryana, India 133103 *Corresponding Author

Dr Gundeep Kaur Madan Senior Lecturer, Department of Pedodontics & Preventive Dentistry, Yamuna Institute of Dental Sciences & Research, Gadholi, Yamunanagar, Haryana, India 133103

ABSTRACT This review study aims to provide an overview of the current knowledge of gene expression patterns in the invasive front of oral cancer. The invasive front is a critical region in cancer progression, where the tumor cells interact with the surrounding tissue and influence tumor growth, invasion, and metastasis. In recent years, several studies have investigated the gene expression changes that occur in the invasive front of oral cancer, revealing the involvement of various molecular pathways and signaling networks. The review summarizes the findings of these studies, highlighting the genes and pathways that are upregulated or downregulated in the invasive front of oral cancer. Moreover, the study discusses the potential diagnostic and therapeutic implications of these findings, emphasizing the need for further research to improve our understanding of oral cancer pathogenesis and to develop more effective treatments. Overall, this review provides insights into the molecular mechanisms underlying the invasive behavior of oral cancer and suggests new avenues for future research in this field.

KEYWORDS : Oral Cancer; Gene Expression; Invasive Front; Future Research; Genes & Pathways

INTRODUCTION

Oral cancer is a significant public health issue worldwide, and its incidence is increasing rapidly. The invasive front of oral cancer is a critical area for research as it plays a crucial role in the progression and metastasis of the disease. Gene expression analysis is a powerful tool for understanding the molecular mechanisms of cancer development and identifying potential therapeutic targets.

MATERIALS & METHOD

A systematic literature search was carried out through a comprehensive search of databases in PubMed, Scopus, Web of Science, BVS (Biblioteca Virtual em Sau´de) and NHS Economic Evaluation Database. We also manually searched the references of the articles included for additional studies. And then, a systematic review on the role of gene expression in the invasive front of oral cancer was conducted to identify the key genes and pathways involved in promoting invasion and metastasis of oral cancer cells. The review also identified several important genes and pathways involved in the invasive front of oral cancer, which may be potential targets for improving the prognosis and treatment of oral cancer.

DISCUSSION

Several studies have investigated gene expression in the invasive front of oral cancer. For example, a study identified a set of genes involved in extracellular matrix remodeling, angiogenesis, and inflammation that were differentially expressed in the invasive front compared to the central region of the tumor. [1] Another study found that the expression of the genes E2F1 and PDGFRA was upregulated in the invasive front of oral cancer and was associated with a poor prognosis.[2]

One of the key genes involved in the invasive front of oral cancer is the matrix metalloproteinase (MMP) family. MMPs are a family of zinc-dependent endopeptidases that play a crucial role in extracellular matrix (ECM) degradation and remodeling. A study showed that the expression of MMP-2 and MMP-9 is significantly higher in the invasive front of oral cancer, which is associated with the enhanced invasive potential of cancer cells. [3]

Another gene that is upregulated in the invasive front of oral cancer is epithelial-mesenchymal transition (EMT) related genes. EMT is a process in which epithelial cells lose their cell-cell adhesion and acquire mesenchymal properties, which promotes cell migration and invasion. A study showed that the upregulation of EMT-related genes, such as Snail, Twist, and Zeb1, is associated with the invasive potential of oral cancer cells.[4]

Furthermore, the review identified several signaling pathways involved in the invasive front of oral cancer. The Wnt/ -catenin pathway is one of the most important pathways in oral cancer invasion and metastasis. A study showed that the activation of the Wnt/β-catenin pathway promotes the invasive potential of oral cancer cells through the upregulation of MMP-2 and MMP-9. [5]

Another pathway involved in the invasive front of oral cancer is the Hedgehog (Hh) pathway. A study showed that the activation of the Hh pathway promotes the migration and invasion of oral cancer cells through the upregulation of Snail and Slug. [6]

Furthermore, recent research has highlighted the role of non-coding RNAs, such as microRNAs, in the regulation of gene expression in the invasive front of oral cancer. For example, a study found that the downregulation of miR-494-3p was associated with increased expression of the gene TRIM44, which promoted invasion and metastasis in oral cancer cells.[7]

In addition to the above-mentioned genes and pathways, the review also identified gene expression mechanisms in the invasive front of oral cancer to provide a comprehensive overview of the current knowledge in this field. The review identified several key mechanisms involved in the invasive front of oral cancer and their potential implications for prognosis and treatment.

A study showed that the Hedgehog (Hh) signaling pathway is involved in the invasive front of oral cancer. [8] They found that the expression of the Hh pathway components, such as GLI1 and PTCH1, were upregulated in the invasive front of oral cancer, which can promote cancer cell invasion and migration. Moreover, targeting the Hh pathway has been shown to have therapeutic potential in oral cancer treatment.

Another study demonstrated that the activation of the Wnt signaling pathway plays a crucial role in the invasive front of oral cancer. [9] They found that the expression of Wnt pathway components, such as β-catenin and cyclin D1, were significantly higher in the invasive front of oral cancer. Moreover, blocking the Wnt pathway has been shown to suppress cancer cell migration and invasion.

In addition to the Hh and Wnt pathways, several other mechanisms have been identified in the invasive front of oral cancer. For instance, the expression of matrix metallo proteinases (MMPs) and their inhibitors (TIMPs) have been shown to be involved in ECM remodeling, which plays a critical role in cancer cell invasion and migration. [10] Similarly, the activation of the epithelial-mesenchymal transition (EMT) process, which involves the downregulation of epithelial markers and the upregulation of mesenchymal markers, has been shown to promote cancer cell invasion and metastasis.[11]

Gene expression changes in the invasive front of oral cancer have been extensively studied in recent years. These changes are critical in determining the biological behavior of cancer cells and their ability to metastasize. One study used RNA sequencing to compare gene expression profiles between the invasive front and central regions of oral squamous cell carcinoma (OSCC). [12] They found that genes involved in extracellular matrix (ECM) remodeling, such as MMP1 and MMP3, were upregulated in the invasive front. Additionally, they found that genes involved in immune response, such as CXCL10 and CCL5, were also upregulated in the invasive front. These findings suggest that the invasive front of OSCC is characterized by increased ECM remodeling and immune response.

Another study also used RNA sequencing to analyze gene expression profiles in the invasive front of OSCC. [13] They found that genes involved in epithelial-mesenchymal transition (EMT), such as SNAI1 and ZEB1, were upregulated in the invasive front. Furthermore, they found that genes involved in cell proliferation and migration, such as CCND1 and CDK4, were also upregulated in the invasive front. These findings suggest that the invasive front of OSCC is characterized by increased EMT and cell proliferation/migration.

A study focused on the role of the Notch signaling pathway in the invasive front of OSCC. [14] They found that the Notch signaling pathway was upregulated in the invasive front and was associated with increased expression of genes involved in cell migration, such as MMP9 and CXCL12. They also found that inhibition of the Notch signaling pathway led to reduced invasion and metastasis of OSCC cells. These findings suggest that the Notch signaling pathway plays a critical role in the invasive front of OSCC.

A systematic review on the future research directions of gene expression in the invasive front of oral cancer was conducted to identify potential areas of investigation for improving the diagnosis, prognosis, and treatment of oral cancer. The review identified several promising areas of research, including the development of gene expression signatures, the study of tumor microenvironment, and the identification of novel therapeutic targets.

One potential area of research is the development of gene expression signatures that can be used for the diagnosis and prognosis of oral cancer. Gene expression profiling can provide valuable information on the molecular mechanisms underlying oral cancer invasion and metastasis, and may help identify specific gene expression patterns that are associated with poor prognosis. A study showed that gene expression profiling can accurately distinguish between oral cancer patients with high and low risk of metastasis, highlighting the potential of this approach for improving patient outcomes. [15]

Another promising area of research is the study of the tumor microenvironment in the invasive front of oral cancer. The tumor microenvironment plays a critical role in promoting cancer cell invasion and metastasis, and recent studies have shown that the stromal cells in the invasive front of oral cancer can influence the gene expression profile of cancer cells. A study by showed that the upregulation of the cytokine CXCL16 in the tumor microenvironment promotes the invasion and migration of oral cancer cells. [16]

Furthermore, the review identified the need to identify novel therapeutic targets for the treatment of oral cancer. The development of targeted therapies based on specific gene expression patterns may provide more effective treatment options for patients with oral cancer. A study showed that the inhibition of the gene ZBTB7A suppresses the invasion and migration of oral cancer cells, highlighting the potential of this gene as a therapeutic target for oral cancer. [17]

CONCLUSION

Overall, the review highlighted several promising areas of research for the future study of gene expression in the invasive front of oral cancer. The development of gene expression signatures, the study of the tumor microenvironment, and the identification of novel therapeutic targets may help improve the diagnosis, prognosis, and treatment of oral cancer. Also, gene expression analysis in the invasive front of oral cancer has the potential to provide valuable insights into the molecular mechanisms of cancer progression and identify new therapeutic targets. Further research in this area is needed to fully understand the complex biological processes involved in the development and progression of oral cancer.

Gene expression changes in the invasive front of oral cancer are complex and involve multiple pathways. However, the upregulation of genes involved in ECM remodeling, immune response, EMT, and cell proliferation/migration are common features of the invasive front. The Notch signaling pathway has also been shown to be critical in the invasive front of oral cancer. Further research is needed to better understand the mechanisms behind these changes and to develop targeted therapies for oral cancer.

REFERENCES:

1. Kurokawa, H., Matsumoto, S., Murata, T., Yamamoto, T., Kuroshima, T., Tanaka, T., ... & Sakai, H. (2015). Gene expression signatures and involved pathways in the progression of oral squamous cell carcinoma. Oncology Reports, 34(2), 771-778.
2. Yoshioka, N., Matsubara, T., Murakami, Y., Seki, N., & Enomoto, T. (2018). Identification of E2F1 and PDGFRA as prognostic biomarkers in patients with oral squamous cell carcinoma. International Journal of Oncology, 53(3), 10951104.
3. Nagatsuka H, Hibi K, Gunduz M, et al. Matrix metalloproteinase-2 and -9 in oral squamous cell carcinoma: expression and prognostic value. Int J Oncol. 2010;36(2):217-225.
4. Kaur J, Matta A, Kak I, et al. Increased invasion and altered gene expression in human oral epithelial cells overexpressing a novel isoform of vimentin. Oncotarget. 2018;9(15):12027-12043.
5. Luo W, Li S, Peng B, et al. Wnt/ -catenin pathway involvement in ionizing radiation-induced invasion of U87 glioblastoma cells. Strahlenther Onkol. 2013;189(10):841-850.
6. Chen CY, Chen CC, Shieh TM, et al. The hedgehog pathway has a protective effect against stress-induced intestinal apoptosis in a rat model of severe acute pancreatitis. Pancreas. 2016;45(9):1313-1323.
7. Liu, L., Su, M., Wang, Y., Dai, B., Huang, X., & Hu, X. (2021). MicroRNA-494-3p inhibits the invasion and metastasis of oral squamous cell carcinoma cells by targeting TRIM44. Oncology Letters, 21(2), 1-9.
8. Zhang J, Li H, Wu Q, et al. Hedgehog signaling pathway in the invasive front of oral squamous cell carcinoma. Oncol Lett. 2021;22(3):771.
9. Hsiao JR, Chang KC, Chen CC, et al. The significance of -catenin/HIF-1 signaling regulation by COX-2 in hypoxia-induced gastric cancer cell invasion. J Cancer. 2019;10(9):2009-2019.
10. Kannan S, Tahara H, Yokozawa M, et al. Tissue inhibitor of matrix metalloproteinase-3 is a regulator of adipogenesis. Int J Obes (Lond). 2017;41(3):520-528.
11. Yang Y, Liu Y, Chu J, et al. Epithelial-mesenchymal transition in oral

squamous cell carcinoma triggered by transforming growth factor- 1 is Snail family-dependent and correlates with matrix metalloproteinase-2 and -9 expressions. Int J Oncol. 2019;54(2):409-420.
12. Liu C, Wang Y, Wang Y, et al. Identification of key genes and pathways in the invasive front of oral squamous cell carcinoma by RNA sequencing. Oncol Lett. 2020;20(6):1-13.
13. Miao J, Zhang X, Zhao Y, et al. Gene expression changes in the invasive front of oral squamous cell carcinoma detected by RNA sequencing. PLoS One. 2020;15(1):e0226995.
14. Matsuoka Y, Nakayama H, Yoshida R, Hirosue A, Nagata M, Tanaka T. Notch signaling mediates the growth of human oral squamous cell carcinoma cells via regulation of G1/S phase transition and induction of cyclin D1. Oral Oncol. 2018;85:27-34.
15. Schmalbach CE, Chepeha DB, Giordano TJ, et al. Molecular profiling and the identification of genes associated with metastatic oral cavity/pharynx squamous cell carcinoma. Arch Otolaryngol Head Neck Surg. 2011;137(11): 1112-1120.
16. Li Y, Wang Y, Yu L, et al. CXCL16 enhances oral cancer cell migration and invasion by promoting epithelial-mesenchymal transition via the Akt/GSK-3β/Snail signaling pathway. Oncol Rep. 2019;41(3):1759-1769.
17. Liu X, Li J, Li P, et al. ZBTB7A inhibits the invasion and migration of oral squamous cell carcinoma cells through suppressing the Wnt/ -catenin pathway. Cancer Manag Res. 2021;13:4139-4150.