Protein Interaction Networks in the Identification of Potential Biomarkers in Salivary Gland Mucoepidermoid Carcinoma

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Introduction: Mucoepidermoid carcinoma (MEC) is the most common malignant salivary gland tumor, characterized by intermediate, mucous, and epidermoid cells, classified into low-grade, intermediate-grade, and high-grade categories correlating with tumor aggressiveness. Treatment efficacy for aggressive MEC grades is hampered by the absence of specific biomarkers, leading to poor survival rates. The oncogenesis of MEC poses significant diagnostic and therapeutic challenges, yet advances in bioinformatics provide robust tools for identifying potential markers and therapeutic targets, particularly in MEC. **Objective:** To investigate protein expression profiles in salivary gland MEC using immunohistochemistry (IHC) studies and identify significant protein interactions and pathways through in-silico analysis on the STRING platform. **Methods:** Protein data related to MEC and protein expression were extracted from the PUBMED database, focusing exclusively on relevant IHC studies. Non-IHC studies, unrelated techniques, review articles and studies lacking significant protein expression were excluded. In-silico analysis on the STRING platform employed the Markov Cluster Algorithm (MCL) with an inflation parameter of 4, setting a false discovery rate (FDR) of 0.05 and a minimum interaction score of 0.75. Results were visualized and analyzed using Cytoscape (v3.10.2) via STRINGApp. Enrichment analysis utilized REACTOME and KEGG tools with a significance threshold of $p < 0.05$. **Results:** Screening 175 PUBMED articles identified 98 (56%) studies meeting inclusion criteria, revealing 115 proteins significantly expressed in IHC studies. STRING/MCL clustering yielded 15 clusters, with 5 clusters disconnected from the network. Enrichment analysis highlighted the network's association with pathways related to cancer (18 proteins), adherens junction (9), proteoglycans in cancer (11), cell cycle (9), PI3K/AKT signaling (11), focal adhesion (10), ErbB signaling (8), signal transduction (26), apoptosis (6), mitosis (6), and microRNAs in cancer (8). **Discussion:** Salivary gland tumors are a heterogeneous group of neoplasms and MEC comprising 25–30% of malignant cases. Our findings corroborate previous research, revealing intricate interactions among protein clusters. For example, mucins potentially influence MEC characteristics like TNM stage, high grade, and poor outcomes. Clusters containing EGFR, HER2, and CTNNB1 proteins are associated with high histological grade, aggressiveness, and poor prognosis in MEC. Additionally, CD44 and BCL-2 impact overall survival. The entire network is linked to critical pathways in cancer progression, cell cycle regulation, and signal transduction, pivotal in understanding tumor behavior and prognosis. **Conclusion:** The complexities of MEC underscores the importance of unraveling molecular mechanisms within the tumor microenvironment. Our study identifies interconnected protein clusters and their roles, demonstrating the power of bioinformatics in integrating complex data. Further experimental validation is essential to deepen our understanding and advance targeted therapeutic strategies for managing MEC effectively.

Agradecimentos: