

Role of the SWI/SNF complex in the development of digestive tumors (Review)

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Abstract. The ATP-dependent switch/sucrose non-fermentable (SWI/SNF) complex serves a crucial role in systematically modifying chromatin structure and regulating cellular epigenetics. A decreased expression or mutations in the SWI/SNF complex can lead to a series of physiological and pathological changes. Several gene sequencing studies have identified diverse mutations in the SWI/SNF subunits across gastrointestinal cancers. Tumor cells with these mutations are dedifferentiated and more aggressive, with early metastases, including to lymph nodes, often associated with poor prognosis. At present, for tumors with SWI/SNF mutations, the main treatment regimen is based on the phenomenon of synthetic lethality. The present review explores the common mutational mechanisms that affect these subunits and their impact on gastrointestinal tumors, as well as the emerging therapeutic approaches, thereby providing a substantive foundation for further clinical research in this field.

Contents

1. Introduction
2. SWI/SNF and human tumors
3. SWI/SNF subunit mutations
4. SWI/SNF deficiency in digestive tumors
5. Progress of treatment
6. Conclusions and opinions

1. Introduction

The switch/sucrose non-fermentable (SWI/SNF) complex, a chromatin remodeler, functions as a direct modulator of transcription in ATP-rich environments, regulating gene expression, cell proliferation, division and differentiation (1). Studies have demonstrated that mutations in all chromatin remodelers, including SWI/SNF, are prevalent in human cancers. Mutations in this complex occur in ~20% of human carcinomas, with a significantly higher incidence in digestive carcinomas [32% in gastric cancer (GC) and 55% in colorectal cancer (CRC)] (2,3). The mammalian SWI/SNF complex belongs to three major subfamilies: Classical BAF (cBAF), polybromo-related BAF and non-cBAF, which consists of BRD9 and GLTSCR1/GLTSCR1L (1). The dynamic activity of the SWI/SNF complex serves an important role in regulating the activation and inhibition of gene expression programs (4).

According to statistics, primary malignant tumors of the digestive system, including esophageal, stomach, colorectal, liver and pancreatic cancer, are one of the main causes of cancer incidence worldwide, and their mortality rate can be as high as 35% (5). Surgical resection remains the most common treatment for cancer of the digestive tract; however, most patients are diagnosed at an advanced stage (6). The introduction of multi-disciplinary models, such as chemoradiotherapy and targeted therapy, has provided new treatment options for patients with tumors. It is necessary for researchers to improve their understanding of digestive tract tumors to optimize disease management and individualized treatment. The present review explores the loss of the SWI/SNF complex in the gastrointestinal tract and its role in the development of digestive tumors.

2. SWI/SNF and human tumors

All three types of SWI/SNF complexes, comprise core, variant and ATP subunits, and typically consist of 12-15 subunits that vary across different tissues and cells (3). Similar to other chromatin remodelers, this complex utilizes energy from ATP hydrolysis to facilitate the release of chromosomes from the histone octamers of nucleosomes, thereby regulating gene expression (Fig. 1). Animal studies have demonstrated that the dynamic opposition between SWI/SNF and polycomb complexes governs normal cell proliferation and

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pathophysiological alterations; for example, early loss of the *BAF53a* subunit prevents cell cycle and disrupts neurogenesis (7-9). In the absence of the BAF complex, this equilibrium is disrupted, reducing resistance to the chromatin polycomb complex. Consequently, decreased dissociation of the polycomb complex results in chromatin inaccessibility, heterochromatin formation and subsequent oncogene activation (10,11).

To date, at least eight human tumors have been linked to mutations in SWI/SNF subunits (12). These lesions affect vital organs across all major systems of the human body, including the genitourinary, nervous, respiratory and digestive systems. A number of these subunits are crucial for the development and differentiation of embryonic stem (ES) cells. Specifically, *BAF155*, *BRG1* and *BRM* contribute to sustaining the self-renewal and differentiation potential of ES cells (13). Furthermore, *BAF250a* regulates cardiac gene expression during the early stages of heart development (14), whereas *BRG1* aids in the differentiation of cardiovascular smooth muscle cells (15); *BAF47* controls the cell cycle and terminal differentiation of skeletal muscle cells (16); and the absence of *ARID1A* causes dentate gyrus malformation in the brain (17). Therefore, it may be inferred that the loss of diverse genes could contribute to the development of various tumors. Accordingly, deficient *BAF47* expression results in malignant rhabdoid tumors and lymphoma (18,19), *SMARCA4* is frequently mutated in lung carcinoma (20), and *SMARCE1* loss leads to aggressive central nervous system tumors (21).

3. SWI/SNF subunit mutations

Core subunits. The coding gene *SMARCB1* (also known as *INI1*, *SNF5* or *BAF47*) is located at q11.23 on chromosome 22 and is crucial for the stability of the SWI/SNF complex, but not its structural integrity. The introduction of exogenous *SMARCB1* into *SMARCB1*-deficient cells has been shown to activate bivalent promoters and enhancers, rescuing the expression of upregulated target genes, which were identified by Gene Ontology analysis (a widely used bioinformatics approach for annotating genes and interpreting large-scale genomics or transcriptomics data) to be related to kidney and neural development (22). As a tumor suppressor gene, oncogenesis occurs only when both *SMARCB1* alleles in a cell are mutated (23). Gene sequencing has revealed that in *SMARCB1*-deficient tumors, chromosome 22q loss frequently extends far beyond *SMARCB1* gene length, with extensive copy number loss and rearrangements, resulting in concurrent defects at multiple gene loci (24,25).

SMARCC1/2 and *SMARCD1/2/3* comprise the primary framework of the BAF complex, and serve a notable role in early assembly of the SWI/SNF complex (26,27). Mutations in *SMARCC1* (also known as *BAF155*), which inhibits fetal differentiation and maturation, facilitate the transformation of stem cells into mature cells in the human gut by augmenting CD117 and cluster cells (28). Conversely, during the resolution of inflammation, *SMARCC1* undergoes polyubiquitination and proteasomal degradation, thereby inhibiting the expression of inflammatory factors (29). *SMARCD2* serves a crucial role in granulocyte maturation and is a promising therapeutic target in leukemia (30,31).

ATP subunits. *SMARCA2* and *SMARCA4* are mutually exclusive subunits that function as ATPases in the SWI/SNF complex, generating energy for chromatin remodeling through hydrolyzing ATP. The bromine domain recognizes acetyl-lysine residues at the N-terminus of histones and hydrolyzes high-energy phosphate bonds of ATP as an energy source (32). The *SMARCA4* (*BRG1*) gene, located at p13.2 on chromosome 19, serves as a valuable marker for investigating rare tumors, such as small cell carcinoma of the ovary, hypercalcemic type, in younger women (<40 years old) (33,34). By contrast, mutations in *SMARCA2* (*BRM*) are less prevalent in human tumors, most of which are reversible epigenetic alterations rather than gene deletions (35). Upon *SMARCA4* inactivation, cells rely on *SMARCA2* to maintain normal vital activity, a phenomenon known as synthetic lethality (36).

Variant subunits. *ARID1A/B*, also referred to as *BAF50a/b*, is the most frequently mutated and extensively studied among these subunits, sharing a highly similar base composition and arrangement with *ARID2*, which exists in the SWI/SNF complex in a mutually exclusive manner. Research has shown that ARIDs contribute to proper spatial folding patterns to maintain structural stability of the complex (26). Deletion of *ARID1B* disordered region 1 can completely inhibit condensation of the BAF complex *in vitro* (37). *ARID1A* depletion alters genome-wide expression, promoting oncogenesis by suppressing enhancer accessibility, whereas *ARID1B* deficiency has negligible effects (38). The majority of *ARID1A* mutations result from premature termination of protein transcription due to insertion/deletion mutations (39). Point mutations impair ARID domain mutual recognition and non-specific DNA binding, thereby inhibiting ES cell differentiation without affecting *ARID1A* protein expression or complex integrity (40). In addition, *ARID1B* loss disrupts binding to the long non-coding RNA (lncRNA) *NEAT1*, which is a component of paraspeckles, resulting in the loss of numerous transcription and chromatin-associated proteins, including the chromatin-modifying enzyme JMJD6, the transcription factor CCCTC-binding factor, which binds to DNA sequence-specific sites and regulates the 3D structure of chromatin, and histones (41).

In conclusion, the recruitment of the SWI/SNF complex is synergistically driven by ARID-mediated non-specific DNA binding, bromodomain interaction with histone N-termini and specific DNA sequence recognition (42-45). Binding of the SWI/SNF complex to chromatin is complex. Transcription typically starts with the recruitment of transcription factors, together with enhanced accessibility of the target DNA. A subset of these transcription factors pre-aggregate around the target nucleosome, increasing accessibility and forming a dynamic open reading frame. Additionally, this complex regulates gene expression via DNA methylation, damage repair and microRNA (miR) processing (42).

4. SWI/SNF deficiency in digestive tumors

As aforementioned, the SWI/SNF complex shows varying degrees of deletion, or epigenetic silencing, in digestive tumors (2). Most undifferentiated gastrointestinal cancers have more than one SWI/SNF subunit mutation (46). These

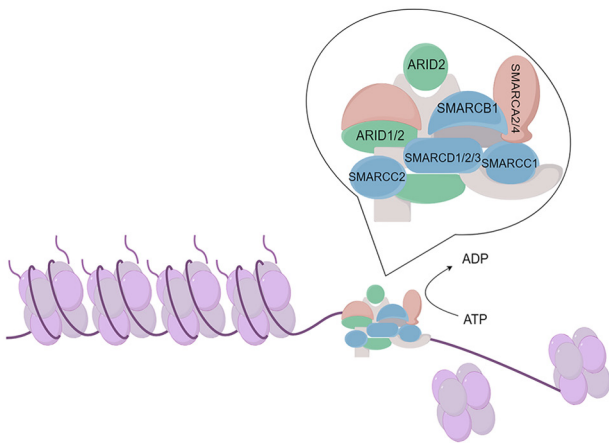


Figure 1. The SWI/SNF complex releases chromosomes from nucleosomes. The SWI/SNF complex, typically composed of 12-15 subunits, uses the energy generated by ATP hydrolysis to facilitate the release of chromosomes from the histone octamer of the nucleosome, thereby regulating gene expression. This figure was generated using Figdraw (<https://www.figdraw.com/#/>). SWI/SNF, switch/sucrose non-fermentable.

patients exhibit non-specific symptoms and clinical findings, which may include dysphagia, weight loss, nausea, abdominal discomfort, pain, palpable masses, melena and constipation. These mutated tumor cells exhibit dedifferentiation, with decreased adhesion and disorganized arrangement, and typically present morphologies resembling flakes, ropes or nests, and thus appear to look like immature cells. Abundant cytoplasm occupies a significant proportion of the cells, whereas the nucleus with a prominent nucleolus is positioned peripherally (19). Due to the presence of poorly differentiated adenocarcinoma and promoter methylation phenotype in metastatic lymph nodes, it was inferred that these SWI/SNF-mutated rhabdoid neoplasms originated from epithelial cells (47). Previously, these tumors with SWI/SNF mutations were often misdiagnosed because of their rhabdoid appearance and the absence of epithelial markers; currently, their diagnosis mainly relies on pathological immunohistochemical staining of the complex subunits, including *SMARCA2/4*, *SMARCB1* and *ARID1A/B*.

Esophageal cancer. Esophageal cancer with SWI/SNF mutations exhibits high aggressiveness, with a notable proportion of patients succumbing to the disease within 1 year, often due to being diagnosed with late-stage cancer (48). A 2023 study reported a pathogenic *SMARCA4* mutation in 2.5% of undifferentiated carcinomas at the esophageal or gastroesophageal junction, which may be relevant to Barrett's esophagus. Notably, >50% of these patients presented with distant metastases at initial diagnosis (49). As a critical component of the tumor suppressor gene family, the loss of *SMARCA4* can directly promote tumor cell proliferation. *SMARCA4* mutations are primarily categorized into two classes (50). Class 1 mutations result in loss of protein function, encompassing truncation mutations, gene fusion and homozygous deletion, whereas class 2 mutations involve missense mutations. Cancers with class 1 mutations tend to be less differentiated than those with class 2 mutations, which are strongly associated with poor patient outcomes, and may co-occur with *APC* and *CTNNB1*

mutations, leading to synergistic effects (49). The mutation rates of *SMARCB1*, *SMARCA2*, *SMARCA4* and *ARID1A* in esophageal adenocarcinoma have been reported to be 2, 9.9, 3.4 and 10.4%, respectively. Furthermore, patients with *ARID1A* mutation were demonstrated to have a 56% reduction in overall survival (OS) time (60.1 months vs. 26.2 months, $P=0.044$) compared with in those with *ARID1A* wild-type esophageal adenocarcinoma (51). Notably, the absence of *ARID1A* may be associated with high microsatellite instability (MSI-H) in tumors.

Stomach cancer. Mutations in SWI/SNF complex genes (*SMARCB1*, *SMARCA2*, *SMARCA4* and *ARID1A*) have been identified in ~35% of patients with GC, with *SMARCA2* and *ARID1A* accounting for 28 and 16%, respectively. Furthermore, concurrent mutations in more than two subunits are frequently detected. These patients are typically of an advanced age and exhibit susceptibility to lymphatic invasion (52). The Cancer Genome Atlas network identified SWI/SNF-deficient tumors in Epstein-Barr virus (EBV) and MSI genotypes, demonstrating effective response to chemotherapy and immunotherapy (53-55). However, in GC cases with high *MLH1* or *EBV* deficiency, *ARID1A* mutations are associated with a poor prognosis (39).

Loss of *ARID1A* function may be caused by mutations and copy number deletions, both of which are enriched in GC with MSI and chromosomal instability (CIN), respectively. According to recent findings, PD-1 targeted therapy improves OS in patients with GC lacking *ARID1A*, whereas 5-fluorouracil therapy significantly benefits only those with the CIN subtype (56). This may be associated with increased activity of carcinogenic signaling pathways, which also further promote the occurrence of *ARID1A*-negative GC. Furthermore, *ARID1A* can regulate the proliferation and invasion of GC cells through non-coding RNAs, such as miR-223-3-p, miR-7641 and the lncRNA *MVIH* (57). *ARID1A* is also involved in cellular DNA damage repair to maintain genomic stability. Furthermore, when *ARID1A* is artificially knocked out in mice, chromosome and gene instability are increased (58).

A single center study conducted in 2022 in China suggested that elevated *SMARCC1* expression may be associated with poor prognosis in patients with GC ($P<0.01$) (59). *SMARCA4*-deficient GC cases generally occur independently of EBV infection and MSI, exhibiting larger tumor volume and deeper infiltration, with a notable tendency for lymph node metastasis (60). In undifferentiated gastrointestinal carcinomas, OS and disease-free survival have been reported to be reduced in patients harboring *SMARCA4* mutations (19). However, Zhang *et al* (61) reported that *SMARCA4* negativity is not a predictor of OS.

Small intestinal cancer. *SMARCA4* serves a crucial role in the development and homeostasis of the mouse gut by regulating the proliferation and differentiation of duodenal stem cells, as well as villi and crypt formation (62). The absence of *SMARCA4* can lead to intestinal inflammatory disorders, triggering autoimmune enteritis (63). Furthermore, evidence has shown that the SWI/SNF complex has a crucial role in the differentiation of intestinal pluripotent ES cells (64). Undifferentiated tumors of the small intestine originating

from SWI/SNF mutations are rare and must be distinguished from other tissue-derived tumors during diagnosis (65).

Liver cancer. Gene sequencing has identified *ARID1A* mutations in ~17% of hepatocellular carcinoma (HCC) cases and *ARID2* mutations in ~6% of cases (66). These tumors are typically characterized by their large size, tendency to induce refractory ascites and increased probability of recurrence. This phenomenon is attributed to the pronounced Warburg effect in *ARID1A*-deficient HCC, which enables tumor cells to sustain high metabolic activity, even in glucose-depleted environments (67). Deletion of the tumor suppressor gene *ARID1A* in hepatocytes can result in the upregulation of CD133 and EPCAM (hepatocyte stem cell markers) and the loss of PROS1 and DCXR (hepatocellular-specific markers), consequently leading to the reacquisition of self-renewal and differentiation potential (68). Furthermore, the tumor driver mTORC1 degrades the ARID1A protein in the liver, impairing chromosome accessibility and activating carcinogenic signaling pathways (such as YAP), thereby promoting HCC (69). Inactivation of *ARID1A* disrupts chromatin spatial structure, interrupts the normal transcription of cancer genes, and increases the aggressiveness of HCC by inhibiting the BRG1-RAD21 axis (70). Increased release of pro-inflammatory factors, such as TNF- α and IL-6, also contributes to *ARID1A*-deficient liver steatosis and HCC development. After the depletion of *ARID1A* in endothelial cells, the concentration of ANG2 (a critical angiogenic factor) is markedly increased, which can promote cell proliferation and migration, providing an enhanced nutritional foundation for HCC growth (71). Additionally, *ARID1A* serves a role in the regulation of the tumor microenvironment, and its loss may augment the responsiveness of HCC to immunotherapy (72).

Furthermore, *ARID2* expression is positively associated with HCC prognosis. It inhibits tumor cell metastasis in HCC by recruiting DNMT1, suppressing epithelial-mesenchymal transition and accelerating the DNA methylation of *Snail* (73). Under normal conditions, the nucleotide excision repair process of DNA damage requires the participation of *ARID2* to counteract the effects of carcinogens, such as ultraviolet light and chemical substances, thereby reducing cellular variation and apoptosis (74).

The SWI/SNF complex acts as tumor suppressor in humans and its reduced expression promotes carcinogenesis through multiple mechanisms. However, one study challenged this perspective. A significant increase in SMARCB1 protein levels was reported to be observed in patients with HCC and was associated with advanced Tumor-Node-Metastasis (TNM) classification (75). The downstream target gene *NUP210*, which encodes the nuclear pore complex, facilitates the interaction between *SMARCB1* and chromatin. *SMARCB1* also sustains HCC via *NUP210*-mediated cholesterol homeostasis and metabolism of exogenous substances. These findings indicated that the SWI/SNF complex may have a dual effect on tumor inhibition and carcinogenesis in the liver. Overexpression of *ARID1A* can promote tumor initiation; however, in established liver tumors, reduced *ARID1A* leads to tumor progression and metastasis due to reduced expression of inhibitory factors (76).

Biliary duct cancer (BDC). SWI/SNF mutations are present in ~50% of gallbladder cancer and BDC, second only to endometrial cancer (77). It has been reported that the SWI/SNF complex subunits ACTL6A and SMARCA4 facilitate TGF- β -induced *LINC00313* gene expression, thereby modulating the Wnt signaling pathway and indirectly promoting the growth of cholangiocarcinoma *in vivo* (78). However, research on the SWI/SNF complex in BDC remains limited. A 2017 study linked *PBRM1* (encoding BAF180, a variant subunit) to advanced BDC (79). Previous studies have suggested that *KRAS* mutations are one of the main pathogenic pathways of (80,81). In addition, mutations of chromatin remodeling genes (*ARID1A* or *PBRM1*) have frequently been observed in cholangiocarcinoma via next generation sequencing (82,83). However, *ARID1A* and *KRAS* co-mutations have been reported to be absent in intra- or extrahepatic BDC, indicating a novel tumorigenesis mechanism (84). Guo *et al* (85) demonstrated that the TGF- β -Smad4 pathway may mediate the loss of resistance to biliary injury, resulting in uncontrolled epithelial proliferation in the presence of *ARID1A* mutations.

Pancreatic cancer. According to an Australian study that performed whole gene sequencing, ~14% of pancreatic ductal adenocarcinoma (PDAC) cases exhibit mutations in the SWI/SNF complex (*ARID1A*, *SMARCA4* and *PBRM1*) (86). *ARID1A* serves a crucial role in maintaining pancreatic cellular homeostasis. Accordingly, *ARID1A* deletion induces acinar cell damage and transformation into the pancreatic duct and mucus accumulation, potentially leading to PDAC (87). Meanwhile, the anticancer activity of T cells in the tumor microenvironment is diminished, along with inhibition of the IFN signaling pathway, resulting in immunosuppression and weakening of the antitumor immune response (71). *ARID1A* knockout in mice has been shown to increase vimentin expression and epithelial-mesenchymal transition markers, resulting in poorly differentiated or undifferentiated pancreatic tumors. These tumors resemble rhabdoid cells, exhibiting highly aggressive behavior, and have severe adverse effects on prognosis (88,89). Furthermore, *ARID1A* silencing irreversibly accelerates PDAC formation (70,90). Notably, the SWI/SNF complex serves a crucial role in the development of islet cells. The deletion of ATPase subunits, such as *SMARCA2* and *SMARCA4*, in endocrine progenitor cells disrupts glucose homeostasis disorder in mice after birth, leading to severe impaired glucose tolerance, hyperglycemia and hypoinsulinemia (91).

CRC. SWI/SNF mutations have been observed in CRC associated with ulcerative colitis, with an *ARID1A* mutation rate of ~44% and a *SMARCA4* mutation rate of ~17% (92). Dysfunction of autophagy in the intestinal epithelium with *SMARCA4* deletion leads to the accumulation of intracellular reactive oxygen species, potentially compromising the intestinal mucosal barrier, thereby triggering intestinal inflammation and tumor formation (93). Mutated *SMARCA4* promotes CRC proliferation through multiple mechanisms (94-96). By contrast, *SMARCA4* has been reported to be crucial for sustaining tumor stem cell activity (97). Notably, knockout of *SMARCA4* in mice has been shown to inhibit colonic tumor growth and induce apoptosis (98). *SMARCB1* exhibits a similar effect (99), as its loss induces CRC cell differentiation

and inhibits neoplasm formation. Chen *et al* (100) revealed that bromodomain containing 9 (*BRD9*), a newly discovered SWI/SNF complex subunit, is significantly enriched in cancer tissues, including colon and lung cancer. Furthermore, tumor progression could be inhibited by Wnt/ β -catenin signaling pathway following *BRD9* deletion. Research on animal models has demonstrated that inactivation of the enhancer H3K27ac and dysregulation of the APC/ β -catenin signaling pathway in infiltrating adenocarcinoma cells with *ARID1A* deletion is crucial for the development of CRC (3,101).

Loss of the SWI/SNF complex is rare in CRC, occurring primarily in cases involving inflammatory bowel disease and the MSI genotype. *SMARCA5* is associated with an imbalance of T helper 17/regulatory T cells in intestinal tissues, contributing to the promotion and exacerbation of colon inflammation, which may be associated with an increased risk of CRC (102,103). In general, CRC with SWI/SNF mutations exhibits higher malignancy and an advanced TNM stage, and the prognosis worsens with mismatch repair defects and the presence of the *BRAF* V600E mutation (104). Notably, *ARID1A* loss is closely associated with lymphatic infiltration, recurrence and metastasis (105). Nevertheless, patients with stage IV CRC who are *ARID1A*-negative have been demonstrated to exhibit improved OS, compared with those patients without an *ARID1A* mutation, which is potentially attributable to the robust response of *ARID1A* mutations to immune checkpoint inhibitors (106).

5. Progress of treatment

The primary treatment options for tumors with SWI/SNF mutations involve the phenomenon of synthetic lethality. Targeted therapy focusing on the collateral homolog *SMARCA2*, as described in the most recent patent design, primarily targets *SMARCA4*-mutated tumors (36). In addition, selective inhibition of *SMARCA2* ATPase activity inhibits the proliferation of *SMARCA4*-deficient cancers (107). In HCC models, JQ1, an inhibitor of bromine protein domain 4, exacerbates DNA double-strand breaks, impairs DNA repair and induces cell death in *ARID2*-deficient cells (108). Notably, JQ1 has been shown to synergize with that cyclin-dependent kinase (CDK)4/6 inhibitors to arrest cell growth in the G₁ phase in drug screening models, potentially offering therapeutic advantages for patients with advanced GC (109).

Treatments based on non-SWI/SNF complex synthetic lethality have been investigated extensively. In CRC, Aurora kinase A (AURKA) promotes mitosis, which is particularly pronounced in cells with *ARID1A* deletion. Inhibition of AURKA activity inhibits chromatin segregation, resulting in programmed cell death (110). Furthermore, PARP and ATR inhibitors synergistically repair DNA damage in *ARID1A*-deficient tumors (111). Chemical modifications of histones alter the overall spatial conformation of chromatin and regulate its transcriptional activity. EZH2 inhibitors reduce chromatin accessibility by selectively altering H3K27Me3 methylation, resulting in growth arrest and apoptosis in *ARID1A*-knockout cells (112). *SMARCA2/4*-deficient cells undergo apoptosis because of limited energy sources, as excess alanine competes with glutamine for cellular uptake; this competition allows alanine supplementation to effectively

suppress *SMARCA2/4*-mutated tumors (113). Recent research has shown that CDK9, a novel epigenetic suppressor, mediates gene silencing through phosphorylation of *SMARCA4*, thereby inhibiting tumor growth (114). Mevalonate pathway inhibitors can also enhance the immune microenvironment of *ARID1A*-mutated ovarian clear cell carcinoma, triggering pyroptosis (115).

6. Conclusions and opinions

The SWI/SNF complex serves a crucial role in epigenetic gene regulation by modulating chromatin accessibility. These subunits contribute to the development and differentiation of gut stem cells, as well as intestinal homeostasis. Recently, multiple studies have identified partial or complete alterations in the SWI/SNF complex in gastrointestinal tumors, which exhibit a high degree of malignancy and poor prognosis. Therefore, the present review summarized the association between the SWI/SNF complex and digestive tract tumors, with the aim of providing data to further support the study of these tumors.

SWI/SNF complex mutations can drive tumor progression primarily by suppressing apoptosis, promoting cell proliferation and inducing other changes that support tumor growth. The loss of tissue-specific markers, and the recovery of stem cell characteristics allow these tumors to exhibit unlimited proliferation and differentiation potential. In addition, the SWI/SNF complex is involved in regulation of the digestive tract microenvironment, which is related to the immune response. With the advancement in research on these tumors, targeted therapy based on the principle of synthetic lethality has begun to garner attention. However, these techniques are still in their preliminary stages of development. Determining the efficacy of these approaches in inhibiting tumor growth and improving patient outcomes require extensive long-term studies prior to practical implementation.

In conclusion, elucidating the structure of the SWI/SNF complex and analyzing tumors associated with SWI/SNF complex mutations is imperative for clinical practice. Additional research is required to substantiate the existing and novel therapeutic options.

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Ethics approval and consent to participate

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Patient consent for publication

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Competing interests

The authors declare that they have no competing interests.

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