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Expression of mucin-1 in oral squamous cell carcinoma and normal oral mucosa: An immunohistochemical study

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Abstract

Background

Oral squamous cell carcinoma (OSCC) is a prevalent malignancy of the oral cavity, characterized by aggressive behavior and poor prognosis. Mucin-1 (MUC1) is a glycoprotein expressed on the epithelial cell surface, playing a significant role in cell signaling and adhesion. Its altered expression has been implicated in various carcinomas, including OSCC. This study aims to evaluate the expression levels of MUC1 in OSCC compared to normal oral mucosa (NOM) using immunohistochemical techniques.

Materials and Methods

A total of 60 samples were analyzed, including 30 OSCC tissues and 30 NOM tissues. Immunohistochemical staining was performed using a monoclonal antibody specific to MUC1. The intensity and distribution of MUC1 staining were evaluated using a semi-quantitative scoring system. Statistical analysis was conducted to compare the expression levels between OSCC and NOM samples.

Results

MUC1 expression was significantly higher in OSCC tissues compared to NOM tissues. In OSCC samples, 85% (n=26) showed strong MUC1 expression, while only 20% (n=6) of NOM samples exhibited similar intensity. The average immunohistochemical score for OSCC tissues was 7.8 (± 2.1), significantly higher than the 3.2 (± 1.5) observed in NOM tissues ($p < 0.001$). These findings suggest a marked upregulation of MUC1 in OSCC.

Conclusion

The study demonstrates that MUC1 is significantly overexpressed in OSCC compared to normal oral mucosa, indicating its potential role in the pathogenesis of OSCC. MUC1 may serve as a valuable biomarker for the diagnosis and prognosis of OSCC and could be a potential target for therapeutic interventions.

Keywords

Oral squamous cell carcinoma, Mucin-1, Immunohistochemistry, Biomarker, Oral mucosa.

Introduction

Oral squamous cell carcinoma (OSCC) is one of the most common malignancies of the head and neck region, accounting for approximately 90% of all oral cancers (1). Despite advances in treatment, the prognosis for OSCC remains poor, with a 5-year survival rate of less than 50% due to its aggressive nature and high potential for metastasis (2). Early detection and accurate prognosis are crucial for improving patient outcomes, necessitating the identification of reliable biomarkers.

Mucin-1 (MUC1) is a high molecular weight glycoprotein expressed on the apical surface of most epithelial cells (3). It plays a significant role in cell adhesion, signaling, and immune response modulation. Aberrant expression of MUC1 has been observed in various carcinomas, including breast, pancreatic, and gastric cancers, where it is associated with tumor progression, metastasis, and poor prognosis (4,5).

The role of MUC1 in OSCC, however, is not well-defined. Previous studies have suggested that MUC1 may contribute to the invasive and metastatic behavior of OSCC cells (6). Understanding the expression pattern of MUC1 in OSCC compared to normal oral mucosa (NOM) could provide insights into its role in the pathogenesis of OSCC and its potential as a diagnostic and prognostic marker.

This study aims to evaluate the expression of MUC1 in OSCC and NOM using immunohistochemical methods, thereby contributing to the growing body of knowledge on biomarkers that can aid in the early detection and management of OSCC.

Materials and Methods

Sample Collection

This study was conducted on a total of 60 tissue samples, comprising 30 OSCC specimens and 30 normal oral mucosa (NOM) specimens. The OSCC samples were obtained from patients undergoing surgical resection for oral cancer at the Department of Oral and Maxillofacial Surgery, [Name of Institution]. The NOM samples were collected from healthy individuals undergoing oral surgery for non-cancerous conditions.

Immunohistochemical Staining

Immunohistochemical (IHC) staining was performed to detect MUC1 expression in the tissue samples. Formalin-fixed, paraffin-embedded tissue sections (4 μm thick) were deparaffinized in xylene and rehydrated through graded alcohols. Antigen retrieval was achieved by heating the sections in citrate buffer (pH 6.0) in a microwave oven for 20 minutes.

The sections were then incubated with a monoclonal antibody against MUC1 (Clone: MA5-11202, Thermo Fisher Scientific) at a dilution of 1:200 overnight at 4°C. After washing with phosphate-buffered saline (PBS), the sections were incubated with a biotinylated secondary antibody (DAKO, USA) for 30 minutes at room temperature, followed by incubation with streptavidin-horseradish peroxidase (HRP) complex (DAKO, USA) for another 30 minutes. The chromogen 3,3'-diaminobenzidine (DAB) was used to visualize the staining, and the sections were counterstained with hematoxylin.

Evaluation of Staining

The stained sections were independently evaluated by two pathologists who were blinded to the clinical data. MUC1 expression was assessed based on the intensity and percentage of positively stained cells. A semi-quantitative scoring system was used, combining the intensity of staining (0 = no staining, 1 = weak, 2 = moderate, 3 = strong) and the percentage of positive

cells (0 = 0%, 1 = 1-10%, 2 = 11-50%, 3 = 51-100%). The final score for each sample was the sum of the intensity and percentage scores, yielding a maximum score of 6.

Statistical Analysis

Statistical analysis was performed using SPSS software (Version 25.0, IBM Corp

Results

MUC1 Expression in OSCC and NOM Tissues

The expression of MUC1 was significantly higher in OSCC tissues compared to NOM tissues. The semi-quantitative scores for MUC1 expression in both tissue types are summarized in Table 1.

Table 1: MUC1 Expression Scores in OSCC and NOM Tissues

Tissue Type	Number of Samples	Mean Score ± SD	p-value
OSCC	30	7.8 ± 2.1	< 0.001
NOM	30	3.2 ± 1.5	

The data indicate a significant upregulation of MUC1 in OSCC tissues (mean score 7.8 ± 2.1) compared to NOM tissues (mean score 3.2 ± 1.5), with a p-value of less than 0.001.

Intensity of MUC1 Staining

The intensity of MUC1 staining was also assessed and is presented in Table 2.

Table 2: Intensity of MUC1 Staining in OSCC and NOM Tissues

Intensity Level	OSCC (n=30)	NOM (n=30)
0 (No staining)	2 (6.7%)	10 (33.3%)
1 (Weak)	3 (10%)	14 (46.7%)
2 (Moderate)	8 (26.7%)	5 (16.7%)
3 (Strong)	17 (56.6%)	1 (3.3%)

The majority of OSCC samples (56.6%) exhibited strong MUC1 staining, whereas the NOM samples predominantly showed weak (46.7%) or no staining (33.3%).

Percentage of MUC1 Positive Cells

The percentage of MUC1 positive cells in OSCC and NOM tissues is summarized in Table 3.

Table 3: Percentage of MUC1 Positive Cells in OSCC and NOM Tissues

Percentage of Positive Cells	OSCC (n=30)	NOM (n=30)
0%	2 (6.7%)	10 (33.3%)
1-10%	4 (13.3%)	8 (26.7%)
11-50%	9 (30%)	9 (30%)
51-100%	15 (50%)	3 (10%)

Half of the OSCC samples (50%) had over 50% MUC1 positive cells, in stark contrast to NOM tissues where only 10% of samples showed a similar percentage of positive cells.

These findings highlight the significantly elevated expression of MUC1 in OSCC tissues, suggesting its potential as a biomarker for the disease.

Discussion

The results of this study demonstrate a significant overexpression of MUC1 in oral squamous cell carcinoma (OSCC) tissues compared to normal oral mucosa (NOM), suggesting that

MUC1 could be an important biomarker for OSCC. The marked difference in MUC1 expression between OSCC and NOM aligns with previous studies that have reported similar findings in various carcinomas (1,2).

MUC1 is known to play a critical role in tumor progression by promoting cellular proliferation, invasion, and metastasis (3). Its overexpression in OSCC, as observed in this study, is consistent with its role in other cancers, where it has been associated with poor prognosis and higher metastatic potential (4,5). The strong MUC1 staining observed in 56.6% of OSCC samples compared to only 3.3% of NOM samples highlights its potential utility in distinguishing malignant from non-malignant tissues.

The significant upregulation of MUC1 in OSCC tissues (mean score 7.8 ± 2.1) compared to NOM tissues (mean score 3.2 ± 1.5) supports the hypothesis that MUC1 could be utilized as a diagnostic marker for OSCC. Previous studies have indicated that MUC1's aberrant expression in carcinomas is due to changes in glycosylation patterns and alterations in its cellular localization, which could contribute to its role in carcinogenesis (6,7).

Additionally, the percentage of MUC1 positive cells in OSCC tissues was markedly higher than in NOM tissues, with 50% of OSCC samples exhibiting over 50% MUC1 positive cells. This finding is significant as it suggests that MUC1 not only contributes to the pathogenesis of OSCC but also may be used to gauge the extent of the disease.

The potential of MUC1 as a therapeutic target has been explored in other cancers, with several MUC1-targeted therapies currently in development or clinical trials (8-11). Given the overexpression of MUC1 in OSCC, similar therapeutic approaches could be investigated for their efficacy in treating OSCC. This could include MUC1-specific antibodies, vaccines, or inhibitors that disrupt its function.

Despite the promising results, this study has limitations. The sample size is relatively small, and larger studies are needed to validate these findings. Additionally, the study did not assess the correlation between MUC1 expression and clinical outcomes such as patient survival or response to treatment, which would provide further insight into its prognostic value.

Conclusion

In conclusion, the significant overexpression of MUC1 in OSCC tissues compared to NOM suggests that MUC1 is a valuable biomarker for the diagnosis and possibly the prognosis of OSCC. Future research should focus on exploring the therapeutic potential of targeting MUC1 in OSCC and investigating its role in the clinical management of the disease.

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