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Research Progress on the Relationship Between WSTF and Cancer

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Abstract

The Williams syndrome transcription factor (WSTF, alternatively termed BAZ1B) represents a versatile nuclear protein that exerts pleiotropic effects on neurodevelopmental processes, chromatin remodeling, DNA damage repair, as well as transcriptional regulation. Accumulating evidence demonstrates that WSTF is a crucial molecular determinant in the pathogenesis and progression of multiple cancers, positioning it as a viable therapeutic target. This review systematically synthesizes the molecular mechanisms by which WSTF drives oncogenesis across malignancies, focusing on its interplay with regulatory factors and signaling pathways. In breast cancer, WSTF participates in estrogen receptor (ER) signaling and contributes to endocrine therapy resistance by modulating ER-dependent gene expression to promote proliferation and invasion. WSTF also interacts with the vitamin D analog EB1089, suppressing tumor progression through altered promoter binding. In gastric cancer, aberrant WSTF expression disrupts cell adhesion, increasing cancer cell dependency on WSTF. Hyperphosphorylation of WSTF in diffuse gastric cancer further implicates it in tumorigenesis. In cervical, glioblastoma, and lung cancers, WSTF activates the PI3K-Akt signaling cascade, enhancing tumor cell proliferation, migration, and invasion. These findings underscore WSTF's oncogenic role and therapeutic potential. Further investigation into WSTF's functions and regulatory mechanisms will deepen our understanding of tumorigenesis and inform novel therapies targeting this chromatin regulator.

Keywords: WSTF; Malignant Tumors; Transcriptional Regulation; PI3K/Akt Pathway

1. Introduction

1.1. Current Status of Cancer Research

Malignant neoplasms persist as a predominant contributor to global mortality. Epidemiological data from the World Health Organization (2019) indicate that cancer was the primary or secondary cause of premature death (prior to 70 years of age) in 183 nations, while ranking third or fourth in 23 other countries (Sung et al., 2021). Epidemiological studies identify China as the country with the most substantial cancer incidence worldwide, exhibiting a steadily increasing annual caseload (Kamaraju et al., 2020). Globally, 2020 witnessed approximately 19.3 million newly diagnosed cancer cases, of which 4.57 million (23.7%) were recorded within China (Qiu et al., 2022). Despite advancements in medical technology, cancer treatment costs continue to rise, and the disease imposes substantial burdens on societal productivity, labor resources, and economic stability (Stemmer et al., 2013; Yabroff et al., 2011). Thus, early screening, timely diagnosis, and effective treatment are critical to mitigating these losses (Luengo-Fernandez et al., 2013). A paradigm shift has characterized oncological therapeutics since the dawn of the 21st century, transitioning sequentially from empirical clinical practice to evidence-based practice approaches, and currently progressing toward individualized precision medicine strategies. (Powell et al., 2022).

1.2. Structure o*f WSTF*

The Williams syndrome transcription factor (WSTF), encoded by the *BAZ1B* gene (HGNC:963; chr7q11.23), is a chromatin-modifying protein that regulates genomic architecture. The BAZ1B gene spans 80 kilobases in length and contains a 4,449-base pair open reading frame. As a member of the BAZ/WAL protein family, the Williams syndrome transcription factor (WSTF) is a large nuclear protein comprising 1,425 amino acid residues with an approximate molecular mass of 171 kilodaltons. This multidomain protein features two evolutionarily conserved functional modules: a plant homeodomain (PHD)-type zinc finger motif and a bromodomain, both of which mediate critical chromatin interactions (Chris Barnett & Jocelyn E. Krebs, 2011; Liu et al., 2020; Sharif et al., 2021; Zanella et al., 2019). Williams syndrome (WS; OMIM 194050) is a contiguous gene deletion syndrome, resulting in a complex developmental disorder characterized by multisystem defects. Common clinical features of WS patients include intellectual disability, distinctive facial features, unique cognitive profiles, congenital heart disease, infantile hypercalcemia, and growth deficiencies (Allegri et al., 2020; Bellugi et al., 1990; Serrano-Juárez et al., 2023). Functionally, WSTF serves as a versatile atypical tyrosine kinase that coordinates multiple essential biological processes. It participates in chromatin organization through nucleosome remodeling, regulates transcription via RNA polymerase I- and III-dependent mechanisms, modulates vitamin D3-dependent signaling pathways, and contributes to genomic stability maintenance through its involvement in DNA damage repair systems (Chris Barnett & Jocelyn E. Krebs, 2011; Sharif et al., 2021). Remarkably, WSTF demonstrates substantial overexpression in malignant lesions relative to adjacent normal tissues, underscoring its promise as an emerging molecular target for anticancer therapy.

2. Biological Functions of WSTF

2.1. Neurodevelopmental Regulation

WSTF serves as a key regulator of neurodevelopment. Haploinsufficiency of the WSTF in neural progenitor populations induces genome-wide transcriptional perturbations and impairs cellular differentiation programs, resulting in dysregulation of multiple downstream genetic networks critical for neurodevelopment. WSTF-targeted genes are enriched in the Wnt signaling pathway, which balances neuronal progenitor proliferation and differentiation. Intriguingly, WSTF can rescue differentiation impairments caused by its haploinsufficiency by attenuating hyperactive Wnt signaling in neural stem cells (Lalli et al., 2016; Zhou et al., 2022).

2.2. Chromatin Remodeling

The WSTF serves as an essential structural and functional element within ATP-dependent chromatin remodeling machinery, particularly within two key complexes: the WSTF-ISWI chromatin regulatory complex (WICH) and the B-WICH complex (Goto et al., 2024; Li et al., 2021; Maga & Hubscher, 2003; Poot et al., 2005; Poot et al., 2004). Research demonstrates that: The WICH complex prevents heterochromatin protein 1 (HP1) from binding to newly replicated DNA (Poot et al., 2004). Biochemical studies reveal that WICH's targeting to nascent replication foci is mediated by high-affinity binding to the Proliferating cell nuclear antigen (PCNA) trimer, facilitating chromatin remodeling at active replication forks.By temporarily maintaining chromatin in a transcriptionally accessible state, WICH delays post-replicative chromatin maturation, thereby preserving chromatin structure (Maga & Hubscher, 2003; Poot et al., 2005).

2.3. Role in DNA Damage Repair

H2A.X represents a specialized variant of histone Histone H2A (H2A)(Dibitetto et al., 2024) that is functionally indispensable for DNA damage response pathways. The distinctive WAC (WSTF/Acf1/cbp146) domain within WSTF exhibits intrinsic tyrosine kinase capability, specifically catalyzing phosphorylation at tyrosine residue 142 (Y142) of H2A.X, generating the γH2AX(a form of H2AX with a phosphate group added at position S139)-pY142 epigenetic mark (Broering et al., 2015; Xiao et al., 2009). This phosphorylation event facilitates molecular interactions with RNA polymerase II (Pol II), establishing a functional linkage between DNA damage signaling and transcriptional regulation in actively cycling cell populations.The DNA damage response involves a sophisticated regulatory mechanism:Upon DNA damage, ATM (a PI3-K-like kinase)-dependent EYA1/3 (eyes absent homologs 1 and 3) phosphatases initially remove pre-existing γH2AX-pY142 modifications, leading to transcriptional silencing at damage sites requiring repair(Yuan et al., 2010). Subsequently, WSTF translocates to DNA lesion sites to restore γH2AX-pY142. This molecular mechanism promotes transcription-coupled homologous recombination (TC-HR) in G1-phase cells, where RNA polymerase II-generated transcripts serve as template donors for precise DNA repair, ensuring preservation of genomic stability (Chris Barnett & Jocelyn E. Krebs, 2011; Ji et al., 2019; Oppikofer et al., 2017).

2.4. Transcriptional Regulation

Emerging evidence demonstrates that nuclear myosin 1 (NM1), WSTF, and SWI/SNF-related

matrix-associated actin-dependent regulator of chromatin subfamily A member 1 (SNF2H) associate with RNA polymerase I (Pol I) and ribosomal DNA (rDNA) loci (Percipalle et al., 2006; Venit et al., 2020). The molecular interplay between NM1 and the WSTF orchestrates the coordinated recruitment of two functionally distinct chromatin remodeling complexes—WICH and the WSTF-containing nucleosome assembly complex (WINAC)—to specific genomic loci. At these target sites, these multi-protein assemblies collaboratively execute chromatin structure modifications that ultimately drive transcriptional activation(Percipalle et al., 2006; Sarshad et al., 2013). The dynamic interplay between NM1 and actin filaments generates biophysical forces that activate kinase-dependent phosphorylation of WSTF at specific regulatory residues (Tyr/Ser). This post-translational modification acts as a molecular switch that induces conformational changes in WSTF, leading to the structural destabilization and subsequent disassembly of the B-WICH chromatin remodeling complex. As a consequence, this regulatory cascade terminates B-WICH-mediated chromatin reorganization at ribosomal DNA loci, thereby modulating rDNA transcriptional output. This dissociation event subsequently prevents the binding of Pol I to gene promoters, thereby effectively inhibiting transcriptional activation (Aydin Ö et al., 2014; Sarshad et al., 2013).

As a critical transcriptional regulator, WSTF performs diverse biological functions under normal physiological conditions. However, emerging evidence has demonstrated the essential role of WSTF in malignant tumor progression, generating substantial research interest in its oncogenic functions. Subsequent sections will systematically review mechanistic insights into WSTF's contributions to cancer pathogenesis.

3. Advances in WSTF Research in Malignant Tumors

3.1. WSTF Promotes Malignant Tumor Development and Progression

Emerging evidence highlights the multifaceted role of the WSTF in oncogenesis, with its involvement spanning transcriptional regulation, immune modulation, and epigenetic remodeling.

3.1.1. RUNX2-Dependent Transcriptional Regulation

Studies show that Runt-related transcription factor 2 (RUNX2) and WSTF form a functional complex in the nuclear matrix, working together to regulate DNA damage response (DDR) through three main mechanisms. First, RUNX2 helps bring WSTF to DNA damage sites, which increases the production of γ-H2AX. This process improves the ability to repair DNA. Second, WSTF usually increases apoptosis by adding phosphate groups to H2AX at position Y142. However, RUNX2 reduces this effect by controlling WSTF's activity, which helps cancer cells avoid programmed cell death. Third, this complex lowers the acetylation levels of histone H3 lysine 9 (H3K9) and Histone H3 lysine 56 (H3K56). These changes modify chromatin structure, which affects DNA repair efficiency and how genes are expressed (Yang et al., 2015). This pathway underscores WSTF's role in promoting cancer progression through cooperation with the RUNX family of transcription factors.

3.1.2. Immunomodulatory Functions in the Tumor Microenvironment

L-Arginine potentiates T cell-mediated anti-tumor responses through metabolic reprogramming, a process orchestrated by the L-arginine-responsive transcriptional regulators BAZ1B, Positive Coactivator 4 (PC4) and Splicing Factor, Arginine/Serine-rich 1 (SFRS1) Interacting Protein 1 (PSIP1), and Translin (TSN). These factors sense intracellular L-arginine concentrations. They dynamically modulate the expression of genes involved in DNA repair, chromatin remodeling, and cell survival, thereby augmenting T cell effector functions. Structural proteomics analysis (limited proteolysis-mass spectrometry LiP-MS) identified early conformational changes in WSTF following L-arginine stimulation, suggesting its potential involvement in the initial signaling cascade. However, genetic ablation of WSTF did not impair L-arginine-induced metabolic adaptation or survival advantages in T cells, whereas depletion of BAZ1B, PSIP1, or TSN markedly attenuated these effects. These findings demonstrate that while WSTF may participate in the early L-arginine response network, BAZ1B and its associated factors serve as the core molecular machinery sustaining T cell anti-tumor activity (Geiger et al., 2016). This study establishes the L-arginine-BAZ1B/PSIP1/TSN axis as a critical regulatory node in tumor immunity, while revealing WSTF's non-essential yet potentially modulatory role in this immunometabolic network.

3.1.3. Epigenetic Control of Tumorigenesis

Extensive research has demonstrated that WSTF contributes to cancer progression through several distinct but interconnected biological processes. The first major mechanism involves post-translational modifications, where males absent on the first (MOF)-mediated acetylation at the K426 residue significantly enhances WSTF's ability to regulate gene expression. Importantly, this acetylation event also facilitates subsequent phosphorylation at the S158 position. Together, these molecular modifications work synergistically to promote aggressive tumor behaviors, including enhanced cell proliferation, increased migratory capacity, and greater invasive potential (Liu et al., 2020).

In cancers harboring $KRAS^{G12}$ mutations, WSTF participates in a unique pathogenic cascade. The mutant KRAS protein induces specific epigenetic alterations at the neuregulin-3 (*NRG3*) gene promoter region, resulting in transcriptional activation. This leads to the formation of stable WSTF/NRG3 protein complexes that are secreted through non-classical pathways. Once released into the extracellular environment, these complexes function as potent signaling molecules that can stimulate nearby wild-type cells through paracrine mechanisms. The activated pathways include several well-characterized oncogenic signaling networks such as RAS, Neurogenic locus notch homolog protein 1 (NOTCH1), and Janus Kinase (JAK) which collectively contribute to microenvironmental changes favorable for tumor progression (Liu et al., 2016).

At the genomic level, comprehensive studies utilizing advanced sequencing technologies have revealed that elevated WSTF expression exerts widespread effects on cellular homeostasis. Specifically, WSTF overexpression leads to the transcriptional repression of critical cell cycle inhibitors including Cyclin-Dependent Kinase Inhibitor 1A (CDKN1A) and Mouse Double Minute 2 (MDM2). Concurrently, it downregulates essential components of the proteasomal

degradation machinery, specifically Proteasome Activator Subunit 3 (PSME3) and Proteasome Activator Subunit 4 (PSME4). This coordinated suppression disrupts both upstream signaling pathways and downstream protein degradation cascades, thereby compromising critical cell cycle checkpoints and fostering a molecular microenvironment conducive to dysregulated proliferation and neoplastic progression (Grochowska et al., 2022).

WSTF has emerged as a central regulator in malignant tumor development and progression, orchestrating diverse oncogenic processes through transcriptional control, immune modulation, and epigenetic remodeling. Its interactions with key factors like RUNX2 and NRG3, modulation of L-arginine metabolism, and influence on tumor suppressors (CDKN1A, MDM2) and proteasomal degradation (PSME3/4) collectively drive cancer cell survival, proliferation, and metastasis. These effects are mediated via two core mechanisms: molecular complex formation and epigenetic regulation, highlighting WSTF's multifaceted role in tumorigenesis. Deeper WSTF research could lead to precise cancer treatments, particularly for resistant cases. Combining lab research with clinical applications strongly supports using WSTF both to predict cancer and to develop targeted drugs.

3.2. WSTF in Breast Cancer Signaling

Estrogen receptor (ER) signaling constitutes a fundamental pathway in breast cancer pathogenesis and therapeutic intervention, with approximately 80% of breast malignancies exhibiting ER-positive status and consequent estrogen-dependent proliferative capacity (Bulun et al., 2009; Lundqvist et al., 2018; Nelson & Bulun, 2001; Sammons et al., 2020; Simpson, 2004; Will et al., 2023).Current clinical strategies predominantly employ endocrine-based therapeutics, including selective estrogen receptor modulators (SERMs) such as tamoxifen and aromatase inhibitors, which effectively attenuate ER signaling cascades to achieve tumor growth suppression (Salvati et al., 2022).

The aromatase enzyme, encoded by *CYP19A1*, catalyzes estrogen synthesis (Lin et al., 2023), and its inhibition by vitamin D analogs like EB1089—which downregulates *CYP19A1* expression and aromatase activity-effectively suppresses growth in aromatase-dependent breast cancer cells (Bulun et al., 2009; Lundqvist et al., 2018). Mechanistically, EB1089 alters nuclear receptor/cofactor interactions at the CYP19A1 promoter, enabling vitamin D receptor (VDR) binding while displacing WSTF, thereby impeding breast cancer progression (Lundqvist et al., 2013). Notably, 1α,25-dihydroxyvitamin D3 and its analogs exhibit antiproliferative and prodifferentiation effects, highlighting their therapeutic potential (Bajbouj et al., 2022; Dennis et al., 2023; Hill et al., 2015). In estrogen-dependent breast cancer, targeting ER signaling remains central, with WSTF identified as an activator of CYP19A1 and ERα promoters, while 1,25(OH)2D3 disrupts WSTF-promoter binding to abolish this activation (Bajbouj et al., 2022). These findings position vitamin D analogs as promising therapeutic agents.

Emerging evidence indicates that Dot1L and Menin (encoded by MEN1) colocalize within the cytoplasmic compartment to cooperatively regulate critical pathways involved in breast cancer progression. These pathways include estrogen signaling, p53 activity, HIF1α-mediated responses, death receptor signaling, as well as cell cycle control and epithelial-mesenchymal transition (EMT)

regulation (Liu et al., 2020; Saatci et al., 2021; Salvati et al., 2022). Dot1L and Menin have been shown to influence estrogen signaling through interactions with nuclear chaperone complexes, particularly the BAZ1B-containing B-WICH and WINAC complexes. Experimental reduction of *BAZ1B* expression in both antiestrogen-sensitive and resistant breast cancer cell lines consistently results in significant suppression of ERα expression, impaired proliferative capacity, and transcriptomic reprogramming affecting estrogen response, Myc signaling, mTOR activity, PI3K/AKT pathway, and metabolic processes. The functional interplay between ERα, Dot1L, Menin and BAZ1B - and their coordinated inhibition - exerts profound effects on the proliferation and survival of endocrine-resistant breast cancer cells. These findings support the potential therapeutic strategy of combined pharmacological targeting of these factors to overcome endocrine resistance in ERα-positive breast malignancies (Liu et al., 2020; Saatci et al., 2021; Salvati et al., 2022).

Research findings demonstrate that WSTF can interact with two key acetyltransferases, p300/CBP-Associated Factor (PCAF) and MOF, to co-regulate the acetylation levels at histone sites H3K9 and Histone H4 lysine 16 (H4K16) (Vintermist et al., 2011). The molecular mechanism can be delineated into three critical steps:First, activation of the Ras signaling pathway induces phosphorylation at serine 158 (S158) of the WSTF protein. This post-translational modification serves as a molecular switch that enhances WSTF's binding affinity for PCAF while simultaneously reducing its interaction with MOF.Second, the altered binding dynamics lead to functional consequences: PCAF enzymatic activity becomes elevated, resulting in increased H3K9 acetylation (H3K9ac). Conversely, MOF activity is diminished, causing decreased H4K16 acetylation (H4K16ac).Third, these coordinated changes in histone acetylation patterns directly modulate the expression of tumor-related genes, including Breast tumor kinase (Brk) and p21. Ultimately, these molecular events promote breast cancer cell proliferation, migration, and enhanced tumorigenic potential in vivo, as evidenced by animal studies.This study reveals WSTF functions as a molecular sensor that transduces Ras signaling to differentially regulate PCAF and MOF activities, thereby establishing a novel epigenetic mechanism controlling oncogene expression. These findings not only advance our understanding of breast cancer pathogenesis but also identify potential therapeutic targets for intervention (Li et al., 2016; Liu et al., 2020).

In summary, WSTF has been identified as a central player that: (1) activates *CYP19A1/ERα* genes, (2) cooperates with PCAF/MOF acetyltransferases to regulate histone marks (H3K9ac/H4K16ac), and (3) integrates Ras pathway signals. Ras-mediated phosphorylation at S158 alters WSTF's binding preferences - increasing PCAF but decreasing MOF interaction - ultimately affecting oncogenes (Brk, p21) to drive cancer progression. Vitamin D compounds counteract this by blocking WSTF's binding to CYP19A1/ERα promoters. These findings establish WSTF as both an epigenetic regulator and therapeutic target. Moving forward, studies should clarify WSTF's regulation mechanisms and explore combination therapies pairing WSTF inhibitors with vitamin D analogs for more precise breast cancer treatment.

3.3. WSTF in Gastric Cancer Signaling Pathways

Dysregulation of cell adhesion represents a hallmark feature across multiple cancer types

(Schnell et al., 2013). In gastric cancer, the adhesion protein Claudin-4 (CLDN4), which mediates intercellular adhesion and maintains cell polarity - shows significant upregulation (Tsukita et al., 2019). Notably, the DNA repair protein MutS Homolog 2 (MSH2) is enriched in cell adhesion-related pathways, where it regulates CLDN4 expression through modulating enhancer-promoter interactions, thereby controlling invasive growth of gastric cancer cells. MSH2 deficiency leads to adhesion pathway dysregulation, rendering aggressive gastric cancer cells dependent on WSTF and consequently sensitive to bromodomain/ Bromodomain and Extra-Terminal motif inhibitors (BET) (extra-terminal motif) inhibition, ultimately promoting gastric carcinogenesis (Nargund et al., 2022; Nargund et al., 2023).

Comprehensive studies show that diffuse gastric cancer develops when several cellular pathways malfunction, including c-MYC signaling, EMT processes, and semaphorin communication. In these cancers, the BAZ1B, With No lysine (K) kinase 1 (WNK1) and myosin light chain kinase (MLCK) show excessive phosphorylation activity, while Adaptor-Associated Kinase 1 (AAK1) activity decreases. The WSTF contributes by phosphorylating BAZ1B at Ser699/705 sites, which activates PI3K/Akt and IL-6/ signal transducer and activator of transcription 3 (STAT3) pathways to promote EMT and invasion. lamin A/C (LMNA) phosphorylation at S392 strongly associates with metastasis. WSTF also influences cancer progression through its roles in maintaining chromatin structure and DNA repair, potentially affecting genetic stability. These multiple mechanisms make WSTF an important factor in diffuse subtype of gastric cancer (DGC) development and potential treatment target (Singh et al., 2024).

In summary, dysregulation of cell adhesion plays a pivotal role in gastric cancer, with WSTF driving tumor progression through coordinated multi-pathway mechanisms: (1) phosphorylating BAZ1B to activate PI3K/Akt and STAT3 pathways, thereby promoting EMT; (2) inducing LMNA hyperphosphorylation to enhance metastatic potential; and (3) compromising genomic stability. Notably, the functional coupling between WSTF and the MSH2-CLDN4 axis establishes it as a promising therapeutic target—WSTF inhibition synergistically enhances the efficacy of BET inhibitors when MSH2 is deficient. These findings elucidate WSTF's critical role in gastric cancer and identify novel therapeutic targets and strategies. Future investigations should focus on elucidating the functional mechanisms of WSTF and its associated signaling pathways, which will deepen our understanding of gastric cancer pathogenesis and inform the development of innovative treatment approaches.

3.4. WSTF Promotes Malignant Tumor Development Through the PI3K/Akt Signaling Pathway

A growing body of research evidence clearly indicates that WSTF commonly contributes to cancer progression in multiple tumor types, primarily by activating the important PI3K/AKT cell signaling pathway. In the specific case of cervical cancer (CC), detailed laboratory studies have demonstrated significantly higher levels of WSTF protein in both patient tumor samples and cultured cancer cell lines when compared to normal healthy tissues. Furthermore, these investigations showed that WSTF expression levels gradually increase in parallel with disease progression, suggesting its potential role in driving more advanced stages of cervical cancer development. Studies demonstrate that WSTF knockdown suppresses CC cell proliferation,

invasion, and migration through PI3K/Akt pathway inhibition, establishing WSTF as a key driver of CC malignancy (Jiang et al., 2021).

Consistent with these observations, the research team led by Liyuan Yang reported similar findings in glioblastoma, an aggressive form of brain cancer. Their study demonstrated that elevated WSTF protein expression in tumor cells promotes key oncogenic processes: accelerated cell proliferation and enhanced migratory capacity. This tumor-promoting effect is mediated through a specific molecular mechanism in which WSTF induces AKT protein phosphorylation, thereby initiating an activation cascade of the PI3K/Akt signaling pathway. Ultimately, this pathway activation drives the characteristic uncontrolled growth and metastatic behavior of glioblastoma cells (Yang et al., 2021).

In lung cancer, Jin Meng's studies revealed that WSTF acts like a cancer-causing gene. It works by switching on two important pathways at the same time - the PI3K/Akt pathway and the IL-6/STAT3 pathway. When both pathways are active, they change how cells behave, making them more likely to undergo EMT (Jiang et al., 2021; Meng et al., 2016). This process helps lung cancer cells in several ways: they grow faster, move more easily, and invade other tissues more effectively. As a result, the cancer spreads quicker and becomes more aggressive (Kim et al., 2006; Mittal, 2016; Zeisberg et al., 2007).

Cumulative evidence demonstrates that WSTF exhibits pleiotropic oncogenic functions across multiple malignancies, notably cervical carcinoma, glioblastoma multiforme, and lung cancer. Mechanistically, WSTF consistently activates the PI3K/AKT signaling cascade, thereby promoting hallmark cancer phenotypes including enhanced proliferative capacity, increased invasive potential, and metastatic dissemination via EMT(Jiang et al., 2021; Meng et al., 2016; Yang et al., 2021). Because multiple studies have now confirmed how important WSTF is in these different cancers, it has become clear that this protein could be a good target for new cancer treatments. The next important step for researchers will be to figure out exactly how WSTF causes these cancer-promoting effects at the molecular level. Understanding these detailed mechanisms could lead to new targeted therapies that might work against several types of cancer.

4. Summary and Perspectives

Scientific research has clearly shown that WSTF encodes an essential protein involved in cancer processes. WSTF has been identified as a crucial cancer-associated gene, with its expression level in malignant cells showing direct associations with neoplastic transformation, disease advancement, and therapeutic responses in diverse malignancies. WSTF exerts its oncogenic effects through pleiotropic mechanisms, including modulation of key cellular signaling pathways, epigenetic regulation of gene expression programs, and chromatin remodeling. These coordinated actions collectively promote tumorigenesis by enhancing malignant cell proliferation and metastatic potential. Although we have learned much about WSTF's cancer roles, future studies should address key questions regarding through additional research.

4.1. Molecular Mechanisms of WSTF in other Malignancies

Although we know that WSTF is involved in cancer development, its exact mechanisms are not yet fully understood. WSTF plays important roles in regulating gene expression, modifying chromatin structure, and repairing DNA damage—all of which are closely linked to cancer initiation and progression. By studying WSTF's functions in greater detail, we may uncover new therapeutic targets for cancer treatment.

4.2. Developing Targeted Therapies Against WSTF

As a promising therapeutic target, WSTF shows potential for inhibiting tumor growth and metastasis. Future research should focus on developing more selective and effective WSTF inhibitors to enhance treatment efficacy while minimizing side effects. Researchers should also explore combination therapies with existing treatments like conventional chemotherapy and immune checkpoint inhibitors to potentially improve therapeutic outcomes.

4.3. The Interaction of WSTF with the Tumor Immune Microenvironment

Recent studies show that the immune cells and molecules around tumors (called the tumor microenvironment) significantly influence cancer growth. Future investigations should focus on two key aspects of WSTF's role in tumor immunology: first, elucidating its mechanisms of immune cell regulation within the tumor microenvironment; and second, determining whether malignant cells utilize WSTF-mediated pathways to evade immune surveillance. These critical questions will help establish WSTF's immunomodulatory functions in cancer pathogenesis. Answers to these questions may lead to new combination therapies that make immunotherapies work better for more patients.

In summary, WSTF is an important transcription factor that contributes significantly to cancer development and progression. Current studies continue to investigate exactly how WSTF works at the molecular level in different cancers. Researchers are also examining whether targeting WSTF could lead to new cancer treatments. The findings from these studies may help scientists develop better therapies and improve outcomes for cancer patients.

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