

Biochemical Mechanisms of Pathogenesis of Squamous Cell Carcinoma of The Oral Cavity: Methods of Study of Oxidative Stress, Inflammation, Microbiome and Molecular Disorders

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Abstract: Squamous cell carcinoma of the oral cavity (OSCC) remains a significant oncological challenge due to its complex, multifactorial pathogenesis. The biochemical basis of tumor development is strongly associated with oxidative stress, characterized by excessive production of reactive oxygen species (ROS), which induce DNA damage, lipid peroxidation, and impairment of cellular repair systems. Despite extensive research, an integrative understanding of how oxidative stress, chronic inflammation, microbiome dysbiosis, and molecular signaling pathways interact in OSCC progression remains insufficient. This study aims to systematize key biochemical and molecular mechanisms underlying OSCC pathogenesis through analysis of oxidative stress markers, inflammatory mediators, microbiological factors, and signaling pathways. The findings demonstrate that oxidative stress initiates carcinogenic processes, while chronic inflammation mediated by cytokines such as IL-6 and TNF- α sustains tumor-promoting conditions. Dysbiosis of the oral microbiome, particularly increased levels of pathogenic bacteria, enhances inflammatory signaling and ROS production. Concurrent activation of pathways such as JAK/STAT3, NF- κ B, and PI3K/AKT/mTOR supports tumor proliferation, angiogenesis, and resistance to apoptosis. The results highlight a unified pathogenic chain linking oxidative damage, inflammation, genetic instability, metabolic reprogramming, and tumor progression. These insights emphasize the clinical importance of biochemical markers such as 8-OHdG, VEGF, MMP-9, and lactate for early diagnosis and prognosis. The study suggests that integrated biomarker panels may significantly improve early detection and enable personalized therapeutic strategies in OSCC management.

Keywords: Oral Squamous Cell Carcinoma, Oxidative Stress, Inflammation, Microbiome, ROS, Biomarkers, Carcinogenesis

Introduction

The central place in the biochemistry of tumor transformation is occupied by oxidative stress caused by the excessive formation of reactive oxygen species (ROS), which have a multilevel damaging effect on cellular structures. ROS induce oxidative DNA damage, including the formation of 8-hydroxydeoxyguanosine (8-OHdG), disrupt the structure of lipid membranes through peroxidation processes, and inactivate enzymes of repair systems, leading to the accumulation of somatic mutations and the formation of genetic instability (Valiko et al., 2007). Of particular importance is the depletion of the body's antioxidant system, represented by superoxide dismutase, catalase and glutathione peroxidase, which leads to the chronization of oxidative damage and the formation of a stable pro-oncogenic background [1]. Against the background of oxidative stress, chronic inflammation develops, which is considered as a key pathogenetic bridge between external carcinogenic factors and the molecular transformation of the cell. Persistent activation of immune cells is accompanied by the release of pro-inflammatory cytokines, including IL-6, TNF- α , and IL-1 β , which form a stable inflammatory microenvironment (Mantovani et al., 2008). IL-6 activates the JAK/STAT3 signaling pathway, enhancing cell proliferation and suppressing apoptosis, whereas TNF- α through the NF- κ B cascade supports chronic inflammation and promotes the formation of resistance of tumor cells to programmed cell death [2]. In the future, the inflammatory environment acquires the character of a tumor microenvironment, in which the processes of angiogenesis and tissue remodeling are activated. The key mediator of this process is vascular endothelial growth factor VEGF, which ensures the formation of new vessels and maintains the metabolic needs of the tumor (Carmeliet, 2005). EGFR and

PI3K/AKT/mTOR signaling pathways that regulate cell growth, proliferation, and survival of tumor cells are simultaneously activated [3][4]. Inactivation of TP53 and RB leads to loss of cell cycle control, which contributes to the accumulation of genetically defective cell clones and tumor progression.

Methodology

The study was conducted using an integrative analytical approach aimed at evaluating the biochemical and molecular mechanisms involved in the pathogenesis of oral squamous cell carcinoma. Data were obtained through comprehensive analysis of biochemical markers associated with oxidative stress, inflammatory response, microbiome alterations, and intracellular signaling pathways [5][6]. Levels of reactive oxygen species and oxidative DNA damage were assessed using indicators such as 8-hydroxydeoxyguanosine, alongside evaluation of antioxidant defense enzymes including superoxide dismutase, catalase, and glutathione peroxidase. Inflammatory status was characterized by measuring pro-inflammatory cytokines, including IL-6, TNF- α , and IL-1 β , and examining activation of signaling pathways such as JAK/STAT3 and NF- κ B.

Microbiological assessment focused on identifying dysbiosis within the oral cavity, particularly the presence of pathogenic species and their associated lipopolysaccharides, which contribute to immune activation and oxidative imbalance [7]. Molecular mechanisms of tumor progression were analyzed through markers of angiogenesis, invasion, and metabolic reprogramming, including VEGF, MMP-9, and lactate levels. The interaction between these parameters was evaluated to establish a comprehensive pathogenic model linking oxidative stress, inflammation, genetic mutations, and tumor microenvironment formation.

The collected data were interpreted using a systems-based framework to identify correlations between biochemical markers and disease progression, enabling the development of an integrated model for early diagnosis and prognostic assessment of OSCC [8][9].

Results and Discussion

An important element of pathogenesis is the oral microbiome, which under conditions of dysbiosis becomes an active participant in carcinogenesis. An increase in the proportion of pathogenic microorganisms such as *Fusobacterium nucleatum* and *Porphyromonas gingivalis* leads to activation of Toll-like receptors, increased NF- κ B-dependent inflammation, and modulation of the immune response (Kostic et al., 2013). Bacterial lipopolysaccharides and enzymes enhance ROS production, contributing to the chronization of the inflammatory process and the formation of a stable pro-oncogenic environment [10]. Thus, the biochemical pathogenesis of PRPR is an integrative system in which oxidative stress initiates damage to cellular structures, chronic inflammation perpetuates the pathological process, signaling proliferation pathways ensure tumor growth, and the microbiome and metabolic changes stabilize the tumor environment. This system is self-sustaining and determines the biological aggressiveness of the disease. Biochemical markers are of particular importance in modern oncology, which make it possible to assess the activity of the tumor process, the degree of inflammation and the prognosis of the disease [11][12]. Their clinical interpretation is essential for early diagnosis and a personalized approach to therapy.

The presented biochemical and molecular markers reflect the key links in the pathogenesis of squamous cell carcinoma of the oral cavity (OCD), covering the processes of oxidative stress, chronic inflammation, metabolic reprogramming, angiogenesis, invasion and genetic instability. Their interpretation allows us to move from a morphological understanding of the tumor to a functional assessment of its biological behavior, which is especially important for early diagnosis and prediction of the course of the disease (Table 1). One of the central links in carcinogenesis is oxidative damage to biomolecules, which is reflected by an increase in the level of 8-OHdG, one of the most sensitive markers of DNA damage [13]. Its increase indicates the direct effect of reactive oxygen species (ROS) on the guanine bases of DNA, which leads to point mutations and the formation of genetic instability. The parallel increase in ROS in the tissues of the oral cavity reflects an active inflammatory process and an imbalance between pro-oxidant and antioxidant systems. Collectively, these changes form the early biochemical background of carcinogenesis, preceding morphologically detectable tumor changes [14]. The processes of invasion and metastasis are closely related to the increased activity of VEGF and MMP-

9. VEGF stimulates angiogenesis by providing the tumor with new vessels and improving its trophic supply, which directly correlates with the metastatic potential. MMP-9 destroys the components of the extracellular matrix and the basement membrane, facilitating the penetration of tumor cells into the surrounding tissues and vascular bed. The metabolic restructuring of tumor cells is reflected by an increase in lactate levels, which is a classic manifestation of the Warburg effect. The shift of energy metabolism towards anaerobic glycolysis leads to acidification of the microenvironment, increased angiogenesis and activation of the invasive properties of the tumor [15]. Lactate also acts as a signaling molecule that enhances the expression of genes associated with aggressive growth.

Microbiological factors represented by lipopolysaccharides (LPS) of bacterial origin are of particular importance. Their increase reflects dysbiosis of the oral microbiome and chronic bacterial stimulation of the immune system.

Conclusion

LPS activate Toll-like receptors and enhance the NF- κ B-dependent inflammatory response, thereby supporting chronic inflammation and enhancing carcinogenesis. In general, the presented marker profile reflects a single pathobiochemical chain: oxidative stress \rightarrow chronic inflammation \rightarrow genetic mutations \rightarrow metabolic restructuring \rightarrow angiogenesis and invasion. The combined interpretation of these indicators allows us to consider them not in isolation, but as an interconnected system of biological indicators reflecting the stage, aggressiveness and prognosis of squamous cell carcinoma of the oral cavity. This opens up prospects for the development of integrated diagnostic panels that can significantly improve the accuracy of early detection and individual disease prediction.

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