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Assessment of CD138 (Syndecan-1) Immunoexpression in Salivary Gland Carcinomas and Its Relationship to Tumor Grade

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Abstract

Background: Salivary gland carcinomas (SGCs) represent a heterogeneous group of malignancies with varied biological behavior and prognosis. Reliable biomarkers that correlate with tumor differentiation and aggressiveness are needed to improve diagnostic accuracy and prognostic stratification. CD138 (Syndecan- 1) is a transmembrane heparan sulfate proteoglycan involved in cell adhesion, proliferation, and tumor progression.

Objective: To evaluate the immunohistochemical expression of CD138 in the stromal and epithelial components of salivary gland carcinomas and determine its association with histopathological grades.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Department of Histopathology/Oral Pathology, Armed Forces Institute of Pathology, Rawalpindi, from November 2024 to May 2025.

Methodology: A cross- sectional analytical study was conducted on 41 cases of histopathologically diagnosed salivary gland carcinomas. Hematoxylin and eosin–stained sections were reviewed to confirm diagnosis and grading. Immunohistochemistry for CD138 was performed, and expression was assessed based on staining intensity and percentage of positive tumor cells. Associations between

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CD138 expression and histopathological grade were analyzed using SPSS v26, with $p \leq 0.05$ considered statistically significant.

Results: A statistically significant association was observed between epithelial CD138 expression and histopathological grade ($p \leq 0.05$), with higher epithelial expression more frequently seen in advanced grades. In contrast, stromal CD138 expression demonstrated variable distribution across tumor grades but did not show a statistically significant association ($p = 0.5$).

Conclusion:

This study demonstrates that altered expression of Syndecan-1 (CD138), particularly within the stromal component, is significantly associated with higher histopathological grades in salivary gland carcinomas. Furthermore, epithelial CD138 expression also shows a strong correlation with the histological grading, especially in high-grade tumors. These findings suggest that CD138 may serve as a valuable adjunct prognostic marker in the assessment of salivary gland carcinomas. However, further large-scale studies are necessary to confirm its clinical utility and potential role in patient management.

Keywords: Salivary gland carcinoma, CD138, Syndecan-1, Immunohistochemistry, Histopathological grading

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Introduction

Salivary gland carcinomas represent an uncommon and complex category of head and neck cancers, distinguished by a remarkable histological variety and unpredictable clinical courses. Their rarity and diversity contribute to significant challenges in both diagnosis and prognosis, as tumors with similar histopathological grades may behave very differently in clinical settings.

To address these challenges, recent research has focused on identifying molecular markers that can enhance diagnostic accuracy and refine prognostic stratification. Among these, Syndecan-1 (CD138) has emerged as a notable candidate due to its role as a cell surface heparan sulfate proteoglycan involved in cell adhesion, matrix interactions, and the modulation of the tumor microenvironment.

Syndecan 1 (CD138) is a heparan sulfate proteoglycan present on the cell surface, participating in cell–cell and cell–matrix interactions, growth factor signaling, and modulation of the tumor microenvironment. Dysregulated expression of Syndecan 1 has been associated with tumor progression, epithelial–mesenchymal transition, invasion, and metastasis in multiple cancer types. Notably, a transition from epithelial membranous expression to increased stromal localization has been correlated with more aggressive tumor phenotypes.

Despite these insights, the clinical significance of CD138 expression in salivary gland carcinomas remains unclear, with available studies providing limited and sometimes conflicting results. This study aims to clarify the relationship between stromal and epithelial CD138 expression and histopathological grading in common salivary gland carcinomas, in pursuit of more reliable biomarkers for prognostic assessment.

Materials and Methods

Study Design and Setting

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This cross-sectional analytical study was conducted at the Department of Histopathology/Oral Pathology, Armed Forces Institute of Pathology, Rawalpindi.

Sample Selection

Forty-one cases of confirmed histopathological diagnosis of mucoepidermoid carcinoma and adenoid cystic carcinoma were included using non-probability consecutive sampling. Cases with inadequate fixation, insufficient tissue, prior chemo-radiotherapy, or incomplete clinical data were excluded.

Histopathological Evaluation

Hematoxylin and eosin–stained slides were reviewed to reconfirm diagnosis and classify tumors according to established histopathological criteria and grading systems.

Immunohistochemical Procedure

Immunohistochemical staining for CD138 was performed using on formalin-fixed, paraffin-embedded sections using a standardized indirect technique. Tumor cell membrane and/or cytoplasmic staining in tumor epithelial cells and stromal components was considered positive.

Expression was assessed semi-quantitatively using the Quick Score (QS) method, calculated as the percentage of positive cells (0–3) and product of staining intensity as weak, moderate, strong (0–3), respectively. QS values were categorized as low (0–3) or high (4–9). Stromal and epithelial compartments were evaluated separately.

Statistical Analysis

Data analysis was performed using SPSS version 26. Quantitative variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages.

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Associations between CD138 expression and histopathological grade were analyzed using appropriate inferential tests. A p-value ≤ 0.05 was considered statistically significant.

Results

Clinicopathological Characteristics

A total of 41 cases of salivary gland carcinomas were included in the study, comprising 51% mucoepidermoid carcinoma and 49% adenoid cystic carcinoma. High-grade tumors accounted for 36.6% of cases, while low-grade tumors represented 53.7%. The distribution of cases according to age, gender, tumor subtype, and histopathological grade is summarized in Table 1.

Table 1. Clinicopathological characteristics of salivary gland carcinoma cases (n = 41)

Variable	Category	Frequency (%)
Age (years)	≤40	29.2
	>40	70.7
Gender	Male	63
	Female	37
Tumor subtype	Mucoepidermoid carcinoma	51
	Adenoid cystic carcinoma	49
Histopathological grade	Low	53.7
	Intermediate	9.8
	High	36.6

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The distribution of tumor sites in SGC cases revealed that Parotid gland was the most affected site, accounting for (46.3%) followed by Submandibular gland (14.6%) and Hard palate for minor glands (7%) while the Upper lip (minor) was a rare site, observed in only 1 case (2.4%).

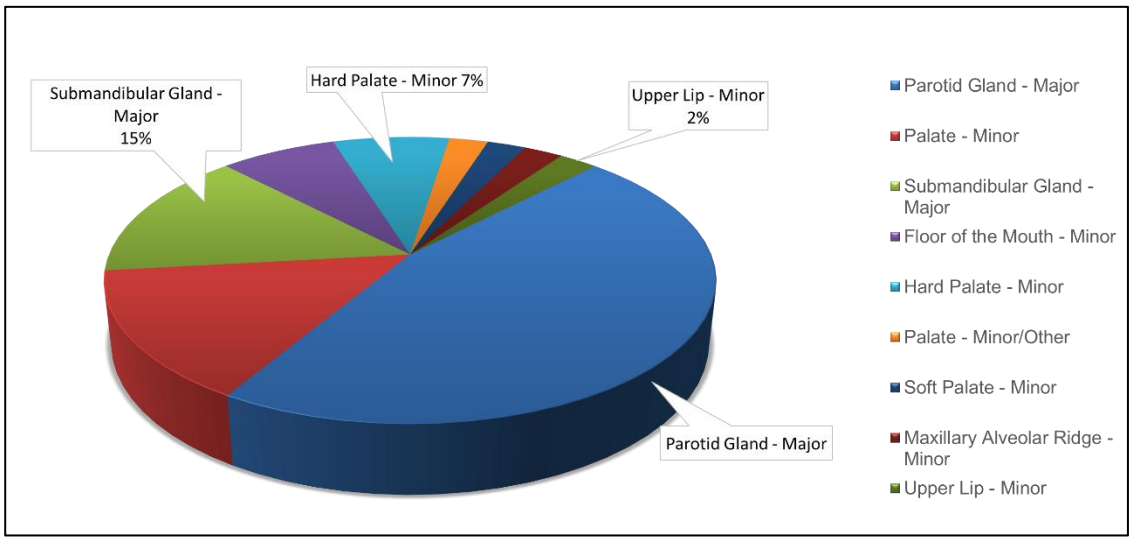

Figure 1: Distribution of tumour sites in SGCs

CD138 Immunohistochemical Expression

The overall patterns of CD138 immunoreactivity in stromal and epithelial components are presented in Table 2. Stromal CD138 expression was predominantly low (63.4%), whereas epithelial expression was predominantly high (73.17%) (Table 2). No statistically significant association was observed between stromal and epithelial expression (p = 1.0), indicating independent expression patterns.

Table 2. Overall CD138 immunoreactivity in stromal and epithelial components

CD138 expression	Stromal n (%)	Epithelial n (%)	**p-value**

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Low (QS 0–3)	63.4	26.6	**1.0**
High (QS 4–9)	36.5	73.17	

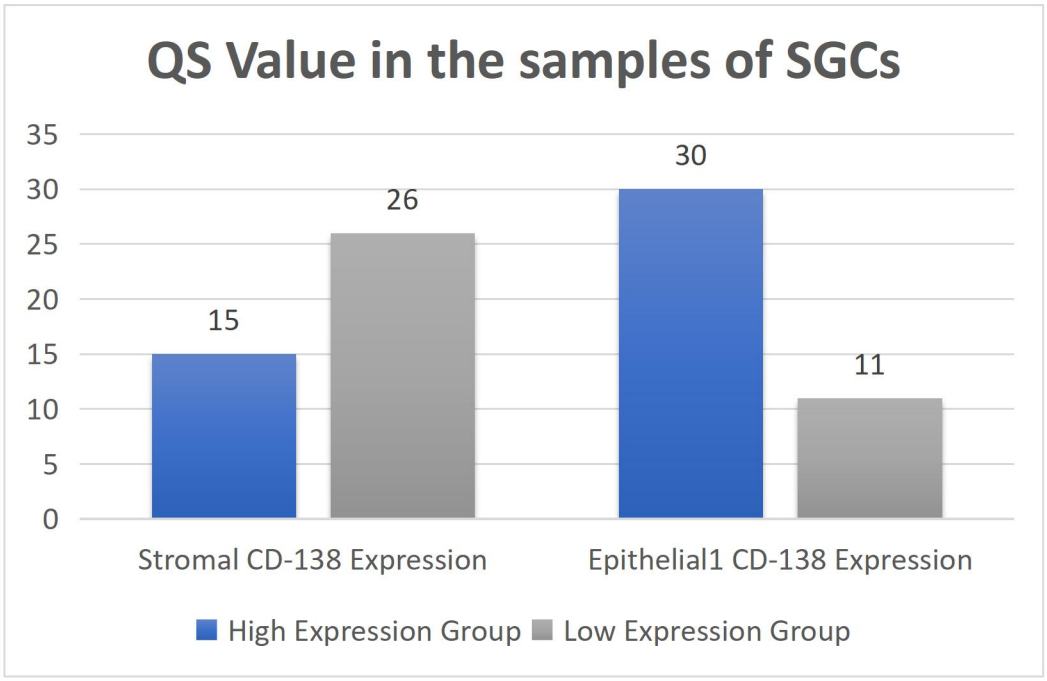

Figure 2: QS values for CD 138 expression in the stromal and epithelial components of SGCs

Association with Histopathological Grade

Epithelial CD138 expression demonstrated a statistically significant association with histopathological grade (Table 3, $p \leq 0.05$), with higher expression more frequently observed in advanced tumor grades.

Table 4. Association of epithelial CD138 expression with histopathological grade

Histological grade	Low epithelial expression n (%)	High epithelial expression n (%)	p-value

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Low	5	16	**≤0.05**
Intermediate	0	5	
High	6	9	

In contrast, stromal CD138 expression showed variable distribution across tumor grades, with low expression observed in both low- and high-grade tumors. Although reduced stromal expression was more frequently seen in high-grade tumors, this association did not reach statistical significance (Table 4, p = 0.5).

Table 3. Association of stromal CD138 expression with histopathological grade

Histological grade	Low stromal expression n (%)	High stromal expression n (%)	p-value
Low	10	3	**0.5**
Intermediate	2	2	
High	17	7	

Figure Representation

Representative photomicrographs illustrating stromal and epithelial CD138 expression patterns across different tumor grades are shown in Figures 3–6. Figure 7-9 shows occasional cases of high-grade tumors showed increased stromal expression and reduced epithelial expression.

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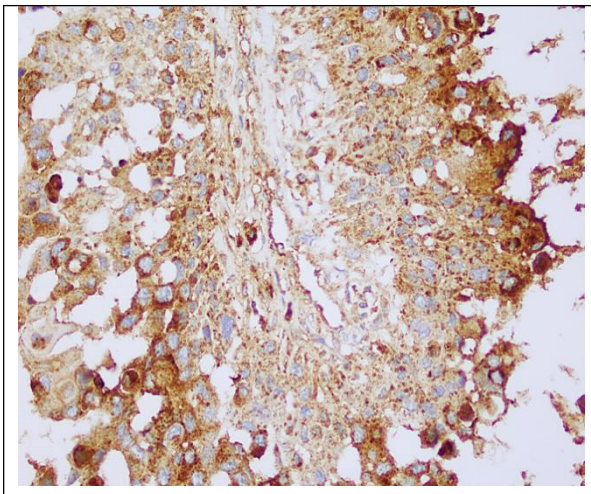

Figure 3. Immunohistochemical staining showing strong epithelial Syndecan-1 expression in high grade MEC (Epithelial component QS 9) (CD138 IHC x 400)

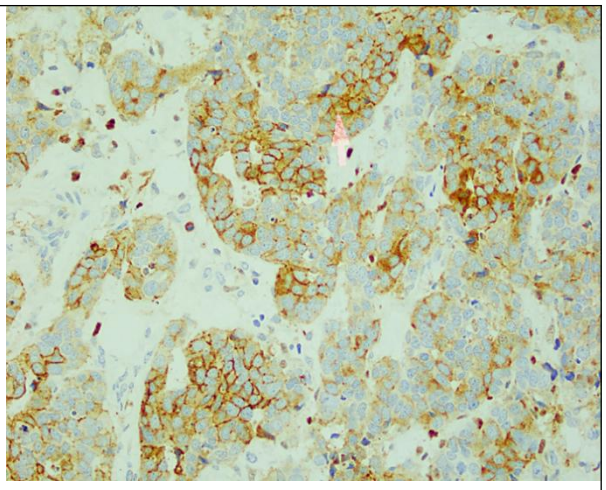

Figure 4. Immunohistochemical staining showing strong epithelial Syndecan-1 expression in high grade AdCC (Epithelial component QS 6) (CD138 IHC x 400)

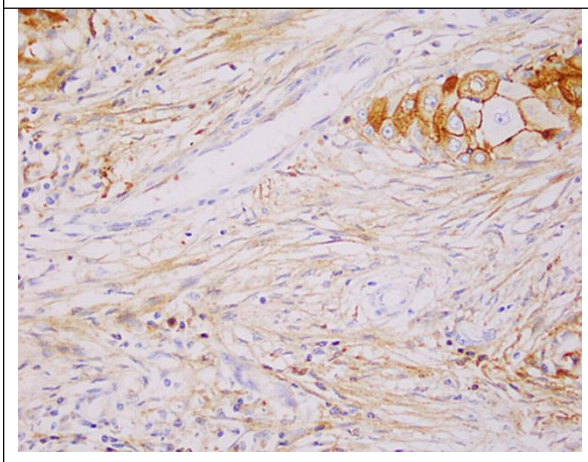

Figure 5. Immunohistochemical staining showing strong stromal Syndecan-1 expression in low grade MEC (Stromal component QS 6) (CD138 IHC x 400)

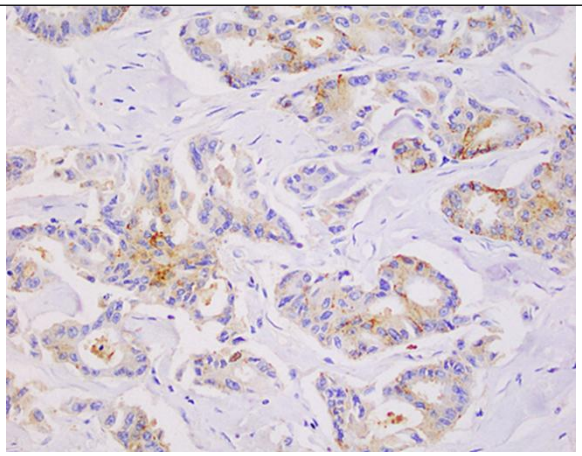

Figure 6. Immunohistochemical staining showing negative stromal Syndecan-1 expression in high grade MEC (Stromal component QS 0) (CD138 IHC x 400)

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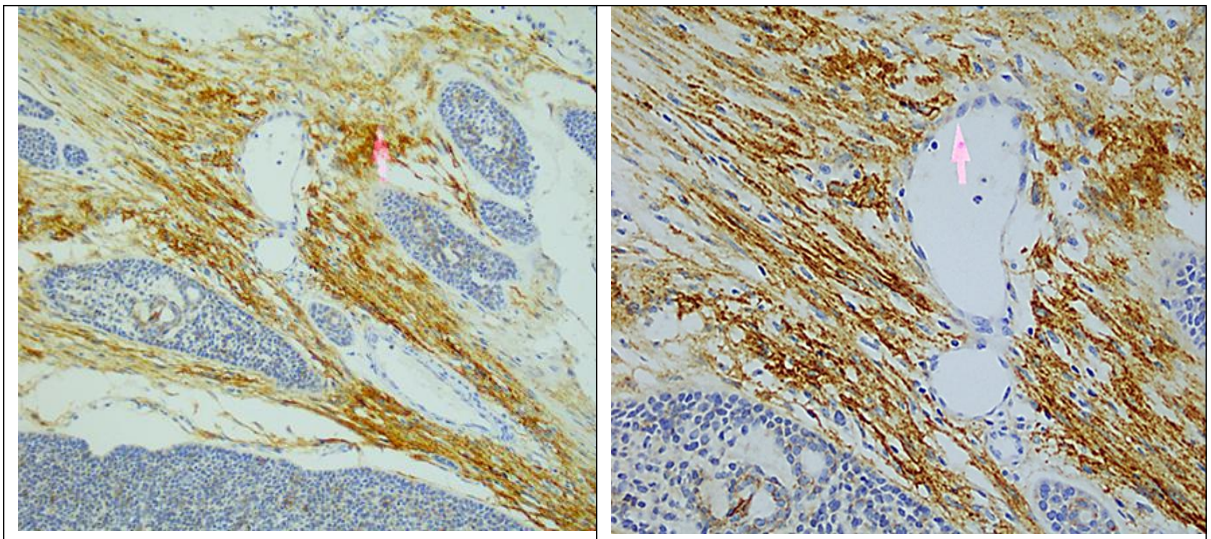

Figure 7. Immunohistochemical staining showing strong stromal Syndecan-1 (CD138) expression in a high-grade salivary gland carcinoma (CD 138 IHC ×200) & (CD 138 IHC x400).

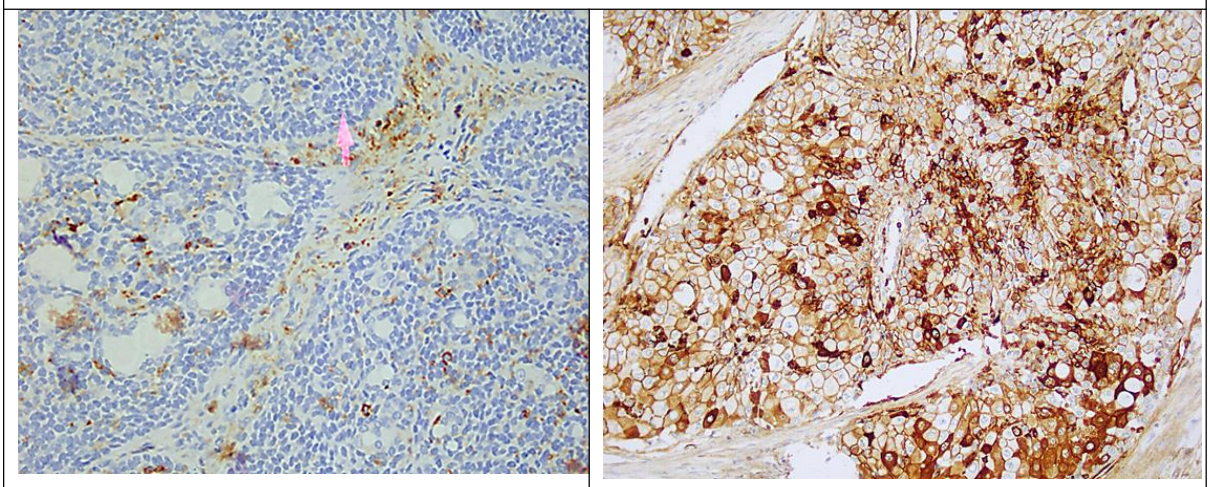

Figure 8. Reduced epithelial Syndecan-1 (CD138) expression in a poorly differentiated salivary gland carcinoma, High Grade AdCC- Negative epithelial positivity (Epithelial component QS 0 (CD138 IHC x 400)

Figure 9. Strong epithelial Syndecan-1 (CD138) expression in Low Grade MEC – Strong Epithelial positivity (Epithelial component QS 9) (CD138 IHC x 200)

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Discussion

The present study demonstrates that epithelial Syndecan-1 (CD138) expression shows a statistically significant association with histopathological grading in salivary gland carcinomas, with higher expression more frequently observed in advanced tumor grades. This suggests that epithelial CD138 may reflect tumor progression and differentiation status, supporting its potential role as a prognostic biomarker.

The increased epithelial expression observed in higher-grade tumors indicates that Syndecan-1 may be involved in regulating tumor cell behavior, including proliferation, adhesion, and differentiation. These findings are consistent with the concept that alterations in epithelial markers contribute to tumor progression and may reflect underlying biological aggressiveness.

In contrast, stromal CD138 expression exhibited variability across tumor grades and did not demonstrate a statistically significant association. Although a general trend of reduced stromal expression in higher-grade tumors was observed, this pattern was not consistent enough to establish a definitive correlation.

Interestingly, occasional cases of high-grade tumors showed increased stromal expression, supporting the concept that tumor stroma is not merely a passive framework but an active participant in tumor progression. Syndecan-1 within the stromal compartment may influence extracellular matrix remodeling, tumor–stroma interactions, and invasive potential.

Previous studies have highlighted the role of stromal Syndecan-1 in promoting aggressive tumor behavior, angiogenesis, and metastasis. However, the lack of statistical significance in the present

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study may be explained by several factors, including the relatively small sample size, biological heterogeneity of salivary gland carcinomas, and the combined analysis of different tumor subtypes such as mucoepidermoid carcinoma and adenoid cystic carcinoma.

The differential expression observed between epithelial and stromal compartments reinforces the concept that Syndecan-1 plays a complex and compartment-specific role in tumor biology. While epithelial expression appears to be more closely linked to tumor differentiation and grading, stromal expression may reflect dynamic interactions within the tumor microenvironment rather than direct correlation with histological grade.

This study has certain limitations. The relatively small sample size may have limited the statistical power to detect significant associations, particularly in stromal analysis. Additionally, the absence of long-term clinical follow-up data restricts the ability to correlate CD138 expression with patient outcomes such as survival and recurrence.

Future Recommendations

Future studies with larger sample sizes and subtype-specific analysis are recommended to further clarify the role of Syndecan-1 in salivary gland carcinomas. Incorporation of survival analysis and molecular profiling may provide deeper insights into its prognostic and therapeutic significance.

Conclusion

Epithelial Syndecan-1 (CD138) expression shows a significant association with histopathological grading in salivary gland carcinomas, suggesting its potential role as a prognostic biomarker. Although stromal expression demonstrated variable patterns and a tendency toward reduced expression in higher-grade tumors, it did not show a statistically significant correlation with tumor

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grade in this cohort. Further large-scale studies are required to clarify the role of stromal CD138 in tumor progression and its prognostic relevance.

Conflict of Interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Ethical Approval

Approved by the Institutional Review Board of AFIP, Rawalpindi.

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