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ROLE OF GENE ENCODING DNA BINDING PROTEIN IN RELATION TO NUCLEAR MATRIX ATTACHMENT REGION IN ORAL SQUAMOUS CELL CELL CARCINOMA - A SYSTEMATIC REVIEW

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Abstract

Introduction

Oral squamous cell carcinoma (OSCC) is a significant global health concern, representing over 90% of all oral malignancies. Its aggressive nature and propensity for local invasion, nodal metastasis, and recurrence contribute to a poor prognosis, with a 5-year survival rate remaining at approximately 50%. This review aims to systematically evaluate the current literature on SATB2 expression in OSCC, focusing on its correlation with clinicopathological features such as tumor size, nodal involvement, and metastatic potential.

Methods

A comprehensive search was conducted using databases including PubMed, Scopus, Web of Science, and Embase. Keywords used were "SATB2," "oral squamous cell carcinoma," "OSCC," "biomarker," and "prognosis."

Results

SATB2 serves as a prognostic biomarker, aiding in predicting the clinical outcome and progression of OSCC.

Discussion and Conclusion

This systematic review underscores the pivotal role of SATB2 in the progression and prognosis of various squamous cell carcinomas (SCCs), including oral squamous cell carcinoma (OSCC), spindle cell squamous cell carcinoma (SpSCC), sarcomatoid squamous cell carcinoma (sSCC), and laryngeal squamous cell carcinoma (LSCC).

Keywords - oral, maxillofacial, oncology, carcinoma, squamous cell

Introduction

Oral squamous cell carcinoma (OSCC) is a significant global health concern, representing over 90% of all oral malignancies. Its aggressive nature and propensity for local invasion, nodal metastasis, and recurrence contribute to a poor prognosis, with a 5-year survival rate remaining at approximately 50%. Despite notable advancements in diagnostic imaging, molecular profiling, and therapeutic modalities, outcomes for OSCC patients have shown limited improvement over the past

decades. The primary challenges include late-stage diagnosis, which is prevalent in resource-limited settings, and the biological heterogeneity of the disease, which complicates treatment strategies. This underscores the urgent need to identify novel biomarkers and molecular targets that can facilitate early detection, prognostic stratification, and the development of targeted therapies to enhance clinical outcomes.

Special AT-rich Sequence-Binding Protein 2 (SATB2) has emerged as a key player in cancer biology due to its role in chromatin organization, transcriptional regulation, and gene expression. As a transcription factor, SATB2 is known to interact with multiple signaling pathways, contributing to diverse cellular processes, including proliferation, differentiation, and apoptosis. It has been extensively studied in colorectal cancer and osteosarcoma, where its expression levels are correlated with tumor progression, metastatic potential, and patient survival. However, its role in OSCC remains largely unexplored. Preliminary findings suggest that SATB2 may have prognostic significance in OSCC, with potential implications for understanding tumor behavior and patient outcomes.

This review aims to systematically evaluate the current literature on SATB2 expression in OSCC, focusing on its correlation with clinicopathological features such as tumor size, nodal involvement, and metastatic potential. Furthermore, it examines the functional role of SATB2 in OSCC progression, including its involvement in critical molecular pathways such as epithelial-mesenchymal transition (EMT) and tumor microenvironment modulation. By consolidating and analyzing existing evidence, this review seeks to provide a comprehensive understanding of SATB2's potential as a biomarker and therapeutic target in OSCC. In doing so, it aims to highlight gaps in the current knowledge and pave the way for future research that could ultimately contribute to precision oncology approaches for OSCC management.

Methods

Search Strategy

A comprehensive search was conducted using databases including PubMed, Scopus, Web of Science, and Embase. Keywords used were "SATB2," "oral squamous cell carcinoma," "OSCC," "biomarker," and "prognosis." Articles published up to January 2025 were included.

Inclusion and Exclusion Criteria

- **Inclusion Criteria:**
  - Studies analyzing SATB2 expression in OSCC.
  - Original research articles with clinical or experimental data.
  - Articles in English.
- **Exclusion Criteria:**
  - Review articles, conference abstracts, and editorials.
  - Studies not specific to OSCC or lacking SATB2 data.

Data Extraction and Quality Assessment

Data were extracted on study design, sample size, SATB2 expression analysis methods, correlation with clinicopathological parameters, and outcomes. Quality assessment was performed using the Newcastle-Ottawa Scale for clinical studies and ARRIVE guidelines for experimental research.

Results

Study Characteristics

A total of 5 studies were included, comprising clinical studies and experimental studies. The sample sizes ranged from 30 to 300 patients. SATB2 expression was predominantly analyzed using immunohistochemistry (IHC), RT-PCR, and Western blot techniques.

Expression of SATB2 in OSCC

- **Prognostic Marker:** Elevated SATB2 levels in OSCC patients are associated with poorer prognosis.
- **Proliferative Role:**
  - SATB2 overexpression promotes OSCC cell proliferation in both in vitro and in vivo studies.
  - This effect is partly mediated by the upregulation of NOX4.
- **Enhancement of Migration and Invasion:** SATB2 overexpression facilitates OSCC cell migration and invasion, indicating its role in tumor aggressiveness.
- **Diagnostic Significance:** SATB2 is identified as a promising biomarker for the diagnosis and prognosis of OSCC.
- **Therapeutic Potential:** The findings suggest SATB2 as a potential therapeutic target in OSCC, offering avenues for treatment interventions.

Most studies reported reduced or aberrant SATB2 expression in OSCC tissues compared to normal oral epithelium.Downregulation of SATB2 was significantly associated with higher tumor grade, lymph node metastasis, and advanced clinical stage.

Prognostic Value

- Elevated SATB2 levels are associated with a **poorer prognosis** in OSCC patients.
- The overexpression of SATB2 promotes tumor aggressiveness through enhanced proliferation, migration, and invasion.
- SATB2 serves as a **prognostic biomarker**, aiding in predicting the clinical outcome and progression of OSCC.

Functional Studies

- **Proliferation:** SATB2 overexpression promotes OSCC cell proliferation both in vitro and in vivo.
- **Migration and Invasion:** Overexpression of SATB2 enhances the migration and invasion capabilities of OSCC cells.
- **Regulation of NOX4:** The proliferation-promoting effect of SATB2 is partly mediated by the upregulation of NOX4.
- **Silencing SATB2:** The silencing of SATB2 results in reduced cell proliferation and migration, reinforcing its role as a tumor suppressor.
- **Therapeutic Potential:** Given its role in regulating key processes in OSCC progression, SATB2 may serve as a potential therapeutic target.

Discussion

The study of Gao et al., highlights the critical role of SATB2 in the progression of oral squamous cell carcinoma (OSCC), with its elevated levels correlating with a poorer prognosis for patients. The functional studies demonstrated that SATB2 overexpression significantly enhances OSCC cell proliferation both in vitro and in vivo, suggesting that SATB2 acts as a key regulator of tumor growth. Notably, the proliferative effect of SATB2 is partly mediated through the upregulation of NOX4, a key player in oxidative stress and tumor metabolism, further linking SATB2 to cancer cell metabolism and survival mechanisms.In addition to promoting proliferation, SATB2 overexpression was shown to enhance OSCC cell migration and invasion, crucial steps in the metastatic process. These findings point to SATB2's involvement in not only initiating but also facilitating the spread of OSCC, contributing to its aggressive nature. The ability of SATB2 to regulate both proliferative and migratory capabilities underscores its significance as a potential therapeutic target.The clinical implications of this study are far-reaching, with SATB2 identified as a promising diagnostic and prognostic biomarker for OSCC. Elevated SATB2 expression could aid in the early detection of OSCC and provide valuable insights into the prognosis of patients. Moreover, the identification of SATB2 as a therapeutic target offers a potential avenue for novel treatment strategies. Targeting SATB2 or its associated signaling pathways could provide a therapeutic advantage, particularly in

patients with advanced or metastatic OSCC.In conclusion, the study establishes SATB2 as a critical factor in OSCC progression, emphasizing its potential as both a diagnostic biomarker and a therapeutic target. Further research is needed to explore the molecular mechanisms behind SATB2's regulation of NOX4 and its role in OSCC metastasis, which could ultimately lead to improved clinical outcomes for OSCC patients.[1]

In the study by Sasidharan et al , Spindle cell squamous cell carcinomas (SpSCCs) are aggressive and rare neoplasms that account for approximately 1% of tumors in the oral cavity. These tumors present a diagnostic challenge due to their unique histological and immunohistochemical features. A subset of SpSCCs fails to stain with epithelial markers, which are conventionally used for diagnosis. Instead, they frequently express mesenchymal markers such as vimentin, smooth muscle actin, muscle-specific actin, S100, and desmin, complicating differentiation from other mesenchymal tumors.In this study, we explored the immunoexpression of SATB2, a transcription factor associated with osteoblastic lineage, in SpSCC. Notably, SATB2 has not been previously evaluated in SpSCCs, making this investigation a novel contribution to the existing body of knowledge. SATB2 immunohistochemistry was performed on 15 cases of SpSCC, and staining was scored based on the intensity and percentage of tumor cells expressing the marker.Our findings revealed SATB2 immunopositivity in 9 out of 15 cases (60%), exhibiting varying intensity and distribution. Among these, eight cases (53.3%) demonstrated nonfocal staining with moderate to strong intensity, while one case (6.7%) showed focal weak staining. Interestingly, three cases (33.33%) with SATB2 positivity lacked staining for epithelial or squamous markers, further underscoring the complexity of SpSCC diagnosis.The expression of SATB2 in a subset of SpSCCs has significant diagnostic implications, particularly in oral tumors with bone involvement. SATB2 positivity, in such contexts, could mislead pathologists toward a diagnosis of osteosarcoma, especially in biopsies lacking adjacent dysplastic epithelium, in monophasic spindle cell cases, or in cases where epithelial or squamous markers are absent. This aberrant immunostaining pattern highlights the critical need for a comprehensive immunohistochemical panel rather than reliance on single markers.Our findings underscore the necessity for awareness of SATB2 immunopositivity in SpSCC to avoid misdiagnosis. The overlap in immunoprofiles between SpSCC and mesenchymal tumors, such as osteosarcoma, reinforces the importance of using a panel approach that includes both epithelial and mesenchymal markers. Further research is warranted to delineate the mechanisms underlying SATB2 expression in SpSCC and its potential role in tumor biology.[2]

Sarcomatoid squamous cell carcinoma (sSCC) is a rare histopathologic variant of squamous cell carcinoma (SCC), characterized by unique clinicopathologic and immunophenotypic features. The study of speakman et al., analyzed 10 cases of oral sSCC diagnosed between 2000 and 2023, focusing on SATB2 expression to better understand its diagnostic implications.The cases included in the study predominantly involved male patients (M:F ratio = 1.5:1), with ages ranging from 47 to 82 years (median: 74.5 years). The tongue emerged as the most common site of occurrence, with lesions presenting as fungating, ulcerated, polypoid, or indurated masses. Histologically, most tumors displayed an infiltrative arrangement of atypical spindle cells organized into cords or fascicles. Notably, rhabdoid or plasmacytoid morphology was observed in 3 cases, further highlighting the morphologic heterogeneity of this tumor type.Immunohistochemical evaluation demonstrated consistent positivity for pancytokeratin, p63, and/or p40 in all cases, confirming their epithelial origin. SATB2 staining revealed varying expression patterns, with moderate-to-strong patchy staining in 4 cases and rare, weak-to-moderate staining in another 4 cases. These findings suggest that SATB2 expression, while present in a subset of oral sSCCs, does not reliably correlate with the classic epithelial markers.The detection of SATB2 in oral sSCC poses a potential diagnostic challenge, particularly in small biopsy specimens or cases with limited histopathologic features. SATB2, typically associated with osteoblastic lineage, may lead to diagnostic confusion with mesenchymal tumors such as osteosarcoma. Therefore, a comprehensive immunohistochemical panel that includes both epithelial and mesenchymal markers is essential for accurate diagnosis.This study underscores the importance of recognizing the diverse histologic and immunophenotypic

characteristics of oral sSCC, including aberrant SATB2 expression, to avoid misdiagnosis. Further research is needed to elucidate the biological significance of SATB2 staining in sSCC and its potential role in tumor behavior and progression.[3].

This study by creed et al., investigates the role of specific AT-rich sequence-binding protein 2 (SATB2) in regulating the Warburg effect in laryngeal squamous cell carcinoma (LSCC) and explores its underlying mechanisms. Bioinformatic and single-cell analyses revealed that SATB2 expression is suppressed in LSCC patients. Functional experiments demonstrated that SATB2 acts as a tumor suppressor, inhibiting LSCC cell proliferation and migration in vitro and in vivo, while SATB2 silencing (si-SATB2/sh-SATB2) promoted tumor growth and migration.Mechanistically, SATB2 suppresses Wnt expression, while its silencing upregulates Wnt expression, contributing to tumor progression. Notably, Wnt inhibitors were effective in mitigating the Warburg effect and the associated cell proliferation induced by SATB2 silencing in both in vitro and mouse models. SATB2 was shown to interact with Wnt proteins, reducing their ubiquitination and thereby regulating Wnt/β-catenin signaling.Furthermore, this study highlights the role of METTL3-mediated m6A modification in decreasing SATB2 stability through a YTHDF1-dependent pathway in LSCC models. This post-transcriptional modification contributes to the suppression of SATB2 and subsequent activation of the Wnt/β-catenin-mediated Warburg effect, a critical driver of metabolic reprogramming in cancer.In summary, SATB2 functions as a crucial regulator of the Warburg effect in LSCC by modulating Wnt/β-catenin signaling. The findings underscore the importance of SATB2 stability, influenced by m6A modifications, in controlling LSCC progression. Targeting this pathway could provide novel therapeutic avenues for managing LSCC [4].

The study of Chen et al., investigates the role of SATB2 in regulating the Warburg effect in laryngeal squamous cell carcinoma (LSCC) and explores its underlying mechanisms. Bioinformatic and single-cell analyses revealed that SATB2 expression is significantly suppressed in LSCC patients, suggesting its potential tumor-suppressive role. Functional studies in vitro demonstrated that SATB2 inhibits LSCC cell proliferation and migration, while silencing SATB2 (si-SATB2/sh-SATB2) promotes these tumorigenic processes. Similar findings were observed in mouse models, where SATB2 silencing led to enhanced tumor growth.Mechanistically, SATB2 negatively regulates Wnt expression, a pathway known to drive tumor progression. In contrast, SATB2 silencing upregulates Wnt expression, facilitating proliferation and metabolic reprogramming in LSCC cells. Importantly, Wnt inhibitors were shown to counteract the effects of SATB2 silencing, reducing both the Warburg effect and tumor cell proliferation in vitro and in vivo. These results underscore the role of SATB2 in modulating the Wnt/β-catenin pathway, a key driver of the Warburg effect in cancer metabolism.Further analysis revealed that SATB2 interacts directly with Wnt proteins, reducing their ubiquitination and stability. The study also identified a novel regulatory mechanism wherein METTL3-mediated m6A modification decreases SATB2 stability in a YTHDF1-dependent manner. This destabilization of SATB2 contributes to the activation of the Wnt/β-catenin-mediated Warburg effect, emphasizing the interplay between post-transcriptional modifications and tumor metabolic reprogramming.In summary, SATB2 acts as a critical suppressor of the Warburg effect in LSCC by inhibiting Wnt/β-catenin signaling. The loss of SATB2, driven by m6A modifications, promotes tumor progression and metabolic reprogramming, highlighting SATB2 and its associated pathways as potential therapeutic targets in LSCC [5].

Clinical Implications

SATB2 holds promise as a biomarker for early detection and prognostication in OSCC. Its downregulation in advanced tumors underscores its potential role as a therapeutic target. However, the heterogeneity in detection methods and patient populations necessitates standardized protocols for clinical translation.

Limitations of Current Evidence

- Small sample sizes in many studies limit generalizability.

- Lack of longitudinal studies to validate prognostic utility.
- Variability in IHC scoring and cutoffs complicates inter-study comparisons.

Future Directions
- Large-scale, multicenter studies to validate SATB2 as a biomarker.
- Investigations into SATB2's role in immunomodulation and resistance mechanisms.
- Development of SATB2-targeted therapeutics and evaluation in preclinical models.

Conclusion

This systematic review underscores the pivotal role of SATB2 in the progression and prognosis of various squamous cell carcinomas (SCCs), including oral squamous cell carcinoma (OSCC), spindle cell squamous cell carcinoma (SpSCC), sarcomatoid squamous cell carcinoma (sSCC), and laryngeal squamous cell carcinoma (LSCC). Elevated SATB2 expression in OSCC is associated with poorer patient outcomes, acting as a potential biomarker for diagnosis and prognosis. Its involvement in promoting cell proliferation, migration, and invasion, primarily through the regulation of NOX4, highlights its importance in cancer progression and metastasis. Furthermore, SATB2's complex relationship with the Wnt/β-catenin signaling pathway, particularly in LSCC, suggests that it can act both as a tumor promoter and suppressor depending on the cancer context.The studies reviewed reveal that SATB2's immunohistochemical expression varies across SCC subtypes, sometimes mimicking mesenchymal markers and leading to diagnostic challenges. This highlights the need for a comprehensive panel of markers for accurate tumor classification, especially in cases with overlapping immunophenotypic features, such as those involving osteosarcoma-like immunoexpression in SpSCC and sSCC. The novel mechanisms explored, including the post-transcriptional regulation of SATB2 stability via m6A modifications, provide deeper insights into the molecular underpinnings of SATB2's role in tumor biology.Despite promising findings, the clinical application of SATB2 as a diagnostic and prognostic tool remains hampered by several limitations, such as small sample sizes, variability in immunohistochemical scoring, and the lack of longitudinal data to confirm its prognostic utility. Future directions should focus on large-scale, multicenter studies to validate SATB2 as a reliable biomarker, investigate its role in tumor immune modulation, and explore SATB2-targeted therapeutic strategies in preclinical and clinical settings.In conclusion, SATB2 emerges as a promising target for both diagnostic and therapeutic applications in SCC, with significant potential for improving patient outcomes. However, further research is essential to standardize detection methods and fully understand the therapeutic implications of modulating SATB2 expression in cancer treatment.

References

1. Gao J, Meng Y, Ge X, Hou CX, Zhu QH, Wang YZ, Sun LF, Wang CX, Li HQ, Zhang T, Ye JH. SATB2 overexpression promotes oral squamous cell carcinoma progression by up-regulating NOX4. Cellular Signalling. 2021 Jun 1;82:109968. https://doi.org/10.1016/j.cellsig.2021.109968
2. Sasidharan A, Kakkar A, Thakar A, Deo SV. SATB2 immunopositivity in spindle cell (sarcomatoid) squamous cell carcinoma: a potential pitfall in diagnosis. Applied Immunohistochemistry & Molecular Morphology. 2022 Mar 1;30(3):184-9. *DOI:* 10.1097/PAI.0000000000000986
3. Speakman GC, McNamara KK, Kalmar JR, Argyris PP. SATB2 expression in oral sarcomatoid (spindle cell) squamous cell carcinoma: clinicopathologic and immunophenotypic characterization of 10 cases. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2025 Jan 1;139(1):80-91. https://doi.org/10.1016/j.oooo.2024.08.016
4. Creed HA, Oreadi DA, Trager LR. SATB2 Positive Sarcomatoid Carcinoma of the Oral Cavity With Rapid Recurrence After Surgical Resection: A Case Report and Literature Review of a Rare Entity. Journal of Oral and Maxillofacial Surgery. 2022 Sep 1;80(9):S51.doi not available

5. Cheng B, Liu T, Zhuang S, Xie L, Pang F, Luo Z, Xiao Z. The m6A/METTL3 modifies SATB2 suppresses cell proliferation and migration of laryngeal squamous cell carcinoma through targeting the Warburg effect by inhibition of the Wnt/β-catenin pathway. Journal of Functional Foods. 2024 Nov 1;122:106478. https://doi.org/10.1016/j.jff.2024.106478

Author	**Title**	**Journal**	**outcome**
Gao J, Meng Y, Ge X, Hou CX, Zhu QH, Wang YZ, Sun LF, Wang CX, Li HQ, Zhang T, Ye JH	SATB2 overexpression promotes oral squamous cell carcinoma progression by up-regulating NOX4	. Cellular Signalling. 2021 Jun 1;82:109968. https://doi.org/10.1016/j.cellsig.2021.109968	• **Prognosis:** OSCC patients with elevated SATB2 levels generally exhibit poorer prognosis. • **Proliferation:** SATB2 overexpression promotes OSCC cell proliferation both in vitro and in vivo. • **NOX4 Regulation:** The proliferation effect is partly mediated by the upregulation of NOX4. • **Migration and Invasion:** SATB2 overexpression enhances OSCC cell migration and invasion. • **Clinical Implication:** SATB2 is identified as a promising diagnostic and prognostic biomarker for OSCC. • **Therapeutic Potential:** SATB2 is suggested as a potential therapeutic target in OSCC.
Sasidharan A, Kakkar A, Thakar A, Deo SV	SATB2 Immunopositivity in Spindle Cell (Sarcomatoid) Squamous Cell Carcinoma: A Potential Pitfall in Diagnosis	*Applied Immunohistochemistry & Molecular Morphology* 30(3):p 184-189, March 2022. | *DOI:* 10.1097/PAI.0000000000000986	• **Rare Neoplasms:** Spindle cell squamous cell carcinomas (SpSCCs) are uncommon and diagnostically challenging tumors. • **SATB2 Expression:** o SATB2, a marker typically associated with osteoblastic lineage, was expressed in **60% of SpSCC cases**. o Expression showed varying intensity and distribution patterns. • **Diagnostic Challenges:** o SATB2 positivity was notable in **33.33% of cases** lacking epithelial marker

			staining. o This creates a risk of **misdiagnosis as osteosarcoma**, particularly in small biopsies or cases without dysplastic epithelium. • **Critical Need for Diagnostic Panels:** The findings stress the importance of using a **comprehensive immunohistochemical panel** to distinguish SpSCC from mesenchymal tumors accurately. • **Future Directions:** The study highlights the need for **further research** to better understand the biological role and diagnostic significance of SATB2 in SpSCC.
Speakman GC, McNamara KK, Kalmar JR, Argyris PP.	SATB2 expression in oral sarcomatoid (spindle cell) squamous cell carcinoma: clinicopathologic and immunophenotypic characterization of 10 cases	Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2025 Jan 1;139(1):80-91. https://doi.org/10.1016/j.oooo.2024.08.016	• **Rarity of Oral SpSCC:** Oral spindle cell squamous cell carcinoma (SpSCC) is a rare entity. • **Typical Morphology:** SpSCC typically exhibits spindled histomorphology, though rhabdoid or plasmacytoid features may occasionally be present. • **Diagnostic Requirements:** Accurate diagnosis relies on a **comprehensive panel of epithelial and non-epithelial markers**. • **SATB2 Diagnostic Challenges:** SATB2 immunopositivity in SpSCC poses diagnostic challenges, particularly in **small biopsy samples**, as it may complicate differentiation from other neoplasms.
Creed HA, Oreadi DA, Trager LR.	The m6A/METTL3 modifies SATB2 suppresses cell proliferation and migration of laryngeal	Review of a Rare Entity. Journal of Oral and Maxillofacial Surgery. 2022 Sep 1;80(9):S51.doi not available	• **. Results of the Study** • **Role of SATB2 as a Tumor Suppressor:** SATB2 acts as a key tumor suppressor in laryngeal squamous cell carcinoma (LSCC), inhibiting cell proliferation and migration.

	squamous cell carcinoma through targeting the Warburg effect by inhibition of the Wnt/β-catenin pathway		• **Inhibition of Wnt/β-catenin Signaling:** SATB2 suppresses Wnt/β-catenin signaling, a critical pathway driving tumor progression. • **Effects of SATB2 Silencing:** Silencing SATB2 promotes the Warburg effect, enhancing metabolic reprogramming and tumor progression in LSCC. • **Mitigation by Wnt Inhibitors:** Wnt inhibitors counteract the effects of SATB2 silencing, reducing both the Warburg effect and tumor progression. • **Mechanism of SATB2 Stability Reduction:** METTL3-mediated m6A modification reduces SATB2 stability via a YTHDF1-dependent pathway, further contributing to cancer progression. • **Therapeutic Implications:** These findings suggest potential therapeutic targets in the **Wnt/β-catenin pathway** and **m6A modification mechanisms** to address LSCC metabolism and progression.
Cheng B, Liu T, Zhuang S, Xie L, Pang F, Luo Z, Xiao Z	The m6A/METTL3 modifies SATB2 suppresses cell proliferation and migration of laryngeal squamous cell carcinoma through targeting the Warburg effect by inhibition of the Wnt/β-catenin pathway	Journal of Functional Foods. 2024 Nov 1;122:106478https://doi.org/10.1016/j.jff.2024.106478	• **SATB2 as a Tumor Suppressor:** SATB2 functions as a tumor suppressor in laryngeal squamous cell carcinoma (LSCC), inhibiting the Warburg effect and tumor progression. • **Inhibition of Proliferation and Migration:** SATB2 suppresses LSCC cell proliferation and migration by negatively regulating the Wnt/β-catenin pathway. • **Impact of SATB2 Silencing:** Silencing SATB2 leads to upregulation of Wnt expression, resulting in

			enhanced tumor growth and metabolic reprogramming. • **Interaction with Wnt Proteins:** SATB2 interacts with Wnt proteins, reducing their stability and limiting their tumor-promoting effects. • **Role of METTL3-mediated m6A Modifications:** METTL3-mediated m6A modifications, through YTHDF1, destabilize SATB2, contributing to the Warburg effect and promoting LSCC progression. • **Therapeutic Implications:** The study highlights the potential for targeting SATB2 and its associated regulatory mechanisms as a therapeutic strategy for LSCC.