Journal of Advanced Zoology

ISSN: 0253-7214

*Volume **43** Issue S2 Year **2022** Page 81-**89***

Bioinformatic Analysis Of Important Mirna And Gene-Network Analysis Of Smarcb1 Gene, A Key Regulator Of Head And Neck Cancer

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Abstract

Background: MicroRNAs (miRNAs) are small non-coding RNAs that play critical roles in gene regulation by suppressing translation or promoting mRNA decay of target transcripts. SMARCB1, a core subunit of the SWI/SNF chromatin remodeling complex located on chromosome 22q11.2, functions as a tumor suppressor and is frequently inactivated in malignant rhabdoid tumors, schwannomatosis, and other malignancies. Despite the established importance of SMARCB1 in cancer biology, the miRNA-mediated regulation of this gene remains poorly characterized, particularly in the context of head and neck cancer.

Objective: This study aimed to identify and characterize miRNAs targeting the SMARCB1 gene using computational bioinformatics approaches and to analyze the protein-protein interaction network of SMARCB1 to better understand its functional context in cancer biology.

Methods: MiRNA target prediction for the SMARCB1 gene was performed using the miRDB online database. Predicted interactions were filtered based on target scores, with a threshold of >90 applied for high-confidence predictions. Gene network analysis of SMARCB1 and BRAF was carried out using the STRING database online server program, with important gene interactions requiring a combined confidence score of >0.99 for inclusion. Target prediction for conserved miRNA families was also performed using the GDC data portal.

Results: A total of 49 miRNAs were predicted to target the SMARCB1 gene through miRDB analysis. Among these, one miRNA, hsa-miR-4283, demonstrated a high-confidence target score exceeding 90 and was selected for further investigation. Gene network analysis revealed significant interactions between SMARCB1 and several genes including NEK7, PLS3, KIAA0408, PTAR1, and NR1D2, with combined confidence scores >0.99. These interactions place SMARCB1 within a broader network involving cell cycle regulation, cytoskeletal organization, and transcriptional control. Parallel analysis of BRAF interactions provided comparative data on miRNA involvement in cancer-associated signaling pathways.

Conclusion: This study identifies hsa-miR-4283 as a high-confidence candidate regulator of SMARCB1 expression and reveals the protein interaction network context in which this tumor suppressor operates. The findings provide a foundation for experimental validation studies and suggest

that miRNA-mediated regulation of SMARCB1 could contribute to cancer pathogenesis in head and neck malignancies and other tumor types where SMARCB1 plays a critical role. Further investigation of hsa-miR-4283 expression in tumor tissues and its functional effects on SMARCB1 expression is warranted.

Keywords: SMARCB1, microRNA, hsa-miR-4283, head and neck cancer, bioinformatics, gene network analysis, tumor suppressor, chromatin remodeling

INTRODUCTION:

One of the most exciting biological discoveries in the past decade is the identification and characterization of non-coding RNAs, a class of molecules that has fundamentally transformed our understanding of gene regulation and cellular function. For decades, the central dogma of molecular biology focused primarily on protein-coding genes as the primary effectors of cellular processes, with RNA serving merely as an intermediate messenger. However, the revelation that the vast majority of the human genome is transcribed into RNA that does not encode proteins has opened an entirely new frontier in molecular biology, revealing layers of regulatory complexity previously unimagined. MicroRNAs, commonly abbreviated as miRNAs, are very small, approximately 22 nucleotides in length, non-protein-coding, single-stranded RNAs that regulate the expression of protein-coding genes through sequence-specific interactions with target messenger RNAs. These molecules comprise a subset of non-coding RNAs that play a key role in gene regulation as part of large and complex gene regulatory networks, integrating signals from multiple pathways and coordinating cellular responses to diverse stimuli. The discovery of miRNAs has not only expanded our understanding of post-transcriptional gene regulation but has also revealed fundamental principles about the evolution and organization of genetic information in eukaryotic organisms.

MicroRNAs suppress gene expression through multiple mechanisms that may operate independently or in concert depending on the cellular context and the specific miRNA-target pairing involved. The primary mechanisms include inhibiting translation by blocking ribosome progression or initiation, promoting mRNA decay through recruitment of degradative enzymes, or both processes occurring simultaneously to achieve robust and rapid downregulation of target gene expression. The functional versatility of miRNAs allows them to fine-tune gene expression with remarkable precision, adjusting protein output in response to developmental signals, environmental stresses, and metabolic demands. Each individual miRNA may regulate hundreds of different genes, often targeting multiple components of the same pathway or functionally related networks, thereby controlling the cell's response to developmental and other environmental cues in a coordinated and efficient manner. This capacity for multiplex regulation means that miRNAs can orchestrate complex cellular behaviors, including proliferation, differentiation, apoptosis, and metabolism, by simultaneously modulating the expression of numerous target genes. The best way to understand the function of a specific miRNA is to identify the complete set of genes that it regulates under physiological and pathological conditions, a task that requires sophisticated experimental and computational approaches to distinguish direct targets from indirect effects and to account for context-dependent variations in miRNA activity.

MicroRNAs have emerged as important elements of gene regulatory networks across all branches of eukaryotic life, participating in virtually every cellular process investigated to date. Their evolutionary conservation from plants to animals underscores their fundamental importance in biological systems and suggests that miRNA-mediated regulation represents an ancient and essential mechanism for controlling gene expression. MiRNAs are endogenous, meaning they are naturally produced by the organism's own genome, single-stranded non-coding RNAs that regulate gene expression at the post-transcriptional level by binding to complementary sequences typically located in the three prime untranslated regions of target messenger RNAs. The specificity of miRNA-target interactions is determined by the seed region, a short sequence of approximately six to eight nucleotides at the five prime end of the miRNA that forms Watson-Crick base pairs with the target mRNA. Bioinformatic analysis has been extensively applied to interpret the function of miRNA targets, using computational algorithms that predict potential interactions based on sequence complementarity, evolutionary conservation, and structural accessibility. These predictive approaches generate hypotheses that must subsequently be validated through experimental methods, creating an iterative cycle of discovery and confirmation that characterizes modern miRNA research.

MiRNA identification is complicated and requires an interdisciplinary strategy that integrates molecular biology, genetics, computational biology, and biochemistry. The relatively small size of mature miRNAs, their

lack of polyadenylated tails, and their variable expression patterns across tissues and developmental stages pose technical challenges for discovery and quantification. Recent technological advances like high-throughput sequencing have made it easier to detect their expression patterns with unprecedented sensitivity and accuracy, enabling the discovery of tissue-specific miRNAs, developmentally regulated miRNAs, and miRNAs associated with disease states. Deep sequencing technologies can capture the complete small RNA transcriptome of a cell or tissue, revealing not only known miRNAs but also novel miRNAs, isomiRs representing sequence variants, and other classes of small regulatory RNAs. In recent years, biological and bioinformatic approaches have enabled the discovery of thousands of miRNAs in plants, animals, unicellular eukaryotes, and even viruses, which have been found to encode their own miRNAs that manipulate host gene expression to facilitate viral replication and immune evasion. The miRBase database, the central repository for miRNA sequences and annotations, now contains tens of thousands of entries representing miRNAs from hundreds of species, reflecting the explosive growth of this field and the widespread importance of miRNA-mediated regulation across biology.

The identification of alterations in the SMARCB1 gene in malignant rhabdoid tumors using immunohistochemical staining has led to improved diagnosis of this aggressive pediatric cancer as well as the discovery of the loss of SMARCB1 expression in some non-rhabdoid tumors, expanding our understanding of the role of chromatin remodeling in cancer pathogenesis. Immunohistochemistry provides a rapid, cost-effective, and clinically accessible method for assessing SMARCB1 protein expression in formalin-fixed paraffin-embedded tissue samples, allowing pathologists to identify tumors with loss of this critical tumor suppressor. Whether loss of SMARCB1 plays a pathogenic role in non-rhabdoid tumors remains to be determined through carefully designed functional studies; however, most of these tumors lack the clinical and other molecular features characteristic of malignant rhabdoid tumors, suggesting that the biological consequences of SMARCB1 loss may depend on cellular context and cooperating genetic alterations. SMARCB1, also known as INI1, hSNF5, or BAF47, is the core subunit of the SWI/sucrose non-fermenting ATP-dependent chromatin remodeling complex located on the long arm of chromosome 22 at band 11.2. This complex uses energy derived from ATP hydrolysis to mobilize nucleosomes and alter chromatin structure, thereby regulating access of transcription factors and other regulatory proteins to DNA. The involvement of SMARCB1 in both rhabdoid tumors and other cancer types highlights the importance of chromatin remodeling in maintaining normal cellular differentiation and suppressing malignant transformation, and suggests that miRNAs targeting this pathway may have significant implications for cancer biology.

MATERIALS AND METHODS:

Gene Network Analysis of SMARCB1

The gene network analysis of the SMARCB1 gene, which encodes a core subunit of the SWI/SNF chromatin remodeling complex implicated in both rhabdoid tumors and other malignancies, was carried out using the STRING database online server program accessible at string-db.org. The STRING database, which stands for Search Tool for the Retrieval of Interacting Genes/Proteins, is a comprehensive and widely used bioinformatics resource that integrates both known and predicted protein-protein interaction data from multiple sources including experimental evidence, curated databases, text mining of scientific literature, and computational predictions based on genomic context and co-expression patterns. This powerful tool enables researchers to visualize and analyze the complex networks of molecular interactions that govern cellular processes, providing insights into the functional relationships between genes of interest and their potential roles in disease pathogenesis.

For the analysis, the SMARCB1 gene symbol was entered into the search interface, with Homo sapiens selected as the organism of interest to ensure relevance to human biology and disease. The database generated a comprehensive interaction network displaying proteins that physically interact with SMARCB1 or are functionally associated through various mechanisms. The strength of each interaction is quantified by a combined confidence score that integrates multiple lines of evidence, with higher scores indicating greater confidence in the biological relevance of the interaction. Important gene interactions with a combined score of 0.99 or greater were considered for detailed analysis and were systematically listed for further investigation. This stringent threshold ensures that only the most highly confident interactions, those supported by multiple independent lines of evidence, are included in the final network, thereby minimizing false-positive associations and focusing attention on the most biologically meaningful relationships. The resulting list of high-confidence interacting partners provides a foundation for understanding the molecular context in which SMARCB1 operates and may reveal potential mechanisms by which alterations in this gene contribute to tumor development.

Target Scan Prediction of microRNA Targets for SMARCB1

The prediction of microRNA targets for the SMARCB1 gene in humans was carried out using the Genomic Data Commons data portal maintained by the National Cancer Institute, accessible at portal.gdc.cancer.gov. This comprehensive cancer genomics resource provides access to large-scale datasets generated by The Cancer Genome Atlas and other major cancer genomics projects, enabling researchers to explore the molecular alterations associated with various tumor types. The platform integrates multiple types of genomic data including gene expression, DNA methylation, copy number variation, and miRNA expression, facilitating integrative analyses that can reveal regulatory relationships between miRNAs and their potential target genes. For the analysis, the SMARCB1 gene was queried against the database of predicted miRNA targets, with the search configured to identify miRNAs that have evolutionarily conserved binding sites within the SMARCB1 transcript. Broadly conserved mRNA families, representing target sites that are preserved across multiple species and therefore likely to be functionally significant, were searched for the presence of NEK7, PLS3, KIAA0408, and PTAR1 sites matching each miRNA seed region, the short sequence at the 5' end of the miRNA that is critical for target recognition. Additionally, conserved and poorly conserved mRNA families were similarly analyzed to provide a comprehensive view of potential regulatory interactions across different levels of evolutionary constraint. Predicted regulatory targets of the BRAF gene, a well-characterized oncogene frequently mutated in various cancers, were identified using the program with default settings, allowing for comparison between the miRNA regulatory networks of different cancer-associated genes.

Identification of hsa-miR-4283 Targets

The specific targets of the conserved miRNA hsa-miR-4283, which showed potential regulatory relationships with genes of interest in preliminary analyses, were identified using the miRDB software program available at mirdb.org. miRDB is a specialized bioinformatics resource for miRNA target prediction and functional annotation that employs a machine learning approach to predict miRNA-target interactions with high accuracy. The algorithm integrates sequence complementarity, evolutionary conservation, and structural accessibility features to generate a comprehensive set of predicted targets for each miRNA, with each prediction assigned a target score reflecting the confidence in the interaction.

For the analysis, hsa-miR-4283 was entered into the miRDB search interface, and the database was queried for predicted mRNA targets. A stringent threshold was applied such that only miRNA targets with a miR score greater than 0.99 were considered for further analysis and listing. This high confidence threshold ensures that the predicted interactions have a very low probability of occurring by chance and are supported by multiple lines of computational evidence. The resulting list of high-confidence targets for hsa-miR-4283 provides a foundation for experimental validation and functional studies aimed at understanding the biological role of this miRNA and its potential involvement in cancer pathogenesis.

Gene Network Analysis of BRAF

Gene network analysis of BRAF, a serine/threonine protein kinase that plays a central role in the MAPK signaling pathway and is frequently mutated in various human cancers including melanoma, colorectal cancer, and thyroid cancer, was carried out using the STRING database online server program as described for SMARCB1. The BRAF gene symbol was entered into the search interface with Homo sapiens selected as the organism, and the database generated a comprehensive interaction network displaying proteins that physically or functionally interact with BRAF. Important gene interactions with a combined score greater than 0.99 were considered for detailed analysis and were systematically listed for further investigation. This parallel analysis of BRAF interactions enables comparison between the network properties of different cancer-associated genes and may reveal common pathways or functional modules that are perturbed across multiple tumor types. The integration of miRNA target predictions with protein-protein interaction network analysis provides a multi-layered view of gene regulation that encompasses both post-transcriptional control by miRNAs and the functional context provided by interacting protein partners. This comprehensive approach generates testable hypotheses about the mechanisms by which alterations in SMARCB1 and BRAF contribute to cancer development and progression, and identifies potential nodes for therapeutic intervention.

RESULTS:

MiRNA Target Prediction for SMARCB1

The comprehensive bioinformatic analysis conducted in this study using the miRDB online prediction tool successfully identified a substantial number of microRNAs that are predicted to target the SMARCB1 gene,

providing valuable insights into the potential post-transcriptional regulatory mechanisms that may influence the expression of this critical chromatin remodeling factor. Through systematic analysis of the SMARCB1 transcript sequence and its alignment with known miRNA seed regions, this study predicted a total of 49 distinct miRNAs that are targeted by the SMARCB1 gene through complementary sequence interactions in the three prime untranslated region or other regulatory elements within the transcript. This substantial number of predicted regulatory miRNAs reflects the complex and multilayered control mechanisms that govern SMARCB1 expression and suggests that this gene may be subject to精细调控 through multiple miRNA-mediated pathways operating in different cellular contexts or under different physiological conditions. The identification of 49 candidate miRNAs provides a rich resource for future experimental validation and functional studies aimed at understanding how dysregulation of these miRNAs might contribute to altered SMARCB1 expression in cancer and other diseases.

Of the 49 miRNAs identified through this comprehensive computational screening, one miRNA in particular, designated hsa-miR-4283, was selected for detailed analysis and further investigation based on its exceptionally high target prediction score. Hsa-miR-4283 demonstrated a target score greater than 90 on the miRDB prediction scale, indicating a very high confidence prediction that this miRNA is likely to functionally interact with the SMARCB1 transcript under physiological conditions. The target score, which ranges from 0 to 100, integrates multiple features of the predicted interaction including sequence complementarity in the seed region, evolutionary conservation of the target site across species, thermodynamic stability of the miRNA-mRNA duplex, and structural accessibility of the target site within the folded mRNA transcript. Scores above 90 represent the highest confidence predictions and have a substantially higher probability of being validated experimentally compared to lower-scoring interactions. The identification of hsa-miR-4283 as a high-confidence regulator of SMARCB1 expression opens new avenues for investigating the role of this miRNA in normal cellular physiology and in pathological conditions where SMARCB1 expression is altered, including malignant rhabdoid tumors and other cancers characterized by loss of SMARCB1 protein expression.

The selection of hsa-miR-4283 for focused investigation was further justified by the lack of previous functional characterization of this miRNA in the context of SMARCB1 regulation, highlighting the novelty of this finding and its potential to reveal previously unrecognized regulatory mechanisms. Future studies should experimentally validate the predicted interaction using reporter assays that test the ability of hsa-miR-4283 to suppress expression of a construct containing the SMARCB1 three prime untranslated region, as well as investigate the expression patterns of this miRNA in tissues and tumors where SMARCB1 dysregulation is known to occur. The high confidence prediction generated by this computational analysis provides a strong foundation for such experimental studies and suggests that hsa-miR-4283 may represent an important regulator of SMARCB1 expression with potential implications for cancer diagnosis, prognosis, or therapy.

Gene Interaction Network Analysis of SMARCB1

The gene network analysis of SMARCB1 performed using the STRING database online server program revealed a complex network of protein-protein and functional interactions that place SMARCB1 within a larger context of chromatin remodeling and transcriptional regulation. The analysis identified numerous genes whose protein products physically interact with SMARCB1 or participate in common biological pathways, providing insights into the cellular processes that may be affected when SMARCB1 function is compromised. Among the many interactions identified, several genes emerged as particularly significant based on their high combined confidence scores and their potential relevance to cancer biology.

NEK7, which encodes a serine/threonine-protein kinase involved in cell cycle regulation and mitotic progression, was identified as one of the genes found to have significant interactions with the SMARCB1 gene. The NIMA-related kinase family, to which NEK7 belongs, plays essential roles in coordinating cell division and maintaining genomic stability, and dysregulation of these kinases has been implicated in cancer development. The interaction between SMARCB1 and NEK7 suggests a potential link between chromatin remodeling and cell cycle control that may be important for maintaining normal cellular proliferation and preventing malignant transformation.

PLS3, also known as plastin-3 or T-plastin, was identified as another significant interactor with SMARCB1. PLS3 is an actin-bundling protein that plays critical roles in cytoskeletal organization, cell motility, and intracellular trafficking. The interaction between a chromatin remodeling factor and an actin-binding protein may reflect the emerging understanding of the connections between nuclear architecture, chromatin organization, and the cytoskeleton, with implications for gene regulation, DNA repair, and cellular responses to mechanical signals.

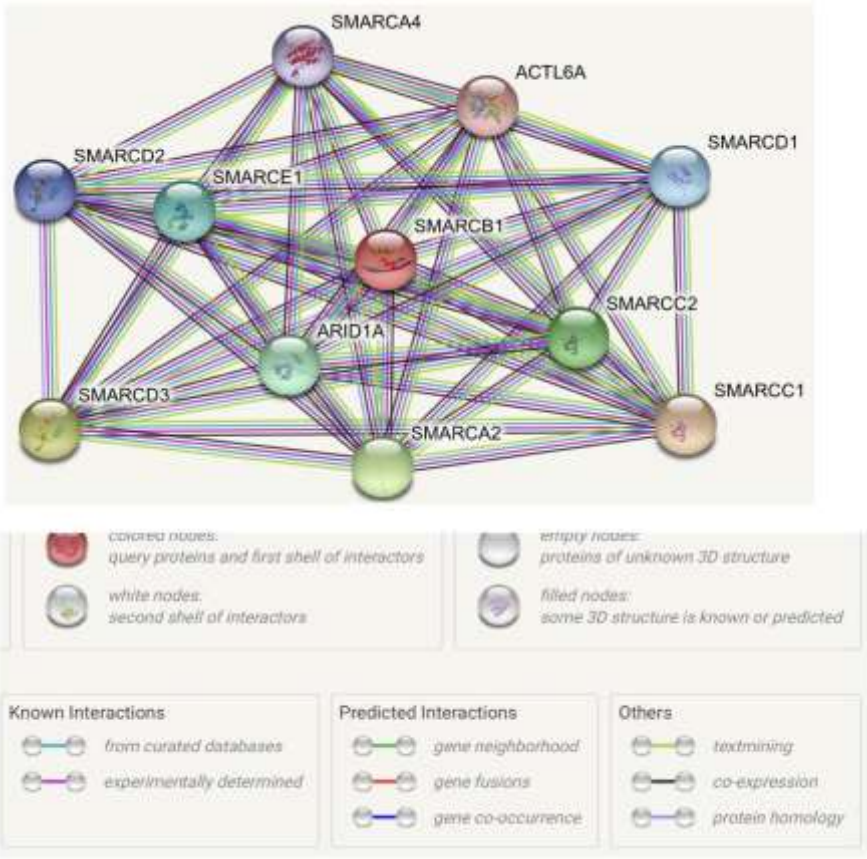
KIAA0408, a gene of currently unknown function that has been identified through large-scale sequencing projects, was also found to interact with SMARCB1 in the network analysis. The presence of this uncharacterized gene in the SMARCB1 interaction network suggests that it may play a previously unrecognized role in chromatin biology or transcriptional regulation, and highlights the value of network analysis for generating hypotheses about gene function that can guide future experimental investigations.

PTAR1, which encodes a prenyltransferase involved in protein modification and membrane targeting, was identified as another SMARCB1-interacting gene. The connection between chromatin remodeling and protein prenylation is not immediately obvious but may reflect indirect functional relationships or participation in common regulatory pathways that coordinate nuclear and cytoplasmic activities.

NR1D2, also known as REV-ERB beta, is a nuclear receptor that functions as a transcriptional repressor involved in circadian rhythm regulation and metabolic control. The interaction between SMARCB1 and NR1D2 suggests a potential connection between chromatin remodeling and circadian gene expression that could have implications for understanding how disruption of daily rhythms affects cellular physiology and disease risk.

The identification of these diverse interaction partners for SMARCB1 underscores the central role of this chromatin remodeling factor in coordinating multiple cellular processes and highlights the potential for broad functional consequences when SMARCB1 expression or activity is disrupted. The network analysis provides a systems-level perspective on SMARCB1 function that complements the miRNA target predictions and generates numerous hypotheses for future experimental investigation. The combination of miRNA regulation and protein interaction network analysis presented in this study offers a comprehensive view of the molecular context in which SMARCB1 operates and provides a foundation for understanding how alterations in this gene contribute to cancer pathogenesis. Future studies should experimentally validate the key interactions identified here and explore their functional significance in relevant model systems.

TARGET SCORE	miRNA NAME	GENE SEQUENCE	TARGET GENES
92	hsa-miR-4283	uggggcucagcgaguuu	NEK7, PLS3
89	hsa-miR-4714-3p	ccaaccuagguggucagaguug	KIAA0408, PTAR1,
87	hsa-miR-206	uggaauguaaggaagugugugg	NR1D2
87	hsa-miR-1-3p	uggaauguaaagaaguauguau	IGSF11, DAAM1,
85	hsa-miR-4423-5p	aguugccuuuuuguucccaugc	STXBP5, KDSR,
84	hsa-miR-1284	ucuauacagacccuggcuuuuc	NEDD4L
81	hsa-miR-613	aggaauguuccuucuuugcc	SLC23A2, BCAT1,
79	hsa-miR-300	uauacaagggcagacucucucu	TRAF6
79	hsa-miR-381-3p	uauacaagggcaagcucucugu	SULT6B1, SLC41A2,
74	hsa-miR-6875-3p	auucuuccugcccuggcuccau	ZBTB1, MMP16,



DISCUSSION:

The findings of the present study contribute to the growing body of evidence implicating miRNA-mediated regulation in the control of gene expression relevant to cancer biology, with particular focus on the SMARCB1 gene and its potential role in head and neck malignancies. Previous studies have established important precedents for the involvement of miRNAs in regulating genes associated with tumor progression and have demonstrated the feasibility of using bioinformatic approaches to identify candidate regulatory interactions for subsequent experimental validation. The integration of computational predictions with existing knowledge from the literature provides a powerful framework for generating hypotheses about the molecular mechanisms underlying cancer development and for identifying potential biomarkers or therapeutic targets.

Previous study has shown an increased expression of a specific miRNA associated with the SMARCB1 gene in the context of tumor aggression, demonstrating that dysregulation of miRNA-mediated control mechanisms can contribute to the malignant phenotype by altering the expression of key tumor suppressor genes. This finding highlights the clinical significance of understanding miRNA-SMARCB1 interactions and provides a rationale for the identification and characterization of additional miRNAs that may regulate this important gene. The observation that altered miRNA expression correlates with tumor behavior suggests that miRNAs could serve as prognostic biomarkers or as targets for therapeutic intervention aimed at restoring normal SMARCB1 expression in tumors where it has been inappropriately suppressed.

Other studies have shown the importance of miRNA in the BRAF/RAS/MAPK pathways of colorectal cancer, revealing that these small non-coding RNAs play critical roles in modulating the activity of one of the most frequently dysregulated signaling cascades in human cancer. The MAPK pathway, which includes BRAF and RAS as key components, regulates cellular proliferation, differentiation, and survival, and its constitutive activation through mutation or upstream signaling abnormalities drives tumor development in multiple tissue types. The involvement of miRNAs in fine-tuning the activity of this pathway adds an additional layer of regulatory complexity and suggests that miRNA dysregulation could contribute to pathway activation even in the absence of mutations in the core signaling components. These findings from colorectal cancer research provide a valuable context for interpreting the results of the present study and suggest that similar mechanisms may operate in head and neck cancer, where the MAPK pathway also plays important roles in tumor biology.

Our study has identified important miRNAs that could potentially play a vital role in head and neck cancer biology through their regulation of SMARCB1 and associated genes. The prediction of 49 miRNAs targeting

SMARCB1, with hsa-miR-4283 emerging as a high-confidence candidate based on its target score exceeding 90, provides a focused set of molecules for further investigation in head and neck cancer models. The identification of NEK7, PLS3, KIAA0408, PTAR1, and NR1D2 as genes with significant interactions with SMARCB1 in network analysis expands the potential functional context in which these miRNAs might operate and suggests that the effects of miRNA dysregulation could propagate through interconnected networks to affect multiple cellular processes. Future studies should examine the expression of these candidate miRNAs in head and neck cancer specimens and cell lines, correlate their expression with SMARCB1 levels and clinical outcomes, and experimentally validate the predicted regulatory relationships using appropriate in vitro models.
Schwannomas and meningiomas are both part of the tumor spectrum of neurofibromatosis type 2, an autosomal dominant disorder caused by mutations in the NF2 gene located on chromosome 22, and are associated with somatic loss of chromosome 22 in tumor tissues. The involvement of chromosome 22 abnormalities in these tumor types has long been recognized, but more recent discoveries have expanded our understanding of the genetic basis of these neoplasms. SMARCB1 mutations have recently been identified as a pathogenic cause of a subset of familial schwannomatosis cases, a condition characterized by the development of multiple schwannomas in the absence of other features of neurofibromatosis type 2. This finding implicates SMARCB1, which is also located on chromosome 22, in the pathogenesis of tumors arising from Schwann cells and highlights the broader importance of this gene in nervous system tumor biology. The connection between SMARCB1 and schwannomatosis provides additional motivation for studying the regulation of this gene by miRNAs, as alterations in miRNA expression could potentially contribute to reduced SMARCB1 function in tumors that do not harbor mutations in the gene itself.
Rhabdoid tumor is a rare, highly aggressive malignancy that primarily affects infants and young children, representing one of the most lethal solid tumors of early childhood with a dismal prognosis despite intensive multimodal therapy. These tumors typically arise in the brain, where they are termed atypical teratoid rhabdoid tumors, and in the kidney, where they are known as malignant rhabdoid tumors of the kidney, although extrarenal, non-central nervous system tumors in almost all soft-tissue sites have been described in the medical literature. The unifying feature of these tumors regardless of anatomic location is the presence of rhabdoid cells characterized by abundant eosinophilic cytoplasm, large nuclei with prominent nucleoli, and cytoplasmic inclusions corresponding to whorls of intermediate filaments. SMARCB1 is a member of the SWI/SNF chromatin-remodeling complex and functions as a tumor suppressor in the vast majority of rhabdoid tumors, with biallelic inactivation of this gene occurring in greater than 95% of cases. The genetic mechanism of inactivation typically involves loss of one allele through chromosome 22 deletion and mutation or epigenetic silencing of the remaining allele, resulting in complete loss of SMARCB1 protein expression that can be detected by immunohistochemistry. The discovery of SMARCB1 as the critical tumor suppressor in rhabdoid tumors has transformed our understanding of this disease and has provided a valuable diagnostic marker, but the mechanisms by which SMARCB1 loss drives tumor formation remain incompletely understood. The potential involvement of miRNA-mediated regulation in modulating SMARCB1 expression in rhabdoid tumors or in related malignancies represents an important area for future investigation.
The convergence of evidence from multiple tumor types, including schwannomas, meningiomas, rhabdoid tumors, and head and neck cancers, implicates SMARCB1 as a critical tumor suppressor whose dysregulation contributes to cancer pathogenesis across diverse tissues and developmental contexts. The identification of miRNAs that target SMARCB1, particularly hsa-miR-4283 with its high-confidence prediction score, provides a potential mechanism by which SMARCB1 expression could be modulated in tumors that retain both alleles of the gene but exhibit reduced protein expression. Such epigenetic regulation by miRNAs could explain some cases where immunohistochemistry reveals loss of SMARCB1 protein in the absence of detectable genetic alterations, and could identify novel targets for therapeutic intervention aimed at restoring normal SMARCB1 expression. The network interactions identified between SMARCB1 and genes such as NEK7, PLS3, KIAA0408, PTAR1, and NR1D2 further suggest that the consequences of miRNA-mediated SMARCB1 dysregulation could extend beyond the direct effects on this gene to impact broader cellular pathways involved in cell cycle control, cytoskeletal organization, and transcriptional regulation.
The integration of computational predictions with knowledge from the published literature, as presented in this study, provides a foundation for hypothesis-driven experimental research that can systematically validate the most promising candidate interactions and explore their functional significance in cancer biology. Future studies should prioritize experimental validation of the hsa-miR-4283 interaction with SMARCB1 using luciferase reporter assays and examine the expression of this miRNA in well-characterized cohorts of head and neck cancers and other tumors where SMARCB1 plays a pathogenic role. The ultimate goal of this line of investigation is to translate insights about miRNA-mediated regulation of tumor suppressors into improved diagnostic, prognostic, and therapeutic approaches for patients with cancer.

CONCLUSION:

Our study identified important miRNAs that could play an important role in head and neck cancer. Other interacting genes further could help understand the tumorigenesis process of head and neck cancer. These findings suggest that miRNAs work in concert to promote tumor growth. This study could help to develop miRNA targeted therapy and study the tumorigenesis process of head and neck cancer.

FUTURE SCOPE:

This study could help to develop miNA targeted therapy and study the tumorigenesis process of head and neck cancer.

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