Evaluation of GLUT-1expression in Oral Leukoplakia – an immunohistochemical study

Nancy Verma[1], Neeraj Grover[1], Kanika Bhalla Prabhat[1], Shreya Singh[1], Shivani Bhandari[2]

[1]Department of Oral and Maxillofacial Pathology and Oral Microbiology, Santosh Dental College and Hospital, Santosh Deemed to be University, Ghaziabad.

[2]Department of Oral and Maxillofacial Pathology and Oral Microbiology, Inderprastha Dental College, Ghaziabad.

Corresponding Author:
Nancy Verma
Email ID: nancy.verma0305@gmail.com

Submission : 08.07.2025 Acceptance: 28.10.2025 Publication : 18.12.2025

https://www.doi.org/10.63778/NHDCJCD-DRJPL/2025_0004

Abstract

Oral potentially malignant disorders (OPMDs) are clinical entities considered to be early indicators of oral carcinogenesis. Among them, leukoplakia stands out as the most commonly encountered lesion, described as a white patch in the oral cavity that cannot be diagnosed as any other disease. Studies suggest that a small percentage of these lesions may progress to oral cancer. The World Health Organization now recommends using the unified term "potentially malignant disorders" instead of separating them into lesions and conditions.

Leukoplakia and erythroplakia are prominent among these disorders, with epithelial dysplasia serving as a key histological marker for assessing the risk of malignant transformation. One of the early events in the carcinogenic process is a shift in glucose metabolism, often mediated by glucose transporter proteins such as GLUT-1.

GLUT-1 is a transmembrane protein responsible for sodium-independent glucose uptake. Its expression is influenced by factors like cellular growth rate, hypoxia, and oncogenic transformation. Numerous malignancies, including those of the prostate and lung, have shown increased GLUT-1 expression. However, limited research has explored its expression in oral epithelial dysplasia (OED).

This study aims to investigate GLUT-1 immunoreactivity in tissues diagnosed with oral leukoplakia and to compare the findings with normal oral epithelium, thereby assessing its potential as an early biomarker for malignant change.

Results:

GLUT-1 immunopositivity was observed in all 30 cases of oral leukoplakia, while the 10 normal mucosal samples showed minimal to no expression. A statistically significant correlation was found between GLUT-1 staining intensity and the severity of epithelial dysplasia ($\chi^2 = 120$, df = 9, $p < 0.001$).

Conclusion:

GLUT-1 expression increases progressively with the severity of dysplasia in leukoplakia. This suggests that GLUT-1 may serve as a valuable biomarker for identifying high-risk lesions with potential for malignant transformation.

Keywords: Oral Epithelial Dysplasia, Oral Potentially Malignant Disorders, GLUT-1, leukoplakia, malignant, precancer lesions.

Introduction

Leukoplakia is clinically defined by the World Health Organization (WHO) as a white patch or plaque in the oral cavity that cannot be categorized as any other known disease either clinically or histopathologically[(1)]. It represents one of the most common oral potentially malignant disorders (OPMDs) observed in dental practice. Among the range of precancerous lesions, leukoplakia and erythroplakia are recognized as the most significant due to their potential for malignant transformation[(2)].

The likelihood of leukoplakia progressing to oral squamous cell carcinoma is closely related to the severity of epithelial dysplasia present, with reported transformation rates ranging from 5% to 43%[(3)]. One of the earliest and most consistent changes during carcinogenesis is an alteration in the cellular energy metabolism pathway, particularly glucose uptake and utilization. Glucose is transported into cells via a group of specialized membrane proteins called glucose transporters (GLUTs), which function through a facilitated diffusion mechanism that does not require energy[(1)].

Among these, GLUT-1 is of particular interest due to its high expression in rapidly dividing cells and its critical role in meeting the increased energy demands of developing or neoplastic tissues. During early embryonic development, GLUT-1 is widely expressed, especially in tissues undergoing rapid proliferation. In postnatal stages, especially after weaning, its expression becomes restricted to specific tissues such as the brain, while tissue-specific isoforms take over in other organs[(4)].

In red blood cells, GLUT-1 accounts for approximately 5–10% of the total membrane protein, highlighting its physiological importance. Under normal aerobic conditions, glucose is metabolized through glycolysis and oxidative phosphorylation, yielding significant energy in the form of ATP. However, in hypoxic environments—or even under normoxic conditions in cancer cells—glucose is often

converted to lactate via aerobic glycolysis, a phenomenon known as the Warburg effect. This metabolic shift supports the rapid growth and survival of malignant cells[5].

This increased reliance on glucose uptake in malignant tissues is often accompanied by upregulation of GLUT-1. Such overexpression has been documented in several cancers, suggesting its potential as a biomarker for early detection of precancerous and cancerous changes. In this study, we aim to explore the expression pattern of GLUT-1 in oral epithelial dysplasia, with a focus on its relevance in identifying early stages of malignant transformation within leukoplakic lesions[6].

This study seeks to explore the diagnostic value of GLUT-1 expression in oral epithelial dysplasia (OED), with the aim of identifying early indicators of malignant progression in leukoplakia. In this study, we evaluated the role of GLUT-1 in detecting early changes in dysplastic epithelium[4].

Materials & Method

Source Of Data

This study employed a combination of retrospective and prospective approaches. A total of 40 formalin-fixed, paraffin-embedded tissue specimens were utilized, including samples diagnosed with varying grades of oral leukoplakia and normal oral mucosa. These were retrieved from the archives of the Department of Oral and Maxillofacial Pathology and Microbiology at Santosh Dental College, Ghaziabad, Uttar Pradesh, India.

Sample Size

The total sample comprised 40 tissue specimens, which included:

- 30 cases of oral leukoplakia of varying histopathological grades
- 10 cases of histologically normal oral mucosa (used as controls)

These samples were selected from previously recorded biopsy cases as well as newly diagnosed cases during the study period at the institution.

This retrospective as well as prospective study was conducted using a total of forty formalin fixed and paraffin embedded soft tissue samples of varying grades of leukoplakia and normal oral mucosa which were retrieved from the archives of the Department of Oral Pathology and Microbiology, Santosh Dental College Ghaziabad U.P., India.

Sample Size

- A total of 40 samples from the archival tissue as well as the cases reported during the study in our institution.
- 30 cases of different histopathological grades of Oral leukoplakia.
- 10 cases of Normal Oral Mucosa.

Statistical Analysis & Results

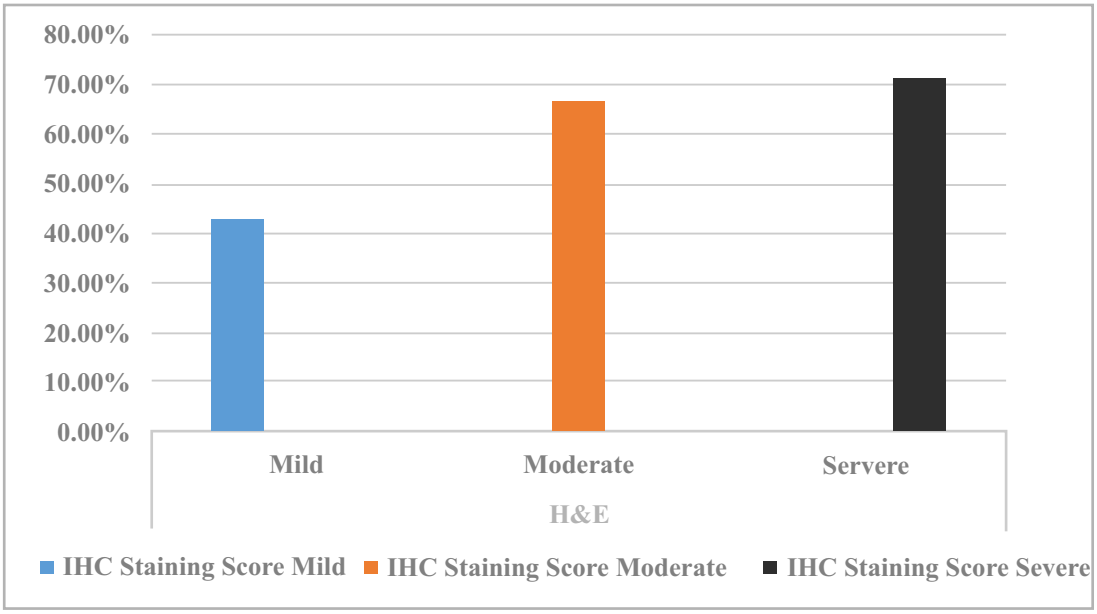
The results were obtained by comparing the IHC staining score with H& E staining and also with the intensity of Glut-1expression in different layer of various dysplastic epithelium.

The Oral leukoplakia cases have showed immunopositivity in all the 30 cases while compare to 10 normal Oral mucous.

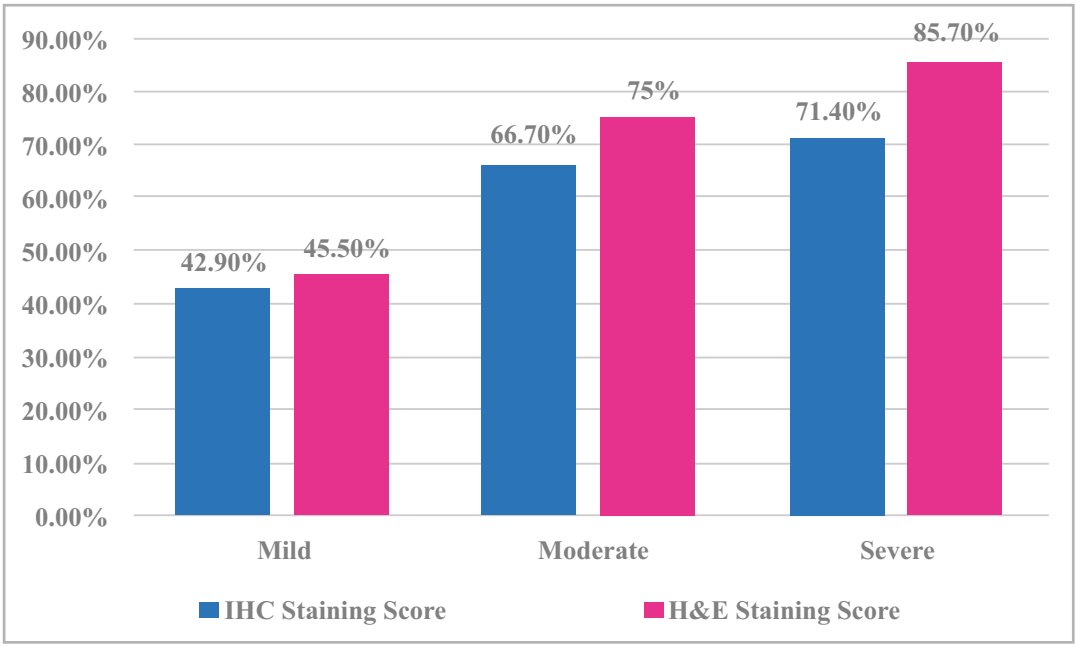
While comparing the H & E and IHC staining score we found that there is a high increase in magnitude from mild to severe dysplasia, in IHC staining the intensity is quite higher and showing a significance of immunohistochemistry over H & E staining i.e. IHC is giving more accurate result in dysplastic epithelium while H & E score is low.

Total score of Glut-1 expression observed in normal mucosa and oral leukoplakia after statistical analyais had a significant value at $P \leq 0.001$.

Graph:1 Association of IHC staining score with H&E Stainings.



Graph:2 Comparison between H& E and IHC staining score.



Discussion

Oral leukoplakia is widely acknowledged as a predominant precursor to oral squamous cell carcinoma, with approximately 18% of these lesions showing progression to malignancy. Among various prognostic factors, the presence and severity of epithelial dysplasia serve as stronger indicators of malignant potential compared to clinical features alone.

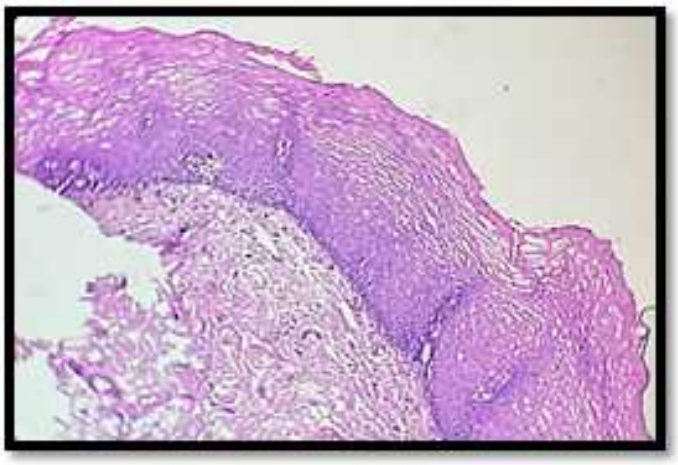
The term "dysplasia" reflects disordered cellular development. Oral potentially malignant disorders (OPMDs) are identified clinically, while histopathological evaluation may reveal a spectrum from hyperplasia and hyperkeratosis to oral epithelial dysplasia (OED) or frank carcinoma. OED is diagnosed based on architectural and cytological changes, particularly loss of stratification and normal epithelial maturation patterns.

OED is typically graded as mild, moderate, or severe depending on how much of the epithelial thickness exhibits dysplastic changes—restricted to the basal third in mild cases, extending to the middle third in moderate cases, and involving the full epithelial thickness in severe dysplasia.

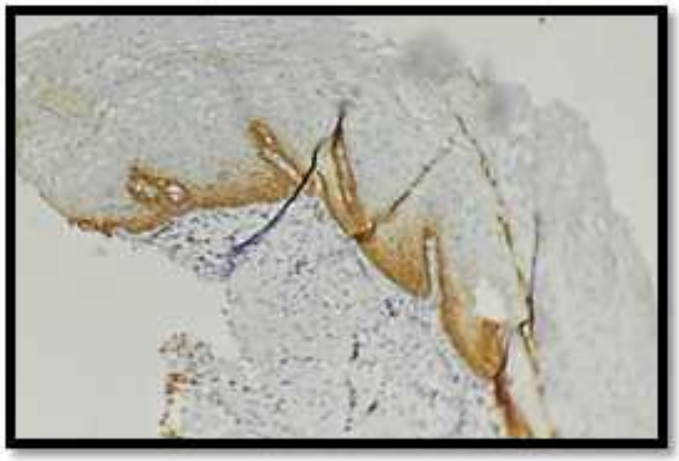
In the current study, all 30 cases of OED demonstrated GLUT-1 immunopositivity. Specifically:

- **Mild dysplasia**: 45% showed positive staining
- **Moderate dysplasia**: 75% positivity observed
- **Severe dysplasia**: 85.7% of cases exhibited GLUT-1 expression.

Histological View Showing Changes In Mild Dysplaisa

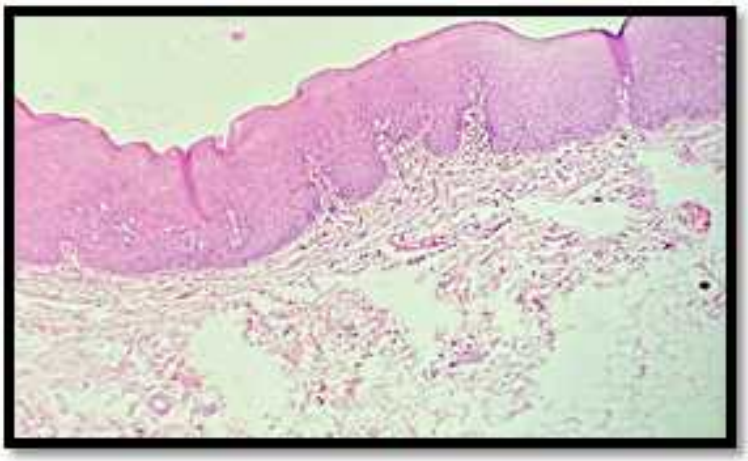


Oral leukoplakia showing dysplastic feature in lower third of epithelium and underlying connective tissue (H and E, ×10x view)

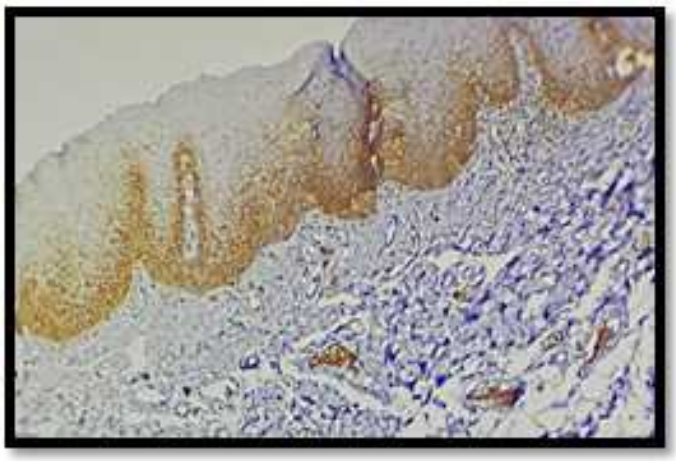


GLUT-1 up to basal layer presence of brown-colored end product in the epithelium at the site of target antigen (IHC, ×10x view)

Histological View Showing Changes In Moderate Dysplaisa

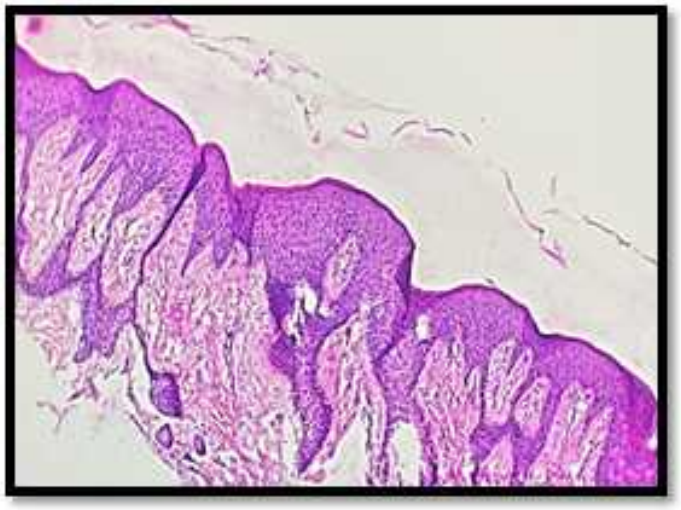


Oral leukoplakia showing dysplastic feature in middle third of epithelium and underlying connective tissue (H and E, ×10x view)

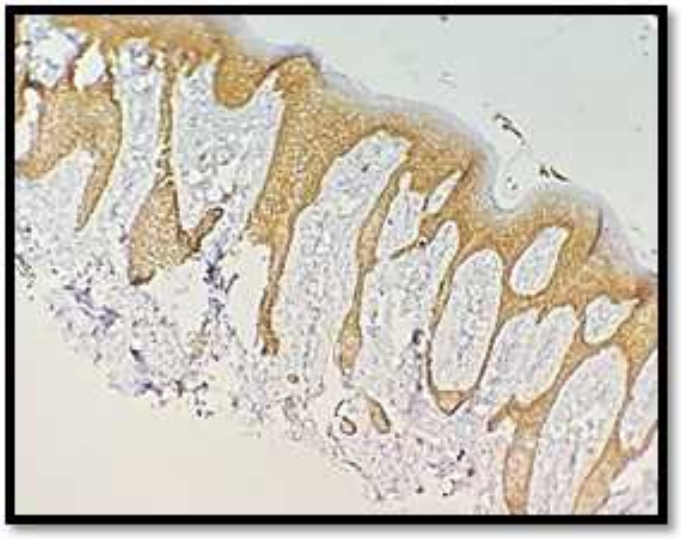


GLUT-1 up to suprabasal layer presence of brown-colored end product in the epithelium at the site of target antigen (IHC, ×10x view)

Histological View Showing Changes In Severe Dysplaisa



Oral leukoplakia showing dysplastic feature in upper third of epithelium and underlying connective tissue (H and E, ×10x view)

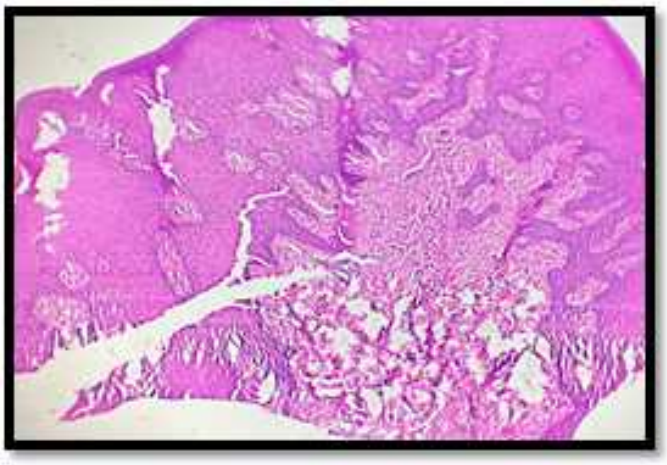


GLUT-1 up to basal and suprabasal layer presence of brown-colored end product in the epithelium at the site of target antigen (IHC, ×10x view)

There was a clear gradation of GLUT-1 expression, beginning in the basal layers in mild dysplasia, extending to two-thirds of the epithelium in moderate dysplasia, and involving the superficial layers in severe dysplasia. This indicates a progressive increase in GLUT-1 expression correlating with the severity of epithelial alteration.

Normal oral mucosa showed minimal to no GLUT-1 expression, supporting its specificity in identifying dysplastic changes. This finding underscores GLUT-1's role in the metabolic reprogramming of dysplastic and potentially neoplastic tissues, aligning with the well-documented Warburg effect—where glucose uptake and glycolysis are elevated in precancerous and cancerous cells, even under oxygen-rich conditions.

Histological View Showing Changes In Normal Oral Mucosa



Normal oral mucosa showing epithelium and connective tissue (HandE, ×10x view)

GLUT-1 expression showing Normal oral mucosa showing epithelium and connective tissue (IHC ×10x view)

Furthermore, comparison between Hematoxylin & Eosin (H&E) staining andimmunohistochemistry (IHC) revealed that IHC provided clearer differentiation among dysplasia grades. The increased intensity of GLUT-1 staining across mild to severe dysplasia groups enhances its utility in borderline or ambiguous histopathological cases.

Table:1 Association of Intensity of Glut-1 Expression with Epithelial Dysplasia.

Intensity of Glut-1 Expression

		Normal		Mild		Moderate		Severe		df	x^2 Value	Value
		N	%	N	%	N	%	N	%			
Epithelial Dysplasia	Mild	0	0	10	100	0	0	0	0	9	120	**0.001***
	Moderate	0	0	0	0	10	100	0	0			
	Severe	0	0	0	0	0	0	10	100			
	Normal	10	100	0	0	0	0	0	0			

Therefore, the present study demonstrates that evaluating GLUT-1 expression may help in identifying high-risk OED cases and offers potential support in diagnostic differentiation, especially where histological interpretation poses challenges.

Conclusion

This study was conducted to evaluate the expression of GLUT-1 in various grades of oral epithelial dysplasia (OED) and compare it with normal oral mucosa, with the goal of identifying early indicators of malignant transformation.

A total of 30 histologically confirmed cases of OED and 10 samples of normal oral mucosa were examined using immunohistochemical staining. The findings demonstrated a clear, progressive increase in both the intensity and extent of GLUT-1 expression from mild to severe dysplasia. In contrast, normal oral tissues showed negligible GLUT-1 activity.

Higher GLUT-1 expression was notably present in the superficial epithelial layers of severe dysplasia cases, whereas it was confined to the basal and suprabasal layers in mild dysplasia. This consistent pattern of increasing expression supports the role of GLUT-1 as a marker associated with advancing dysplastic severity.

The study highlights that the process of malignant transformation in the oral epithelium is multifactorial and involves early metabolic alterations. GLUT-1 may serve as a useful adjunctive biomarker to standard H&E staining, especially in cases where histopathological grading is challenging. Its increased expression aligns with higher dysplasia grades and thus may assist in identifying lesions with a greater risk of progression to oral squamous cell carcinoma.

Immunohistochemistry for GLUT-1, therefore, has the potential to enhance diagnostic precision and aid in the early detection of high-risk lesions. Further investigations with larger sample sizes are recommended to validate its prognostic value and explore its utility in clinical decision-making.

Source of Support: Nil

Conflict of Interest: Nil

References

1. Warnakulasuriya S, Johnson NW, van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. J Oral Pathol Med. 2007;36:575–80.
2. Neville BW, Douglas DD, Allen CM, Bouquot JE. Oral and Maxillofacial Pathology. USA: WB Sunders Co; 1995. pp. 280–8.
3. Amagasa T, Yamashiro M, Ishikawa H. Oral Leukoplakia Related to Malignant Transformation. Oral Science International; 2006;3:45–55.
4. Gould GW, Holman GD. The glucose transporter family: Structure, function and tissue-specific expression. Biochem J. 1993;295(Pt 2):329–41.
5. Reisser C, Eichhorn K, Herold-Mende C, Born AI, Bannasch P. Expression of facilitative glucose transport proteins during development of squamous cell carcinomas of the head and neck. Int J Cancer. 1999;80:194–8.
6. Annibaldi A, Widmann C. Glucose metabolism in cancer cells. Curr Opin Clin Nutr Metab Care. 2010;13:466–70.