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Review

The Role and Therapeutic Potential of ARSB Gene in Tumor Development

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Abstract: Arylsulfatase B (ARSB), also known as *N*-acetylgalactosamine-4-sulfatase, is a lysosomal enzyme specifically involved in the degradation of chondroitin sulfate and dermatan sulfate. In recent years, studies have demonstrated that ARSB plays multifaceted roles in tumor extracellular matrix remodeling, signal transduction, and immune regulation. Across different cancer types, ARSB exhibits heterogeneous expression patterns and displays tumor type–dependent dual regulatory functions. Mechanistically, ARSB modulates multiple signaling pathways, including Wnt/β-catenin, PI3K/AKT, and MAPK, and influences PD-L1 expression, thereby participating in tumor proliferation, invasion, and immune evasion. This review systematically summarizes the gene structure and biological functions of ARSB, its roles across various cancer types, prognostic value based on TCGA pan-cancer data,and discusses therapeutic strategies such as enzyme replacement therapy and gene therapy, highlighting its potential as a target for personalized cancer treatment.

Keywords: lysosomal enzyme; ARSB; tumor development; signaling pathway

1. Introduction

1.1. Current Status of Cancer

Cancer is a complex and heterogeneous disease characterized by sustained proliferation, invasion, metastasis, and evasion of immune surveillance. It remains one of the leading causes of death worldwide [1]. Contemporary research has revealed that cancer initiation and progression are not solely driven by intrinsic abnormalities of tumor cells but are also profoundly influenced by the surrounding tumor microenvironment.

1.2. Composition and Function of the Tumor Microenvironment

The tumor microenvironment (TME) comprises a diverse array of components, including immune cells [2], fibroblasts [3], and the extracellular matrix (ECM) [4]. These elements interact either through secreted factors or direct cellular contact to collaboratively influence cancer initiation and progression [5–7]. For instance, alterations in ECM stiffness [4], immune cell infiltration patterns [2], and metabolic reprogramming [6,8] within the TME have been shown to significantly affect tumor cell migration, proliferation, and therapeutic responsiveness [3,7]. Among these components, the ECM has recently emerged as a critical target in cancer research [9]. As a major structural and functional component of the TME, the ECM serves not only as mechanical support but also as a dynamic regulator of the microenvironment and a reservoir of signaling molecules [10]. It consists primarily of structural proteins [11], adhesive glycoproteins [12], proteoglycans and glycosaminoglycans (GAGs) [13], and

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basement membrane components [14]. Through regulation of tumor cell adhesion, migration, and intracellular signaling, the ECM actively contributes to cancer progression, immune evasion, and the development of therapeutic resistance [15].

1.3. Reappraisal of Lysosomal Enzyme Function

Traditionally, lysosomes have long been regarded as the "digestive system" of the cell, primarily responsible for the degradation of macromolecules. However, recent studies have revealed that lysosomal enzymes exert far more complex functions in cancer, including roles in signal transduction [16], immune evasion [17], metabolic regulation, and cellular reprogramming [18].

Lysosomal enzymes are pivotal in ECM homeostasis. Beyond directly degrading and recycling ECM components such as collagen and GAGs, they also modulate key signaling pathways, including those involved in autophagy, and transcriptional regulation, thereby facilitating ECM remodeling [19]. Under pathological conditions, lysosomal dysfunction can lead to aberrant ECM accumulation or degradation, contributing to fibrosis, neurodegenerative disorders, and tumor progression [20]. Moreover, the exocytotic release of lysosomal enzymes plays a role in tissue repair and microenvironmental remodeling, indicating their potential involvement in tumor invasion and metastasis [21].

2. Methodology

This review was synthesized based on literature retrieved from PubMed, Web of Science, Scopus, Google Scholar, and CNKI (China National Knowledge Infrastructure), including both English and Chinese sources published between 1980 and 2024.

Search terms included:

"Arylsulfatase B", "ARSB", "ARSB and cancer", "ARSB and tumor", "ARSB and carcinoma", "ARSB and malignancy", "Sulfatases", and their Chinese equivalents for CNKI.

Given the limited number of original studies on ARSB in cancer, we broadened the scope to include original research articles, reviews, and conference abstracts that provided mechanistic, clinical, or therapeutic insights related to ARSB.

After screening and evaluation, a total of 38 articles directly related to ARSB were included in this review for detailed analysis and synthesis.

3. The ARSB Gene and Its Protein

3.1. Genomic Localization and Splice Variants

ARSB, also known as *N*-acetylgalactosamine-4-sulfatase, is the only known enzyme capable of removing the 4-sulfate groups from dermatan sulfate (DS) and chondroitin sulfate (CS) [22]. These two GAGs play essential roles in maintaining ECM integrity and lysosomal homeostasis. Their abnormal accumulation disrupts lysosomal acidification, membrane stability, and autophagic flux, particularly in the tumor microenvironment, where altered lysosomal activity can remodel the cancer cell–matrix interface and affect cell survival and invasiveness [6].

The ARSB gene is located on chromosome 5q14.1 and encodes a highly conserved lysosomal enzyme belonging to the sulfatase superfamily [23] (Figure 1). Multiple splice variants of the gene have been identified. Among them, transcript variant 1 (NM_000046.5) encodes the functional ARSB protein, consisting of 533 amino acid residues, while transcript variant 2 (NM_198709.3) encodes a 413-amino acid protein due to a 3′-end deletion [24].

3.2. Protein Structure and Catalytic Properties

The ARSB protein functions as a homodimer within the lysosome and belongs to the class of metal ion–dependent hydrolases. Its *N*-terminal segment (residues 1–36) constitutes a signal peptide responsible for lysosomal targeting. Notably, Cys91 undergoes post-translational modification to formylglycine, which participates in ester bond formation at the catalytic site, a crucial determinant of its enzymatic function. ARSB catalyzes the hydrolysis of the 4-sulfate groups from CS and DS, facilitating the degradation of GAGs [25].

3.3. Subcellular Localization and Biological Functions

Although ARSB is predominantly localized in the lysosome, it has also been detected on the cell membrane and in the nucleus, suggesting potential non-canonical roles in signal transduction and transcriptional regulation [26]. Alterations in ARSB expression significantly affect the sulfation patterns of the ECM, thereby modulating the binding

and release of critical mediators such as galectin-3 and SHP2, with effects on cell proliferation, migration, and immune responses [22].

3.4. Mutations and Disease Associations

Loss-of-function mutations in ARSB are the primary cause of Mucopolysaccharidosis type VI (MPS VI), an autosomal recessive lysosomal storage disorder characterized by systemic accumulation of GAGs. Clinically, MPS VI manifests as skeletal abnormalities, hepatosplenomegaly, pulmonary dysfunction, and cardiac valve disease [27,28]. Currently, over 160 ARSB mutations have been reported, including missense mutations, splice-site alterations, and large deletions, all of which significantly impair ARSB enzymatic activity [29–31].

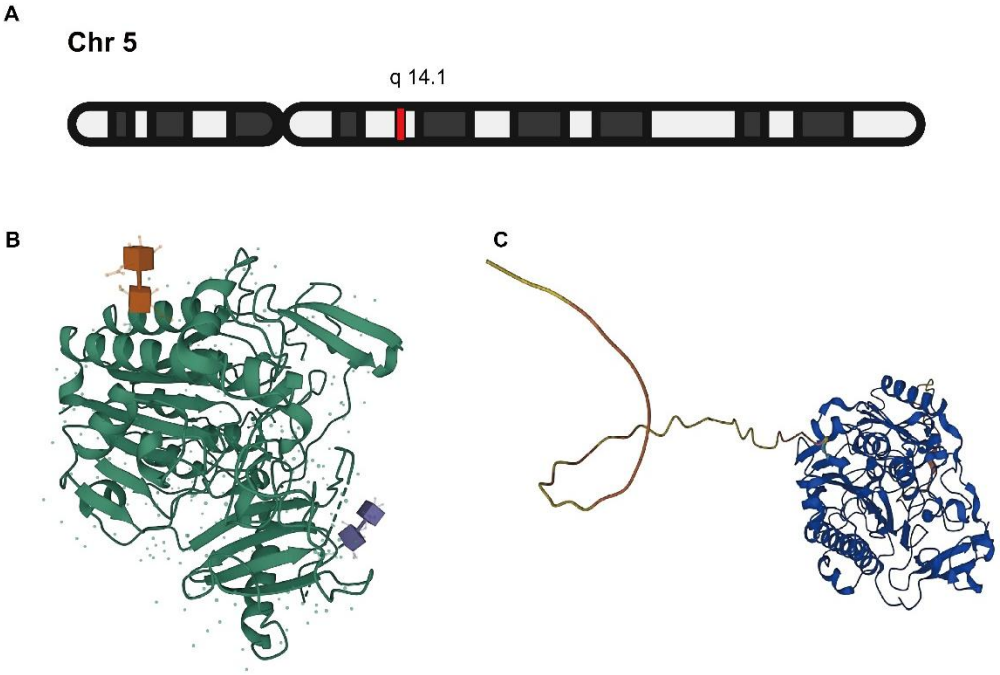

Figure 1. ARSB Gene and Protein Overview. Brief Gene Structure (**A**), Representative (**B**) and Predicted Structures (**C**) of the ARSB Protein [32].

4. ARSB Expression Across Human Cancers

4.1. Findings from TCGA Pan-Cancer Analysis

We extracted ARSB gene expression data from the standardized TCGA pan-cancer dataset in the UCSC Xena database, including both normal and tumor tissue samples. Expression values were $\log_2^{(x+1)}$ transformed. To ensure analytical reliability, cancer types with fewer than three samples were excluded, resulting in 31 cancer types for analysis. Statistical comparisons between normal and tumor tissues were performed using R (version 3.6.4) and the unpaired Wilcoxon rank-sum test.

Our pan-cancer analysis revealed significant heterogeneity in ARSB expression across various tumor types and is significantly associated with both overall survival (OS) and disease-specific survival (DSS) in multiple malignancies.

As shown (Figure 2), upregulated ARSB expression was observed in several tumors, including (Figure 2A) glioblastoma multiforme (GBM), lower grade glioma and glioblastoma (GBMLGG), stomach adenocarcinoma (STAD), stomach and esophageal carcinoma (STES), Liver hepatocellular carcinoma (LIHC), kidney renal clear cell carcinoma (KIRC), kidney renal papillary cell carcinoma (KIRP), head and neck squamous cell carcinoma (HNSC), and skin cutaneous melanoma (SKCM).

In contrast, (Figure 2B) downregulation of ARSB was noted in prostate adenocarcinoma (PRAD), colon adenocarcinoma (COAD), and bladder urothelial carcinoma (BLCA). No statistically significant differences in ARSB expression were found in esophageal carcinoma (ESCA) and thyroid carcinoma (THCA).

Survival analyses (Figure 3) demonstrated that high ARSB expression was significantly associated with poor OS and DSS in several tumor types, including GBM, GBMLGG, STAD, and STES. In contrast, low ARSB expression was correlated with poor OS and DSS in tumors such as BLCA and kidney chromophobe carcinoma (KICH).

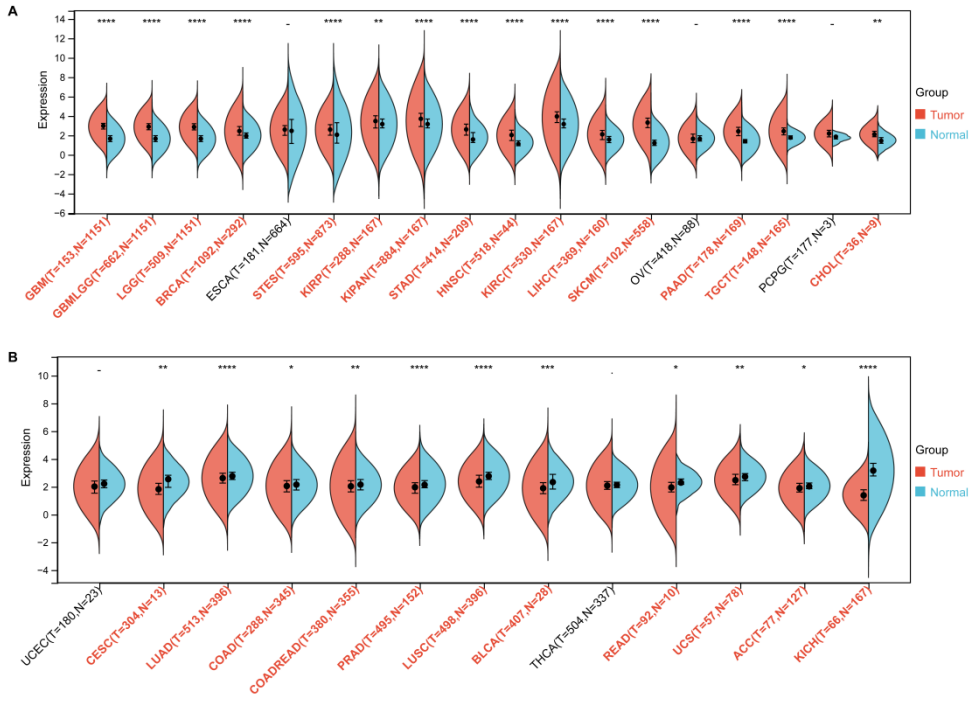

Figure 2. Distribution of ARSB expression across tumor types. ARSB expression data were extracted from the UCSC Xena pan-cancer dataset. (**A**) ARSB expression across tumors showing significant upregulation in 15 cancer types. (**B**) ARSB expression across tumors showing significant downregulation in 11 cancer types. Significance levels are indicated as follows: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$ (unpaired Wilcoxon rank-sum test).

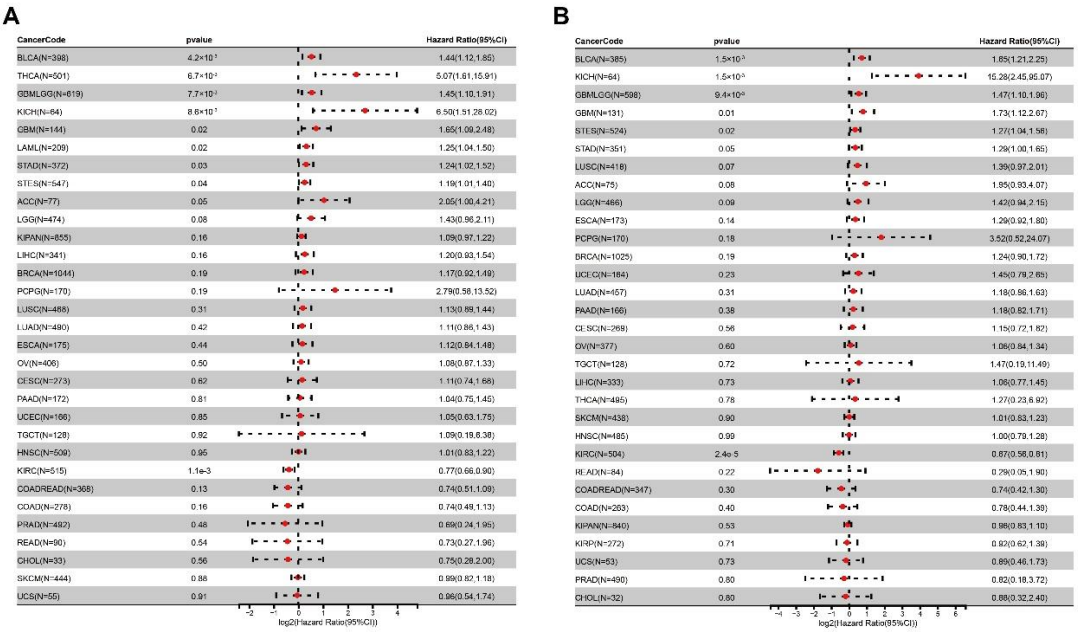

Figure 3. Association between ARSB expression and OS (**A**). Association between ARSB expression and DSS (**B**). Cox regression and log-rank tests were used to assess survival associations. High ARSB expression predicted poor prognosis in 5 cancers and low expression predicted poor outcome in 3.

These expression patterns suggest that ARSB does not exert a uniformly pro-tumorigenic or tumor-suppressive role across all malignancies. Instead, its regulatory effects may depend on tumor type, cellular context, and the tumor microenvironment, reflecting a complex and potentially biphasic regulatory function.

4.2. Summary of Current Research on ARSB in Cancer

ARSB exhibits differential expression across various cancer types (Table 1). Notably, MPS VI results from diverse mutations in the ARSB gene [33]—including missense, nonsense, splice-site mutations, and small deletions—that lead to absent or significantly reduced ARSB activity. In cancers where ARSB activity is diminished, although the precise cause (such as gene mutations) is not always identified, a decline in ARSB function is consistently observed.

Table 1. ARSB expression and functional significance across different cancer types.

Cancer	ARSB	Significance
Breast Cancer	Significantly Decreased	ARSB is significantly downregulated in breast cancer cells, particularly estrogen-responsive types [34]. Functional studies suggest a tumor-suppressive role via regulation of C4S metabolism and proteoglycans such as syndecan-1 and decorin [35].
Melanoma	Significantly Decreased	ARSB expression is significantly decreased in melanoma tissues and B16F10 cells. ARSB deficiency enhances cell invasiveness and MMP-2 expression, whereas treatment with exogenous recombinant ARSB suppresses tumor growth and improves survival outcomes in murine models [36,37].
Prostate Cancer	Downregulated	ARSB is downregulated in prostate cancer, as demonstrated by immunohistochemistry and enzymatic assays, with concurrent increases in CS levels [38]. Reduced ARSB expression is significantly associated with higher Gleason scores and PSA recurrence, and serves as a prognostic biomarker superior to traditional clinical indicators [39,40].
Colon Cancer	Progressively Decreased	ARSB expression and activity progressively decline from adenoma to carcinoma [26], with further reduction in invasive subtypes. Its co-expression with maspin and ARSA predicts poor prognosis [41], while ARSB silencing enhances MMP9, RhoA activation, and cell migration [42].
Hepatocellular Carcinoma	Upregulated	ARSB is upregulated in hepatocellular carcinoma, and its circular RNA (circARSB) encodes a functional peptide, circARSB-321aa, which activates the PI3K/AKT pathway to promote cell proliferation and migration, suggesting a pro-tumorigenic role [43].
Stomach Adenocarcinoma	Upregulated	ARSB is upregulated in gastric cancer tissues and correlates with TNM stage. ARSB silencing inhibits proliferation and migration, induces apoptosis, and suppresses Wnt/β-catenin signaling, indicating a pro-tumorigenic role [44].
Lung Cancer	Significantly Upregulated	ARSB activity is significantly increased in lung adenocarcinoma and squamous cell carcinoma. A tumor-specific ARSB isoform (B1) [45] with a unique isoelectric point (pI = 6.7) and phosphorylation was identified, suggesting potential pro-tumorigenic roles in metabolic regulation or microenvironmental adaptation [46].
Thyroid Cancer	Unknown	A genome-wide association study identified a significant correlation between the ARSB SNP rs13184587 and susceptibility to differentiated thyroid cancer (DTC) in an Italian population ($p = 8.54 \times 10^{-6}$), suggesting a potential role of the ARSB locus in DTC genetic predisposition [47].

5. Mechanistic Roles of ARSB in Cancer

Recent studies have shown that ARSB influences multiple signaling pathways and regulatory axes involved in tumor initiation and progression, demonstrating complex, tissue-specific regulatory mechanisms, as summarized in the Table 2.

The decline in ARSB activity promotes cancer progression primarily through decreased SHP2 activity and increased Galectin-3 levels. In addition, cancers with elevated ARSB activity are mainly associated with the activation of the Wnt/β-Catenin and PI3K/AKT signaling pathways (Figure 4).

Table 2. Mechanistic roles of ARSB in different cancer types.

Cancer	Pathway/ Regulatory Axis	Significance
Prostate Cancer	C4S/SHP2/JNK/ EGFR Pathway	ARSB downregulation leads to C4S accumulation, which inhibits SHP2 activity, activates JNK signaling, promotes c-Jun nuclear translocation and EGFR upregulation, thereby enhancing EGF-induced proliferation in prostate cancer cells [48].

	Galectin-3/AP-1/ Versican Pathway	ARSB loss increases C4S and versican expression via enhanced AP-1 activity due to reduced Galectin-3 binding [49]. In prostate cancer, low ARSB enhances versican–EGFR interaction, potentially affecting EGFR signaling [39,50,51].
	Wnt/β-Catenin Pathway	ARSB downregulation in prostate cancer promotes C4S accumulation, inhibits SHP2, and induces epigenetic silencing of DKK3, thereby activating Wnt/β-catenin signaling [52].

Table 2. *Cont.*

Cancer	Pathway/ Regulatory Axis	Significance
Prostate Cancer	Non-canonical Wnt/CHST15/ CSE Pathway	ARSB downregulation activates the Wnt3A/Rac1/p38 MAPK/GATA-3 axis, promoting CHST15 expression and CSE accumulation, thereby inducing EMT and enhancing invasiveness [53].
Melanoma	MAPK/ERK Pathway	ARSB downregulation in melanoma inhibits SHP2 via C4S accumulation, activates p38 MAPK/MITF signaling, and upregulates GPNMB, promoting malignancy [54]. ARSB restoration reverses these effects, reduces Sp1, and suppresses MMP2/9 expression, limiting invasiveness [37].
	HDAC3/c-Jun/ PD-L1 Regulatory Axis	ARSB loss promotes nuclear c-Jun accumulation and HDAC3-mediated H3K27 acetylation at the PD-L1 promoter, increasing PD-L1 expression. Exogenous ARSB interacts with IGF2R and suppresses PD-L1, enhancing immune cytotoxicity [55].
Stomach Adenocarcinoma	Wnt/β-Catenin Pathway	ARSB upregulates β-catenin and c-Myc to promote proliferation and migration, while its knockdown inhibits the pathway and induces apoptosis [44].
Colon Cancer	BMP4/Wnt9A/CHST11 Pathway	ARSB downregulation increases C4S sulfation, which traps BMP4 at the membrane and reduces Smad3 phosphorylation and CHST11 expression. Meanwhile, reduced Galectin-3 binding promotes Wnt9A upregulation via Sp1, which further suppresses CHST11. This bidirectional regulation may alter glycosylation and progression in colorectal cancer [56].
	Maspin/ARSB Regulatory Axis	ARSB downregulation with increased maspin is linked to greater invasion and lymphatic metastasis, suggesting a cooperative role in immune evasion and tumor progression [57].
Hepatocellular Carcinoma	PI3K/AKT Pathway	circARSB encodes the oncogenic peptide circARSB-321aa, which activates PI3K/AKT signaling to promote proliferation and migration, suggesting its potential as a therapeutic target and prognostic marker [43].
Hepatocellular Carcinoma	Warburg Effect	ARSB loss promotes the Warburg effect by reducing oxygen consumption and increasing lactate production, disrupting redox balance even under normoxia [58].

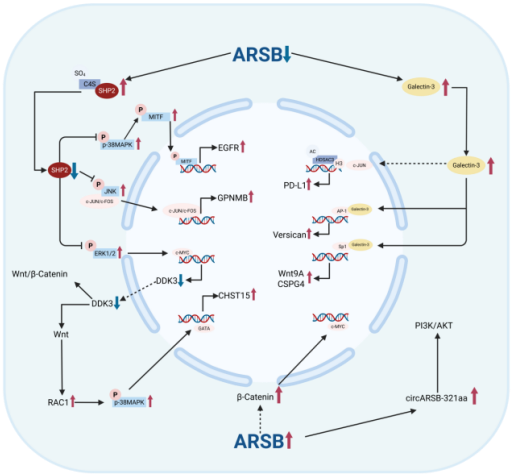

Figure 4. Mechanistic roles of ARSB in cancer. Reduced ARSB activity leads to C4S accumulation due to impaired removal of sulfate groups at the non-reducing end. This enhances Galectin-3-mediated transcriptional activation of versican [59], CSGP4 [36], Wnt9A [60], and PD-L1 [61] via interaction with AP-1 and Sp1. Concurrently, increased C4S promotes SHP2 binding, reducing its phosphatase activity and resulting in sustained phosphorylation of ERK [36,52,62], JNK [48], and p38 MAPK [53,54]. Downstream, nuclear translocation of c-Myc [52] and MITF [54] upregulates GPNMB [54] and EGFR [48], while repressing DDK3 [52]. In contrast, high ARSB activity enhances β-catenin levels, facilitating c-Myc-driven transcription [44], and promotes circARSB-321aa expression, thereby activating the PI3K/AKT pathway [43].

6. Therapeutic Implications of ARSB in Cancer

Aberrant expression and function of ARSB in various cancers highlight its potential as a valuable therapeutic target. Drawing on its well-established role in the treatment of genetic disorders, particularly MPS VI, current evidence suggests that ARSB-targeted cancer therapy may be explored on three major fronts.

6.1. Insights from ARSB-Deficiency Therapies into Cancer Intervention

As the causative gene for MPS VI, ARSB has been the focus of extensive therapeutic research. Its clinical management provides a foundational reference for translational approaches in oncology.

6.1.1. Enzyme Replacement Therapy (ERT)

ERT using recombinant human ARSB (galsulfase) has been shown to significantly improve tissue damage and functional impairment in MPS VI patients [27]. However, long-term ERT can induce anti-ARSB antibodies, potentially diminishing therapeutic efficacy. This underscores the need to consider immunogenicity mitigation strategies—such as PEGylation, antibody screening, or adjuvant modulation—if ARSB-based ERT is to be repurposed for cancer treatment.

6.1.2. Long-Term Replacement Potential of Gene Therapy

Gene therapy offers a promising strategy for sustained correction or regulation of pathogenic genes, enabling targeted and durable interventions in complex diseases such as cancer. Its advantages include high specificity, long-term efficacy, and applicability to various treatment-resistant malignancies [63,64]. A 2024 study reported that liver-targeted AAV8.TBG.hARSB achieved stable expression of ARSB enzyme activity for over three years in MPS VI patients—reaching 38–67% of normal levels—without serious adverse events [30]. This approach suggests the feasibility of localized and controllable ARSB restoration in cancer, particularly for focal tumors with ARSB downregulation, such as melanoma and prostate cancer.

6.1.3. Metabolic Reprogramming and Microenvironmental Modulation

ARSB enzymatic activity is oxygen-dependent, and its deficiency has been shown to induce metabolic reprogramming and promote the Warburg effect [58]. This suggests ARSB may serve as a regulator of oxidative metabolism in metabolically active tumors. Restoration of ARSB expression may help re-establish metabolic balance within the tumor microenvironment, potentially enhancing the efficacy of other treatments such as chemotherapy, radiotherapy, or immunotherapy.

6.2. Replacement Strategies for ARSB-Deficient Cancers

In cancers such as melanoma, prostate cancer, and colorectal cancer, ARSB is frequently downregulated, leading to C4S accumulation, SHP2 inactivation, dysregulation of MAPK and JNK signaling, and activation of immune evasion pathways [36,48,55]. Exogenous recombinant ARSB has been shown to suppress tumor progression and prolong survival in preclinical models [37]. Drawing from MPS VI treatment experience, several considerations are essential for ARSB replacement in cancer. Localized delivery: Higher intratumoral concentrations are required than in systemic deficiency, possibly achievable via nanocarriers or IGF2R-targeted systems [55,65] elicit anti-ARSB antibodies, necessitating immune tolerance strategies [66]. Combination therapies: ARSB restoration may enhance sensitivity to immune checkpoint inhibitors [67], and be synergistic with metabolic modulators or anti-angiogenic agents [68].

6.3. ARSB Inhibition Strategies for Cancers with High ARSB Expression

In gastric and liver cancers, high ARSB expression is associated with activation of Wnt/β-catenin and PI3K/AKT pathways, promoting proliferation, migration, and treatment resistance [43,44]. Thus, ARSB may serve as an upstream target for growth inhibition and signaling reprogramming.

Future ARSB inhibitors for cancer should be highly specific, low-molecular-weight, and stable, referencing steroid sulfatase inhibitor development [69]. Local delivery is preferred to limit off-target effects and immunogenicity [70], and combination therapy may enhance Wnt or PI3K/AKT blockade.

Given the role of the tumor stroma in progression and resistance [71], and the ability of ARSB to induce EMT [53], combining ARSB inhibition with anti-stromal strategies may further improve outcomes [72].

7. Review and Outlook on ARSB in Cancer

Several reviews have discussed the role of ARSB in disease pathogenesis and its potential as a therapeutic target [22,73]. While existing literature has explored its biological functions in metabolic disorders and selected cancers, systematic analyses are still lacking. Key gaps include: (1) mechanistic studies of its context-dependent dual roles—oncogenic in gastric cancer vs. tumor-suppressive in prostate cancer [40]; (2) integrated bioinformatic reviews utilizing datasets such as TCGA to define expression profiles, prognostic value, and regulatory networks.

However, current findings on ARSB expression remain inconsistent across studies. These discrepancies likely stem from tumor-specific biology—such as microenvironmental differences and glycosaminoglycan composition—as well as methodological variations. For example, some studies assess mRNA only, while others evaluate protein levels or enzymatic activity via IHC, western blot, or activity assays. Antibody specificity, sample preservation, and detection thresholds further complicate interpretation. Older studies [45,46] also lacked clear distinction between ARSB and ARSA, possibly contributing to misidentification.

This review builds upon current knowledge by combining bioinformatics and experimental validation, offering a comprehensive summary of ARSB's roles and therapeutic implications across cancer types, along with challenges in clinical translation. Reviews on the sulfatase family also highlight ARSB's broader biological relevance beyond MPS VI, including tumor suppression and signaling regulation [22].

In summary, ARSB plays a complex, tumor-specific role in cancer development by modulating GAGs sulfation, thereby influencing signaling, the tumor microenvironment, and immune response. Therapeutic strategies targeting ARSB—via gene therapy, enzyme restoration, or inhibition—show promise, especially in ARSB-deficient tumors. Preclinical melanoma models demonstrate that recombinant ARSB exerts antitumor effects [69], supporting its translational potential.

Future research should focus on cancer-type–specific functions of ARSB, standardization of detection protocols, and further preclinical validation across broader malignancies. Clinical trials evaluating ARSB-targeted therapies—starting with galsulfase in cancers with strong preclinical evidence—are essential to determine safety and efficacy. Development of specific ARSB inhibitors may also benefit cancers with ARSB overexpression. Continued investigation into ARSB biology will likely contribute to the advancement of novel and effective cancer therapies.

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Abbreviations

ACC	Adrenocortical carcinoma	KIRP	Kidney renal papillary cell carcinoma
AP-1	Activator Protein-1	LAML	Acute Myeloid Leukemia
ARSB	*N*-acetylgalactosamine-4-sulfatase	LGG	Brain Lower Grade Glioma
BLCA	Bladder Urothelial Carcinoma	LIHC	Liver hepatocellular carcinoma
BMP4	Bone Morphogenetic Protein 4	LUAD	Lung adenocarcinoma
BRCA	Breast invasive carcinoma	LUSC	Lung squamous cell carcinoma
C4S	chondroitin 4-sulfate	MESO	Mesothelioma
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	MITF	microphthalmia-associated transcription factor
CHOL	Cholangiocarcinoma	MMP-2	pro-matrix metalloproteinase-2
CHST11	Carbohydrate Sulfotransferase 11	MMP9	matrix metalloproteinase 9
CHST15	Carbohydrate Sulfotransferase 15	MPS VI	Mucopolysaccharidosis VI
c-Jun	cellular Jun	OS	Overall Survival
COAD	Colon adenocarcinoma	OS*	Osteosarcoma
COADREAD	Colon adenocarcinoma/Rectum adenocarcinoma	OV	Ovarian serous cystadenocarcinoma

CS	chondroitin sulfate	p38 MAPK	p38 Mitogen-Activated Protein Kinase
CSE	chondroitin sulfate E	PAAD	Pancreatic adenocarcinoma
DLBC	Diffuse Large B-cell Lymphoma	PCPG	Pheochromocytoma and Paraganglioma
DNA	Deoxyribonucleic Acid	PD-L1	Programmed Death-Ligand 1
DS	dermatan sulfate	PEG	Polyethylene Glycol
DSS	Disease-Specific Survival	PI3K/AKT	Phosphoinositide 3-Kinase/Protein Kinase B
ECM	extracellular matrix	PRAD	Prostate adenocarcinoma
EGF	Epidermal Growth Factor	PSA	Prostate-Specific Antigen
EGFR	Epidermal Growth Factor Receptor	Rac1	Ras-related C3 botulinum toxin substrate 1
EMT	Epithelial-Mesenchymal Transition	READ	Rectum adenocarcinoma
ERK1/2	Extracellular Signal-Regulated Kinase 1/2	SARC	Sarcoma
ERT	Enzyme Replacement Therapy	SHP2	Src Homology 2 Domain-Containing Phosphatase 2
ESCA	Esophageal carcinoma	SKCM	Skin Cutaneous Melanoma
FPPP	FFPE Pilot Phase II	Smad3	Mothers Against Decapentaplegic Homolog 3
GAGs	glycosaminoglycans	Sp1	Specificity Protein 1
Galectin-3	Galactoside-Binding Lectin 3	STAD	Stomach adenocarcinoma
GATA-3	GATA Binding Protein 3	STES	Stomach and Esophageal carcinoma
GBM	Glioblastoma multiforme	TGCT	Testicular Germ Cell Tumors
GBMLGG	lower grade glioma and glioblastoma	THCA	Thyroid carcinoma
GPNMB	transmembrane glycoprotein NMB; glycoprotein non-metastatic melanoma protein B	THYM	Thymoma
H3K27	Histone H3 Lysine 27	TME	tumor microenvironment
HDAC3	Histone Deacetylase 3	UCEC	Uterine Corpus Endometrial Carcinoma
HNSC	Head and Neck squamous cell carcinoma	UCS	Uterine Carcinosarcoma
JNK	c-Jun *N*-terminal Kinase	UVM	Uveal Melanoma
KICH	Kidney Chromophobe	Wnt/β-Catenin	Wingless/Integrated, Beta-Catenin
KIPAN	Pan-kidney cohort	Wnt3A	Wingless-Type MMTV Integration Site Family, Member 3A
KIRC	Kidney clear cell carcinoma	Wnt9A	Wingless-Type MMTV Integration Site Family, Member 9A

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