FACULTAD DE CIENCIAS DE LA SALUD

Trabajo de fin de Carrera titulado:

The Regulatory Role of MSI2 in Solid Tumors: A Scoping Review

Realizado por:

JOSEPH GONZALO ARCOS OÑA

Director del proyecto:

MARÍA FERNANDA GUTIÉRREZ BRAVO, PhD.

Como requisito para la obtención del título de:

MAGISTER EN BIOMEDICINA

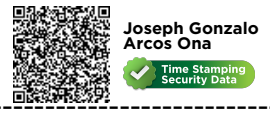
QUITO, 6 DE AGOSTO del 2025

DECLARACIÓN JURAMENTADA

Yo, JOSEPH GONZALO ARCOS OÑA, ecuatoriano, con Cédula de ciudadanía N° 1723437735, declaro bajo juramento que el trabajo aquí desarrollado es de mi autoría, que no ha sido presentado anteriormente para ningún grado o calificación profesional, y se basa en las referencias bibliográficas descritas en este documento.

A través de esta declaración, cedo los derechos de propiedad intelectual a la

UNIVERSIDAD INTERNACIONAL SEK, según lo establecido en la Ley de Propiedad Intelectual, reglamento y normativa institucional vigente.



JOSEPH GONZALO ARCOS OÑA

C.I.: 1723437735

DECLARACIÓN DEL DIRECTOR DE TESIS

Declaro haber dirigido este trabajo a través de reuniones periódicas con el estudiante, orientando sus conocimientos y competencias para un eficiente desarrollo del tema escogido y dando cumplimiento a todas las disposiciones vigentes que regulan los Trabajos de Titulación.

Firmado electrónicamente por:
MARIA FERNANDA GUTIERREZ BRAVO
Validar únicamente con FirmaEC

MARÍA FERNANDA GUTIÉRREZ BRAVO, PhD.
PhD. Biomedicina y Biotecnología.

LOS PROFESORES INFORMANTES:

Ing. Jorge Patricio Espinosa Espinosa, MSc.

Ing. Manuel Andrés Herrera Yela, MSc.

Después de revisar el trabajo presentado lo han calificado como apto para su defensa oral ante el tribunal examinador.

ESPINOSA ESPINOSA JORGE PATRICIO - 60393089B

Digitally signed by ESPINOSA ESPINOSA JORGE PATRICIO - 60393089B
Date: 2025.08.16 09:09:32 -05'00'

Firmado electrónicamente por:
MANUEL ANDRES HERRERA YELA
Validar únicamente con FirmaEC

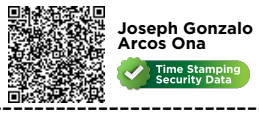
Ing. Jorge Patricio Espinosa Espinosa, MSc.

Ing. Manuel Andrés Herrera Yela, MSc.

Quito, 6 de agosto de 2025

DECLARACIÓN DE AUTORÍA DEL ESTUDIANTE

Declaro que este trabajo es original, de mi autoría, que se han citado las fuentes correspondientes y que en su ejecución se respetaron las disposiciones legales que protegen los derechos de autor vigentes.



JOSEPH GONZALO ARCOS OÑA

C.I.: 1723437735

DEDICATORIA

A mi abuela Mercedes

y mi madre Alicia.

Artículo de tesis

The Regulatory Role of MSI2 in Solid Tumors: A Scoping Review

Joseph Arcos [1], Maria Fernanda Gutierrez [2,*]

[1]Biomedicine Master´s Programme. Health Sciences Faculty, Universidad Particular Internacional SEK (UISEK), Quito 170302, Ecuador.

[2] Experimental and Applied Biomedicine Research Group, Health Sciences Faculty, Universidad Particular Internacional SEK (UISEK), Quito 170302, Ecuador.

* Correspondence Author: maria.gutierrezb@uisek.edu.ec

Resumen: Musashi-2 (MSI2) es una proteína de unión a ARN que interactua ampliamente en procesos oncogénicos, sin embargo, su papel en tumores sólidos sigue sin estar completamente definido. En esta revisión sistemática, se sesgaron artículos publicados entre 2014 y 2025 mediante una busqueda sistematizada en PubMed, Embase, Scielo y Lilacs de acuerdo con los protocolos PRISMA. Los criterios de inclusión abarcaron estudios sobre la expresión y función de MSI2 en tumores de cabeza, pecho, gastrointestinales, genitourinarios y ginecológicos. Después de eliminar duplicados y realizar una selección por título, resumen y texto completo, se incluyeron 97 artículos para realizar una síntesis de los resutlados. Dichos resultados muestran de forma consistente que la sobreexpresión de MSI2 se correlaciona con un mal pronóstico, un estadio avanzado del tumor y resistencia a la terapia. Desde el punto de vista molecular, MSI2 ejerce su influencia oncogénica a través de la regulación postranscripcional de rutas de señalización asociadas al cáncer, como PI3K/Akt/mTOR, Wnt/β-catenina, TGF-β/SMAD, JAK/STAT y Notch. MSI2, al unirse y estabilizar los transcritos pro-tumorales e inhibir los supresores tumorales, impulsa la proliferación celular, transición epitelio-mesénquimo, invasividad y reconfiguración metabólica hacia la glicolisis y síntesis de lípidos. Estos cambios favorecen un entorno propicio para la evasión inmunitaria y la resistencia a diversas terapias, como la quimioterapia, como gemcitabina, la radioterapia y las terapias dirigidas (ej. inhibidores del EGFR). Además, mejora las propiedades de las células madre cancerosas y potencia la proliferación y la pluripotencia en varios tumores malignos. En general, estas pruebas subrayan el valor de MSI2 como biomarcador pronóstico y como nueva diana terapéutica. La inhibición de la actividad de MSI2, a través de la unión de microARNs o de enfoques de knockdown, ha demostrado ser prometedora en la reducción de la progresión tumoral y en la mejora de la resistencia a los fármacos en modelos preclínicos. Aunque la heterogeneidad de los estudios y la falta de ensayos clínicos a gran escala siguen limitando las conclusiones definitivas, estos resultados resaltan la importancia de dilucidar las funciones de MSI2 en diferentes tipos de tumores. Se recomienda llevar a cabo futuras investigaciones centradas en terapias dirigidas a MSI2 y en el desarrollo de biomarcadores integradores para perfeccionar las estrategias personalizadas de tratamiento del cáncer.

***Palabras clave*:** Musashi-2, tumores sólidos, proteína de unión a ARN, señalización oncogénica, resistencia a terapias, biomarcador, rutas metabólicas del cáncer.

Abstract: Musashi-2 (MSI2) is an RNA-binding protein widely implicated in oncogenic processes, but its role in solid tumors remains incompletely defined. In this systematic review, articles published between 2014 and 2025 were identified through comprehensive searches of PubMed, Embase, Scielo, and Lilacs according to PRISMA guidelines. Eligibility criteria included studies investigating MSI2 expression and function in glioblastoma, thyroid, lung, breast, gastrointestinal, genitourinary, and gynecological cancers. After removal of duplicates and screening by title, abstract and full text, 97 articles were included for quantitative and qualitative synthesis. The results consistently show that MSI2 overexpression correlates with poor prognosis, advanced tumor stage and resistance to therapy. In the molecular level, MSI2 exerts its oncogenic influence through post-transcriptional regulation of cancer-associated signaling pathways, including PI3K/Akt/mTOR, Wnt/β-catenin, TGF-β/SMAD, JAK/STAT, and Notch. By binding and stabilizing pro-tumor transcripts while inhibiting tumor suppressors, MSI2 drives cellular proliferation, epithelial-to-mesenchymal transition, invasiveness, and metabolic rewiring toward glycolysis and lipid synthesis. These changes promote an environment conducive to immune evasion and resistance to various therapies, including chemotherapy (e.g., gemcitabine), radiation therapy, and targeted therapies (e.g., EGFR inhibitors). It promotes cancer stem-like properties and enhances self-renewal and pluripotency in several malignancies. Altogether, this evidence underscores the value of MSI2 as both a prognostic biomarker and an emerging therapeutic target. Inhibition of MSI2 activity, via microRNAs binding or knockdown approaches, has shown promise in reducing tumor progression and overcoming drug resistance in pre-clinical models. While the heterogeneity of the studies and the lack of large-scale clinical trials still limit definitive conclusions, these findings highlight the importance of elucidating MSI2 functions in different tumor types. Future research focusing on MSI2-targeted therapies and integrative biomarker development is warranted to refine personalized cancer treatment strategies.
***Keywords*:** Musashi-2, solid tumors, RNA-binding protein, oncogenic signaling, therapy resistance, prognostic biomarker, oncogenic pathways.

1. Introduction

MSI2 AND SOLID TUMORS

Cancer is a disease of worldwide interest since the 1950s and has been defined as a set of nearly 100 heterogeneous diseases that affect the cell genomics. It is caused by a series of mutations which, after accumulating at the molecular level, systematically affect the host (DeVita et al., 2015). Alterations in human genetics and/or epigenetics make cancer a multifactorial disease, and result in abnormal growth of carcinogenic cells, along with the likelihood of migration to multiple tissues or organs of the body (Saini et al., 2020).

Nowadays, about 161 types of cancer have been described, classified according to the type of tissue, organ, and/or differentiated cell in which it is developing. The prevalence of cancer as of 2024, by the NIH is: bladder cancer, breast cancer, colorectal cancer, kidney cancer (renal cells), lung cancer, lymphoma, pancreatic cancer, prostate cancer, skin cancer, and endometrial cancer (NIH, 2024). Due to their aggressiveness, colorectal, lung, and breast cancer rank in the top three global mortality rates (GLOBOCAN, 2022).

RNA-binding proteins are known to be evolutionarily conserved and involved in a multitude of processes associated with transcribed RNA, including stabilization, splicing, transport, and degradation (H. Li et al., 2022). MSI2, a member of the RNA-binding protein (RNA-BP) family, exerts direct influence on proliferation, self-renewal, and pluripotency of pluripotent hematopoietic cells during embryogenesis (Yeh et al., 2023). MSI2 is an RNA-binding protein that plays a role in several cancer pathways, functioning as an activator of hallmarks of cancer, i.e., metastasis, invasion, cell proliferation, and immune evasion. A series of studies have defined a comprehensive compendium of the signaling pathways in which MSI2 is involved. The main signaling pathways affected by MSI2 include Numb/Notch, PTEN/Akt/mTOR, TGF-ß/SMAD, JAK/STAT, and KRAS. Its interaction with various proteins, mRNA, and microRNAs establishes MSI2 as a deregulator of homeostatic biological processes (L. Jiang et al., 2022).

The presence of carcinogenic and cancerous cells, along with increased levels of MSI2 in solid tumors, has been associated with some hallmarks of cancer. These hallmarks include sustaining proliferative signaling, deregulating cellular metabolism, and activating invasion and metastasis. They are also associated with poor prognosis and clinicopathological characteristics in patients diagnosed with solid tumors presented in Figure 1 (W. Wu et al., 2022). Also, the principal alterations in cellular metabolism resulting from elevated MSI2 levels during the development of solid tumors encompass increased cell proliferation, promotion of invasion and metastasis, enhanced epithelial-mesenchymal transition (EMT), and drug resistance. Solid cancers, such as glioblastoma, thyroid cancer, non-small cell lung cancer (NSCLC), breast cancer, esophageal cancer, gastric cancer, pancreatic cancer, liver cancer, colorectal cancer, prostate cancer, bladder cancer, cervical cancer, endometriosis, and ovarian cancer, tend to develop MSI2-mediated tumors (Figure 1).

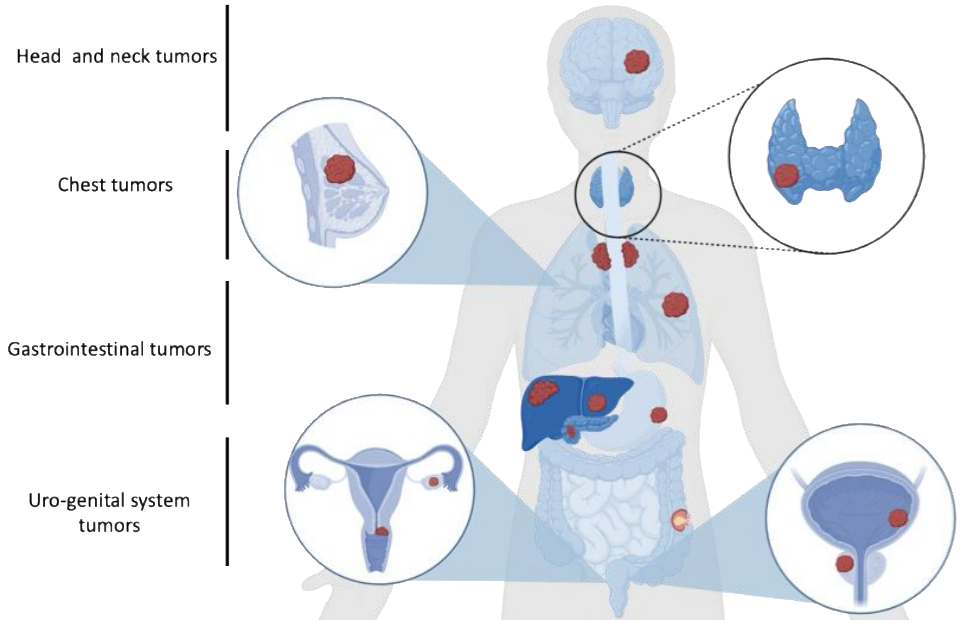


Figure 1. Solid tumors in which MSI2 RNA-binding protein has been reported to be altered. Head and neck tumors: Glioblastoma and thyroid cancer. Chest tumors: Non-small cell lung cancer (NSCLC), breast cancer. Gastrointestinal tumors: Esophageal cancer, gastric cancer, pancreatic cancer, liver cancer, and colorectal cancer. Urinary and genital system: Prostatic cancer, bladder cancer, cervical cancer, and ovarian cancer. Created with: Biorender.com

MSI2 quantification, therefore, emerges as a significant prognostic factor for cancer patients, given the established correlation between elevated MSI2 levels and a worse overall survival prognosis in patients with solid tumors. Consequently, MSI2 has emerged as a molecular marker for predicting patient survival, attributable to its interactions with multiple signaling pathways implicated in the development of solid tumors (Y. Yang et al., 2022). However, the way it works in solid tumors is still being studied. For these reasons, a scoping review was conducted to systematically map the research done in this area, as well as to identify any existing gaps in knowledge. This has led to the following research question: **What is the current literature's description of the role of MSI2 in solid tumors and pathways related to cancer hallmarks**?

2. Methods

PROTOCOL REGISTRATION

The current scoping review does not require the protocol to be registered a priori on platforms such as Prospero.

ELIGIBILITY CRITERIA

The protocol was developed using the Preferred Reporting Items for Scoping reviews (PRISMA-ScR) (Tricco et al., 2018). Journal articles written in English and published between 2014 and 2025 were included in this review.

INFORMATION SOURCES

To find relevant bibliography regarding MSI2 and solid tumors, PubMed, Embase, Scielo and Lilacs were used as databases for the research. All the papers were selected and cited in the RIS format so they could be uploaded to Rayyan.ai for screening. The screening of the papers was developed in three categories: accepted, maybe and excluded. For excluded papers, the reviewers set an argument based on the reason of rejecting the article (e.g. background, foreign language, publication type) (See Figure 2). The most recent search was performed on 09/07/2025.

SEARCH STRATEGY

The following query strategy was prepared by the investigators to retrieve documents from PubMed: ((msi2[TW] OR "musashi 2"[TW]) AND ("solid tumors"[TW] OR "solid tumours"[TW] OR "glioblastoma"[TW] OR "pancreatic cancer"[TW] OR "esophageal cancer"[TW] OR "breast cancer"[TW] OR "NSCLC"[TW] OR "non-small cell lung cancer"[TW] OR "colorectal cancer"[TW] OR "gastric cancer"[TW] OR "bladder cancer"[TW] OR "thyroid cancer"[TW] OR "liver cancer"[TW] OR “hepatocellular cancer”[TW] OR "cervical cancer"[TW] OR "ovarian cancer"[TW] OR "prostate cancer"[TW]). On the other hand, the query structured for Embase search was: ('msi2 protein human'/exp OR 'msi2 protein human' OR 'msi2') AND (2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py OR 2022:py OR 2023:py OR 2024: py) AND ('glioblastoma' OR 'pancreatic cancer' OR 'esophageal cancer' OR 'breast cancer' OR 'nsclc' OR 'non-small cell lung cancer' OR 'colorectal cancer' OR 'gastric cancer' OR 'bladder cancer' OR 'thyroid cancer' OR 'liver cancer' OR 'hepatocellular cancer' OR 'cervical cancer' OR 'ovarian cancer' OR 'prostate cancer'). The search strategy for Scielo and Lilacs was the research of the terms "msi2" and "Musashi 2".

SELECTION OF SOURCES OF EVIDENCE

For the screening and selection process, 2 reviewers independently performed a blind peer-review using Rayyan.ai, based on the titles and abstracts of each article. The criteria of acceptance were based on the relevance of the information regarding the pathways of solid tumors and the regulation of Msi2 on them. Second, a full-text blind review was executed to increase the significance of the selection criteria of the journal articles chosen. The reviews obtained from the query were removed from the screening process. However, they were cited alongside the indexed abstracts in the discussion section.

DATA CHARTING

Two reviewers independently charted the data, screened the results, and continuously updated the data-charting form in an iterative process to determine which variables to extract.

DATA ITEMS

We abstracted data on article characteristics (e.g., journal article title, year published, DOI, study type, solid tumor type, altered pathway, MSI2 status, effect type.)

SYNTHESIS OF RESULTS

We grouped the studies by the types of solid tumors presented, and summarized the pathway, populations, and study designs for each group, along with the MSI2 status reported and broad findings. The pathways and alterations that are associated with the RNA-binding protein MSI2 have been linked to the MSigDB human collections "H", within the context of the cancer hallmarks gene sets (Mootha et al., 2003; Subramanian et al., 2005). Items that did not fall into the hallmarks were assigned to independent groups. The researchers named these groups.

3. Results and discussion

Upon conducting a query of the databases, a total of 86 articles were retrieved from PubMed, while Embase returned 116 publications. According to the research, the number of articles found in Scielo and Lilacs were 0 and 13, respectively. The journal articles were exclusively focused on MSI2 action in solid tumors. A total of 132 articles were selected for further evaluation through abstract and title screening, after the removal of duplicates (see Figure 2). Following the removal of 28 articles through the screening of abstract and title, a full-text screening was conducted, resulting in the identification of 71 papers to be included in the review (See Figure 2). The exclusion criteria are detailed on the flow diagram in Figure 2. The variable operationalization chart is summarized in the Supplementary Table 1.

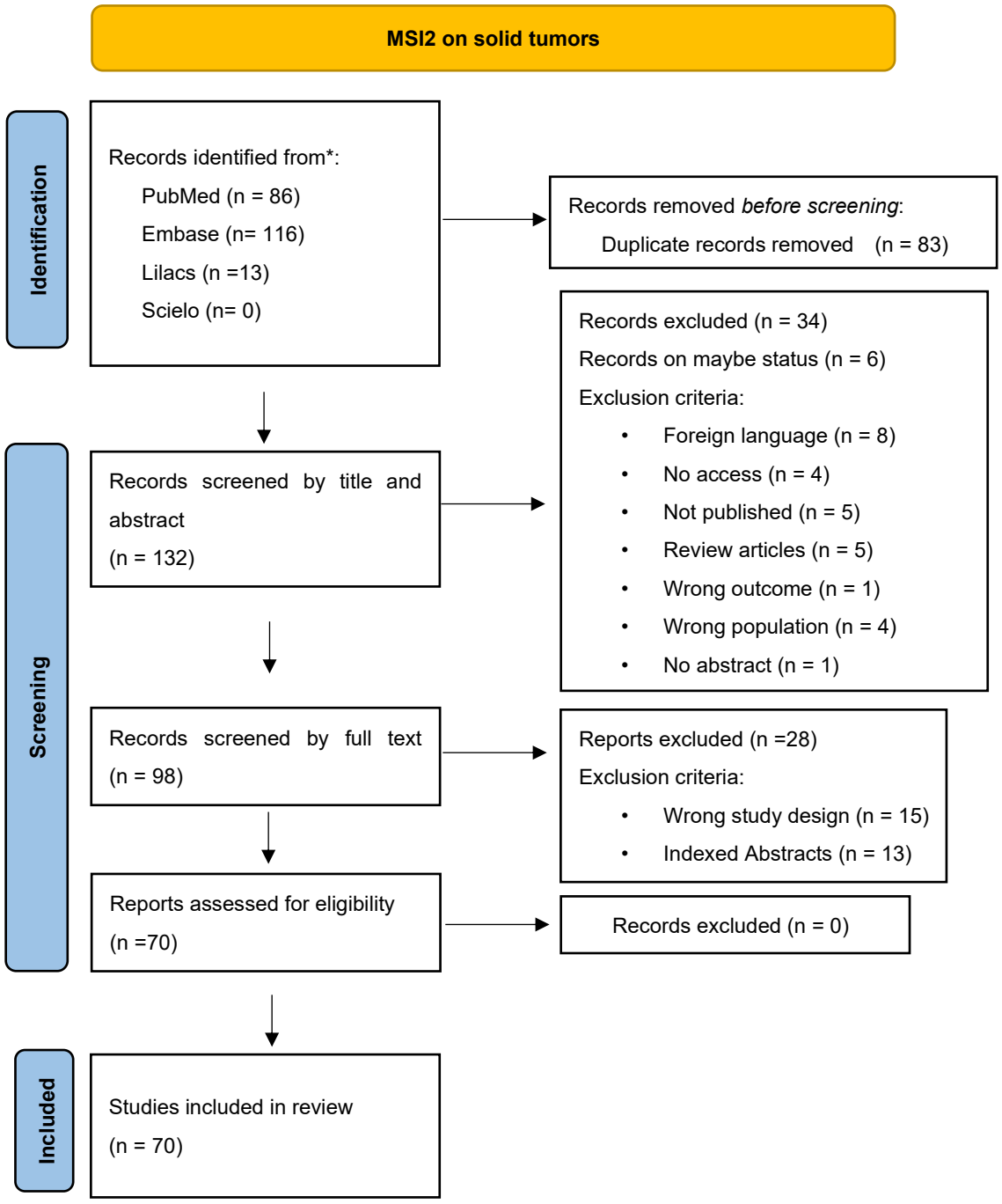


Figure 2. Flow diagram illustrating the selection process of studies evaluating the status of MSI2 and solid tumors. This diagram follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and outlines the inclusion and exclusion criteria applied during the study selection process for this scoping review.

The 70 papers included in this review were classified into five categories: bone tumors, head and neck tumors, chest tumors, gastrointestinal tumors, and tumors affecting the urinary and genital system. Accordingly, three articles on glioblastoma and two on thyroid cancer were added to the "Head and Neck Tumors" category. Moreover, the "Chest Tumors" category embraced twelve articles on non-small cell lung cancer (NSCLC) and eight articles on breast cancer. In the "Gastrointestinal Tumor" group, four articles focused on gastric cancer, ten on colorectal cancer, eleven on pancreatic cancer, five on liver cancer, and two on esophageal cancer were assigned to the gastrointestinal category. Next, the "Urinary and Genital System" category was addressed by tailoring one article on prostatic cancer, three on cervical cancer, four on bladder cancer, and four on ovarian cancer. Finally, into the "Bone Tumors" category, we added one article for the Ewing's Sarcoma group. In this review, we found that the most frequently studied solid tumors were non-small cell lung cancer (NSCLC, 17.1 %), pancreatic cancer (15.7%), colorectal cancer (14.3%), and breast cancer (11.4%) (Figure 3).

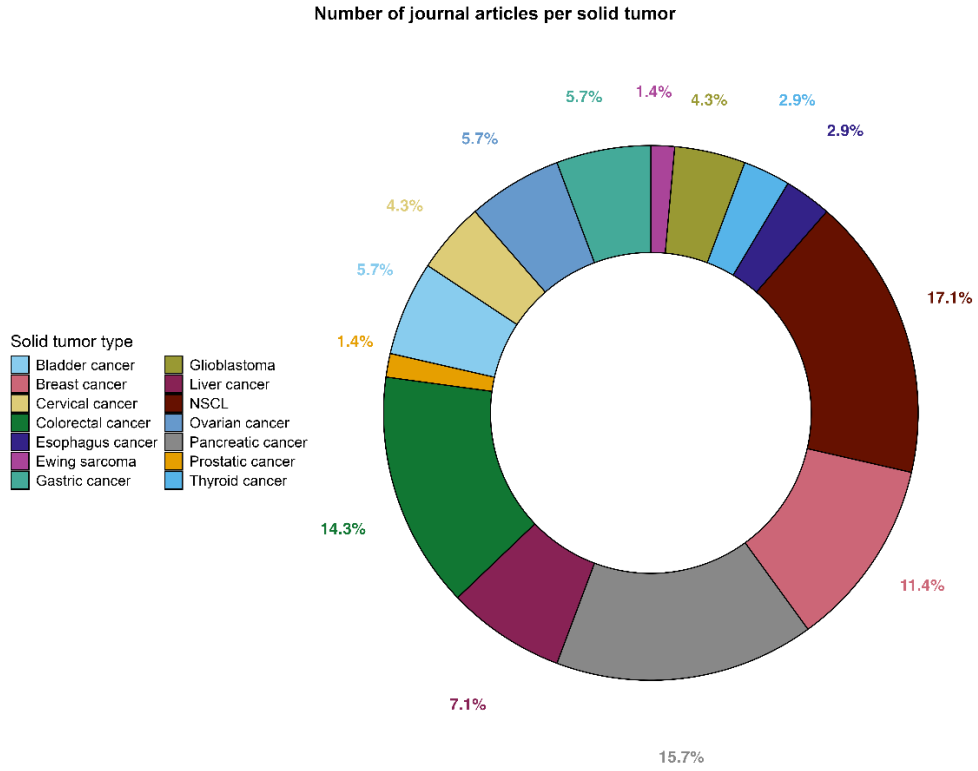


Figure 3. Distribution of the selected studies based on the type of solid tumors addressed.

To explore the different experimental models used and exhibit the influence of MSI2 in solid tumor pathways, we identified the experimental models in each study. Our research revealed that the in vitro model was the most frequently utilized, followed by the *in vivo* and *in silico* models. Additionally, certain solid tumors were not investigated using all three experimental models. Precisely, Ewing's sarcoma and thyroid cancer were studied using *in vitro* approaches, while cervical and ovarian cancers lacked model-based investigations. The results are summarized in Figure 4 and Supplementary Table 2.

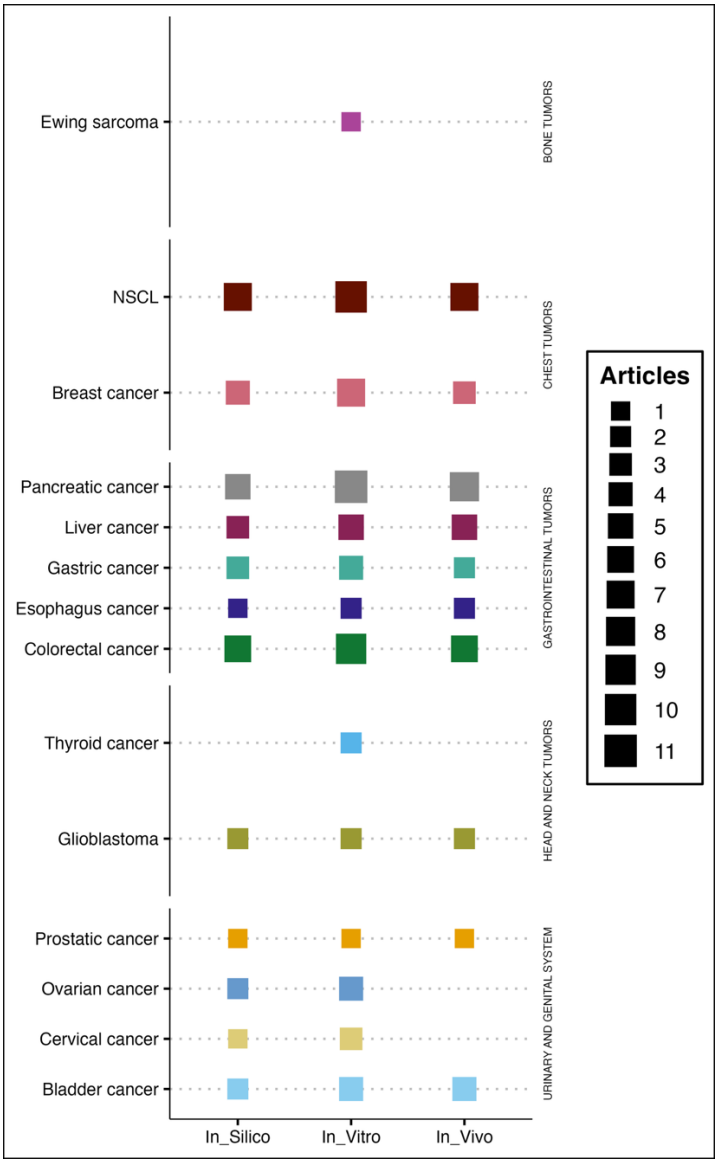


Figure 4. Experimental model counting of the papers included in the scoping review after the full-text screening. On the "*x*" axis are placed the different experimental models (*in vitro*, *in vivo,* and/or *in silico*), while on the "*Y*" axis are the solid tumor types. The size of the square represents the number of experiments developed ineach tumor type.

We found 30 biological processes that are connected to the hallmark gene sets defined in the MSigDB datasets. In addition, we assigned five independent biological processes that weren't included in the MSigDB hallmarks: m6A methylation, the LIN28/LET7 axis, the Hippo signaling pathway, the spliceosome and nucleocytoplasmic transport, and long non-coding RNAs and microRNAs. Among the MSigDB hallmarks, those most frequently altered by MSI2 were HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION, HALLMARK_PI3K_AKT_MTOR_SIGNALING, HALLMARK_IL6_JAK_STAT3_SIGNALING, HALLMARK_KRAS_SIGNALING_UP, HALLMARK_WNT_BETA_CATENIN_SIGNALING, HALLMARK_NOTCH_SIGNALING, HALLMARK_P53_PATHWAY, HALLMARK_ANGIOGENESIS,

HALLMARK_APOPTOSIS, HALLMARK_HYPOXIA, and HALLMARK_TNFA_SIGNALING_VIA_NFKB. (Figure 5; Supplementary Table 3).

To elucidate the diverse roles of MSI2 in tumorigenesis, we categorized its pathway alterations across five major tumor types (Bone, Head and Neck, Chest, Gastrointestinal, and Genitourinary), providing a framework to assess its influence within distinct oncogenic contexts.

HEAD AND NECK TUMORS

Glioblastoma

Upon reviewing the publications reporting MSI2-driven glioblastoma progression, 3 pathways were discussed: m6A methylation, MSI2/SNORD12B/FIP1L1/ZBTB4 and TGF-β/SMAD3 . The findings from each study are described below.

MSI2 is consistently overexpressed in glioblastoma tissues compared to normal brain tissue, where it contributes to tumor aggressiveness by modulating post-transcriptional and metabolic regulatory pathways (X. Deng et al., 2023). These findings are in line with studies reporting that the alterations over m6A effectors impact the stability and translation of transcripts linked to tumor growth, stemness, and therapy resistance (Dixit et al., 2020; P. Li et al., 2022; G. Xie & Richard, 2024; Yuan et al., 2022; Zepecki et al., 2020). MSI2 influences mRNA stability, splicing, and translation of oncogenic transcripts through indirect regulation of m6A RNA methylation. Its suppression disrupts this regulatory axis, leading to the destabilization of m6A-modified oncogenic mRNAs and inhibition of signaling pathways associated with glioblastoma growth (X. Deng et al., 2023). m6A dysregulation by YTHDF2 upregulates oncogenes such as MYC and VEGFA and contributes to shaping an immunosuppressive tumor microenvironment (Benavides-Serrato et al., 2023; Dixit et al., 2020; P. Li et al., 2022; Radhi et al., 2023; G. Xie & Richard, 2024; Yuan et al., 2022; Zepecki et al., 2020).

In parallel, MSI2 has been shown to facilitate metabolic reprogramming by enhancing glycolysis and lipid biosynthesis (W. Dong et al., 2021). MSI2 binds to SNORD12B, stabilizing it and promoting its accumulation without altering its transcription. This interaction drives the alternative polyadenylation of ZBTB4, reducing in reduced expression through increased usage of its distal polyadenylation site. The downregulation of ZBTB4 facilitates the upregulation of glycolytic and lipogenic enzymes, including HK2 and ACLY, supporting glioblastoma cell proliferation (W. Dong et al., 2021). Glioblastoma cells are known to upregulate glycolytic enzymes such as HK2, PKM2, LDHA, and ENO1, consistent with a pronounced Warburg effect (Kathagen-Buhmann et al., 2015; Koukourakis et al., 2017; X. Liang et al., 2022; Sanzey et al., 2015; Stanke et al., 2021; Udawant et al., 2021). This shift away from oxidative phosphorylation promotes rapid proliferation and contributes to resistance against therapies like temozolomide and radiotherapy (Koukourakis et al., 2017; X. Liang et al., 2022; Shukla et al., 2018; Stanke et al., 2021; Trejo-Solís et al., 2023). Moreover, glioblastoma stem cells further adapt by increasing polyunsaturated fatty acid synthesis and reducing neutral lipid storage, supporting self-renewal and survival (Shakya et al., 2019). Conversely, MSI2 knockdown reduces SNORD12B expression and half-life, diminishing its competitive binding to FIP1L1 and reducing repression of ZBTB4. This restores ZBTB4 tumor-suppressive activity,

leading to direct transcriptional repression of HK2, ACLY, and MSI2 itself, ultimately impeding glioblastoma metabolism and proliferation (W. Dong et al., 2021). Members of the POZ and Krüppel family have been associated with poor prognosis, increased aneuploidy, EMT, and metastasis when downregulated (L. Chen et al., 2020; Jeong et al., 2023; Roussel-Gervais et al., 2017). Although these findings are consistent with the MSI2/SNORD12B/FIP1L1/ZBTB4 regulatory loop, no additional studies have addressed the dysregulation of the regulatory loop between ZBTB4, FIP1L1, or SNORD12B in glioblastoma.

It is also described that MSI2 is involved in oncogenic signaling through a positive feedback loop with TGF-β receptor 1 (TGFβR1), (Constam et al., 1992; Golestaneh & Mishra, 2005; Peñuelas et al., 2009) and phosphorylated SMAD3 (Z. Zhang et al., 2014), which promotes the expression of epithelial–mesenchymal transition (EMT) transcription factors such as Snail1 and Snail2, as shown in figure 6 (L. Fan et al., 2019; X. Jiang et al., 2019; Qiu et al., 2021; X. Xu et al., 2023). MSI2 modulates EMT marker expression by upregulating vimentin and downregulating E-cadherin, while its depletion induces a shift toward an epithelial-like phenotype. Moreover, MSI2 contributes to chemoresistance by maintaining O6-methylguanine-DNA methyltransferase (MGMT) expression (X. Jiang et al., 2019), which has been described as a marker of resistance to temozolomide (TMZ), and its downregulation sensitizes glioblastoma cells to TMZ treatment (Binabaj et al., 2018; Brandner, McAleenan, Kelly, Spiga, Cheng, Dawson, Schmidt, Faulkner, Christopher, et al., 2021; Brandner, McAleenan, Kelly, Spiga, Cheng, Dawson, Schmidt, Faulkner, Wragg, et al., 2021; Butler et al., 2020; Hao et al., 2024; Kristensen et al., 2016; Mansouri et al., 2018; Rivera et al., 2010). These findings were supported by integrated *in vitro, in vivo*, and *in silico* analyses with glioblastoma cell lines (e.g., LN-18, H4), xenograft models, clinical tumor samples, and public datasets such as The Cancer Genome Atlas (TCGA). In medulloblastoma, MSI2 has been found as a SOX2-associated protein (Sheng et al., 2016).

Thyroid cancer

In thyroid cancer, MSI2 expression has been reported to be modulated by Hsa-miR143-3p, which binds to the 3'UTR of MSI2 mRNA, resulting in reduced MSI2 levels. This causes cell cycle arrest, decreased cell proliferation, and increased apoptosis, as indicated by altered expression of BAX, caspase-3, and BCL-2. The same study described EMT inhibition and downregulation of MMP-2 and MMP-9, following miR-143-3p treatment, suggesting an influence on tumor invasiveness (Z. L. Wang et al., 2020). However, these findings were later called into question following the article's retraction (Z.-L. Wang et al., 2022). The metalloproteinases 9 and 2 are involved in the EMT, cell migration, and invasion ability regulation (e.g., the increase of invasiveness and migration capacity of papillary thyroid cancer cells mediated by the lncRNA AGAP2-AS1 influence over MMP2) (Z. Li et al., 2023; Shao et al., 2020).

According to current evidence, Hsa-miR143-3p may exert a biological role in papillary thyroid carcinoma (PTC) by targeting HMGA2, leading to reduced cell proliferation and supporting its potential as a therapeutic candidate (Ding et al., 2022). Its activity is associated with increased expression of pro-apoptotic markers such as BAX and caspase-3. Furthermore, the downregulation of the anti-apoptotic protein BCL-2 in PTC cells was shown to sensitize them to apoptotic signaling (S. Huang et al., 2023; X. Li et al., 2019, 2020; G. Zhou & Wang, 2023).

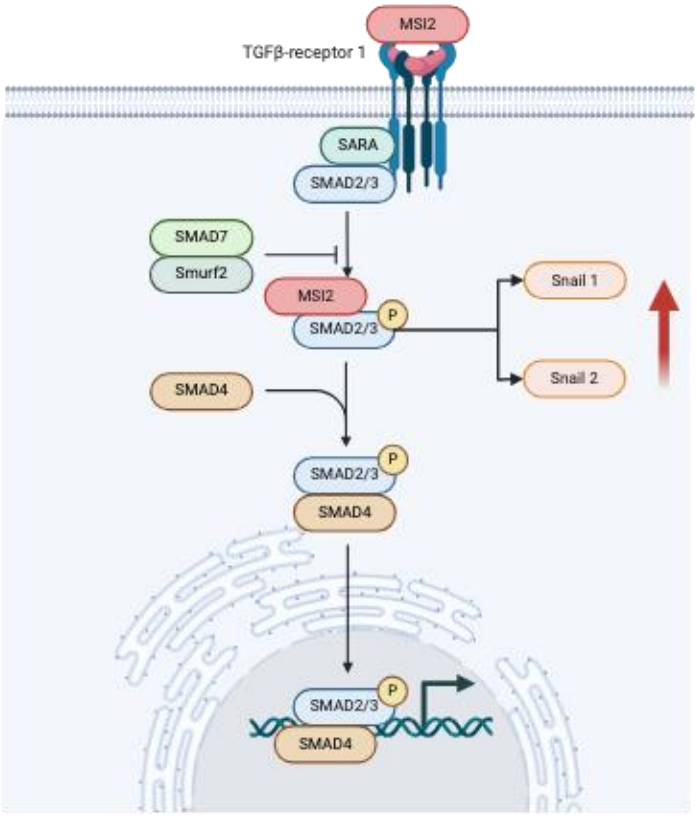


Figure 5. TGF-β/SMAD3 pathway regulated by MSI2 overepression. Created on BioRender.com

CHEST TUMORS

Non-Small Cell Lung Cancer and lung tumors

Among the 12 studies examining MSI2 expression, the JAK2/STAT3 and TGF-β/SMAD3 signaling pathways were consistently identified as key targets of dysregulation. Both pathways are well-established mediators of tumorigenesis in humans, driving EMT, metastasis, tumor growth, angiogenesis, cell survival, and therapy resistance (Sloan et al., 2023; H. Yang et al., 2015).

MSI2 binds to the 3′UTRs of TGFβR1 and SMAD3 mRNAs, enhancing their stability and translation (See Figure 7). This activity sustains TGF-β signaling, which is closely associated with the induction of EMT, increased cell invasion, and metastatic potential. It has also been described that a decrease in human epithelial markers, such as Claudins (Figure 7), and an increase in human EMT-inducing transcription factors, including SNAIL, SLUG, and ZEB1/2, have been reported (Kudinov et al., 2016, 2017; Kumar et al., 2013; Makhov et al., 2021). MSI2 also interferes with SMAD2/3-dependent transcription, indirectly supporting the suppression of epithelial gene expression (Topchu et al., 2021).

MSI2 activates inflammatory pathways, particularly NF-κB signaling, with IL-6 secretion by cancer-associated fibroblasts (Samart et al., 2023) and supporting the mesenchymal phenotype, reinforcing these changes (Kumar et al., 2013; Szymura et al., 2019).

In NSCLC, impaired TGF-β signaling is linked to metastasis and recurrence (Korkut et al., 2018; Levy & Hill, 2006). Even with upstream disruptions, elevated SMAD2/3 stimulates EMT by inducing N-cadherin expression (H. Yang et al., 2015). MSI2 enhances this process by stabilizing TGFBR1 and SMAD3 transcripts, thereby sustaining EMT signaling. This is further potentiated by cytoskeletal remodeling proteins such as Vimentin and MYH15 further contribute to increased stiffness and invasiveness (T. Chen et al., 2019; Kucuksayan et al., 2018; H. Yang et al., 2015). Additionally, loss of epithelial markers, including Claudin-7, which is reduced in about two-thirds of NSCLC tumors, has been associated with poorer outcomes (Yamamoto et al., 2010). At the transcriptional level, MSI2 activity is modulated by tumor suppressor factors. For example, KLF4 inhibits MSI2 by binding to its promoter region, which in turn downregulates the JAK2/STAT3 pathway (Figure 7) (D. Di Luo & Zhao, 2022). This downregulation is especially relevant given that JAK2 amplification and a higher STAT3 signaling have been associated with immune evasion through increased PD-L1 expression, as well as the maintenance of cancer stem-like traits via IFN/JAK/STAT1 signaling (Y. Han et al., 2022; Ikeda et al., 2016; M. Li et al., 2018; H. Pan et al., 2021; D.-Y. Zhu et al., 2019). MSI2 is also known to directly bind to the 3′UTRs of key receptor tyrosine kinase (RTK) mRNAs, including EGFR and VEGFR2, promoting their stabilization and translation.
Increased MSI2 expression is also related to elevated EGFR protein levels, especially phosphorylation of tyrosine 1068 (Makhov et al., 2021). This also alters ERBB family signaling dynamics by reducing ERBB3 expression, thereby supporting sustained oncogenic signaling (Bychkov et al., 2023; Makhov et al., 2021). RTKs are frequently overexpressed in NSCLC and are associated with poor clinical outcomes. An evaluation of 56 RTKs displayed that 33 were expressed in at least 25% of early-stage tumors, with EGFR, ERBB2, ERBB3, and the insulin receptor notably elevated in tumors that later metastasized (Q. Chen et al., 2024; Müller-Tidow et al., 2005; Xiao & Schmid, 2020). EGFR itself is commonly altered through activating mutations or gene amplification, promoting tumor growth and resistance to tyrosine kinase inhibitors (TKIs). Such mutations occur in 15–55% of NSCLC cases, with higher prevalence in Asian populations (up to 40%) compared to non-Asian populations (about 20%) (Bironzo et al., 2021; R.-F. Dong et al., 2021; Gelatti et al., 2019; Harrison et al., 2020; Hsu et al., 2019; Knebel et al., 2017). Similarly, VEGFR2, expressed in 20–34% of tumors, has been associated with aggressive clinical behavior and poor survival outcomes, particularly in patients receiving immunotherapy (Kaira et al., 2022; Volz et al., 2020; Watanabe et al., 2021).

These alterations can influence downstream pathways such as RAS/RAF/MEK/ERK and PI3K/AKT/mTOR, which promote tumor growth, treatment resistance, and immune evasion. It has been described that KRAS and BRAF mutations activate the RAS/RAF/MEK/ERK cascade (Figure 7), supporting proliferation and reducing sensitivity to MEK inhibitors through feedback regulation (Brant et al., 2016; J. Han et al., 2021; Nguyen-Ngoc et al., 2015; Ullah et al., 2021; Yaeger & Corcoran, 2019). Within this regulatory cascade, MSI2 has been shown to suppress PTEN expression by binding to its mRNA, resulting in increased AKT activity and phosphorylation of downstream targets such as GSK3α/β. Alterations in the PI3K/AKT/mTOR axis, such as mutations in PIK3CA

(9.5%), PTEN (5.5%), and AKT1 (0.9%) appear in 14.9% of EGFR TKI–resistant NSCLC tumors (Beck et al., 2014; W. Fang et al., 2020; Fumarola et al., 2014; Heavey et al., 2014; Yip, 2015). It has also been described that MSI2 contributes to cancer stemness by binding to the 3′UTR of Nanog mRNA, increasing its expression, and indirectly upregulating SOX2 and ALDH activity (Yiming et al., 2021). Nanog protein is frequently upregulated in drug-resistant cells, enhancing self-renewal and tumorigenicity. In combination, co-expression with Oct4 protein activates Wnt/β-catenin signaling, facilitating EMT and promoting invasive behavior (L. Liu et al., 2020). Alongside with its promotion of stem-like features, SOX2 and ALDH (e.g. ALDH1A1, ALDH1A3, and ALDH3A1) overexpression further contributes to therapy resistance by enhancing DNA repair and anti-apoptotic pathways (Choe et al., 2018; W. Gao et al., 2020; J. Kang et al., 2016; D. Li et al., 2023; Mirzaei et al., 2022; Patel et al., 2008; Rebollido-Ríos et al., 2020; Velcheti et al., 2013; S. Wang et al., 2023). These stem-like features are associated with resistance to EGFR tyrosine kinase inhibitors such as gefitinib and Osimertinib (Yiming et al., 2021).

Furthermore, MSI2 promotes the activation of the mTOR pathway. It enhances mTORC1 signaling, as evidenced by increased phosphorylation of S6K1, 4E-BP1, and S6 ribosomal protein, and supports mTORC2 activation, leading to enhanced AKT phosphorylation at Ser473 (M. Wang et al., 2020). Notably, mTOR activity may also increase without canonical genetic alterations, possibly through kinases such as PIM (Moore et al., 2021), which have a central role in cell migration, proliferation, apoptosis, and immunomodulation processes, and have been implicated in different types of hematological cancers (Bellon & Nicot, 2023).

From a therapeutic perspective, MSI2 silencing increases the effectiveness of EGFR-targeted therapies, including erlotinib, afatinib, and Osimertinib, in preclinical models (Yiming et al., 2021). Largazole, a compound that binds directly to the RRM1 domain of the MSI2 transcript, has been shown to reduce MSI2 mRNA and protein levels and suppress the activation of multiple oncogenic pathways, including mTORC1/2, JAK/STAT, TGF-β, and EMT signaling (M. Wang et al., 2020). (Y. Han et al., 2022; Ikeda et al., 2016; M. Li et al., 2018; H. Pan et al., 2021; D.-Y. Zhu et al., 2019)

Conversely, miR-598 negatively regulates MSI2 by directly binding to its mRNA, decreasing cell migration and invasion (J. Guo et al., 2021). Several microRNAs, including miR-33a, miR-16-5p, miR-1260b, miR-142-3p, miR-495-3p, and miR-101-3p, have been shown to directly target mRNAs encoding factors of the cell cycle, metabolism, apoptosis, and autophagy, such as METTL3, LDH-A, SOCS6, CDC25C, Sphk1, and ATG4(Arora et al., 2022a, 2022b; Cui et al., 2021; Du et al., 2017; J. Meng et al., 2024; Xia et al., 2019). Alongside, miR-520c-3p is involved in PI3K/AKT/mTOR signaling, while miR-221/222 modulate Notch1 signaling via Reck, influencing cancer stemness (Gulhane et al., 2022; Y. Guo et al., 2021).

MSI2 influences tumor metabolic adaptation and DNA repair. Knockdown of MSI2 in mouse models results in the downregulation of genes such as Gli1, Tubb3, and Ccr1, which are involved in survival, neural differentiation, and immune signaling, respectively. Additional mouse genes that rely on MSI2 activity include Ptgds (prostaglandin synthesis), Arl2bp (STAT3-associated nuclear binding), Rnf157 (an E3 ligase linked to cell survival), and

Syt11 (a vesicular trafficking protein), highlighting the broad pro-tumorigenic influence of MSI2 (Barber et al., 2025). In humans, this activity has been widely described as MSI2 depletion, which is linked to reduced hallmarks expression contributing to anti-tumorigenic configurations in NSCLC cells (Bychkov et al., 2022; Kudinov et al., 2016).

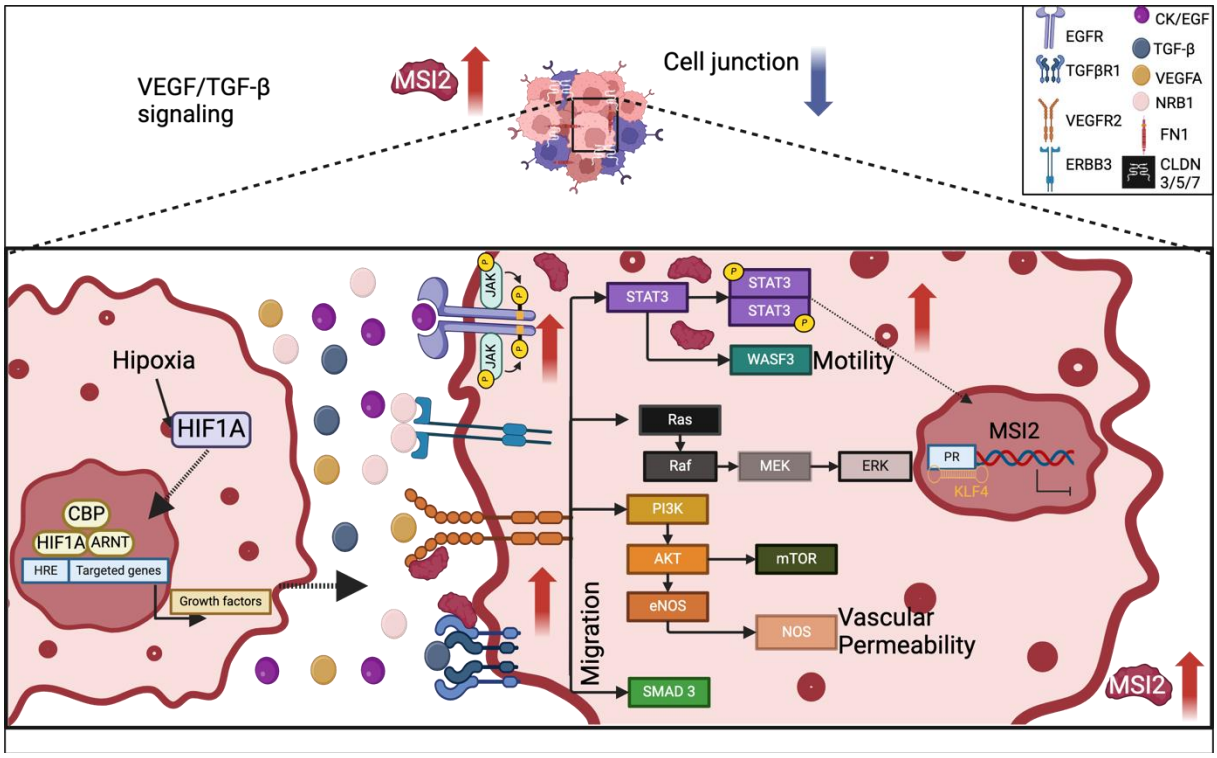


Figure 6. MSI2 regualtion of RTKs, tight junction, and inactievation of MSI2 mediated by KLF4. Created on BioRender.com

Breast cancer

Among the eight reviewed articles on breast cancer, triple-negative breast cancer (TNBC) was the subtype most consistently affected by MSI2, with alterations reported in four studies. In TNBC, MSI2 was primarily associated with dysregulation of the PI3K/AKT/mTOR and epithelial–mesenchymal transition (EMT) signaling pathways.

Copy number gains of MSI2 were identified in the cell-free DNA (cfDNA) of breast cancer patients but were absent in individuals with false-positive screening results, indicating a tumor-specific amplification detectable prior to biopsy (Barbirou et al., 2022a). This finding supports MSI2's potential as a noninvasive biomarker, particularly for early detection in patients with dense breast tissue. Similarly, cfDNA profiles differ markedly between breast cancer patients and healthy individuals; patients exhibit elevated cfDNA levels enriched with tumor-associated features such as mutations and amplifications in TP53, PIK3CA, ESR1, and ERBB2, as well as copy number alterations that reflect tumor heterogeneity(Ambriz-Barrera et al., 2024; Barbirou et al., 2022b; J. Fan et al., 2023; Herzog et al., 2022; Khurram et al., 2023; Moss et al., 2020; Page et al., 2017; Stover et al., 2018) These alterations, absent in healthy controls, provide relevant information for diagnosis, disease monitoring, and treatment response

evaluation. Additionally, breast-specific DNA methylation signatures found exclusively in patient-derived cfDNA enable sensitive detection of localized disease and support longitudinal therapeutic assessment.

Beyond its biomarker role, MSI2 influences oncogenesis through post-transcriptional and signaling mechanisms. By binding to p21 mRNA, MSI2 reduces its translation, facilitating cell cycle progression (Y. M. Choi et al., 2016). Consistent with this, breast cancer patients exhibit significantly higher p21 promoter methylation compared to healthy controls, correlating with a reduction of p21 mRNA expression by up to 79%, suggesting epigenetic silencing contributes to p21 downregulation in tumor cells (Askari et al., 2013). MSI2 also contributes to apoptotic resistance by downregulating BAX and upregulating BCL-2, while also enhancing ERK signaling and p38 MAPK phosphorylation. It promotes EMT, as indicated by increased cell migration and invasion, and directly binds to vimentin to stabilize its expression (Y. M. Choi et al., 2016). Inhibition of ERK signaling in breast cancer models, including TNBC, has been associated with reduced proliferation, induction of apoptosis, cell cycle arrest, and increased cellular senescence (Amin et al., 2023; Bhagwat et al., 2019; Bhatt et al., 2021; Q. He et al., 2019). This suppression also decreases BCL-2 expression and increases BAX levels, thereby sensitizing cells to apoptosis (G. Hu et al., 2019; Xing et al., 2021). Moreover, phosphorylated p38 MAPK is primarily activated by cancer-associated fibroblasts (CAFs), which activate EMT markers and promote tumor cells' invasion and metastasis (Wen et al., 2019). While MSI2 has been shown to promote p38 MAPK phosphorylation, the specific molecular mechanisms by which it interacts with CAF-mediated signaling remain to be clarified.

MSI2 supports pro-survival signaling in breast cancer by activating the PI3K/AKT pathway (Figure 7), supported by increased phospho-AKT and reduced PTEN activity. This leads to elevated MMP-9 expression and enhanced nuclear translocation of NFκB, promoting tumor progression (Jadhao et al., 2025). PI3K/AKT/mTOR signaling directly regulates MMP9-driven mechanisms of proliferation and apoptosis in breast cancer cells (W. Liang et al., 2021), and its dysregulation is frequently associated with NFκB activation, therapy resistance, and poor prognosis (Alves & Ditzel, 2023; C. Dong et al., 2021; Ellis & X., 2019; Ippen et al., 2019; Khan et al., 2019; Martorana et al., 2021; Miricescu et al., 2020; Verret et al., 2019; K. Zhu et al., 2022). High MSI2 expression has been shown to correlate with elevated levels of MYC, SOX2, and CD133 (Jadhao et al., 2025). These genes are associated with stemness, tumor progression, and therapeutic resistance, and their regulation involves feedback loops that can be modulated by targeting pathways such as Wnt/β-catenin, PTEN, and NF-κB (Brugnoli et al., 2019; Das et al., 2019; Golden et al., 2024; Liou, 2019; Y. Meng et al., 2020; W. Zheng et al., 2024). Jadhao et al. (2025) validated these findings in TNBC human cells, zebrafish, and mouse xenograft models.

MSI2 also promotes stemness and tumor progression in breast cancer through the activation of multiple signaling pathways. In MDA-MB-231 cells, MSI2 indirectly suppresses m-Numb, leading to the upregulation of Notch1/2 and Hes2, along with increased expression of stemness markers such as CD44 and GBX2 (Troschel et al., 2020). Notch1/2 upregulation has also been reported in human breast cancer samples, where it supports tumor growth, stem cell maintenance, metastasis, and therapy resistance. In aggressive subtypes like TNBC, downstream Notch effectors such as HES1 and HEY1 can repress tumor suppressors like PTEN (Chimento et al., 2022; Ilhan et al.,

2020; Katoh & Katoh, 2019; Krishna et al., 2019; Pappas et al., 2021; X. Sun et al., 2019; K. Yao et al., 2024). High CD44 expression, particularly in TNBC, is linked to increased migration, invasion, metastasis, therapy resistance, and poor prognosis, highlighting its role in cancer stem cell maintenance (Bai et al., 2020; L. Guo et al., 2022; Mesrati et al., 2021; A. Sethi et al., 2024; Vadhan et al., 2022; H. Xu et al., 2020; P. Zhang et al., 2020). Troschel et al. (2020) further demonstrated that MSI2 knockdown reduces GBX2 expression by 40%, confirming its regulatory role.

In the Wnt pathway of human TNBC, MSI2 overexpression leads to nuclear accumulation of β-catenin, which binds TCF/LEF transcription factors and drives transcription of Wnt target genes associated with proliferation and invasion. MSI2 further interacts with LIN28 to directly destabilize MST1/2 and LATS1/2 mRNAs, reducing Hippo signaling activity. This enables YAP1 stabilization and nuclear translocation, activating pro-tumorigenic genes such as CYR61 and CTGF, and enhancing stemness via OCT4, NANOG, and SOX2 expression. These changes are associated with the increased population of $CD44^{+}/CD24^{-}$/low cancer stem-like cells and increased sphere-forming capacity (H. Zou et al., 2022). Wnt pathway activation also induces overexpression of TCF/LEF family members, including LEF1 and TCF3, which are frequently upregulated in breast tumors and associated with immune cell infiltration and unfavorable clinical outcomes (Hashemi et al., 2023; H. Huang et al., 2024; Lima et al., 2023; Mahanujam, 2025; Niu et al., 2019; Y. Zou et al., 2020). Alongside these observations, several studies have reported a reduced expression of Hippo pathway components in breast cancer (such as MST1/2, LATS1/2, SAV1, MOB1, YAP, TAZ, and TEAD1) compared to adjacent normal tissues. This contributes to uncontrolled proliferation, metastasis, poor prognosis, and therapy resistance, particularly in endocrine-resistant and TNBC cases (Bhavnagari & Shah, 2025; J. Chen et al., 2021; Kyriazoglou et al., 2020; Parambil et al., 2024; Z. Wang et al., 2021, 2022; Yousefi et al., 2022).

Alternatively, the isoform MSI2a exerts a tumor-suppressive influence as shown in vitro cell lines, in vivo mouse xenografts, and ex vivo analysis of human TNBC tissues (M. Li et al., 2020). MSI2a binds to the 3'UTR of TP53INP1 mRNA, stabilizing the transcript and enhancing p53 phosphorylation through ATM, EP300, HIPK2, and DNA-PKcs regulation. This reduces ERK1/2 phosphorylation, inhibits cell proliferation and migration, and reverses EMT by downregulating mesenchymal markers (SLUG, N-cadherin, vimentin) and upregulating epithelial markers (E-cadherin, β-catenin, ZO-1). Loss of MSI2a, conversely, destabilizes TP53INP1 and activates ERK1/2 via the p73/DUSP10 pathway, enhancing tumor progression and metastasis (M. Li et al., 2020). Although the role of HIPK2 in p53 phosphorylation remains to be clarified, existing evidence indicates that reduced HIPK2 levels are linked to increased expression of multidrug resistance proteins such as MDR1 and BCRP, decreased apoptosis, and resistance to adriamycin in breast cancer cells (X. Pan et al., 2021). Moreover, ATM regulates BRCA1-dependent p300-mediated p53 acetylation (Q. Li et al., 2019), and DNA-PKcs plays a distinct role in DNA repair resection control and checkpoint activation (Mladenov et al., 2019).

Additionally, MSI2 expression may be modulated by SDC1 knockdown, although the direction remains unclear. Specifically, SDC1 depletion affects the expression of KLF4, MSI2, and miR-10b (Valla et al., 2021). Finally, microRNA miR-155-5p mimic treatment has been shown to downregulate MSI2 expression, while inhibition of

NFκB reduces MMP-9 activity, limiting migration and reinforcing the importance of MSI2 in coordinating several interconnected oncogenic programs (Jadhao et al., 2025).

GASTROINTESTINAL TUMORS

Esophageal cancer

Overexpression of MSI2 has been shown to promote proliferation, invasion, and metastasis in esophageal squamous cell carcinoma (ESCC) human samples (M. Wang et al., 2020). In cell lines, MSI2 knockdown reduces the mRNA and protein expression of β-catenin, c-Myc, and cyclin D1, suggesting that MSI2 may sustain proliferative signaling through Wnt pathway effectors. miR-942 is significantly increased in ESCC and directly activates the Wnt/β-catenin pathway by targeting and suppressing negative regulators (sFRP4, GSK3β, TLE1). This leads to enhanced cancer stem cell-like properties and tumor growth. c-Myc also promotes miR-942 expression, further amplifying pathway activation (Ge et al., 2015).

Simultaneously, decreased expression of Gli-1 and Patched indicates attenuation of Hedgehog (HH) pathway activity, further diminishing tumor-promoting transcriptional programs. In addition, elevated MSI2 expression enhances the invasive capacity of cancer cells by increasing the levels of MMP-2 and MMP-9, enzymes that degrade extracellular matrix components and facilitate tumor cell migration (Z. Li et al., 2017). Key components of the HH pathway, including Gli1, SMO, PTCH1, and SHH, are overexpressed or activated in ESCC tissues and cell lines, promoting cancer cell proliferation, stemness, and migration. High levels of HH pathway activity have been associated with worse prognosis in ESCC patients (J. Chen et al., 2023; L. Hu et al., 2023; N. Li et al., 2020; C. Wang et al., 2020; G. Zhao et al., 2020).

Gastric cancer

Four papers were analyzed; across these studies, MSI2 consistently emerged as a key regulator through its interactions with lncRNAs and miRNAs.

Different publications report that multiple pathways are interconnected in gastric cancer, including Wnt/β-catenin, PI3K/AKT, p38 MAPK/STAT3, Hippo, and TGF-β, which drive both the proliferation and migration of gastric cancer cells. These pathways are regulated by various noncoding RNAs, proteins, and microenvironmental factors, making them important targets for potential therapeutic intervention in gastric cancer (Feng et al., 2023; X. Guo et al., 2021; J. Han et al., 2025; Y. Hu et al., 2025; Y. Lin et al., 2018; W. Liu & Xu, 2019; H. Meng et al., 2019; Um et al., 2008; Veen et al., 2021; P. Zheng et al., 2018). In gastric cancer, MSI2 has been linked indirectly to enhanced tumor aggressiveness through different experimental models. *In vitro* assays using human samples and cell lines show that MSI2 overexpression accelerates colony formation and increases cell migration and invasion, promotes pro-angiogenic signals, contributing to aggressive tumor behavior and decreased overall survival (Z. Yang et al., 2019). On the other hand, *in vivo* profiling of MSI2-deficient pancreatic tumor cells revealed

reduced expression of stem cell regulators (Wnt7a, Aldh, Lin28), proto-oncogenes (cMet, Fos, Fyn), and Reg family genes, which are associated with gastrointestinal malignancies (Fox et al., 2016).

Although the Wnt signaling pathway is frequently altered in gastric cancer, there is no direct evidence that WNT7A itself is modified (Astudillo, 2020, 2021; Cao et al., 2021; M. Gao et al., 2021; Koushyar et al., 2020; Ning et al., 2022; Pi et al., 2020; Schmidt et al., 2020; Y. Wang et al., 2022; H.-J. Xie et al., 2020). Regarding ALDH, it has been described that multiple isoforms are associated with tumor progression and therapy resistance, while others correlate with better prognosis. (Y. Cai et al., 2022; C. Choi et al., 2020; S. Kang et al., 2020; Kawakami et al., 2020; Q. Li et al., 2022; Nguyen et al., 2024; L. Wang et al., 2022, 2024; S. Yao et al., 2022; Yin et al., 2020), while LIN28A and LIN28B are frequently upregulated and contribute to tumor growth, metastasis, and stemness through several regulatory mechanisms (W. Liang et al., 2020; Shen et al., 2020; J. Xu et al., 2021; Zhuo et al., 2022).

Proto-oncogenes like c-Fos are stabilized by methylation and autophagy, promoting proliferation, stemness, and resistance (E. Kim et al., 2023; J. H. Lee et al., 2023; Y. Xu et al., 2023; F. Zeng et al., 2024). FYN is upregulated and drives metastasis via STAT3-mediated EMT (J. Yu et al., 2020), while MET amplification drives proliferation, survival, and invasion (Kaurich et al., 2023; G. Li et al., 2023; H. Lin et al., 2025; C. Wang et al., 2022).
Lastly, REG3A acts as a tumor suppressor, whereas other REGs may promote inflammation(C. Sun et al., 2021; L. Wang et al., 2021). Despite these genes being associated with multiple cancer hallmarks and poor clinical outcomes, current data are inconclusive regarding a direct regulatory link between deregulation and MSI2 expression or activity in gastric cancer.

Some lncRNAs (e.g., LINC942) stabilize MSI2 and its downstream effects on c-MYC, supporting chemoresistance, survival, proliferation and tumor progression in gastric cancer. For instance, MSI2 is regulated at the post-translational level in gastric cancer, where the lncRNA LINC942 binds to MSI2 and prevents its proteasomal degradation by inhibiting interaction with the SCF^β-TRCP E3 ubiquitin ligase, as demonstrated in gastric cancer cell lines and murine xenografts (Y. Zhu et al., 2022). Stabilized MSI2 then binds to m6A-modified regions of c-MYC transcripts via its RRM1 domain, enhancing c-MYC mRNA stability and preventing its protein degradation, thereby reducing apoptosis and promoting chemoresistance under cisplatin treatment. These findings suggest a regulatory axis wherein LINC942 sustains MSI2 protein levels, which in turn stabilize c-MYC, facilitating tumor cell survival. Other studies have shown that c-MYC is similarly stabilized through m6A-dependent interactions with RNA-binding proteins such as IGF2BP1 and LIN28B, aided by lncRNAs including LOC101929709 and GLCC1. (Hou et al., 2022; Y.-D. Hu et al., 2018; Khanna et al., 2009; M. Liu et al., 2020; F. Luo & Lin, 2022; X.-X. Sun et al., 2018; T. Xu et al., 2022; D. Yang et al., 2021; L. Zhang et al., 2010; W. Zhao et al., 2023).
Additionally, in silico analysis reveals MSI2 as a competitive endogenous RNA (ceRNAs), which interacts with multiple components of a ceRNA network involving lncRNAs such as MCF2L-AS1, CCDC18-AS1, and TMPO-AS1, through shared microRNAs like hsa-miR-105-5p and hsa-miR-1-3p (X. Zheng et al., 2020). Disruption of MSI2 expression may destabilize this network, reinforcing high-risk molecular profiles. These interactions affect downstream genes involved in proliferation, immune regulation, and DNA replication. Collectively, these results

support the altered ceRNA network in gastric cancer. (Jin et al., 2022; Landeros et al., 2020; D. Peng et al., 2022; Qi et al., 2020; J. Xu et al., 2023; Yesharim et al., 2022; X. Zeng et al., 2022; J. Zhang et al., 2021; K. Zhang et al., 2020).

Pancreatic cancer

It has been established that MSI2 functions as a regulator of tumor progression, stem-like cell maintenance, and therapeutic resistance in pancreatic ductal adenocarcinoma (PDAC), as demonstrated in *in vivo* mouse models, *in vitro* human pancreatic cancer cell lines, and *in vivo* patient-derived xenografts.

Its expression increases during the transition from pancreatic intraepithelial neoplasia (PanIN) to invasive carcinoma, marking a subpopulation of tumor-initiating cells. In vivo transplantation of mouse pancreatic tumor cells showed that only $MSI2^+$ cells formed lethal tumors, while $MSI2^-$ cells did not. $MSI2^+$ cells were also overrepresented among circulating tumor cells and remained viable following high-dose gemcitabine treatment, indicating intrinsic drug resistance. In this study, increased ALDH and LIN28 expression caused by MSI2 upregulation also contributes to gemcitabine resistance. Genetic deletion of Msi2 in mice significantly reduced tumor burden, arrested progression at low-grade PanINs, and extended survival (Fox et al., 2016). Interestingly, inhibiting c-MET or BRD4 in combination with gemcitabine, in mouse tumors, reduces this resistant population, and MSI2 knockdown in patient-derived xenografts suppresses tumor growth (J. S. Kim et al., 2024; Tadros et al., 2017). Restoration of c-MET in MSI2-deficient pancreatic cancer cells rescues colony formation, confirming its downstream role (Fox et al., 2016). The upregulation of MSI2 is also implicated in post-transcriptional regulation, which enhances the ubiquitin-proteasome system, thereby promoting proteasome and ribosome biogenesis pathways in gemcitabine-resistant pancreatic cancer (Gu et al., 2020).

MSI2 also has a post-transcriptional regulatory mechanism associated with Numb downregulation. Still, it does not alter its mRNA levels, which activate Notch signaling and promote tumor stemness, cell survival, proliferation, migration, and therapy resistance (Rajbhandari et al., 2023). This leads to the upregulation of MDM2, which promotes the degradation of wild-type p53, in xenograft mouse models (Sheng et al., 2016, 2017). It's important to note that Notch activation in pancreatic cancer is also regulated by interactions between tumor cells, immune cells, stromal cells, and specific molecular modulators (Avritt et al., 2023; H. Chen et al., 2024; K. Chen et al., 2020; Elantary et al., 2025; L. Li et al., 2022; Y. Liu, Cao, et al., 2023; Sumi et al., 2021; Yan et al., 2024; J. Yu et al., 2021).

In gemcitabine-resistant pancreatic cancer cells, microRNAs such as hsa-miR-485-3p target MSI2, forming a regulatory network that is associated with increased resting CD4+ memory T cell populations. Also, enrichment in immune-related pathways, such as IL-6/JAK/STAT3 signaling (See Figure 7), and IFN-γ gene ontology (GO) was identified *in silico* (Gu et al., 2020). It has been described that immune evasion and poor anti-tumor responses in pancreatic cancer are displayed, especially by a complex interplay of stromal cells, immune checkpoints, chemokines, and suppressive enzymes, which, in turn, limit memory T cell formation, infiltration, and function (Adair et al., 2023; Brooks et al., 2024; Carpenter et al., 2020; Jain et al., 2022; Kern et al., 2019; Knoblock et al., 2017; J. Lin et al., 2020; Mathes et al., 2020; Van Poelgeest et al., 2020; Zambon et al., 2011). Additionally, a correlation

has been described between elevated MSI2 levels and high Ki-67 levels (Sheng et al., 2016, 2017), which is linked to more aggressive disease and poorer outcomes.

The transcriptional regulation of MSI2 in cancer involves a critical KLF4/FOXF2/MSI2 axis, which integrates opposing signals to modulate tumor progression. FOXF2 directly activates MSI2 transcription, concomitantly increasing the expression of Cyclin D1, CDK2, and phosphorylated RB, enhancing anti-apoptotic proteins (e.g., BCL-2 family), and suppressing pro-apoptotic effectors such as Bax, Bad, and cleaved caspase-3 (Zhong et al., 2024). While these changes were initially described in the context of FOXF2 regulation, the findings collectively suggest that elevated MSI2 expression promotes G1–S cell cycle progression, inhibits apoptosis, and supports proliferation, invasion, and migration (Aldoss et al., 2024; Al-Shammari et al., 2022; Ayoub et al., 2024; Barton et al., 2020; El-Far et al., 2020; Inada et al., 2023; Mahmoud et al., 2022; Overman et al., 2020; Yadav et al., 2022; H. Zhao et al., 2020).

Conversely, KLF4 negatively regulates MSI2 by binding directly to its promoter and repressing its oncogenic functions. Studies in human pancreatic ductal adenocarcinoma (PDAC) cell lines and in vivo models of subcutaneous and orthotopic liver metastases demonstrated that loss of KLF4 relieves this repression, resulting in MSI2 upregulation and PDAC progression (K. Guo et al., 2017).

Together, these observations define the KLF4/FOXF2/MSI2 axis as a key regulatory pathway, balancing MSI2 expression and influencing downstream oncogenic pathways, although its direct relationship to the hallmark functions of MSI2 remains to be fully delineated (Hope et al., 2010; Ito et al., 2010; Park et al., 2015; M.-H. Wang et al., 2015).

MSI2 functions as a regulator of pancreatic tumorigenesis by orchestrating progenitor cell fate decisions and enhancing oncogenic signaling pathways. In an in vivo mouse model, MSI2-positive pancreatic progenitors, characterized by expression of stemness-associated transcription factors such as SOX4, GATA6, TEAD2, OCT4, and Notch, along with early transformation markers including TOP2A and HMGB2, give rise to multilineage preneoplastic populations upon MYC induction. These populations progress into distinct tumor subtypes, including acinar cell carcinoma (ACC), pancreatic ductal adenocarcinoma (PDAC), adenosquamous carcinoma (ASCP), and anaplastic tumors through epigenetically regulated lineage specification, followed by accumulation of copy number variations. Tumor subtype identity is associated with differential pathway activation: ACCs exhibit metabolic reprogramming, while ASCPs engage RAS, Notch, and MAPK signaling (Rajbhandari et al., 2023).

MSI2 orchestrates multiple signaling cascades that converge on the regulation of epithelial–mesenchymal transition (EMT), thereby promoting tumor invasion, metastasis, and progression. By enhancing EGF-induced EGFR phosphorylation at Tyr1068, MSI2 activates downstream ERK/MAPK signaling and assembles a regulatory complex with ZEB1, phosphorylated ERK, and c-MYC (Sheng et al., 2020). This complex upregulates ZEB1, which represses E-cadherin, and induces mesenchymal markers including vimentin, MMP9, and α-SMA, while sustaining ERK-driven c-MYC expression to amplify oncogenic transcriptional programs.

In parallel, MSI2 suppresses Numb expression, activating Hedgehog signaling, accelerating EMT, and tumor progression (Sheng et al., 2020). MSI2 also directly binds to NLK mRNA, which in turn suppresses E-cadherin and upregulates vimentin and β-catenin, reinforcing EMT and activating PI3K/AKT/mTOR signaling to drive cell migration, invasion, and liver metastasis. This NLK-mediated pathway is counteracted by miR-149, which post-transcriptionally suppresses MSI2 (L. Huang et al., 2024).

Moreover, MSI2 impairs Hippo pathway signaling by binding and destabilizing SAV1 and MOB1 mRNAs, thereby inhibiting the kinase cascade and derepressing YAP/TAZ activity (H. Yang et al., 2020). The resultant upregulation of YAP/TAZ target genes further enhances tumor cell proliferation, migration, and invasion, suggesting a multilayered EMT-promoting network coordinated by MSI2.

Clinically, elevated MSI2 expression inversely correlates with inositol-3-phosphate synthase 1 (ISYNA1), associating with advanced pathological stage and poor prognosis. (L. Zhou et al., 2020). In PDAC, reduced ISYNA1 expression specifically correlates with greater tumor depth and increased vascular invasion, supporting its association with more aggressive tumor phenotypes (M. Dong et al., 2019). MSI2-mediated ISYNA1 repression facilitates ZEB1 upregulation and p21 suppression, enhancing migratory, invasive, and proliferative phenotypes (L. Zhou et al., 2020).

Liver Cancer

MSI2 functions as an oncogenic driver in liver cancer, with its expression negatively regulated by miR-3144-3p. Impairment of miR-3144-3p through ADAR1-mediated enzyme editing leads to MSI2 overexpression, which enhances tumor growth, proliferation, migration, and invasion. It has also been described that MSI2 expression correlates positively with the expression of the proto-oncogene MET, a key mediator of cancer progression (H. S. Kim et al., 2023). Mechanistically, MSI2 promotes tumorigenesis by enhancing the translation of key internal ribosome entry site (IRES)-containing mRNAs, including MYC, JUN, and VEGFA, factors widely involved with cancer onset and development. Thus, MYC protein levels increase without changes in mRNA levels, indicating a translational effect. Furthermore, MSI2 inhibits the processing of lncRNA MIR22HG into mature miR-22, a microRNA that normally suppresses MYC translation, indirectly contributing to elevated MYC protein levels. These combined translational mechanisms support the self-renewal and tumor-initiating capacity of tumor-initiating stem-like cells (TICs) (Yeh et al., 2023). MSI2 also maintains the stemness properties of CD44v6+ LCSCs by binding directly to LFNG mRNA and protein, enhancing Notch1 signaling and downstream activation of Hes1 and Hey1. This pathway promotes self-renewal, proliferation, migration, invasion, and drug resistance in liver cancer stem cells (LCSCs) and cancer stem cells (CSCs). In stemness-enriched hepatocellular carcinoma (HCC) spheroid cells, the expression of MSI2, MYC, and NANOG was elevated, and a correlation was observed between MSI2 and NANOG expression. Additionally, in human HCC tissue samples, NANOG co-localized with MSI2 and MYC in TICs (Yeh et al., 2023). Also, it has been described that MSI2 overexpression upregulates the RNA-binding protein LIN28A, which is involved in stemness regulation. The knockdown of LIN28A attenuates MSI2-induced stemness and chemoresistance, with clinical samples showing a positive correlation between MSI2 and LIN28A linked to poor prognosis, in HCC patients (T. Fang et al., 2017) LIN28A, through the TLR4 pathway

and in cooperation with histone methylases, helps generate TICs, which are linked to tumor recurrence and metastasis (Machida et al., 2023).

It has also been reported that MSI2 promotes the invasive capacity of HCC cells by inducing EMT (M. Liang et al., 2013). This phenotypic plasticity is closely associated with the upregulation of oncogenic factors such as MYC, MET, and NANOG described previously (Bae et al., 2022; K. Jiang et al., 2013; Y. Ren et al., 2016). MYC overexpression in HCC activates EMT-driving transcription factors, such as ZEB1, and represses epithelial phenotype promoters, including MIZ1 (Chahine et al., 2024; X. Jiang et al., 2021; Y. Ren et al., 2016). Whereas the stem cell marker NANOG is highly expressed in circulating tumor cells (CTCs) with mesenchymal or mixed phenotypes in patients with HCC. These cells often co-express EMT markers, such as Vimentin and Twist, and show reduced epithelial markers, including E-cadherin (Gawlik-Rzemieniewska & Bednarek, 2016; K. Jiang et al., 2013; L. Liu et al., 2020; Z. Ren et al., 2015; Tian et al., 2021). As previously mentioned, MET, especially RTK c-MET, is overexpressed in HCC, whose activation can be induced by high glucose or HGF stimulation, thus promoting EMT and triggering key oncogenic pathways, such as PI3K/Akt/mTOR and MEK/ERK (Bagirsakci et al., 2020; G. Chi et al., 2021; Çömez et al., 2021; Hui et al., 2022; Jayachandran et al., 2020; Kóbori et al., 2019; Koudelková et al., 2016; Rangel et al., 2016; Rustgi et al., 2020).

MSI2 is also positively correlated with CD44v6 expression in HCC tissues, associating its incidence with aggressive tumor features and resistance to sorafenib (X. Wang et al., 2019). Patients with CD44v6+ cells express higher levels of MET and maintain stemness through the HGF/MET/NANOG signaling pathway (Cheng et al., 2022). Increased expression of transcription factors such as Nanog, Oct4, and Sox2 has been observed in CD44v6+ LCSCs compared to CD44v6- cells (X. Wang et al., 2019).

MSI2 may also predict poor outcomes in hepatitis B virus (HBV)-related HCC via direct influence on the Wnt/β-catenin pathway. MSI2 is overexpressed in HBV-related HCC tissues compared to noncancerous tissues and is associated with cancer progression, migration, and invasiveness. Knockdown of MSI2 in HCC cells downregulates the expression of β-catenin, T cell factor (TCF-4), and lymphoid enhancer factor (LEF-1) at both the mRNA and protein levels. These proteins are effectors of the Wnt/β-catenin pathway and enhance the abilities of cells to migrate and invade (M.-H. Wang et al., 2015). Mutations in CTNNB1, which stabilize β-catenin, and loss-of-function mutations in AXIN1 are found in about 35% of HCC cases. These mutations are the precursor for activation of downstream genes that promote tumor growth and survival (Aceto et al., 2022; Cotellese et al., 2023; Evert et al., 2022; Gajos-Michniewicz & Czyż, 2023; S. He & Tang, 2020; Krutsenko et al., 2021; Matsumoto & Kikuchi, 2024; Nakagawa et al., 2024; G. Sethi et al., 2021; Wei et al., 2024). Importantly, pharmacological inhibition of MSI2-RNA interactions disrupts oncogene translation, impairs hepatitis C virus (HCV) replication, and suppresses tumor growth in animal models, highlighting MSI2 as a promising therapeutic target for malignancies driven by dysregulated post-transcriptional control in liver cancer (Yeh et al., 2023).

Colorectal cancer

It has been determined that MSI2 is an oncogenic RNA-binding protein in colorectal cancer (CRC), where its overexpression correlates with aggressive clinicopathological features, including poor prognosis and liver metastasis (Qi et al., 2020). This overexpression could be regulated through lncRNA-mediated ceRNA networks, where SNHG7, ASMTL-AS1, and LINC02604 capture miRNAs, such as hsa-let-7d-5p, hsa-mir-92a-3p, and hsa-mir-423-5p, which target MSI2 and in turn enhance its expression (Shakeri et al., 2024). Furthermore, MSI2 expression demonstrates a strong relationship with the upregulation of serum chemokines and broader immune/inflammatory responses in CRC (X. Meng et al., 2024). For example, MSI2 drives malignant progression through post-transcriptional repression of tumor suppressor mRNAs by direct binding to conserved motifs within their 3′UTRs, as validated by in vivo CLIP-seq analyses (Li et al., 2015; Kharin et al., 2021). Additionally, MSI2 directly upregulates KIF18A, ZFHX4, PEG10, and EIF4EBP1 at the translational level (X. Zhang et al., 2022). The upregulation of these genes and lncRNAs enhances CRC cell proliferation, migration, and invasion, and promotes tumor progression by inhibiting PTEN, which activates the PI3K/Akt pathway, leading to increased expression of metastasis-related proteins (MMP2, MMP9) (Cha et al., 2015; X. Chen et al., 2018; G. Liu et al., 2025; Y. Liu, Sun, et al., 2023; Marquis et al., 2020; Nagahara et al., 2011; Ye et al., 2022; H. Zhu et al., 2013). At the post-transcriptional level, MSI2 may contribute to the repression of tumor suppressor mRNAs, such as PTEN, LRIG1, CDH1 (E-cadherin), ZO-1, TGFβ1, NUMB, and BMPR1A, thereby activating multiple oncogenic pathways. MSI2 has been found to repress NUMB expression, contributing to NOTCH signaling dysregulation in tumorigenesis (LM et al., 2018). While PTEN suppression hyperactivates the PI3K/PDK1/AKT/mTORC1 axis, evidenced by increased phosphorylation of AKT (T308), ribosomal protein S6, and 4EBP1, which promotes protein synthesis, ribosome biogenesis, and cellular proliferation while suppressing oxidative phosphorylation (N. Li et al., 2015; Qi et al., 2020). Concurrently, LRIG1 repression enhances ErbB receptor signaling, and coordinated downregulation of epithelial markers (CDH1, ZO-1) with upregulation of TGFβ1 facilitates EMT and metastatic dissemination (Figure 7) (Kharin et al., 2021; N. Li et al., 2015).

MSI2 also exerts its oncogenic influence by promoting immune and inflammatory responses. Overexpression of MSI2 in colitis-associated colon cancer (CAC) models has been shown to significantly elevate serum levels of chemokines (e.g., MCP-1, CCL5, CCL11, G-CSF) and inflammatory cytokines (e.g., IL-1β, TNF-α, IL-6, IFN-γ, IL-17a), enhancing immune cell recruitment and activation within the tumor microenvironment. Transcriptomic analyses confirm MSI2 regulates immune-related pathways (including TNF-α/IFNG responses) and activates nucleocytoplasmic transport and NF-κB signaling, amplifying inflammatory cascades and chemokine production (X. Meng et al., 2024). Overall, MSI2 acts as a key regulator linking chemokine upregulation to enhanced immune cell infiltration and inflammatory signaling in CRC (X. Meng et al., 2024).

MSI2 loss was shown to inhibit CRC malignancy by reducing cell proliferation, viability, migration, and invasion, both in vitro and in vivo. This inhibition was also associated with triggering ferroptosis through alterations in the intracellular redox state, increased ROS and lipid peroxidation, disrupted iron homeostasis, reduced glutathione (GSH) levels, and mitochondrial injury. For instance, MSI2 directly interacts with phosphorylated ERK (p-ERK). When MSI2 is knocked down or deficient, the activity of the p-ERK/p38/MAPK signaling axis is reduced, which in turn leads to decreased phosphorylation and activity of MAPKAPK2. This repression of MAPKAPK2 is

associated with reduced phosphorylation of downstream targets, such as HSPB1, and contributes to increased ferroptosis. Due to this regulation, there is decreased expression of proliferation markers (PCNA and Ki67), as well as increased expression of ACSL4, which is a marker associated with ferroptosis. (X. Meng et al., 2023). Notably, these effects are independent of canonical Wnt/β-catenin signaling, as MSI2 induces no nuclear β-catenin accumulation or activation of Wnt target genes despite binding APC and CTNNB1 transcripts (N. Li et al., 2015; S. Wang et al., 2015). Instead, MSI2 mimics APC loss by suppressing overlapping tumor suppressors (e.g., PTEN, BMPR1A), driving crypt transformation and tumor initiation (Kharin et al., 2021).

Both MSI1 and MSI2 are expressed in colorectal cancers and have similar oncogenic effects. Loss of both proteins is required to fully suppress tumor growth *in vivo* in chemical [inflammation-driven (colitis-associated) CRC] and genetic [Familial adenomatous polyposis (hereditary CRC)] models, indicating functional redundancy in promoting intestinal tumorigenesis. (N. Li et al., 2015). Clinically, MSI2 is highly expressed in 32.9% of colorectal cancer cases, and its overexpression is associated with depth of invasion, lymph node metastasis, distant metastasis, liver metastasis, TNM clinical stage, and carcinoembryonic antigen (CEA) level. Moreover, MSI2 overexpression, lymph node metastasis, and distant metastasis are considered independent prognostic factors for overall survival in CRC patients. MSI2 high expression is specifically related to liver metastasis, and combining MSI2 expression with TNM stage improves liver metastasis prediction (Kharin et al., 2021; Zong et al., 2016). Functionally, MSI2 is essential for the survival and proliferation of HCT116 cells, where its knockout inhibits growth, delays G1-to-S phase transition, and reduces xenograft tumorigenesis. Transcriptomic profiling of MSI2-KO HCT116 cells reveals downregulation of RNA processing pathways (spliceosome, nucleocytoplasmic transport) and enrichment in neurological disease pathways (ALS, Huntington's, Parkinson's, Prion's). GSEA analysis further correlates MSI2 depletion with Myc, TNFα-NFκB, and KRAS signaling downregulation in CRC (X. Zhang et al., 2022). MSI2 binds to miR-30a-3p, which helps to interact with AGO2 and suppresses CGRRF1, a protein that normally breaks down KRAS. By blocking CGRRF1, MSI2 stabilizes KRAS, increasing KRAS/ERK signaling and making cancer cells more resistant to chemotherapy (Figure 7) (Lu et al., 2024).
Therapeutically, all-trans retinoic acid (ATRA) reduces MSI2 protein levels in CRC cell lines, suggesting differentiation-based strategies that may restore normal pathways signaling (LM et al., 2018). Additionally, it has been shown that palmatine exerts a direct inhibitory effect on MSI2 by binding to its RRM2 protein, thereby hindering cancer cell growth (X. Zhang et al., 2022). Overall, MSI2 acts as a key regulator linking chemokine upregulation to enhanced immune cell infiltration and inflammatory signaling in CRC (X. Meng et al., 2024).

URINARY AND GENITAL SYSTEM

Prostatic cancer

MSI2 alters the androgen receptor (AR) signaling pathway in prostate cancer. Specifically, MSI2 binds directly to the 3’ UTR of AR mRNA, increasing its stability, leading to upregulation of AR downstream target genes, such as KLK3 and NKX3.1. It has also been described that androgens directly stimulate the prostate-specific homeobox transcription factor NKX3.1 (Budreika et al., 2025); as a result, the AR pathway is activated, promoting prostate

cancer cell proliferation and tumor growth (J. Zhao et al., 2020). AR is frequently upregulated in prostate cancer, particularly as the disease progresses and becomes resistant to hormone therapy. This can promote cancer progression through ligand-independent mechanisms and by regulating genes involved in cell cycle and survival, such as c-Myc. Additionally, signaling pathways like Akt can further enhance AR levels in prostate cancer cells. (Fujita & Nonomura, 2018; L. Gao et al., 2013; Ha et al., 2011; Heinlein & Chang, 2004; X. Li et al., 2024; Özturan et al., 2022; Pandini et al., 2005; Singh & Figg William, 2004; Q. Wang et al., 2009; J. Zhao et al., 2020). Also, polymorphisms in the KLK3 promoter can enhance AR binding, leading to higher KLK3 expression and increased prostate cancer risk (Koistinen et al., 2021; H. Lin et al., 2021; Matin et al., 2019).

Bladder cancer

MSI2 promotes cancer cell migration and metastasis via the JAK2/STAT3 pathway in bladder cancer (M. Wang et al., 2020). Overexpression of MSI2 increases the phosphorylation of JAK2 and STAT3, which in turn upregulates downstream genes like WASF3, involved in the transduction of signals that involve changes in cell shape, function and motility, Figure 7 (C.Yang et al., 2016), and can promote EMT by the effect of lncRNA DANCR and MSI2-binding protein, whose regulation is linked to increased N-cadherin and vimentin, and depletion of E-cadherin(Zhan et al., 2018). EMT in bladder cancer is regulated by a complex network of signaling pathways, transcription factors (Snail, Twist1, and ZEB1), non-coding RNAs (VIM-AS1/miR-655/ZEB1 axis), and interactions with the tumor microenvironment (m6A RNA methylation) (Ashrafizadeh et al., 2020; H. Cai et al., 2024; M. Chi et al., 2022; C. Huang, 2025; J. Huang et al., 2022; McConkey et al., 2009; X. Meng et al., 2022; Ping et al., 2023; Xiong et al., 2021; N. Zhang et al., 2021). In addition, MSI2 expression has been shown to enhance KRAS translation, which thus indirectly activates the PI3K/AKT and MAPK pathways, which are growth-related effector signaling pathways downstream of KRAS. Additionally, MSI2 enhanced KRAS translation upregulates the translational initiator eIF4E, further promoting protein synthesis and cell growth.. This action of MSI2 has been described as influencing HRAS expression and function. Besides, HRAS mutations are found in about 15% of bladder cancer cases, with higher mutation frequency and mRNA expression in bladder urothelial carcinoma compared to other cancers (Y.-T. Chen et al., 2020; Y. Peng et al., 2025).

MSI2 drives oncogenic KRAS signaling and is inversely correlated with miR-143 in human tumors. MSI2 directly binds the conserved UAGUA motif within the KRAS 3′ UTR, post-transcriptionally upregulating KRAS protein levels. Genetic suppression of MSI2 reduced KRAS abundance, consequently diminishing phosphorylation of AKT and ERK1/2. This attenuation of PI3K and MAPK signaling pathways resulted in significant growth arrest and apoptosis. Conversely, MSI2 overexpression amplified KRAS expression and enhanced PI3K/AKT and MAPK activation, thereby accelerating cellular proliferation.(Tsujino et al., 2019).

Cervical cancer

MSI2 is described as an oncogenic driver in cervical cancer, where its overexpression correlates with poor survival and drives increased proliferation, invasion, and sphere formation. Mechanistically, MSI2 directly binds the c-FOS 3′-UTR to enhance its translation, activating pro-invasion signaling (P. Dong et al., 2017). In cervical cancer (CC) cell lines, this activation may lead to continuous activation of the Serum Response Element (SRE) motif in

the c-FOS promoter, promoting malignant transformation (Van Riggelen et al., 2005). MSI2 concurrently suppresses PTEN and induces EMT by increasing SNAIL, Vimentin, CD44, and decreasing E-cadherin (P. Dong et al., 2017). Loss of PTEN activates the PI3K/AKT/mTOR pathway, promoting EMT and cancer progression (H. He et al., 2023; H. Liu et al., 2020; R. Sun et al., 2024; W. Zhang et al., 2021). MSI2 expression is tightly regulated by tumor-suppressor miRNAs, such as miR-128-3p, miR-143, and miR-107, which directly target MSI2, and their downregulation predicts poor prognosis. Importantly, p53 activation increases miR-143 and miR-107 levels, leading to suppression of MSI-2 and establishing the p53-miR-143/miR-107-MSI-2 axis. It has been described that antineoplastic antibiotics such as Mithramycin A activate p53, restoring miR-143/miR-107, reducing MSI2 levels, and potently inhibiting oncogenic phenotypes (P. Dong et al., 2017; R. Wang et al., 2020). Clinically, MSI2 is upregulated in CC tissues and correlates with advanced FIGO stage, lymph node metastasis, and serves as an independent prognostic marker for poorer overall and progression-free survival (Y. Liu et al., 2018).

Endometriosis and ovarian cancer

Endometriosis is a benign gynecological disorder characterized by the growth of ectopic endometrial-like tissue (M. Chen et al., 2020; Y.-M. Yang & Yang, 2017; Zubrzycka et al., 2021). Although not malignant, this condition shares molecular features with specific ovarian carcinomas. A key pathogenic feature common to both is epithelial-mesenchymal transition (EMT), facilitating cellular invasion and dissemination (Agostinis et al., 2021; Cela et al., 2021; S. Guo et al., 2024; Konrad et al., 2020; X. Li et al., 2017; Ni & Li, 2024; J. Wang et al., 2023; Z. Wang et al., 2024; Y. Xie et al., 2023; W. Zheng et al., 2023; M. Zou et al., 2024; 许, 2022).

Endometriosis is a chronic condition where tissue resembling the uterine lining grows outside the uterus. While endometriosis itself is not cancer, it shares some biological features with certain ovarian cancers. One key similarity is the process of Epithelial-Mesenchymal Transition (EMT), which facilitates abnormal cell movement and invasion in both diseases.

MSI2 is significantly upregulated in ovarian carcinoma tissues compared to adjacent noncancerous tissues, and its overexpression is an independent predictor of poor overall survival. Especially, in advanced-stage (III-IV) and serous ovarian carcinomas (J. Lee et al., 2016). Moreover, elevated MSI2 expression enhances tumor cell viability, migration, and invasion, and promotes EMT, as evidenced by reduced E-cadherin expression and increased N-cadherin and vimentin expression. These changes correlate with activation of the PI3K/AKT pathway, as indicated by increased levels of phospho-PI3K and phospho-AKT (L. W. Zhao et al., 2020). Proteins like CD24 and XTP8 further activate this pathway, enhancing EMT (J. Deng et al., 2019; L. Liu et al., 2019; Nakamura et al., 2017; R. Zhao et al., 2024).

In addition, two miRNA pathways have been described as regulators of MSI2. First, in endometriosis MSI2 is translationally repressed by miR-145 via direct binding to the 3′UTR (modulated upstream by the long non-coding RNA PCAT1) (L. Wang et al., 2020). Second, in ovarian cancer MSI2 is targeted by miR-149; it has been determined that overexpression of miR-149 suppresses MSI2 and reverses EMT markers (L. W. Zhao et al., 2020).

Concurrently, MSI2 sustains cancer stemness by upregulating SOX2 during endometriosis (L. Wang et al., 2020). SOX2 expression in endometriosis is regulated by hormonal signals. Analysis of lymph node metastases in endometriosis patients revealed significant enrichment of SOX2-positive cells in tumors dual-positive for estrogen receptor (ER) and progesterone receptor (PR). Current research in endometriosis has shown SOX2 to have robust co-localization with ER in these lesions, indicating that estrogen signaling directly drives SOX2 overexpression in endometriosis-associated tissues. This functional interplay between ER activation and SOX2 upregulation suggests a mechanism for sustaining stemness and metastatic competence in hormone-sensitive disease. (Velho et al., 2023).

Furthermore, in ovarian cancer experimental models MSI2 positively regulates the cancer stem-cell (CSC) marker ALDH4A1 to drive chemoresistance by inducing MDR1 and dysregulates the cell cycle via the repression of p21 and NUMB, which leads to NOTCH1/3 pathway activation (J. Lee et al., 2016; Löblein et al., 2021). Along with MDR1 overexpression, resistant cells often shift their metabolism toward aerobic glycolysis, by displaying proteins upregulation like NOC2L and Hexokinase 2 (HK2) (T.-Y. Lin et al., 2024; McCorkle et al., 2021; Ozturk et al., 2025). MSI2 knockdown attenuates these pro-tumorigenic phenotypes, including stemness maintenance, metabolic activity, and therapy resistance to paclitaxel (J. Lee et al., 2016).

BONE TUMORS

Current research does not directly address whether the incidence of MSI2 affects other bone tumors besides Ewing's sarcoma. Most available studies focus on the role of MSI2 in other cancers and bone cell differentiation rather than bone tumor development or progression.

Ewing’s sarcoma

Ewing's sarcoma is mainly regulated by the EWSR1-FLI1 fusion protein, which acts as a powerful transcription factor, changing gene expression and chromatin structure to drive tumor growth and spread. This regulation involves genetic, epigenetic, and microenvironmental factors that together control how the tumor behaves and responds to treatment (Apfelbaum et al., 2022; Chellini et al., 2023; García-Domínguez et al., 2021, 2022; Gong et al., 2023; Hesla et al., 2021; Hughes et al., 2023; Issaq et al., 2020; Koppenhafer et al., 2022; M. Li & Chen, 2022; Marques et al., 2023; Orth et al., 2021; Shi et al., 2020; L. Yu et al., 2023; Zöllner et al., 2021). Recent research has demonstrated that both MSI2 and lncRNA TUG1 are upregulated in Ewing's sarcoma tissues and cell lines. Their expression correlates with tumor cell proliferation, migration, invasion, and decreased patient survival. Functionally, MSI2 is negatively regulated by the tumor suppressor miR-199a-3p, which directly binds to its 3'UTR. While the lncRNA TUG1 acts as a competing endogenous RNA, sequestering miR-199a-3p and thereby enhancing MSI2 expression. This upregulation of MSI2 promotes pro-tumorigenic phenotypes (H. Li et al., 2021).

CACHEXIA AND MSI2

Cachexia is a common and severe complication in cancer, especially in advanced stages, where it affects 50–80% of patients, with particularly high rates in cancers like pancreatic and gastrointestinal tumors. The underlying pathophysiology involves chronic systemic inflammation driven by cytokines (e.g., IL-6, TNF-α) and tumor-derived factors that disrupt metabolism, leading to muscle and fat loss (Da Silva et al., 2020; Law, 2022; Y. Li et al., 2021; Mariean et al., 2023; McGovern et al., 2022; Pavăl et al., 2022; Poulia et al., 2020; Setiawan et al., 2023; Van De Worp et al., 2020; Q. Wu et al., 2023). Particularly, in pancreatic cancer, MSI2 upregulates the ubiquitin-proteasome, which may promote cachexia by accelerating the breakdown of muscle proteins, leading to severe muscle loss and weakness (Libramento et al., 2025; Martin et al., 2023; Mulder et al., 2020).

Cachexia is not a specific feature of cancer; it has been largely described in muscular atrophies, such as Myotonic dystrophy. Myotonic dystrophy type 1 (DM1) is a disorder characterized by muscle weakness and wasting that may be amplified by MSI2 overexpression (Sabater-Arcis et al., 2021). Recent research has identified MSI2 as a key player in DM1 muscle dysfunction, acting through the regulation of autophagy and microRNA pathways. Muscle cells from DM1 patients exhibit increased levels of MSI2, which suppresses the maturation of microRNA miR-7. Low levels of miR-7 lead to excessive autophagy, resulting in muscle atrophy and weakness in DM1 patients (Sabater-Arcis et al., 2021). Further, MSI2 overexpression is related to muscle pathology in the HSALR DM1 mouse model, which typically exhibits mild or no muscle atrophy. The forced overexpression of MSI2 has been shown to induce key features of muscle degeneration, including activation of autophagy, as evidenced by an increased LC3-II/LC3-I ratio and elevated ATG7 levels, along with a reduction in P62 protein (Sabater-Arcis et al., 2024).

MSI2 overexpression is involved in driving the progression of muscular atrophy in DM1 (Sabater-Arcis et al., 2021). Concurrently, MSI2 is overexpressed in multiple solid cancers associated with cachexia, including pancreatic, gastric, lung, liver, and colorectal cancers (Baracos et al., 2018; X. Li et al., 2017; Porporato, 2016; 许, 2022).

This shared dysregulation suggests MSI2 may act as a convergent molecular mechanism promoting muscle atrophy in both contexts. The overexpression in cancer is hypothesized to contribute directly to the muscle wasting characteristic of cachexia.

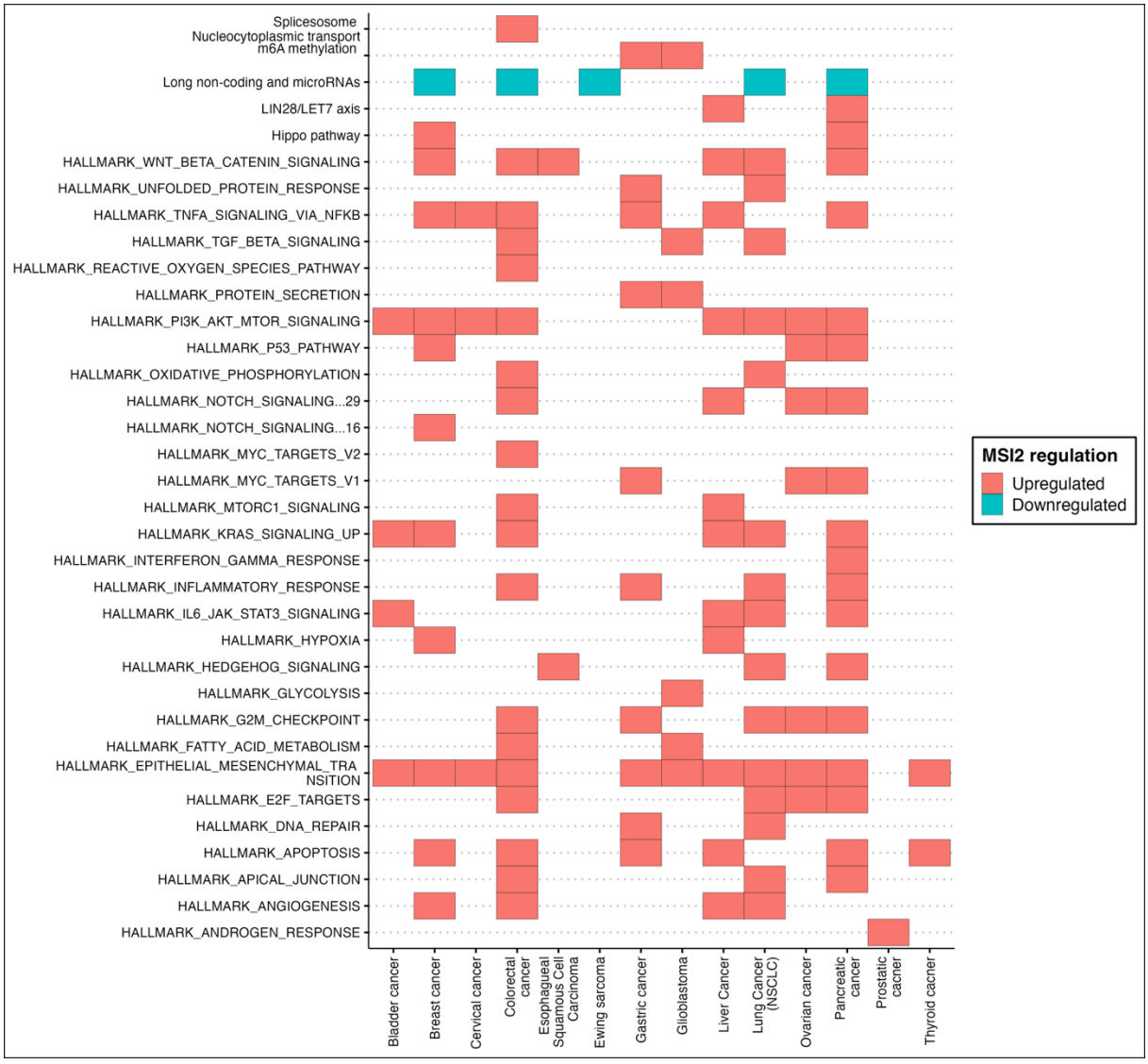


Figure 7. Hallmarks from MSigDB and additional categories illustrate the role of MSI2 as an oncoprotein that exerts its function. The x-axis shows the 14 solid tumors in which MSI2 exerts its role, and the y-axis shows the MSigDB hallmarks. Red boxes indicate upregulation, and blue boxes indicate downregulation.

4. Conclusion

Musashi-2 has been widely studied for its role in cancer. The literature shows that MSI2 is frequently upregulated in a variety of solid tumors, which is often linked to tumor progression, metastasis, poor prognosis, and chemoresistance. Its ability to bind and stabilize certain oncogenic mRNAs, while blocking the expression of tumor suppressors, allows cancer cells to acquire aggressive properties and enhance their survival mechanisms. By acting on pathways such as PI3K/Akt/mTOR, Wnt/β-catenin and TGF-β/SMAD, MSI2 confers a distinct advantage on malignant cells, helping them to survive under metabolic stress and evade treatment. In glioblastoma, for example, MSI2 stimulates glycolysis and lipid biosynthesis, enabling rapid cell division and contributing to therapy

resistance. A similar phenomenon is observed in pancreatic cancer, where MSI upregulation of c-MET and other oncogenic targets supports both tumor growth and chemoresistance.

Emerging evidence also points to MSI2 role in promoting EMT, enabling cancer cell dissemination to distant organs. Especially, due to the dysregulation of factors and mesenchymal effectors, such as SNAIL1/2, SLUG, and ZEB1/2, along with cytoskeletal proteins like vimentin and E-cadherin. In addition, MSI2 has been associated with enhanced stem-like properties characterized by increased markers of self-renewal and pluripotency. These attributes foster a tumor cell subpopulation resistant to conventional therapies and prone to relapse

MSI2-driven metabolic regulation is observed frequently in high-incidence malignancies. In glioblastoma, MSI2 promotes glycolysis and lipogenesis via the SNORD12B–ZBTB4 axis. In pancreatic cancer, MSI2 drives gemcitabine resistance through the ALDH and LIN28 regulation. In hepatocellular carcinoma, MSI2 enhances MYC and VEGFA translation. Despite these advances, most experimental studies remain reductionist. The 91,5% are limited to in vitro systems, the in silico 56,3% and only 52,1% employ patient-derived xenograft (PDX) models. This PRISMA-based scoping review identified 71 eligible studies that consistently link MSI2 overexpression with a poor prognosis. However, no metabolic study has progressed to Phase III clinical trials. Bone tumors remain poorly understood. Few studies address their metabolic programming, and the role of MSI2 in their development remains unclear. These gaps emphasize the need for humanized preclinical models and metabolic imaging tools to enable the translational validation of MSI2-targeted strategies.

The broad functional range of MSI2 highlights its potential as both a prognostic biomarker and a therapeutic target. Elevated levels often correlate with poorer patient outcomes and more advanced disease stages. Interfering with MSI2 expression, either through knockdown strategies or small molecule inhibitors, has shown promising preliminary results in reducing tumor proliferation and sensitizing cancer cells to existing therapies. This dual prognostic and therapeutic role underscores the clinical significance of MSI2 and prompts further investigation into how it can best be exploited for diagnostic and therapeutic purposes.

In conclusion, MSI2 emerges as a molecular driver of solid tumor progression by coordinating metabolic adaptations, maintaining oncogenic signaling networks, and influencing immune evasion. A deeper understanding of MSI2 mechanisms and interactions in driving tumor growth, metastasis, and therapy resistance places this RNA-binding protein as a promising target in precision oncology for solid tumors.

Authors contribution: Conceptualization, F.G.; Data curation, J.A. and F.G.: Formal analysis, J.A. and F.G.; Investigation, J.A. and F.G.; Methodology, F.G.; Writing – original draft, J.A.; Writing -review & editing, F.G.
Financing/founding: This research did not receive external funding.
Conflicts of Interest: The authors declare no conflict of interest.

References

Aceto, G., Cotellese, R., Selvaggi, F., & Catalano, T. (2022). Targeting Wnt/β-Catenin Pathways in Primary Liver Tumours: From Microenvironment Signaling to Therapeutic Agents. *Cancers*, *14*. https://doi.org/10.3390/cancers14081912

Adair, S., Conarroe, C., Bullock, T., Bauer, T., Gamache, A., & Padilla, F. (2023). Interrogating the CD27:CD70 axis in αCD40-dependent control of pancreatic adenocarcinoma. *Frontiers in Cell and Developmental Biology*, *11*. https://doi.org/10.3389/fcell.2023.1173686

Agostinis, C., Balduit, A., Mangogna, A., Zito, G., Romano, F., Ricci, G., Kishore, U., & Bulla, R. (2021). Immunological Basis of the Endometriosis: The Complement System as a Potential Therapeutic Target. *Frontiers in Immunology*, *11*. https://doi.org/10.3389/fimmu.2020.599117

Aldoss, I., Zhang, J., Shimamoto, K., Saygin, C., Robbins, M., Agrawal, V., Aribi, A., Karaoğlu, D. A., Pourhassan, H., Koller, P., Ali, H., Blackmon, A., Otoukesh, S., Sandhu, K., Ball, B., Artz, A., Malki, M. Al, Salhotra, A., Tinajero, J., … Pullarkat, V. (2024). Venetoclax in combination with a pediatric-inspired regimen for the treatment of newly diagnosed adults with Philadelphia chromosome-negative acute lymphoblastic leukemia. *Haematologica*. https://doi.org/10.3324/haematol.2024.286427

Al-Shammari, G., Abdelhalim, M., Al-Ayed, M., Al-Harbi, L., & Yahya, M. (2022). The Protective Effect of α-Lipoic Acid against Gold Nanoparticles (AuNPs)-Mediated Liver Damage Is Associated with Upregulating Nrf2 and Suppressing NF-κB. *Nutrients*, *14*. https://doi.org/10.3390/nu14163327

Alves, C. L., & Ditzel, H. J. (2023). Drugging the PI3K/AKT/mTOR Pathway in ER+ Breast Cancer. In *International Journal of Molecular Sciences* (Vol. 24, Issue 5). https://doi.org/10.3390/ijms24054522

Ambriz-Barrera, F., Rojas-Jiménez, E., Díaz-Velásquez, C., De-La-Cruz-Montoya, A. H., Martínez-Gregorio, H., Ruiz-De-La-Cruz, M., Huertas, A., Montealegre, A. L., Castro-Rojas, C., Acosta, G., Vaca-Paniagua, F., & Perdomo, S. (2024). Mutational spectrum of breast cancer by shallow whole-genome sequencing of cfDNA and tumor gene panel analysis. *PLOS ONE*, *19*. https://doi.org/10.1371/journal.pone.0308176

Amin, T., Sharma, R. P., Mir, K. B., Slathia, N., Chhabra, S., Tsering, D., Kotwal, P., Bhagat, M., Nandi, U., Parkesh, R., Kapoor, K., & Goswami, A. (2023). Quinoxalinone substituted pyrrolizine (4h)-induced dual inhibition of AKT and ERK instigates apoptosis in breast and colorectal cancer by modulating mitochondrial membrane potential. *European Journal of Pharmacology*, 175945. https://doi.org/10.1016/j.ejphar.2023.175945

Apfelbaum, A., Wrenn, E., & Lawlor, E. (2022). The importance of fusion protein activity in Ewing sarcoma and the cell intrinsic and extrinsic factors that regulate it: A review. *Frontiers in Oncology*, *12*. https://doi.org/10.3389/fonc.2022.1044707

Arora, S., Singh, P., Tabassum, G., Dohare, R., & Syed, M. (2022a). miR-16-5p regulates aerobic glycolysis and tumorigenesis of NSCLC cells via LDH-A/lactate/NF-κB signaling. *Life Sciences*, 120722. https://doi.org/10.1016/j.lfs.2022.120722

Arora, S., Singh, P., Tabassum, G., Dohare, R., & Syed, M. (2022b). miR-495-3p regulates sphingolipid metabolic reprogramming to induce Sphk1/ceramide mediated mitophagy and apoptosis in NSCLC. *Free Radical Biology & Medicine*. https://doi.org/10.1016/j.freeradbiomed.2022.07.001

Ashrafizadeh, M., Hushmandi, K., Hashemi, M., Akbari, M., Kubatka, P., Raei, M., Koklesová, L., Shahinozzaman, M., Mohammadinejad, R., Najafi, M., Sethi, G., Kumar, A., & Zarrabi, A. (2020). Role of microRNA/Epithelial-to-Mesenchymal Transition Axis in the Metastasis of Bladder Cancer. *Biomolecules*, *10*. https://doi.org/10.3390/biom10081159

Askari, M., Sobti, R., Nikbakht, M., & Sharma, S. (2013). Aberrant promoter hypermethylation of p21 (WAF1/CIP1) gene and its impact on expression and role of polymorphism in the risk of breast cancer. *Molecular and Cellular Biochemistry*, *382*, 19–26. https://doi.org/10.1007/s11010-013-1696-5

Astudillo, P. (2020). Wnt5a Signaling in Gastric Cancer. *Frontiers in Cell and Developmental Biology*, *8*. https://doi.org/10.3389/fcell.2020.00110

Astudillo, P. (2021). A Non-canonical Wnt Signature Correlates With Lower Survival in Gastric Cancer. *Frontiers in Cell and Developmental Biology*, *9*. https://doi.org/10.3389/fcell.2021.633675

Avritt, F., Carpenter, E., Bednar, F., Zhang, Y., Bonilla, M., Burns, W., Brown, K., Irizarry-Negron, V., Menjivar, R., Yang, S., Du, W., Yan, W., Steele, N., Donahue, K., Di Magliano, P., & Kemp, S. (2023). Notch signaling regulates immunosuppressive tumor-associated macrophage function in pancreatic cancer. *Cancer Immunology Research*. https://doi.org/10.1158/2326-6066.CIR-23-0037

Ayoub, M., Faris, C., Juranovic, T., Chela, H., & Daglilar, E. (2024). The Use of Glucagon-like Peptide-1 Receptor Agonists in Patients with Type 2 Diabetes Mellitus Does Not Increase the Risk of Pancreatic Cancer: A U.S.-Based Cohort Study. *Cancers*, *16*. https://doi.org/10.3390/cancers16091625

Bae, S., Sung, P., Cha, J., Jang, J., Park, N., Choi, J., & Yoon, S. (2022). MiR-23b-3p suppresses epithelial-mesenchymal transition, migration, and invasion of hepatocellular carcinoma cells by targeting c-MET. *Heliyon*, *8*. https://doi.org/10.1016/j.heliyon.2022.e11135

Bagirsakci, E., Bağcı, G., Topel, H., Cakan-Akdogan, G., Comez, D., & Atabey, N. (2020). lncRNA HOTAIR overexpression induced downregulation of c-Met signaling promotes hybrid epithelial/mesenchymal phenotype in hepatocellular carcinoma cells. *Cell Communication and Signaling : CCS*, *18*. https://doi.org/10.1186/s12964-020-00602-0

Bai, J., Chen, W.-B., Zhang, X., Kang, X., Jin, L., Zhang, H., & Wang, Z. (2020). HIF-2α regulates CD44 to promote cancer stem cell activation in triple-negative breast cancer via PI3K/AKT/mTOR signaling. *World Journal of Stem Cells*, *12 1*, 87–99. https://doi.org/10.4252/wjsc.v12.i1.87

Baracos, V., Martin, L., Korc, M., Guttridge, D., & Fearon, K. (2018). Cancer-associated cachexia. *Nature Reviews Disease Primers*, *4*. https://doi.org/10.1038/nrdp.2017.105

Barber, A. G., Quintero, C. M., Hamilton, M., Rajbhandari, N., Sasik, R., Zhang, Y., Kim, C., Husain, H., Sun, X., & Reya, T. (2025). Regulation of lung cancer initiation and progression by the stem cell determinant Musashi. *ELife*, *13*, RP97021. https://doi.org/10.7554/eLife.97021

Barbirou, M., Miller, A. A., Gafni, E., Mezlini, A., Zidi, A., Boley, N., & Tonellato, P. J. (2022a). Evaluation of cfDNA as an early detection assay for dense tissue breast cancer. *Scientific Reports 2022 12:1*, *12*(1), 1–14. https://doi.org/10.1038/s41598-022-12457-1

Barbirou, M., Miller, A. A., Gafni, E., Mezlini, A., Zidi, A., Boley, N., & Tonellato, P. J. (2022b). Evaluation of cfDNA as an early detection assay for dense tissue breast cancer. *Scientific Reports*, *12*(1), 8458. https://doi.org/10.1038/s41598-022-12457-1

Barton, K., Siddiqui, F., Pompa, R., Freytag, S., Khan, G., Dobrosotskaya, I., Ajlouni, M., Zhang, Y., Cheng, J., Movsas, B., & Kwon, D. (2020). Phase I trial of oncolytic adenovirus-mediated cytotoxic and interleukin-12 gene therapy for the treatment of metastatic pancreatic cancer. *Molecular Therapy Oncolytics*, *20*, 94–104. https://doi.org/10.1016/j.omto.2020.11.006

Beck, J., Ismail, A., & Tolomeo, C. (2014). Targeting the phosphatidylinositol 3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) pathway: an emerging treatment strategy for squamous cell lung carcinoma. *Cancer Treatment Reviews*, *40 8*, 980–989. https://doi.org/10.1016/j.ctrv.2014.06.006

Bellon, M., & Nicot, C. (2023). Targeting Pim kinases in hematological cancers: molecular and clinical review. *Molecular Cancer*, *22*(1), 18. https://doi.org/10.1186/s12943-023-01721-1

Benavides-Serrato, A., Saunders, J., Kumar, S., Holmes, B., Benavides, K., Bashir, M., Nishimura, R., & Gera, J. (2023). m6A-modification of cyclin D1 and c-myc IRESs in glioblastoma controls ITAF activity and resistance to mTOR inhibition. *Cancer Letters*, 216178. https://doi.org/10.1016/j.canlet.2023.216178

Bhagwat, S., Mcmillen, W., Cai, S., Zhao, B., Whitesell, M., Shen, W., Kindler, L., Flack, R., Wu, W., Anderson, B., Zhai, Y., Yuan, X., Pogue, M., Van Horn, R., Rao, X., Mccann, D., Dropsey, A., Manro, J., Walgren, J., … Peng, S.-B. (2019). ERK Inhibitor LY3214996 Targets ERK Pathway–Driven Cancers: A Therapeutic Approach Toward Precision Medicine. *Molecular Cancer Therapeutics*, *19*, 325–336. https://doi.org/10.1158/1535-7163.MCT-19-0183

Bhatt, A., Wright, T., Barnes, V., Chakrabarty, S., Matossian, M., Lexner, E., Ucar, D., Miele, L., Flaherty, P., Burow, M., & Cavanaugh, J. (2021). Diverse and converging roles of ERK1/2 and ERK5 pathways on mesenchymal to epithelial transition in breast cancer. *Translational Oncology*, *14*. https://doi.org/10.1016/j.tranon.2021.101046

Bhavnagari, H., & Shah, F. (2025). Decoding gene expression profiles of Hippo signaling pathway components in breast cancer. *Molecular Biology Reports*, *52 1*, 216. https://doi.org/10.1007/s11033-025-10299-4

Binabaj, M., Bahrami, A., Shahidsales, S., Joodi, M., Mashhad, J., Hassanian, S., Anvari, K., & Avan, A. (2018). The prognostic value of MGMT promoter methylation in glioblastoma: A meta-analysis of clinical trials. *Journal of Cellular Physiology*, *233*, 378–386. https://doi.org/10.1002/jcp.25896

Bironzo, P., Reale, M., Sperone, T., Tabbò, F., Caglio, A., Listì, A., Passiglia, F., Di Maio, M., Righi, L., Bussolino, F., Scagliotti, G., & Novello, S. (2021). Clinical and Molecular Features of Epidermal Growth Factor Receptor (EGFR) Mutation Positive Non-Small-Cell Lung Cancer (NSCLC) Patients Treated with Tyrosine Kinase Inhibitors (TKIs): Predictive and Prognostic Role of Co-Mutations. *Cancers*, *13*. https://doi.org/10.3390/cancers13102425

Brandner, S., McAleenan, A., Kelly, C., Spiga, F., Cheng, H.-Y., Dawson, S., Schmidt, L., Faulkner, C., Christopher, W., Jefferies, S., Higgins, J., & Kurian, K. (2021). MGMT promoter methylation testing to predict overall survival in people with glioblastoma treated with temozolomide: a comprehensive meta-analysis based on a Cochrane Systematic Review. *Neuro-Oncology*, *23*, 1457–1469. https://doi.org/10.1093/neuonc/noab105

Brandner, S., McAleenan, A., Kelly, C., Spiga, F., Cheng, H.-Y., Dawson, S., Schmidt, L., Faulkner, C., Wragg, C., Jefferies, S., Higgins, J., & Kurian, K. (2021). MGMT promoter methylation testing to predict overall survival in people with glioblastoma treated with temozolomide: a comprehensive meta-analysis based on a Cochrane Systematic Review. *Neuro-Oncology*, *23 9*, 1457–1469. https://doi.org/10.1093/neuonc/noab105

Brant, R., Sharpe, A., Liptrot, T., Dry, J., Harrington, E., Barrett, J., Whalley, N., Womack, C., Smith, P., & Hodgson, D. (2016). Clinically Viable Gene Expression Assays with Potential for Predicting Benefit from MEK Inhibitors. *Clinical Cancer Research*, *23*, 1471–1480. https://doi.org/10.1158/1078-0432.CCR-16-0021

Brooks, D., Liu, M. Y. R., & Guo, M. (2024). Regulation and impact of tumor-specific CD4+ T cells in cancer and immunotherapy. *Trends in Immunology*. https://doi.org/10.1016/j.it.2024.02.005

Brugnoli, F., Grassilli, S., Al-Qassab, Y., Capitani, S., & Bertagnolo, V. (2019). CD133 in Breast Cancer Cells: More than a Stem Cell Marker. *Journal of Oncology*, *2019*. https://doi.org/10.1155/2019/7512632

Budreika, A., Phoenix, J., Kostlan, R., Deegan, C., Ferrari, M., Young, K., Fanning, S., & Kregel, S. (2025). The Homeobox Transcription Factor NKX3.1 Displays an Oncogenic Role in Castration-Resistant Prostate Cancer Cells. *Cancers*, *17*. https://doi.org/10.3390/cancers17020306

Butler, M., Pongor, L., Su, Y.-T., Xi, L., Raffeld, M., Quezado, M., Trepel, J., Aldape, K., Pommier, Y., & Wu, J. (2020). MGMT Status as a Clinical Biomarker in Glioblastoma. *Trends in Cancer*, *6 5*, 380–391. https://doi.org/10.1016/j.trecan.2020.02.010

Bychkov, I., Deneka, A., Topchu, I., Makhov, P., Kudinov, A., Nikonova, A., Karanicolas, J., Golemis, E., Lengner, C. J., Borghaei, H., Patel, J., & Boumber, Y. (2022). Abstract 874: MSI2 regulates VEGFR2 signaling and tumor progression in NSCLC. *Cancer Research*. https://doi.org/10.1158/1538-7445.am2022-874

Bychkov, I., Deneka, A., Topchu, I., Pangeni, R. P., Lengner, C., Karanicolas, J., Golemis, E. A., Makhov, P., & Boumber, Y. (2023). Musashi-2 (MSI2) regulation of DNA damage response in lung cancer. *BioRxiv*, 2023.06.13.544756. https://doi.org/10.1101/2023.06.13.544756

Cai, H., Ke, Z.-B., Chen, J.-Y., Li, X.-D., Zhu, J.-M., Xue, Y., Ruan, Z., Wang, Z., Lin, F., Zheng, Q., Wei, Y., Xue, X., & Xu, N. (2024). Ubiquitin-specific protease 5 promotes bladder cancer progression through stabilizing Twist1. *Oncogene*. https://doi.org/10.1038/s41388-023-02936-8

Cai, Y., Zeng, R., Peng, J., Liu, W., He, Q., Xu, Z., & Bai, N. (2022). The downregulated drug-metabolism related ALDH6A1 serves as predictor for prognosis and therapeutic immune response in gastric cancer. *Aging (Albany NY)*, *14*, 7038–7051. https://doi.org/10.18632/aging.204270

Cao, J., Zhang, X., Xu, P., Wang, H., Wang, S., Zhang, L., Li, Z., Xie, L., Sun, G., Xia, Y., Lv, J., Yang, J., & Xu, Z. (2021). Circular RNA circLMO7 acts as a microRNA-30a-3p sponge to promote gastric cancer progression via the WNT2/β-catenin pathway. *Journal of Experimental & Clinical Cancer Research : CR*. https://doi.org/10.1186/s13046-020-01791-9

Carpenter, E., Brown, K., Donahue, K., Di Magliano, P., Anderson, M., Zhang, Y., Nwosu, Z., Vinta, A., Nevison, A., Lee, H.-J., Sirihorachai, V., Irizarry-Negron, V., Menjivar, R., Velez-Delgado, A., Lazarus, J., Crawford, H., Frankel, T., Yan, W., Bednar, F., … Kemp, S. (2020). Regulatory T cell depletion alters the tumor microenvironment and accelerates pancreatic carcinogenesis. *Cancer Discovery*. https://doi.org/10.1158/2159-8290.cd-19-0958

Cela, V., Malacarne, E., Obino, M., Marzi, I., Papini, F., Vergine, F., Pisacreta, E., Zappelli, E., Pietrobono, D., Scarfò, G., Daniele, S., Franzoni, F., Martini, C., & Artini, P. (2021). Exploring Epithelial–Mesenchymal Transition Signals in Endometriosis Diagnosis and In Vitro Fertilization Outcomes. *Biomedicines*, *9*. https://doi.org/10.3390/biomedicines9111681

Cha, Y.-L., Li, P.-D., Yuan, L., Zhang, M.-Y., Zhang, Y., Rao, H., Zhang, H., Zheng, X., & Wang, H. (2015). EIF4EBP1 Overexpression Is Associated with Poor Survival and Disease Progression in Patients with Hepatocellular Carcinoma. *PLoS ONE*, *10*. https://doi.org/10.1371/journal.pone.0117493

Chahine, J., Davis, S., Culfaci, S., Tuma, P., & Kallakury, B. (2024). Chromosome 8q24 amplification associated with human hepatocellular carcinoma predicts MYC/ZEB1/MIZ1 transcriptional regulation. *Scientific Reports*, *14*. https://doi.org/10.1038/s41598-024-75219-1

Chellini, L., Scarfò, M., Bonvissuto, D., Sette, C., & Paronetto, M. (2023). The DNA/RNA helicase DHX9 orchestrates the KDM2B-mediated transcriptional regulation of YAP1 in Ewing sarcoma. *Oncogene*. https://doi.org/10.1038/s41388-023-02894-1

Chen, H., Robledo, M., Rose, J., Adams, C., Jaskula-Sztul, R., Guenter, R., Chen, W., & Golivi, Y. (2024). Abstract 4387: Interplay of Notch1 and Notch3 signaling regulates pancreatic neuroendocrine tumor proliferation. *Cancer Research*. https://doi.org/10.1158/1538-7445.am2024-4387

Chen, J., Wan, R., Li, Q., Rao, Z., Wang, Y., Zhang, L., & Teichmann, A. (2021). Utilizing the Hippo pathway as a therapeutic target for combating endocrine-resistant breast cancer. *Cancer Cell International*, *21*. https://doi.org/10.1186/s12935-021-01999-5

Chen, J., Zhu, Y., Zhao, D., Zhang, L., Zhang, J., Xiao, Y., Wu, Q., Wang, Y., & Zhan, Q. (2023). Co-targeting FAK and Gli1 inhibits the tumor-associated macrophages-released CCL22-mediated esophageal squamous cell carcinoma malignancy. *MedComm*, *4*. https://doi.org/10.1002/mco2.381

Chen, K., Zhang, C., Qian, L., Chen, L., Fan, J., Wang, P., Qu, C., Chen, Z., Geng, Y., & Meng, Z. (2020). A Notch-Dependent Inflammatory Feedback Circuit between Macrophages and Cancer Cells Regulates Pancreatic Cancer Metastasis. *Cancer Research*, *81*, 64–76. https://doi.org/10.1158/0008-5472.CAN-20-0256

Chen, L., Wang, L., Qin, J., & Wei, D.-S. (2020). CtBP2 interacts with ZBTB18 to promote malignancy of glioblastoma. *Life Sciences*, 118477. https://doi.org/10.1016/j.lfs.2020.118477

Chen, M., Zhou, Y., Xu, H., Hill, C., Ewing, R., He, D., Zhang, X., & Wang, Y. (2020). Bioinformatic analysis reveals the importance of epithelial-mesenchymal transition in the development of endometriosis. *Scientific Reports*, *10*. https://doi.org/10.1038/s41598-020-65606-9

Chen, Q., Jia, G., Zhang, X., & Wenxue. (2024). Targeting HER3 to overcome EGFR TKI resistance in NSCLC. *Frontiers in Immunology*, *14*. https://doi.org/10.3389/fimmu.2023.1332057

Chen, T., Zhu, J., Cai, T., Du, W., Zhang, Y., Zhu, Q., Liu, Z., & Huang, J.-A. (2019). Suppression of non-small cell lung cancer migration and invasion by hsa-miR-486-5p via the TGF-β/SMAD2 signaling pathway. *Journal of Cancer*, *10*, 6014–6024. https://doi.org/10.7150/jca.35017

Chen, X., Zeng, K., Xu, M., Hu, X., Liu, X., Xu, T., He, B., Pan, Y.-Q., Sun, H., & Wang, S. (2018). SP1-induced lncRNA-ZFAS1 contributes to colorectal cancer progression via the miR-150-5p/VEGFA axis. *Cell Death & Disease*, *9*. https://doi.org/10.1038/s41419-018-0962-6

Chen, Y.-T., Huang, Z.-Y., Tang, H.-H., Kuo, W.-T., Wu, S.-Y., Lan, S., Chang, K., Lin, P.-L., Lee, M.-F., Cheng, H.-C., Liu, H., Huang, C.-Y., Huang, G., & Su, C. (2020). Pterostilbene Sensitizes Cisplatin-Resistant Human Bladder Cancer Cells with Oncogenic HRAS. *Cancers*, *12*. https://doi.org/10.3390/cancers12102869

Cheng, B., Zhao, Y., Zheng, M.-L., Chen, W., Liu, M., Peng, W., Wang, X., Wang, R.-H., Bai, S., & Li, Y. (2022). CD44v6+ Hepatocellular Carcinoma Cells Maintain Stemness Properties through Met/cJun/Nanog Signaling. *Stem Cells International*, *2022*. https://doi.org/10.1155/2022/5853707

Chi, G., Pei, J.-H., Li, X., & He, Y. (2021). IL-35 promotes EMT through STAT3 activation and induces MET by promoting M2 macrophage polarization in HCC. *Biochemical and Biophysical Research Communications*, *559*, 35–41. https://doi.org/10.1016/j.bbrc.2021.04.050

Chi, M., Liu, J., Mei, C., Shi, Y., Liu, N., Jiang, X., Liu, C., Xue, N., Hong, H., Xie, J., Sun, X., Yin, B.-K., Meng, X., & Wang, B. (2022). TEAD4 functions as a prognostic biomarker and triggers EMT via PI3K/AKT pathway in bladder cancer. *Journal of Experimental & Clinical Cancer Research : CR*, *41*. https://doi.org/10.1186/s13046-022-02377-3

Chimento, A., D'Amico, M., Pezzi, V., & De Amicis, F. (2022). Notch Signaling in Breast Tumor Microenvironment as Mediator of Drug Resistance. *International Journal of Molecular Sciences*, *23*. https://doi.org/10.3390/ijms23116296

Choe, C.-H., Kim, H., Min, S., Park, S., Seo, J., & Roh, S. (2018). SOX2, a stemness gene, induces progression of NSCLC A549 cells toward anchorage-independent growth and chemoresistance to vinblastine. *OncoTargets and Therapy*, *11*, 6197–6207. https://doi.org/10.2147/OTT.S175810

Choi, C., Kweon, S., Cho, S., Kim, H. Y., & Shin, M. (2020). Association between ALDH2 Polymorphism and Gastric Cancer Risk in a Korean Population. *Journal of Korean Medical Science*, *35*. https://doi.org/10.3346/jkms.2020.35.e148

Choi, Y. M., Kim, K. B., Lee, J. H., Chun, Y. K., An, I. S., An, S., & Bae, S. (2016). DBC2/RhoBTB2 functions as a tumor suppressor protein via Musashi-2 ubiquitination in breast cancer. *Oncogene 2017 36:20*, *36*(20), 2802–2812. https://doi.org/10.1038/onc.2016.441

Çömez, D., Kahraman, E., Atabey, N., Bağcı, G., Topel, H., Bagirsakci, E., Korhan, P., Yilmaz, Y., & Güneş, A. (2021). High glucose induced c-Met activation promotes aggressive phenotype and regulates expression of glucose metabolism genes in HCC cells. *Scientific Reports*, *11*. https://doi.org/10.1038/s41598-021-89765-5

Constam, D., Philipp, J., Malipiero, U., Dijke, P., Schachner, M., & Fontana, A. (1992). Differential expression of transforming growth factor-beta 1, -beta 2, and -beta 3 by glioblastoma cells, astrocytes, and microglia. *Journal of Immunology*, *148 5*, 1404–1410. https://doi.org/10.4049/jimmunol.148.5.1404

Cotellese, R., Selvaggi, F., Catalano, T., Aceto, G., & Esposito, D. (2023). Infectious Agents Induce Wnt/β-Catenin Pathway Deregulation in Primary Liver Cancers. *Microorganisms*, *11*. https://doi.org/10.3390/microorganisms11071632

Cui, D., Feng, Y., & Qian, R. (2021). Up-regulation of microRNA miR-101-3p enhances sensitivity to cisplatin via regulation of small interfering RNA (siRNA) Anti-human AGT4D and autophagy in non-small-cell lung carcinoma (NSCLC). *Bioengineered*, *12*, 8435–8446. https://doi.org/10.1080/21655979.2021.1982274

Da Silva, S. P., Santos, J., Silva, M. C., Da Costa, R. G., & Medeiros, R. (2020). Cancer cachexia and its pathophysiology: links with sarcopenia, anorexia and asthenia. *Journal of Cachexia, Sarcopenia and Muscle*, *11*, 619–635. https://doi.org/10.1002/jcsm.12528

Das, B., Pal, B., Bhuyan, R., Li, H., Sarma, A., Gayan, S., Talukdar, J., Sandhya, S., Bhuyan, S., Gogoi, G., Gouw, A., Baishya, D., Gotlib, J., Kataki, A., & Felsher, D. (2019). MYC regulates the HIF-2α stemness pathway via Nanog and Sox2 to maintain self-renewal in cancer stem cells versus non-stem cancer cells. *Cancer Research*. https://doi.org/10.1158/0008-5472.CAN-18-2847

Deng, J., Bai, X., Feng, X., Ni, J., Beretov, J., Graham, P., & Li, Y. (2019). Inhibition of PI3K/Akt/mTOR signaling pathway alleviates ovarian cancer chemoresistance through reversing epithelial-mesenchymal transition and decreasing cancer stem cell marker expression. *BMC Cancer*, *19*. https://doi.org/10.1186/s12885-019-5824-9

Deng, X., Sun, X., Hu, Z., Wu, Y., Zhou, C., Sun, J., Gao, X., & Huang, Y. (2023). Exploring the role of m6A methylation regulators in glioblastoma multiforme and their impact on the tumor immune microenvironment. *FASEB Journal*, *37*(9). https://doi.org/10.1096/FJ.202301343

DeVita, V. T., Lawrence, T. S., & Rosenberg, S. A. (2015). DeVita, Hellman, and Rosenberg's cancer . In *Principles & practice of oncology: Tenth edition* (pp. 1-2280 BT-DeVita, Hellman, and Rosenberg's Can). Wolters Kluwer Health Adis (ESP) . http://www.scopus.com/inward/record.url?scp=84976580788&partnerID=8YFLogxK

Ding, C., Shi, T., Wu, G., Man, J., Han, H., & Cui, Y. (2022). The anti-cancer role of microRNA-143 in papillary thyroid carcinoma by targeting high mobility group AT-hook 2. *Bioengineered*, *13*, 6629–6640. https://doi.org/10.1080/21655979.2022.2044277

Dixit, D., Prager, B., Gimple, R., Poh, H. X., Wang, Y., Wu, Q., Qiu, Z., Kidwell, R., Kim, L., Xie, Q., Vitting-Seerup, K., Bhargava, S., Dong, Z., Jiang, L., Zhu, Z., Hamerlik, P., Jaffrey, S., Zhao, J. C., Wang, X., & Rich, J. (2020). The RNA m6A reader YTHDF2 maintains oncogene expression and is a targetable dependency in glioblastoma stem cells. *Cancer Discovery*. https://doi.org/10.1158/2159-8290.CD-20-0331

Dong, C., Wu, J., Chen, Y., Nie, J., & Chen, C. (2021). Activation of PI3K/AKT/mTOR Pathway Causes Drug Resistance in Breast Cancer. *Frontiers in Pharmacology*, *12*. https://doi.org/10.3389/fphar.2021.628690

Dong, M., Zhou, L., Sheng, W., Shi, X., & Zhou, J. (2019). [Clinicopathological significance of ISYNA1 expression in pancreatic ductal adenocarcinoma]. *Zhonghua Wai Ke Za Zhi [Chinese Journal of Surgery]*, *57 3*, 206–211. https://doi.org/10.3760/cma.j.issn.0529-5815.2019.03.009

Dong, P., Xiong, Y., Hanley, S. J. B., Yue, J., & Watari, H. (2017). Musashi-2, a novel oncoprotein promoting cervical cancer cell growth and invasion, is negatively regulated by p53-induced miR-143 and miR-107 activation. *Journal of Experimental & Clinical Cancer Research : CR*, *36*(1), 150. https://doi.org/10.1186/s13046-017-0617-y

Dong, R.-F., Zhu, M.-L., Liu, M., Xu, Y.-T., Yuan, L.-L., Bian, J., Xia, Y., & Kong, L. (2021). .EGFR mutation mediates resistance to EGFR tyrosine kinase inhibitors in NSCLC: From molecular mechanisms to clinical research. *Pharmacological Research*, 105583. https://doi.org/10.1016/j.phrs.2021.105583

Dong, W., Liu, X., Yang, C., Wang, D., Xue, Y., Ruan, X., Zhang, M., Song, J., Cai, H., Zheng, J., & Liu, Y. (2021). Glioma glycolipid metabolism: MSI2–SNORD12B–FIP1L1–ZBTB4 feedback loop as a potential treatment target. *Clinical and Translational Medicine*, *11*(5), e411. https://doi.org/10.1002/CTM2.411

Du, M., Zhang, Y., Mao, Y., Mou, J., Zhao, J., Xue, Q., Wang, D.-L., Huang, J.-F., Gao, S., & Gao, Y. (2017). MiR-33a suppresses proliferation of NSCLC cells via targeting METTL3 mRNA. *Biochemical and Biophysical Research Communications*, *482 4*, 582–589. https://doi.org/10.1016/j.bbrc.2016.11.077

Elantary, M., El-Naggar, S., Elkomy, H., Ragab, M., Moustafa, S., Basyouni, O., El-Najjar, F., Gamal, D. El, Elsherbiny, A., & Ragab, E. (2025). New insights into Notch signaling as a crucial pathway of pancreatic cancer stem cell behavior by chrysin-polylactic acid-based nanocomposite. *Discover Oncology*, *16*. https://doi.org/10.1007/s12672-025-01846-3

El-Far, A., Lebda, M., Noreldin, A., Atta, M., Elewa, Y., Elfeky, M., & Mousa, S. (2020). Quercetin Attenuates Pancreatic and Renal D-Galactose-Induced Aging-Related Oxidative Alterations in Rats. *International Journal of Molecular Sciences*, *21*. https://doi.org/10.3390/ijms21124348

Ellis, H., & X., C. (2019). PI3K Inhibitors in Breast Cancer Therapy. *Current Oncology Reports*, *21*. https://doi.org/10.1007/s11912-019-0846-7

Evert, M., Chen, X., Calvisi, D., Xu, C., Zhang, Y., & Xu, Z. (2022). β-Catenin signaling in hepatocellular carcinoma. *The Journal of Clinical Investigation*, *132*. https://doi.org/10.1172/JCI154515

Fan, J., Yin, Y., Hu, B., & Peng, B. (2023). The mutational landscape of Chinese breast cancer by liquid biopsy. *Journal of Clinical Oncology*. https://doi.org/10.1200/jco.2023.41.16_suppl.e13117

Fan, L., Chen, Z., Wu, X., Cai, X., Feng, S., Lu, J., Wang, H., & Liu, N. (2019). Ubiquitin-Specific Protease 3 Promotes Glioblastoma Cell Invasion and Epithelial–Mesenchymal Transition via Stabilizing Snail. *Molecular Cancer Research*, *17*, 1975–1984. https://doi.org/10.1158/1541-7786.MCR-19-0197

Fang, T., Lv, H., Wu, F., Wang, C., Li, T., Lv, G., Tang, L., Guo, L., Tang, S., Cao, D., Wu, M., Yang, W., & Wang, H. (2017). Musashi 2 contributes to the stemness and chemoresistance of liver cancer stem cells via LIN28A activation. *Cancer Letters*, *384*, 50–59. https://doi.org/10.1016/j.canlet.2016.10.007

Fang, W., Huang, Y., Gu, W., Gan, J., Wang, W., Zhang, S., Wang, K., Zhan, J., Yang, Y., Huang, Y., Zhao, H., & Zhang, L. (2020). PI3K-AKT-mTOR pathway alterations in advanced NSCLC patients after progression on EGFR-TKI and clinical response to EGFR-TKI plus everolimus combination therapy. *Translational Lung Cancer Research*, *9*, 1258–1267. https://doi.org/10.21037/tlcr-20-141

Feng, Q., Nie, F., Gan, L.-H., Wei, X., Liu, P., Liu, H., Zhang, K., Fang, Z., Wang, H., & Fang, N. (2023). Tripartite motif 31 drives gastric cancer cell proliferation and invasion through activating the Wnt/β-catenin pathway by regulating Axin1 protein stability. *Scientific Reports*, *13*. https://doi.org/10.1038/s41598-023-47139-z

Fox, R. G., Lytle, N. K., Jaquish, D. V., Park, F. D., Ito, T., Bajaj, J., Koechlein, C. S., Zimdahl, B., Yano, M., Kopp, J. L., Kritzik, M., Sicklick, J. K., Sander, M., Grandgenett, P. M., Hollingsworth, M. A., Shibata, S., Pizzo, D., Valasek, M. A., Sasik, R., … Reya, T. (2016). Image-based detection and targeting of therapy resistance in pancreatic adenocarcinoma. *Nature 2016 534:7607*, *534*(7607), 407–411. https://doi.org/10.1038/nature17988

Fujita, K., & Nonomura, N. (2018). Role of Androgen Receptor in Prostate Cancer: A Review. *The World Journal of Men's Health*, *37*, 288–295. https://doi.org/10.5534/wjmh.180040

Fumarola, C., Bonelli, M., Petronini, P., & Alfieri, R. (2014). Targeting PI3K/AKT/mTOR pathway in non small cell lung cancer. *Biochemical Pharmacology*, *90 3*, 197–207. https://doi.org/10.1016/j.bcp.2014.05.011

Gajos-Michniewicz, A., & Czyż, M. (2023). WNT/β-catenin signaling in hepatocellular carcinoma: The aberrant activation, pathogenic roles, and therapeutic opportunities. *Genes & Diseases*, *11*, 727–746. https://doi.org/10.1016/j.gendis.2023.02.050

Gao, L., Schwartzman, J., Gibbs, A., Lisac, R., Kleinschmidt, R., Wilmot, B., Bottomly, D., Coleman, I., Nelson, P., McWeeney, S., & Alumkal, J. (2013). Androgen Receptor Promotes Ligand-Independent Prostate Cancer Progression through c-Myc Upregulation. *PLoS ONE*, *8*. https://doi.org/10.1371/journal.pone.0063563

Gao, M., Liu, L., Yang, Y., Li, M., Qingqing, & Chang, Z. (2021). LncRNA HCP5 Induces Gastric Cancer Cell Proliferation, Invasion, and EMT Processes Through the miR-186-5p/WNT5A Axis Under Hypoxia. *Frontiers in Cell and Developmental Biology*, *9*. https://doi.org/10.3389/fcell.2021.663654

Gao, W., Qi, C.-Q., Feng, M.-G., Yang, P., Liu, L., & Sun, S.-H. (2020). SOX2-induced upregulation of lncRNA LINC01561 promotes non-small-cell lung carcinoma progression by sponging miR-760 to modulate SHCBP1 expression. *Journal of Cellular Physiology*, *235*, 6684–6696. https://doi.org/10.1002/jcp.29564

García-Domínguez, D., Hajji, N., López-Alemany, R., Sánchez-Molina, S., Figuerola-Bou, E., Civanto, F. M., Rello-Varona, S., Andrés-León, E., Benito, A., Keun, H., Mora, J., Tirado, Ò., De Álava, E., & Hontecillas-Prieto, L. (2022). Selective histone methyltransferase G9a inhibition reduces metastatic development of Ewing sarcoma through the epigenetic regulation of NEU1. *Oncogene*, *41*, 2638–2650. https://doi.org/10.1038/s41388-022-02279-w

García-Domínguez, D., Hajji, N., Sánchez-Molina, S., Figuerola-Bou, E., De Pablos, R., Espinosa-Oliva, A., Andrés-León, E., Terrón-Camero, L., Flores-Campos, R., Pascual-Pasto, G., Robles, M., Machado, I., Llombart-Bosch, A., Magagnoli, G., Scotlandi, K., Carcaboso, A., Mora, J., De Álava, E., & Hontecillas-Prieto, L. (2021). Selective inhibition of HDAC6 regulates expression of the oncogenic driver EWSR1-FLI1 through the EWSR1 promoter in Ewing sarcoma. *Oncogene*, *40*, 5843–5853. https://doi.org/10.1038/s41388-021-01974-4

Gawlik-Rzemieniewska, N., & Bednarek, I. (2016). The role of NANOG transcriptional factor in the development of malignant phenotype of cancer cells. *Cancer Biology & Therapy*, *17*, 1–10. https://doi.org/10.1080/15384047.2015.1121348

Ge, C., Wu, S., Wang, W., Liu, Z., Zhang, J., Wang, Z., Li, R., Zhang, Z., Li, Z., Dong, S., Wang, Y., Xue, Y., Yang, J., Tan, Q., Wang, Z., & Song, X. (2015). miR-942 promotes cancer stem cell-like traits in esophageal squamous cell carcinoma through activation of Wnt/β-catenin signalling pathway. *Oncotarget*, *6*, 10964–10977. https://doi.org/10.18632/ONCOTARGET.3696

Gelatti, A., Drilon, A., & Santini, F. (2019). Optimizing the sequencing of tyrosine kinase inhibitors (TKIs) in epidermal growth factor receptor (EGFR) mutation-positive non-small cell lung cancer (NSCLC). *Lung Cancer*, *137*, 113–122. https://doi.org/10.1016/j.lungcan.2019.09.017

GLOBOCAN. (2022). *Cancer Today*. https://gco.iarc.fr/today/en/dataviz/bars?mode=cancer&group_populations=1&populations=904

Golden, B. O., Gonzalez, D., Yochum, G., Coulter, D., & Rizzino, A. (2024). SOX2 represses c-MYC transcription by altering the co-activator landscape of the c-MYC super-enhancer and promoter regions. *The Journal of Biological Chemistry*, *300*. https://doi.org/10.1016/j.jbc.2024.107642

Golestaneh, N., & Mishra, B. (2005). TGF-beta, neuronal stem cells and glioblastoma. *Oncogene*, *24 37*, 5722–5730. https://consensus.app/papers/tgfbeta-neuronal-stem-cells-and-glioblastoma-golestaneh-mishra/411bac12ceb654b5a7592cf5af726eee/

Gong, H., Xue, B., Ru, J., Pei, G., & Li, Y. (2023). Targeted Therapy for EWS-FLI1 in Ewing Sarcoma. *Cancers*, *15*. https://doi.org/10.3390/cancers15164035

Gu, J., Zhang, J., Huang, W., Tao, T., Huang, Y., Yang, L., Yang, J., Fan, Y., & Wang, H. (2020). Activating miRNA-mRNA network in gemcitabine-resistant pancreatic cancer cell associates with alteration of memory CD4+ T cells. *Annals of Translational Medicine*, *8*(6), 279–279. https://doi.org/10.21037/ATM.2020.03.53

Gulhane, P., Nimsarkar, P., Kharat, K., & Singh, S. (2022). Deciphering miR-520c-3p as a probable target for immunometabolism in non-small cell lung cancer using systems biology approach. *Oncotarget*, *13*, 725–746. https://doi.org/10.18632/oncotarget.28233

Guo, J., Liu, T., Su, M., & Yan, Q. (2021). miR-598 Represses Cell Migration and Invasion of Non-Small-Cell Lung Cancer by Inhibiting MSI2. *Journal of Nanomaterials*, *2021*(1), 9997806. https://doi.org/https://doi.org/10.1155/2021/9997806

Guo, K., Cui, J., Quan, M., Xie, D., Jia, Z., Wei, D., Wang, L., Gao, Y., Ma, Q., & Xie, K. (2017). The Novel KLF4/MSI2 Signaling Pathway Regulates Growth and Metastasis of Pancreatic Cancer. *Clinical Cancer Research : An Official Journal of the American Association for Cancer Research*, *23*(3), 687–696. https://doi.org/10.1158/1078-0432.CCR-16-1064

Guo, L., Ke, H., Zhang, H., Zou, L., Yang, Q., Lu, X., Zhao, L., & Jiao, B. (2022). TDP43 promotes stemness of breast cancer stem cells through CD44 variant splicing isoforms. *Cell Death & Disease*, *13*. https://doi.org/10.1038/s41419-022-04867-w

Guo, S., Chen, Q., Liang, J., Wu, H., Li, L., & Wang, Y. (2024). Correlation of Glycolysis-immune-related Genes in the Follicular Microenvironment of Endometriosis Patients with ART Outcomes. *Reproductive Sciences*. https://doi.org/10.1007/s43032-024-01518-7

Guo, X., Qin, M.-D., Hong, H., Xue, X., Fang, J., Jiang, L., Kuang, Y., & Gao, L. (2021). Circular RNA hsa_circ_0072309 inhibits the proliferation, invasion and migration of gastric cancer cells via inhibition of PI3K/AKT signaling by activating PPARγ/PTEN signaling. *Molecular Medicine Reports*, *23*. https://doi.org/10.3892/mmr.2021.11988

Guo, Y., Wang, G., Wang, Z., Ding, X., Qian, L., Li, Y., Ren, Z., Liu, P., Wenjing, Li, D., Li, Y., Zhao, Q., Lü, J., Li, Q., Wang, Q., & Yu, Z. (2021). Reck-Notch1 Signaling Mediates miR-221/222 Regulation of Lung Cancer Stem Cells in NSCLC. *Frontiers in Cell and Developmental Biology*, *9*. https://doi.org/10.3389/fcell.2021.663279

Ha, S., Ruoff, R., Kahoud, N., Franke, T., & Logan, S. (2011). Androgen receptor levels are upregulated by Akt in prostate cancer. *Endocrine-Related Cancer*, *18 2*, 245–255. https://doi.org/10.1530/ERC-10-0204

Han, J., Liu, Y., Yang, S., Wu, X., Li, H., & Wang, Q. (2021). MEK inhibitors for the treatment of non-small cell lung cancer. *Journal of Hematology & Oncology*, *14*. https://doi.org/10.1186/s13045-020-01025-7

Han, J., Shin, Y.-H., Kim, E., Park, H.-M., & Kim, J.-Y. (2025). Proteomic Characterization of NEDD4 Unveils Its Potential Novel Downstream Effectors in Gastric Cancer. *Journal of Proteome Research*. https://doi.org/10.1021/acs.jproteome.4c01109

Han, Y., Zhang, Y., Tian, Y., Zhang, M., Xiang, C., Zhen, Q., Liu, J.-B., Shang, Y., Zhao, Y., Si, H., & Sui, A. (2022). The Interaction of the IFNγ/JAK/STAT1 and JAK/STAT3 Signalling Pathways in EGFR-Mutated Lung Adenocarcinoma Cells. *Journal of Oncology*, *2022*. https://doi.org/10.1155/2022/9016296

Hao, Z., Wang, J., Lv, Y., Wu, W., Zhang, S., Hao, S., Chu, J., Wan, H., Feng, J., & Ji, N. (2024). Identification of MGMT promoter methylation as a specific lipid metabolism biomarker, reveals the feasibility of atorvastatin application in glioblastoma. *Metabolism: Clinical and Experimental*, 155794. https://doi.org/10.1016/j.metabol.2024.155794

Harrison, P., Vyse, S., & Huang, P. (2020). Rare epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer. *Seminars in Cancer Biology*, *61*, 167–179. https://doi.org/10.1016/j.semcancer.2019.09.015

Hashemi, M., Hasani, S., Hajimazdarany, S., Ghadyani, F., Olyaee, Y., Khodadadi, M., Ziyarani, M. F., Dehghanpour, A., Salehi, H., Kakavand, A., Goharrizi, M. A. S. B., Aref, A., Salimimoghadam, S., Akbari, M., Taheriazam, A., Hushmandi, K., & Entezari, M. (2023). Biological functions and molecular interactions of Wnt/β-catenin in breast cancer: Revisiting signaling networks. *International Journal of Biological Macromolecules*, 123377. https://doi.org/10.1016/j.ijbiomac.2023.123377

He, H., Lin, C., Lu, Y., & Wu, H. (2023). Knockdown of miR-24 Suppressed the Tumor Growth of Cervical Carcinoma Through Regulating PTEN/PI3K/AKT Signaling Pathway. *Biochemical Genetics*. https://doi.org/10.1007/s10528-023-10491-w

He, Q., Xue, S., Tan, Y., Zhang, L., Shao, Q., Xing, L., Li, Y., Xiang, T., Luo, X., & Ren, G. (2019). Dual inhibition of Akt and ERK signaling induces cell senescence in triple-negative breast cancer. *Cancer Letters*, *448*, 94–104. https://doi.org/10.1016/j.canlet.2019.02.004

He, S., & Tang, S. (2020). WNT/β-catenin signaling in the development of liver cancers. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *132*, 110851. https://doi.org/10.1016/j.biopha.2020.110851

Heavey, S., O'Byrne, K., & Gately, K. (2014). Strategies for co-targeting the PI3K/AKT/mTOR pathway in NSCLC. *Cancer Treatment Reviews*, *40 3*, 445–456. https://doi.org/10.1016/j.ctrv.2013.08.006

Heinlein, C., & Chang, C. (2004). Androgen receptor in prostate cancer. *Endocrine Reviews*, *25 2*, 276–308. https://doi.org/10.1210/ER.2002-0032

Herzog, H., Aktas, B., & Nel, I. (2022). Abstract P2-01-16: Targeted sequencing of plasma-derived vs. urinary cfDNA from patients with triple negative breast cancer. *Cancer Research*. https://doi.org/10.1158/1538-7445.sabcs21-p2-01-16

Hesla, A., Papakonstantinou, A., & Tsagkozis, P. (2021). Current Status of Management and Outcome for Patients with Ewing Sarcoma. *Cancers*, *13*. https://doi.org/10.3390/cancers13061202

Hope, K. J., Cellot, S., Ting, S. B., MacRae, T., Mayotte, N., Iscove, N. N., & Sauvageau, G. (2010). An RNAi screen identifies Msi2 and Prox1 as having opposite roles in the regulation of hematopoietic stem cell activity. *Cell Stem Cell*, *7*(1), 101–113. https://doi.org/10.1016/j.stem.2010.06.007

Hou, J., Huang, P., Lan, C., Geng, S., Xu, M., Liu, Y., Chang, H., Wang, Z., Gu, H., Wang, Y., Yang, G., & Cui, H. (2022). ZC3H15 promotes gastric cancer progression by targeting the FBXW7/c-Myc pathway. *Cell Death Discovery*, *8*. https://doi.org/10.1038/s41420-022-00815-x

Hsu, P.-C., Jablons, D., Yang, C.-T., & You, L. (2019). Epidermal Growth Factor Receptor (EGFR) Pathway, Yes-Associated Protein (YAP) and the Regulation of Programmed Death-Ligand 1 (PD-L1) in Non-Small Cell Lung Cancer (NSCLC). *International Journal of Molecular Sciences*, *20*. https://doi.org/10.3390/ijms20153821

Hu, G., Liu, H., Wang, M., & Peng, W. (2019). IQ Motif Containing GTPase-Activating Protein 3 (IQGAP3) Inhibits Kaempferol-Induced Apoptosis in Breast Cancer Cells by Extracellular Signal-Regulated Kinases 1/2 (ERK1/2)

Signaling Activation. *Medical Science Monitor : International Medical Journal of Experimental and Clinical Research*, *25*, 7666–7674. https://doi.org/10.12659/MSM.915642

Hu, L., Cao, H., Zheng, L., & Li, R. (2023). BBOX1-AS1 Activates Hedgehog Signaling Pathway to Facilitate the Proliferation and Stemness of Esophageal Squamous Cell Carcinoma Cells via miR-506-5p/EIF5A/PTCH1 Axis. *Current Molecular Pharmacology*. https://doi.org/10.2174/1874467216666230130132927

Hu, Y., Zhang, Y., Ding, M., & Xu, R. (2025). HOXA10-AS Enhances Gastric Cancer Cell Proliferation, Migration, and Invasion via the p38 MAPK/STAT3 Signaling Pathway. *Journal of Biochemical and Molecular Toxicology*, *39 3*. https://doi.org/10.1002/jbt.70187

Hu, Y.-D., Yu, K.-K., Wang, G., Zhang, D.-P., Shi, C., Ding, Y.-H., Hong, D., Zhang, D., He, H.-Q., Sun, L., Zheng, J.-N., Sun, S., & Qian, F. (2018). Lanatoside C inhibits cell proliferation and induces apoptosis through attenuating Wnt/&bgr;-catenin/c-Myc signaling pathway in human gastric cancer cell. *Biochemical Pharmacology*, *150*, 280. https://doi.org/10.1016/j.bcp.2018.02.023

Huang, C. (2025). Abstract 5123: Up-regulation of KRT14 promotes EMT in basal muscle-invasive bladder cancer through IGF2BP1/FTO dependence on methyladenosine-modified SNAI1. *Cancer Research*. https://doi.org/10.1158/1538-7445.am2025-5123

Huang, H., Jin, H., Lei, R., He, Z., He, S., Chen, J., Saw, P., Qiu, Z., Ren, G., & Nie, Y. (2024). lncRNA-WAL Promotes Triple-Negative Breast Cancer Aggression by Inducing β-Catenin Nuclear Translocation. *Molecular Cancer Research*, *22*, 1036–1050. https://doi.org/10.1158/1541-7786.MCR-23-0334

Huang, J., Zhou, W., Hao, C., He, Q.-M., & Tu, X. (2022). The feedback loop of METTL14 and USP38 regulates cell migration, invasion and EMT as well as metastasis in bladder cancer. *PLOS Genetics*, *18*. https://doi.org/10.1371/journal.pgen.1010366

Huang, L., Sun, J., Ma, Y., Chen, H., Tian, C., & Dong, M. (2024). MSI2 regulates NLK-mediated EMT and PI3K/AKT/mTOR pathway to promote pancreatic cancer progression. *Cancer Cell International*, *24*(1), 1–11. https://doi.org/10.1186/S12935-024-03444-9/FIGURES/5

Huang, S., Cui, M., Wang, R., Yang, G., Wang, N., Cui, L., & Guangwei. (2023). Combined treatment with Prunella vulgaris and Radix bupleuri activated the Bax/Bcl-2 and Caspase-3 signal pathways in papillary thyroid carcinoma cells. *Nucleosides, Nucleotides & Nucleic Acids*, *42*, 731–742. https://doi.org/10.1080/15257770.2023.2189464

Hughes, C., Fields, K., Danis, E., Hsu, J., Neelakantan, D., Vincent, M., Gustafson, A., Oliphant, M., Sreekanth, V., Zaberezhnyy, V., Costello, J., Jedlicka, P., & Ford, H. (2023). SIX1 and EWS/FLI1 co-regulate an anti-metastatic gene network in Ewing Sarcoma. *Nature Communications*, *14*. https://doi.org/10.1038/s41467-023-39945-w

Hui, K., Yang, M., Rangappa, K., Jung, S., Ahn, K., Chinnathambi, A., Alharbi, S., Sethi, G., Mohan, C., Ko, H., & Deivasigamani, A. (2022). Procaine Abrogates the Epithelial-Mesenchymal Transition Process through Modulating c-Met Phosphorylation in Hepatocellular Carcinoma. *Cancers*, *14*. https://doi.org/10.3390/cancers14204978

Ikeda, S., Okamoto, T., Okano, S., Umemoto, Y., Tagawa, T., Morodomi, Y., Kohno, M., Shimamatsu, S., Kitahara, H., Suzuki, Y., Fujishita, T., & Maehara, Y. (2016). PD-L1 Is Upregulated by Simultaneous Amplification of the PD-L1 and JAK2 Genes in Non–Small Cell Lung Cancer. *Journal of Thoracic Oncology*, *11*, 62. https://doi.org/10.1016/j.jtho.2015.09.010

Ilhan, M., Kucukkose, C., Efe, E., Gunyuz, Z. E., Firatligil, B., Dogan, H., Ozuysal, M., & Yalcin-Ozuysal, O. (2020). Pro-metastatic functions of Notch signaling is mediated by CYR61 in breast cells. *European Journal of Cell Biology*, 151070. https://doi.org/10.1016/j.ejcb.2020.151070

Inada, A., Yasunami, Y., Yoshiki, A., Nabeshima, Y., & Inada, O. (2023). Greb1 Transiently Accelerates Pancreatic β-Cell Proliferation in Diabetic Mice Exposed to Estradiol. *The American Journal of Pathology*, *193 8*, 1081–1100. https://doi.org/10.1016/j.ajpath.2023.04.012

Ippen, F., Grosch, J., Subramanian, M., Kuter, B., Liederer, B., Plise, E., Mora, J., Nayyar, N., Schmidt, S., Giobbie-Hurder, A., Martinez-Lage, M., Carter, S., Cahill, D., Wakimoto, H., & Brastianos, P. (2019). Targeting the PI3K/Akt/mTOR-pathway with the pan-Akt inhibitor GDC-0068 in PIK3CA-mutant breast cancer brain metastases. *Neuro-Oncology*. https://doi.org/10.1093/neuonc/noz105

Issaq, S., Mendoza, A., Kidner, R., Rosales, T., Duveau, D., Heske, C., Rohde, J., Boxer, M., Thomas, C., Deberardinis, R., & Helman, L. (2020). EWS-FLI1–regulated Serine Synthesis and Exogenous Serine are Necessary for Ewing Sarcoma Cellular Proliferation and Tumor Growth. *Molecular Cancer Therapeutics*, *19*, 1520–1529. https://doi.org/10.1158/1535-7163.MCT-19-0748

Ito, T., Kwon, H. Y., Zimdahl, B., Congdon, K. L., Blum, J., Lento, W. E., Zhao, C., Lagoo, A., Gerrard, G., Foroni, L., Goldman, J., Goh, H., Kim, S.-H., Kim, D.-W., Chuah, C., Oehler, V. G., Radich, J. P., Jordan, C. T., & Reya, T. (2010). Regulation of myeloid leukaemia by the cell-fate determinant Musashi. *Nature*, *466*(7307), 765–768. https://doi.org/10.1038/nature09171

Jadhao, M., Hsu, S.-K., Deshmukh, D., Liu, P.-F., Weng, S.-F., Chen, Y.-F., Li, C.-Y., Wang, C.-Y., Tsai, E.-M., Wang, L.-F., & Chiu, C.-C. (2025). Prolonged DEHP exposure enhances the stemness and metastatic potential of TNBC cells in an MSI2-dependent manner. *International Journal of Biological Sciences*, *21*(4), 1705–1729. https://doi.org/10.7150/ijbs.101598

Jain, T., Iyer, S., Ferrantella, A., Vaish, U., Sharma, P., & Dudeja, V. (2022). Abstract B038: Toll like receptor 4 (TLR4) agonism by lipopolysaccharide (LPS) in pancreatic cancer model stimulates anti-tumor immunity in CD4+T cell dependent fashion. *Cancer Research*. https://doi.org/10.1158/1538-7445.panca22-b038

Jayachandran, A., Bridle, K., Shrestha, R., & Crawford, D. (2020). TNF-α-mediated epithelial-to-mesenchymal transition regulates expression of immune checkpoint molecules in hepatocellular carcinoma. *Molecular Medicine Reports*, *21*, 1849–1860. https://doi.org/10.3892/mmr.2020.10991

Jeong, J.-H., Park, S.-H., Kim, H., Nam, H., Kim, S.-H., Jeong, M., Kong, M.-J., Son, J., Jeong, J., Song, J.-H., Kim, S. W., & Choi, K.-C. (2023). ZBTB7A suppresses glioblastoma tumorigenesis through the transcriptional repression of EPB41L5. *Experimental & Molecular Medicine*, *55*, 43–54. https://doi.org/10.1038/s12276-022-00908-8

Jiang, K., Sun, C., Liu, Y., Huang, S., Wang, C., Qin, X., Sun, L., Gao, D., Li, Y., Zhang, S., & Kang, X. (2013). NANOG promotes liver cancer cell invasion by inducing epithelial-mesenchymal transition through NODAL/SMAD3 signaling pathway. *The International Journal of Biochemistry & Cell Biology*, *45 6*, 1099–1108. https://doi.org/10.1016/j.biocel.2013.02.017

Jiang, L., Xue, S., Xu, J., Fu, X., Wei, J., & Zhang, C. (2022). Prognostic value of Musashi 2 (MSI2) in cancer patients: A systematic review and meta-analysis. In *Frontiers in oncology* (Vol. 12, p. 969632). https://doi.org/10.3389/fonc.2022.969632

Jiang, X., Tan, J., Wen, Y., Liu, W., Wu, S., Wang, L., Wangou, S., Liu, D., Du, C., Zhu, B., Xie, D., & Ren, C. (2019). MSI2-TGF-β/TGF-β R1/SMAD3 positive feedback regulation in glioblastoma. *Cancer Chemotherapy and Pharmacology*, *84*(2), 415–425. https://doi.org/10.1007/S00280-019-03892-5/METRICS

Jiang, X., Zhang, H., Liu, Y., Wang, G., Weijie, Yao, Y., Gao, M., Chen, X., Xia, P., Xu, K., Yuan, Y., & Zhang, Z. (2021). MYC-targeted WDR4 promotes proliferation, metastasis, and sorafenib resistance by inducing CCNB1 translation in hepatocellular carcinoma. *Cell Death & Disease*, *12*. https://doi.org/10.1038/s41419-021-03973-5

Jin, W., Liu, J., Yang, J., Feng, Z., Feng, Z., Huang, N., Yang, T., & Yu, L. (2022). Identification of a key ceRNA network associated with ferroptosis in gastric cancer. *Scientific Reports*, *12*. https://doi.org/10.1038/s41598-022-24402-3

Kaira, K., Imai, H., Kawasaki, T., Hashimoto, K., Miura, Y., Shiono, A., Yamaguchi, O., Mouri, A., Kobayashi, K., Yasuda, M., & Kagamu, H. (2022). Potential of VEGFR2 expression as a predictive marker of PD-1 blockade in patients with advanced NSCLC. *Oncology Reports*, *48*. https://doi.org/10.3892/or.2022.8429

Kang, J., Lee, S.-H., Hong, D., Lee, J.-S., Ahn, H.-S., Ahn, J.-H., Seong, T. W., Lee, C.-H., Jang, H., Hong, K.-M., Lee, C., Lee, J.-H., & Kim, S. (2016). Aldehyde dehydrogenase is used by cancer cells for energy metabolism. *Experimental & Molecular Medicine*, *48*. https://doi.org/10.1038/emm.2016.103

Kang, S., Shin, C., Sung, J., & Kim, N. (2020). Association between ALDH2 Polymorphism and Gastric Cancer Risk in Terms of Alcohol Consumption: A Meta-Analysis. *Alcoholism, Clinical and Experimental Research*. https://doi.org/10.1111/acer.14508

Kathagen-Buhmann, A., Schulte, A., Weller, J., Holz, M., Herold-Mende, C., Glass, R., & Lamszus, K. (2015). Glycolysis and the pentose phosphate pathway are differentially associated with the dichotomous regulation of glioblastoma cell migration versus proliferation. *Neuro-Oncology*, *18 9*, 1219–1229. https://doi.org/10.1093/neuonc/now024

Katoh, M., & Katoh, M. (2019). Precision medicine for human cancers with Notch signaling dysregulation (Review). *International Journal of Molecular Medicine*, *45*, 279–297. https://doi.org/10.3892/ijmm.2019.4418

Kaurich, Q., Huang, J., & Awasthi, N. (2023). Enhancing nanoparticle paclitaxel antitumor response through targeted inhibition of c-Met pathway by merestinib in gastric cancer models. *Journal of Clinical Oncology*. https://doi.org/10.1200/jco.2023.41.4_suppl.372

Kawakami, R., Mashima, T., Kawata, N., Kumagai, K., Migita, T., Sano, T., Mizunuma, N., Yamaguchi, K., & Seimiya, H. (2020). ALDH1A3-mTOR axis as a therapeutic target for anticancer drug-tolerant persister cells in gastric cancer. *Cancer Science*, *111*, 962–973. https://doi.org/10.1111/cas.14316

Kern, K., Rangelova, E., Gorchs, L., Moro, F., Bankhead, P., Meng, Q., Sadeak, I., & Kaipe, H. (2019). Human Pancreatic Carcinoma-Associated Fibroblasts Promote Expression of Co-inhibitory Markers on CD4+ and CD8+ T-Cells. *Frontiers in Immunology*, *10*. https://doi.org/10.3389/fimmu.2019.00847

Khan, M., Jain, V., Rizwanullah, Md., Ahmad, J., & Jain, K. (2019). PI3K/AKT/mTOR pathway inhibitors in triple-negative breast cancer: a review on drug discovery and future challenges. *Drug Discovery Today*. https://doi.org/10.1016/j.drudis.2019.09.001

Khanna, A., Böckelman, C., Hemmes, A., Junttila, M., Wiksten, J., Lundin, M., Junnila, S., Murphy, D., Evan, G., Haglund, C., Westermarck, J., & Ristimäki, A. (2009). MYC-dependent regulation and prognostic role of CIP2A in gastric cancer. *Journal of the National Cancer Institute*, *101 11*, 793–805. https://doi.org/10.1093/jnci/djp103

Kharin, L., Bychkov, I., Karnaukhov, N., Voloshin, M., Fazliyeva, R., Deneka, A., Frantsiyants, E., Kit, O., Golemis, E., & Boumber, Y. (2021). Prognostic role and biologic features of Musashi-2 expression in colon polyps and during colorectal cancer progression. *PLOS ONE*, *16*(7), e0252132. https://doi.org/10.1371/JOURNAL.PONE.0252132

Khurram, I., Khan, M. U., Ibrahim, S., Saleem, A., Khan, Z., Mubeen, M., Khawar, A., & Ali, Q. (2023). Efficacy of cell-free DNA as a diagnostic biomarker in breast cancer patients. *Scientific Reports*, *13*. https://doi.org/10.1038/s41598-023-42726-6

Kim, E., Rahmawati, L., Aziz, N., Kim, H., Kim, J. H., Kim, K.-H., Yoo, B., Parameswaran, N., Kang, J.-S., Hur, H., Manavalan, B., Lee, J., & Cho, J. Y. (2023). Protection of c-Fos from autophagic degradation by PRMT1-mediated methylation fosters gastric tumorigenesis. *International Journal of Biological Sciences*, *19*, 3640–3660. https://doi.org/10.7150/ijbs.85126

Kim, H. S., Na, M. J., Son, K. H., Yang, H. D., Kim, S. Y., Shin, E., Ha, J. W., Jeon, S., Kang, K., Moon, K., Park, W. S., & Nam, S. W. (2023). ADAR1-dependent miR-3144-3p editing simultaneously induces MSI2 expression and suppresses SLC38A4 expression in liver cancer. *Experimental & Molecular Medicine 2022 55:1*, *55*(1), 95–107. https://doi.org/10.1038/s12276-022-00916-8

Kim, J. S., Keum, J. Y., Park, C. H., & Bang, S. (2024). Abstract 5876: ALDH3A1 as a predictive marker for gemcitabine treatment in pancreatic cancer. *Cancer Research*. https://doi.org/10.1158/1538-7445.am2024-5876

Knebel, F., Bettoni, F., Shimada, A., Cruz, M., Alessi, J., Negrão, M., Reis, L., Katz, A., & Camargo, A. (2017). Sequential liquid biopsies reveal dynamic alterations of EGFR driver mutations and indicate EGFR amplification as a new mechanism of resistance to osimertinib in NSCLC. *Lung Cancer*, *108*, 238–241. https://doi.org/10.1016/j.lungcan.2017.04.004

Knoblock, D., Liu, A., Beatty, G., McAllister, F., & Bengsch, F. (2017). CTLA-4/CD80 pathway regulates T cell infiltration into pancreatic cancer. *Cancer Immunology, Immunotherapy*, *66*, 1609–1617. https://doi.org/10.1007/s00262-017-2053-4

Kóbori, L., Gurzu, S., Jung, I., & Fodor, D. (2019). Epithelial Mesenchymal and Endothelial Mesenchymal Transitions in Hepatocellular Carcinoma: A Review. *BioMed Research International*, *2019*. https://doi.org/10.1155/2019/2962580

Koistinen, H., Künnapuu, J., & Jeltsch, M. (2021). KLK3 in the Regulation of Angiogenesis—Tumorigenic or Not? *International Journal of Molecular Sciences*, *22*. https://doi.org/10.3390/ijms222413545

Konrad, L., Dietze, R., Riaz, M., Scheiner-Bobis, G., Behnke, J., Horné, F., Hoerscher, A., Reising, C., & Meinhold-Heerlein, I. (2020). Epithelial–Mesenchymal Transition in Endometriosis—When Does It Happen? *Journal of Clinical Medicine*, *9*. https://doi.org/10.3390/jcm9061915

Koppenhafer, S., Goss, K., Voigt, E., Croushore, E., Terry, W., Ostergaard, J., Gordon, P., & Gordon, D. (2022). Inhibitor of DNA Binding 2 (ID2) Regulates the Expression of Developmental Genes and Tumorigenesis in Ewing Sarcoma. *Oncogene*, *41*, 2873–2884. https://doi.org/10.1038/s41388-022-02310-0

Korkut, A., Zaidi, S., Kanchi, R., Rao, S., Gough, N., Schultz, A., Li, X., Lorenzi, P., Berger, A., Robertson, G., Kwong, L., Datto, M., Roszik, J., Ling, S., Ravikumar, V., Manyam, G., Rao, A., Shelley, S., Liu, Y., … Akbani, R. (2018). A Pan-Cancer Analysis Reveals High-Frequency Genetic Alterations in Mediators of Signaling by the TGF-β Superfamily. *Cell Systems*, *7 4*, 422–437. https://doi.org/10.1016/j.cels.2018.08.010

Koudelková, P., Dituri, F., Mikulits, W., & Giannelli, G. (2016). Role of epithelial to mesenchymal transition in hepatocellular carcinoma. *Journal of Hepatology*, *65 4*, 798–808. https://doi.org/10.1016/j.jhep.2016.05.007

Koukourakis, M., Tsolou, A., Pouliliou, S., Lamprou, I., Papadopoulou, M., Ilemosoglou, M., Kostoglou, G., Ananiadou, D., Sivridis, E., & Giatromanolaki, A. (2017). Blocking LDHA glycolytic pathway sensitizes glioblastoma cells to radiation and temozolomide. *Biochemical and Biophysical Research Communications*, *491 4*, 932–938. https://doi.org/10.1016/j.bbrc.2017.07.138

Koushyar, S., Powell, A., Vincan, E., & Phesse, T. (2020). Targeting Wnt Signaling for the Treatment of Gastric Cancer. *International Journal of Molecular Sciences*, *21*. https://doi.org/10.3390/ijms21113927

Krishna, B., Jana, S., Singhal, J., Horne, D., Awasthi, S., Salgia, R., & Singhal, S. (2019). Notch Signaling in Breast Cancer: From Pathway Analysis to Therapy. *Cancer Letters*. https://doi.org/10.1016/j.canlet.2019.07.012

Kristensen, L. S., Michaelsen, S. R., Dyrbye, H., Aslan, D., Grunnet, K., Christensen, I. J., A1 Poulsen, Hans S. Grønbæk, K., & Broholm, H. (2016). Assessment of Quantitative and Allelic MGMT Methylation Patterns as a Prognostic Marker in Glioblastoma. In *Journal of Neuropathology and Experimental Neurology* (Vol. 75, pp. 246–255). https://doi.org/10.1093/jnen/nlv024

Krutsenko, Y., Monga, S., & Singhi, A. (2021). β-Catenin Activation in Hepatocellular Cancer: Implications in Biology and Therapy. *Cancers*, *13*. https://doi.org/10.3390/cancers13081830

Kucuksayan, H., Akgun, S., Ozes, O., Alikanoğlu, A., Yıldız, M., Dal, E., & Akça, H. (2018). TGF-β-SMAD-miR-520e axis regulates NSCLC metastasis through a TGFBR2-mediated negative feedback loop. *Carcinogenesis*. https://doi.org/10.1093/carcin/bgy166

Kudinov, A. E., Deneka, A., Nikonova, A. S., Beck, T. N., Ahn, Y. H., Liu, X., Martinez, C. F., Schultz, F. A., Reynolds, S., Yang, D. H., Cai, K. Q., Yaghmour, K. M., Baker, K. A., Egleston, B. L., Nicolas, E., Chikwem, A., Andrianov, G., Singh, S., Borghaei, H., … Boumber, Y. (2016). Musashi-2 (MSI2) supports TGF-β signaling and inhibits claudins to promote non-small cell lung cancer (NSCLC) metastasis. *Proceedings of the National Academy of Sciences of the United States of America*, *113*(25), 6955–6960. https://doi.org/10.1073/PNAS.1513616113/SUPPL_FILE/PNAS.1513616113.SAPP.PDF

Kudinov, A. E., Karanicolas, J., Golemis, E. A., & Boumber, Y. (2017). Musashi RNA-Binding Proteins as Cancer Drivers and Novel Therapeutic Targets. *Clinical Cancer Research : An Official Journal of the American Association for Cancer Research*, *23*(9), 2143–2153. https://doi.org/10.1158/1078-0432.CCR-16-2728

Kumar, M., Allison, D., Baranova, N., Wamsley, J., Katz, A., Bekiranov, S., Jones, D., & Mayo, M. (2013). NF-κB Regulates Mesenchymal Transition for the Induction of Non-Small Cell Lung Cancer Initiating Cells. *PLoS ONE*, *8*. https://doi.org/10.1371/journal.pone.0068597

Kyriazoglou, A., Liontos, M., Zakopoulou, R., Kaparelou, M., Tsiara, A., Papatheodoridi, A., Georgakopoulou, R., & Zagouri, F. (2020). The Role of the Hippo Pathway in Breast Cancer Carcinogenesis, Prognosis, and Treatment: A Systematic Review. *Breast Care*, *16*, 6–15. https://doi.org/10.1159/000507538

Landeros, N., Santoro, P., Carrasco-Avino, G., & Corvalán, A. (2020). Competing Endogenous RNA Networks in the Epithelial to Mesenchymal Transition in Diffuse-Type of Gastric Cancer. *Cancers*, *12*. https://doi.org/10.3390/cancers12102741

Law, M. (2022). Cancer cachexia: Pathophysiology and association with cancer-related pain. *Frontiers in Pain Research*, *3*. https://doi.org/10.3389/fpain.2022.971295

Lee, J., An, S., Choi, Y. M., Lee, J., Ahn, K. J., Lee, J. H., Kim, T. J., An, I. S., & Bae, S. (2016). Musashi-2 is a novel regulator of paclitaxel sensitivity in ovarian cancer cells. *International Journal of Oncology*, *49*(5), 1945–1952. https://doi.org/10.3892/IJO.2016.3683/HTML

Lee, J. H., Park, S.-A., Park, I., Yoon, B. K., Lee, J.-S., & Lee, J. M. (2023). Stem Cell Properties of Gastric Cancer Stem-Like Cells under Stress Conditions Are Regulated via the c-Fos/UCH-L3/β-Catenin Axis. *Molecules and Cells*, *46*, 476–485. https://doi.org/10.14348/molcells.2023.0011

Levy, L., & Hill, C. (2006). Alterations in components of the TGF-beta superfamily signaling pathways in human cancer. *Cytokine & Growth Factor Reviews*, *17 1-2*, 41–58. https://doi.org/10.1016/J.CYTOGFR.2005.09.009

Li, D., Cao, Y., Luo, C.-W., Zhang, L.-P., & Zou, Y.-B. (2023). The Clinical Significance and Prognostic Value of ALDH1 Expression in Non-small Cell Lung Cancer: A Systematic Review and Meta-analysis. *Recent Patents on Anti-Cancer Drug Discovery*. https://doi.org/10.2174/0115748928265992230925053308

Li, G., Shi, H., Zhang, P., Li, X., Lan, W., Li, L., Chung, D., & Schaab, K. (2023). Abstract C145: ANS014004, a novel small-molecule type II c-Met inhibitor effectively overcomes clinical-resistance MET mutations and exhibits antitumor activity in preclinical models of MET-amplified non-small cell lung cancer (NSCLC) and gastric cancer. *Molecular Cancer Therapeutics*. https://doi.org/10.1158/1535-7163.targ-23-c145

Li, H., Huang, F., Liu, X., Liu, H., Dai, M., & Zeng, J. (2021). LncRNA TUG1 promotes Ewing's sarcoma cell proliferation, migration, and invasion via the miR-199a-3p-MSI2 signaling pathway. *Neoplasma*. https://doi.org/10.4149/neo_2021_201110N1198

Li, H., Meng, X., You, X., Zhou, W., Ouyang, W., Pu, X., Zhao, R., & Tang, H. (2022). Increased expression of the RNA-binding protein Musashi-2 is associated with immune infiltration and predicts better outcomes in ccRCC patients. *Frontiers in Oncology*, *12*, 949705. https://doi.org/10.3389/fonc.2022.949705

Li, L., Chen, S., Cai, K., Liu, Y., Yu, C., Zheng, D., He, Z., & Sun, C. (2022). RHBDL2 promotes the proliferation, migration, and invasion of pancreatic cancer by stabilizing the N1ICD via the OTUD7B and activating the Notch signaling pathway. *Cell Death & Disease*, *13*. https://doi.org/10.1038/s41419-022-05379-3

Li, M., & Chen, C. (2022). Regulation of Metastasis in Ewing Sarcoma. *Cancers*, *14*. https://doi.org/10.3390/cancers14194902

Li, M., Li, A. Q., Zhou, S. L., Lv, H., Wei, P., & Yang, W. T. (2020). RNA-binding protein MSI2 isoforms expression and regulation in progression of triple-negative breast cancer. *Journal of Experimental and Clinical Cancer Research*, *39*(1), 1–18. https://doi.org/10.1186/S13046-020-01587-X/FIGURES/8

Li, M., Zheng, R., & Yuan, F. (2018). MiR-410 affects the proliferation and apoptosis of lung cancer A549 cells through regulation of SOCS3/JAK-STAT signaling pathway. *European Review for Medical and Pharmacological Sciences*, *22 18*, 5987–5993. https://doi.org/10.26355/eurrev_201809_15933

Li, N., Yousefi, M., Nakauka-Ddamba, A., Li, F., Vandivier, L., Parada, K., Woo, D. H., Wang, S., Naqvi, A. S., Rao, S., Tobias, J., Cedeno, R. J., Minuesa, G., Y, K., Barlowe, T. S., Valvezan, A., Shankar, S., Deering, R. P., Klein, P. S., … Lengner, C. J. (2015). The Msi Family of RNA-Binding Proteins Function Redundantly as Intestinal Oncoproteins. *Cell Reports*, *13*(11), 2440–2455. https://doi.org/10.1016/J.CELREP.2015.11.022/ATTACHMENT/65C5D6F1-D7FD-4965-AED9-A4345E0C34F0/MMC8.PDF

Li, N., Yu, Y., & Wang, B. (2020). *Downregulation of AAA-domain-containing protein 2 restrains cancer stem cell properties in esophageal squamous cell carcinoma via blockade of the Hedgehog signaling pathway*. https://consensus.app/papers/downregulation-of-aaadomaincontaining-protein-2-li-yu/d943ae8c0aaf5eb0af89376a25954292/

Li, P., Richard, H., Zhu, K., Li, L., & Huang, S. (2022). The Roles and Regulation of m6A Modification in Glioblastoma Stem Cells and Tumorigenesis. *Biomedicines*, *10*. https://doi.org/10.3390/biomedicines10050969

Li, Q., Hao, Q., Cao, W., Li, J., Wu, K., Elshimali, Y., Zhu, D., Chen, Q.-H., Chen, G., Pollack, J., Vadgama, J., & Wu, Y. (2019). PP2Cδ inhibits p300-mediated p53 acetylation via ATM/BRCA1 pathway to impede DNA damage response in breast cancer. *Science Advances*, *5*. https://doi.org/10.1126/sciadv.aaw8417

Li, Q., Qiu, Q., Zhang, L., Zhang, X., Wang, Y., Geng, Z., Ge, S., Zuo, L., Song, X., Li, J., & Hu, J. (2022). [ALDH3B1 expression is correlated with histopathology and long-term prognosis of gastric cancer]. *Nan Fang Yi Ke Da Xue Xue Bao = Journal of Southern Medical University*, *42 5*, 633–640. https://doi.org/10.12122/j.issn.1673-4254.2022.05.02

Li, X., Liu, C.-Z., Zhao, X., Wang, R., Gu, N., Shen, H., Li, X., Wang, L., & Li, C. (2020). Effects of CDK6 regulated by miR-298 on proliferation and apoptosis of thyroid cancer cells. *Oncology Letters*, *19*, 2909–2915. https://doi.org/10.3892/ol.2020.11398

Li, X., Shen, W., Zhang, L., Zhao, S., Wang, B., Zhang, S., & Li, Q. (2019). Downregulation of long noncoding RNA CASC15 inhibits progression, migration and invasion of papillary thyroid cancer. *Archives of Medical Science : AMS*, *19*, 1869–1878. https://doi.org/10.5114/aoms.2019.89982

Li, X., Xiong, H., Mou, X., Huang, C., Thomas, E. R., Yu, W., Jiang, Y., & Chen, Y. (2024). Androgen receptor cofactors: A potential role in understanding prostate cancer. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *173*, 116338. https://doi.org/10.1016/j.biopha.2024.116338

Li, X., Zhang, M., Wang, Y., & Xie, F. (2017). The research advances on mechanisms underlying endometriosis-associated hyperalgesia. *International Journal of Anesthesiology and Resuscitation*, *38*, 171–174. https://doi.org/10.3760/CMA.J.ISSN.1673-4378.2017.02.017

Li, Y., Jin, H., Chen, Y., Huang, T., Mi, Y., & Zou, Z. (2021). Cancer cachexia: molecular mechanism and pharmacological management. *The Biochemical Journal*, *478 9*, 1663–1688. https://doi.org/10.1042/BCJ20201009

Li, Z., Jin, H., Mao, G., Wu, L., & Guo, Q. (2017). Msi2 plays a carcinogenic role in esophageal squamous cell carcinoma via regulation of the Wnt/&bgr;-catenin and Hedgehog signaling pathways. *Experimental Cell Research*, *361*, 170. https://doi.org/10.1016/j.yexcr.2017.10.016

Li, Z., Wei, J., Chen, B., Wang, Y., Yang, S., Wu, K., & Meng, X.-Y. (2023). The Role of MMP-9 and MMP-9 Inhibition in Different Types of Thyroid Carcinoma. *Molecules*, *28*. https://doi.org/10.3390/molecules28093705

Liang, M., Zhang, Q., Tang, Y.-Q., Qu, C., Zhou, X., Hong, J., He, L., & Hu, L. (2013). Musashi2 predicts poor prognosis and invasion in hepatocellular carcinoma by driving epithelial–mesenchymal transition. *Journal of Cellular and Molecular Medicine*, *18*, 49–58. https://doi.org/10.1111/jcmm.12158

Liang, W., Shi, J., Xia, H., & Wei, X. (2021). A Novel Ruthenium-Fluvastatin Complex Downregulates SNCG Expression to Modulate Breast Carcinoma Cell Proliferation and Apoptosis via Activating the PI3K/Akt/mTOR/VEGF/MMP9 Pathway. *Oxidative Medicine and Cellular Longevity*, *2021*. https://doi.org/10.1155/2021/5537737

Liang, W., Xia, B., He, C., Zhai, G., Li, M., & Zhou, J. (2020). Overexpression of LINC00691 promotes the proliferation and invasion of gastric cancer cells via the Janus kinase/signal transducer and activator of transcription signalling pathway. *The International Journal of Biochemistry & Cell Biology*, 105751. https://doi.org/10.1016/j.biocel.2020.105751

Liang, X., Wang, Z., Dai, Z., Zhang, H., Zhang, J., Luo, P., Liu, Z.-B., Liu, Z., Yang, K., Cheng, Q., & Zhang, M. (2022). Glioblastoma glycolytic signature predicts unfavorable prognosis, immunological heterogeneity, and ENO1 promotes microglia M2 polarization and cancer cell malignancy. *Cancer Gene Therapy*, *30*, 481–496. https://doi.org/10.1038/s41417-022-00569-9

Libramento, Z., Tichy, L., & Parry, T. (2025). Muscle wasting in cancer cachexia: Mechanisms and the role of exercise. *Experimental Physiology*. https://doi.org/10.1113/EP092544

Lima, B. M., De Azevedo, A. L. K., Giner, I. S., Gomig, T., Ribeiro, E., & Cavalli, I. (2023). Biomarker potential of the LEF1/TCF family members in breast cancer: Bioinformatic investigation on expression and clinical significance. *Genetics and Molecular Biology*, *46*. https://doi.org/10.1590/1678-4685-GMB-2022-0346

Lin, H., Huang, P.-Y., Cheng, C.-H., Tung, H.-Y., Fang, Z., Berglund, A., Chen, A., French-Kwawu, J., Harris, D., Pow-Sang, J., Yamoah, K., Cleveland, J., Awasthi, S., Rounbehler, R., Gerke, T., Dhillon, J., Eeles, R., Kote-Jarai, Z., Muir, K., … Park, J. (2021). KLK3 SNP–SNP interactions for prediction of prostate cancer aggressiveness. *Scientific Reports*, *11*. https://doi.org/10.1038/s41598-021-85169-7

Lin, H., Qu, L., Wei, H., Guo, M., Chen, X., Lin, Q., Zhang, H., Dai, S., & Chen, Y. (2025). Characterization of Bozitinib as a potential therapeutic agent for MET-amplified gastric cancer. *Communications Biology*, *8*. https://doi.org/10.1038/s42003-025-07490-5

Lin, J., Huffman, A., Vonderheide, R., Kim, S., & Byrne, K. (2020). CCL5 mediates CD40-driven CD4+ T-cell tumor infiltration and immunity. *JCI Insight*. https://doi.org/10.1172/jci.insight.137263

Lin, T.-Y., Gu, S.-Y., Lin, Y.-H., Shih, J.-H., Lin, J.-H., Chou, T.-Y., Lee, Y.-C., Chang, S.-F., & Lang, Y.-D. (2024). Paclitaxel-resistance facilitates glycolytic metabolism via Hexokinase-2-regulated ABC and SLC transporter genes in ovarian clear cell carcinoma. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *180*, 117452. https://doi.org/10.1016/j.biopha.2024.117452

Lin, Y., Zhang, C., Li, S., Li, Z., & Sun, F. (2018). LncRNA LOC554202 promotes proliferation and migration of gastric cancer cells through regulating p21 and E-cadherin. *European Review for Medical and Pharmacological Sciences*, *22 24*, 8690–8697. https://doi.org/10.26355/eurrev_201812_16634

Liou, G.-Y. (2019). CD133 as a regulator of cancer metastasis through the cancer stem cells. *The International Journal of Biochemistry & Cell Biology*, *106*, 1–7. https://doi.org/10.1016/j.biocel.2018.10.013

Liu, G., Zhang, Y., Cao, Z., & Zhao, Z. (2025). Targeting KIF18A triggers antitumor immunity and enhances efficiency of PD-1 blockade in colorectal cancer with chromosomal instability phenotype. *Cell Death Discovery*, *11*. https://doi.org/10.1038/s41420-025-02437-5

Liu, H., Zhang, L., Ding, X., & Sui, X. (2020). LINC00861 inhibits the progression of cervical cancer cells by functioning as a ceRNA for miR-513b-5p and regulating the PTEN/AKT/mTOR signaling pathway. *Molecular Medicine Reports*, *23*. https://doi.org/10.3892/mmr.2020.11662

Liu, L., Wu, N., Wang, Y., Zhang, X., Xia, B., Tang, J., Cai, J., Zhao, Z., Liao, Q., & Wang, J. (2019). TRPM7 promotes the epithelial–mesenchymal transition in ovarian cancer through the calcium-related PI3K / AKT oncogenic signaling. *Journal of Experimental & Clinical Cancer Research : CR*, *38*. https://doi.org/10.1186/s13046-019-1061-y

Liu, L., Zhu, H., Liao, Y., Wu, W., Liu, L., Liu, L., Wu, Y.-L., Sun, F., & Lin, H. (2020). Inhibition of Wnt/β-catenin pathway reverses multi-drug resistance and EMT in Oct4+/Nanog+ NSCLC cells. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *127*, 110225. https://doi.org/10.1016/j.biopha.2020.110225

Liu, M., Yao, B., Gui, T., Guo, C., Wu, X., Li, J., Lingling, Deng, Y., Xu, P., Wang, Y., Yang, D., Li, Q., Zeng, X., Li, X., Hu, R., Ge, J., Yu, Z., Chen, Y.-G., Chen, B., … Zhao, Q. (2020). PRMT5-dependent transcriptional repression of c-Myc target genes promotes gastric cancer progression. *Theranostics*, *10*, 4437–4452. https://doi.org/10.7150/thno.42047

Liu, W., & Xu, Q. (2019). Upregulation of circHIPK3 promotes the progression of gastric cancer via Wnt/β-catenin pathway and indicates a poor prognosis. *European Review for Medical and Pharmacological Sciences*, *23 18*, 7905–7912. https://doi.org/10.26355/eurrev_201909_19004

Liu, Y., Cao, Y.-L., Deng, X., Liu, J., Tang, X., Ji, Y., Li, F., Liu, P., Zhai, S., Zhang, Z., Zhang, R., Lin, J., Shi, Y., Lin, J., Fu, D., Shen, B., & Li, H. (2023). A microprotein N1DARP encoded by LINC00261 promotes Notch1 intracellular domain (N1ICD) degradation via disrupting USP10-N1ICD interaction to inhibit chemoresistance in Notch1-hyperactivated pancreatic cancer. *Cell Discovery*, *9*. https://doi.org/10.1038/s41421-023-00592-6

Liu, Y., Fan, Y., Wang, X., Huang, Z., Shi, K., & Zhou, B. (2018). Musashi-2 is a prognostic marker for the survival of patients with cervical cancer. *Oncology Letters*, *15*(4), 5425–5432. https://doi.org/10.3892/OL.2018.8077

Liu, Y., Sun, M.-X., Zhang, B., & Zhao, W. (2023). KIF18A improves migration and invasion of colorectal cancer (CRC) cells through inhibiting PTEN signaling. *Aging (Albany NY)*, *15*, 9182–9192. https://doi.org/10.18632/aging.205027

LM, O., R, K., G, M., BM, B., T, Z., & SR, M. (2018). Increased Musashi-2 and Decreased NUMB Protein Levels Observed in Human Colorectal Cancer are reverted to Normal Levels by ATRA-Induced Cell Differentiation. *International Journal of Cancer Research & Therapy*, *3*(2). https://doi.org/10.33140/IJCRT/03/02/00003

Löblein, M. T., Falke, I., Eich, H. T., Greve, B., Götte, M., & Troschel, F. M. (2021). Dual knockdown of musashi rna-binding proteins msi-1 and msi-2 attenuates putative cancer stem cell characteristics and therapy resistance in ovarian cancer cells. *International Journal of Molecular Sciences*, *22*(21), 11502. https://doi.org/10.3390/IJMS222111502/S1

Lu, R., Zhang, Y., Chen, R., Li, L., Huang, C., Zhou, Z., Cao, Y., Li, H., Li, J., Zhang, Y., Wang, Y., Huang, J., Zhao, X., Feng, J., Yu, J., & Du, C. (2024). A novel regulatory axis of MSI2-AGO2/miR-30a-3p-CGRRF1 drives cancer chemoresistance by upregulating the KRAS/ERK pathway. *Neoplasia (New York, N.Y.)*, *59*. https://doi.org/10.1016/j.neo.2024.101082

Luo, D. Di, & Zhao, F. (2022). KLF4 suppresses the proliferation and metastasis of NSCLC cells via inhibition of MSI2 and regulation of the JAK/STAT3 signaling pathway. *Translational Oncology*, *22*, 101396. https://doi.org/10.1016/J.TRANON.2022.101396

Luo, F., & Lin, K. (2022). N6-methyladenosine (m6A) reader IGF2BP1 accelerates gastric cancer aerobic glycolysis in c-Myc-dependent manner. *Experimental Cell Research*, 113176. https://doi.org/10.1016/j.yexcr.2022.113176

Machida, K., Tsukamoto, H., Tahara, S., Liang, J., Montana, J., Sher, L., Jung, J., Machida, T., Hernandez, J., Chen, C.-L., & Kumar, D. U. (2023). LIN28 and histone H3K4 methylase induce TLR4 to generate tumor-initiating stem-like cells. *IScience*, *26*. https://doi.org/10.1016/j.isci.2023.106254

Mahanujam, A. (2025). The Role of Beta-Catenin and the Wnt Signalling Pathway in Breast Cancer Initiation, Progression and Metastasis: A Literature Review. *Undergraduate Research in Natural and Clinical Science and Technology (URNCST) Journal*. https://doi.org/10.26685/urncst.715

Mahmoud, M., Ali, N., Mostafa, I., Hasan, R., & Sobeh, M. (2022). Coriander Oil Reverses Dexamethasone-Induced Insulin Resistance in Rats. *Antioxidants*, *11*. https://doi.org/10.3390/antiox11030441

Makhov, P., Bychkov, I., Faezov, B., Deneka, A., Kudinov, A., Nicolas, E., Brebion, R., Avril, E., Cai, K. Q., Kharin, L. V., Voloshin, M., Frantsiyants, E., Karnaukhov, N., Kit, O. I., Topchu, I., Fazliyeva, R., Nikonova, A. S., Serebriiskii, I. G., Borghaei, H., … Boumber, Y. (2021). Musashi-2 (MSI2) regulates epidermal growth factor receptor (EGFR) expression and response to EGFR inhibitors in EGFR-mutated non-small cell lung cancer (NSCLC). *Oncogenesis 2021 10:3*, *10*(3), 1–14. https://doi.org/10.1038/s41389-021-00317-y

Mansouri, A., Hachem, L., Mansouri, S., Nassiri, F., Laperriere, N., Xia, D., Lindeman, N., Wen, P., Chakravarti, A., Mehta, M., Hegi, M., Stupp, R., Aldape, K., & Zadeh, G. (2018). MGMT promoter methylation status testing to guide therapy for glioblastoma: refining the approach based on emerging evidence and current challenges. *Neuro-Oncology*, *21 2*, 167–178. https://doi.org/10.1093/neuonc/noy132

Mariean, C. R., Tiucă, O., Mariean, A., & Cotoi, O. (2023). Cancer Cachexia: New Insights and Future Directions. *Cancers*, *15*. https://doi.org/10.3390/cancers15235590

Marques, J., Pavlovic, B., Ngo, Q., Pedot, G., Roemmele, M., Volken, L., Kisele, S., Perbet, R., Wachtel, M., & Schafer, B. (2023). The chromatin remodeler CHD4 sustains Ewing Sarcoma cell survival by controlling global chromatin architecture. *Cancer Research*. https://doi.org/10.1158/0008-5472.CAN-22-3950

Marquis, C., Fonseca, C., Queen, K., Wood, L., Vandal, S., Malaby, H., Clayton, J., & Stumpff, J. (2020). Chromosomally unstable tumor cells specifically require KIF18A for proliferation. *Nature Communications*, *12*. https://doi.org/10.1038/s41467-021-21447-2

Martin, A., Gallot, Y., & Freyssenet, D. (2023). Molecular mechanisms of cancer cachexia-related loss of skeletal muscle mass: data analysis from preclinical and clinical studies. *Journal of Cachexia, Sarcopenia and Muscle*, *14*, 1150–1167. https://doi.org/10.1002/jcsm.13073

Martorana, F., Motta, G., Pavone, G., Motta, L., Stella, S., Vitale, S., Manzella, L., & Vigneri, P. (2021). AKT Inhibitors: New Weapons in the Fight Against Breast Cancer? *Frontiers in Pharmacology*, *12*. https://doi.org/10.3389/fphar.2021.662232

Mathes, A., Utikal, J., Werner, J., Shevchenko, I., Karakhanova, S., Bazhin, A., Umansky, V., Müller, V., & Groth, C. (2020). Enhanced expression of CD39 and CD73 on T cells in the regulation of anti-tumor immune responses. *Oncoimmunology*, *9*. https://doi.org/10.1080/2162402X.2020.1744946

Matin, F., Jeet, V., Srinivasan, S., Cristino, A., Panchadsaram, J., Clements, J., & Batra, J. (2019). MicroRNA-3162-5p-Mediated Crosstalk between Kallikrein Family Members Including Prostate-Specific Antigen in Prostate Cancer. *Clinical Chemistry*, *65 6*, 771–780. https://doi.org/10.1373/clinchem.2018.295824

Matsumoto, S., & Kikuchi, A. (2024). Wnt/β-catenin signaling pathway in liver biology and tumorigenesis. *In Vitro Cellular & Developmental Biology. Animal*. https://doi.org/10.1007/s11626-024-00858-7

McConkey, D., Choi, W., Marquis, L., Martin, F., Williams, M., Shah, J., Svatek, R., Das, A., Adam, L., Kamat, A., Siefker-Radtke, A., & Dinney, C. (2009). Role of epithelial-to-mesenchymal transition (EMT) in drug sensitivity and metastasis in bladder cancer. *Cancer and Metastasis Reviews*, *28*, 335–344. https://doi.org/10.1007/s10555-009-9194-7

McCorkle, J., Gorski, J., Liu, J., Riggs, M., McDowell, A., Lin, N., Wang, C., Ueland, F., & Kolesar, J. (2021). Lapatinib and poziotinib overcome ABCB1-mediated paclitaxel resistance in ovarian cancer. *PLoS ONE*, *16*. https://doi.org/10.1371/journal.pone.0254205

McGovern, J., Dolan, R., Skipworth, R., Laird, B., & McMillan, D. (2022). Cancer cachexia: a nutritional or a systemic inflammatory syndrome? *British Journal of Cancer*, *127*, 379–382. https://doi.org/10.1038/s41416-022-01826-2

Meng, H., Li, Y., Han, D., & Zhang, C. (2019). MiRNA-93-5p promotes the biological progression of gastric cancer cells via Hippo signaling pathway. *European Review for Medical and Pharmacological Sciences*, *23 11*, 4763–4769. https://doi.org/10.26355/eurrev_201906_18058

Meng, J., Song, Z., Cong, S., Sun, Q., Qinyun, Shi, W., & Wang, L. (2024). Regulatory role of the miR-142-3p/CDC25C axis in modulating autophagy in non-small cell lung cancer. *Translational Lung Cancer Research*, *13*, 552–572. https://doi.org/10.21037/tlcr-24-82

Meng, X., Na, R., Peng, X., Li, H., Ouyang, W., Zhou, W., You, X., Li, Y., Pu, X., Zhang, K., Xia, J., Wang, J., Tang, H., Zhuang, G., & Peng, Z. (2024). Musashi-2 potentiates colorectal cancer immune infiltration by regulating the post-translational modifications of HMGB1 to promote DCs maturation and migration. *Cell Communication and Signaling*, *22*(1), 1–24. https://doi.org/10.1186/S12964-024-01495-Z/FIGURES/8

Meng, X., Peng, X., Ouyang, W., Li, H., Na, R., Zhou, W., You, X., Li, Y., Pu, X., Zhang, K., Xia, J., Wang, J., Zhuang, G., Tang, H., & Peng, Z. (2023). Musashi-2 Deficiency Triggers Colorectal Cancer Ferroptosis by Downregulating the MAPK Signaling Cascade to Inhibit HSPB1 Phosphorylation. *Biological Procedures Online*, *25*(1), 1–23. https://doi.org/10.1186/S12575-023-00222-1/FIGURES/9

Meng, X., Xiao, W., Sun, J., Li, W., Yuan, H., Yu, T., Zhang, X., & Dong, W. (2022). CircPTK2/PABPC1/SETDB1 axis promotes EMT-mediated tumor metastasis and gemcitabine resistance in bladder cancer. *Cancer Letters*, 216023. https://doi.org/10.1016/j.canlet.2022.216023

Meng, Y., Xu, Q., Chen, L., Wang, L., & Hu, X. (2020). The function of SOX2 in breast cancer and relevant signaling pathway. *Pathology, Research and Practice*, *216 8*, 153023. https://doi.org/10.1016/j.prp.2020.153023

Mesrati, M. H., Syafruddin, S., Mohtar, M., & Syahir, A. (2021). CD44: A Multifunctional Mediator of Cancer Progression. *Biomolecules*, *11*. https://doi.org/10.3390/biom11121850

Miricescu, D., Totan, A., Stănescu-Spînu, I.-I., Badoiu, S., Ștefani, C., & Greabu, M. (2020). PI3K/AKT/mTOR Signaling Pathway in Breast Cancer: From Molecular Landscape to Clinical Aspects. *International Journal of Molecular Sciences*, *22*. https://doi.org/10.3390/ijms22010173

Mirzaei, S., Paskeh, M. D. A., Entezari, M., Mirmazloomi, S. R., Hassanpoor, A., Aboutalebi, M., Rezaei, S., Hejazi, E. S., Kakavand, A., Heidari, H., Salimimoghadam, S., Taheriazam, A., Hashemi, M., & Samarghandian, S. (2022). SOX2 function in cancers: Association with growth, invasion, stemness and therapy response. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *156*, 113860. https://doi.org/10.1016/j.biopha.2022.113860

Mladenov, E., Fan, X.-X., Dueva, R., Soni, A., & Iliakis, G. (2019). Radiation-dose-dependent functional synergisms between ATM, ATR and DNA-PKcs in checkpoint control and resection in G2-phase. *Scientific Reports*, *9*. https://doi.org/10.1038/s41598-019-44771-6

Moore, G., Lightner, C., Elbai, S., Brady, L., Nicholson, S., Ryan, R., O'Sullivan, K., O'Byrne, K., Blanco-Aparicio, C., Cuffe, S., O'Neill, M., Heavey, S., Finn, S., & Gately, K. (2021). Co-Targeting PIM Kinase and PI3K/mTOR in NSCLC. *Cancers*, *13*. https://doi.org/10.3390/cancers13092139

Mootha, V. K., Lindgren, C. M., Eriksson, K.-F., Subramanian, A., Sihag, S., Lehar, J., Puigserver, P., Carlsson, E., Ridderstråle, M., Laurila, E., Houstis, N., Daly, M. J., Patterson, N., Mesirov, J. P., Golub, T. R., Tamayo, P., Spiegelman, B., Lander, E. S., Hirschhorn, J. N., … Groop, L. C. (2003). PGC-1α-responsive genes involved in oxidative phosphorylation are coordinately downregulated in human diabetes. *Nature Genetics*, *34*(3), 267–273. https://doi.org/10.1038/ng1180

Moss, J., Zick, A., Grinshpun, A., Carmon, E., Maoz, M., Ochana, B., Abraham, O., Arieli, O., Germansky, L., Meir, K., Glaser, B., Shemer, R., Uziely, B., & Dor, Y. (2020). Circulating breast-derived DNA allows universal detection and monitoring of localized breast cancer. *Annals of Oncology : Official Journal of the European Society for Medical Oncology*, *31 3*, 395–403. https://doi.org/10.1016/j.annonc.2019.11.014

Mulder, S., Dasgupta, A., King, R., Abrego, J., Attri, K., Murthy, D., Shukla, S., & Singh, P. (2020). JNK signaling contributes to skeletal muscle wasting and protein turnover in pancreatic cancer cachexia. *Cancer Letters*. https://doi.org/10.1016/j.canlet.2020.07.025

Müller-Tidow, C., Diederichs, S., Bulk, E., Pohle, T., Steffen, B., Schwäble, J., Plewka, S., Thomas, M., Metzger, R., Schneider, P., Brandts, C., Berdel, W., & Serve, H. (2005). Identification of metastasis-associated receptor tyrosine kinases in non-small cell lung cancer. *Cancer Research*, *65 5*, 1778–1782. https://doi.org/10.1158/0008-5472.CAN-04-3388

Nagahara, M., Nishida, N., Iwatsuki, M., Ishimaru, S., Mimori, K., Tanaka, F., Nakagawa, T., Sato, T., Sugihara, K., Hoon, D., & Mori, M. (2011). Kinesin 18A expression: Clinical relevance to colorectal cancer progression. *International Journal of Cancer*, *129*. https://doi.org/10.1002/ijc.25916

Nakagawa, S., Ikenoue, T., Yamaguchi, K., Takane, K., Furukawa, Y., & Tabata, S. (2024). Wnt/β-catenin signaling regulates amino acid metabolism through the suppression of CEBPA and FOXA1 in liver cancer cells. *Communications Biology*, *7 1*, 510. https://doi.org/10.1038/s42003-024-06202-9

Nakamura, K., Terai, Y., Tanabe, A., Ono, Y., Hayashi, M., Maeda, K., Fujiwara, S., Ashihara, K., Nakamura, M., Tanaka, Y., Tanaka, T., Tsunetoh, S., Sasaki, H., & Ohmichi, M. (2017). CD24 expression is a marker for predicting clinical outcome and regulates the epithelial-mesenchymal transition in ovarian cancer via both the Akt and ERK pathways. *Oncology Reports*, *37*, 3189–3200. https://doi.org/10.3892/or.2017.5583

Nguyen, A., Facey, C., & Boman, B. (2024). The Significance of Aldehyde Dehydrogenase 1 in Cancers. *International Journal of Molecular Sciences*, *26*. https://doi.org/10.3390/ijms26010251

Nguyen-Ngoc, T., Bouchaab, H., Adjei, A., & Peters, S. (2015). BRAF Alterations as Therapeutic Targets in Non–Small-Cell Lung Cancer. *Journal of Thoracic Oncology*, *10*, 1396. https://doi.org/10.1097/JTO.0000000000000644

Ni, C., & Li, D. (2024). Ferroptosis and oxidative stress in endometriosis: A systematic review of the literature. *Medicine*, *103*. https://doi.org/10.1097/MD.0000000000037421

NIH. (2024). *A to Z List of Cancer Types - NCI*. https://www.cancer.gov/types

Ning, Tao, H., Shan, Z., & Zhou, X. (2022). Activation of WNT/CTNNB1/TCF7L2 in Epstein-Barr virus-positive gastric cancer regulates epithelial mesenchymal transition. *Biochemical and Biophysical Research Communications*, *609*, 54–61. https://doi.org/10.1016/j.bbrc.2022.03.150

Niu, J., Wang, X., Liang, C., Zhang, Y., Liu, F., Li, H.-Y., Xie, S.-Q., Sun, H., & Fang, D. (2019). Suppression of epidermal growth factor receptor-mediated β-catenin nuclear accumulation enhances the anti-tumor activity of phosphoinositide 3-kinase inhibitor in breast cancer. *Cell Biology International*, *43*. https://doi.org/10.1002/cbin.11183

Orth, M., Surdez, D., Marchetto, A., Grossetête, S., Gerke, J., Zaidi, S., Alonso, J., Sastre, A., Baulande, S., Sill, M., Cidre-Aranaz, F., Ohmura, S., Kirchner, T., Hauck, S., Reischl, E., Gymrek, M., Pfister, S., Strauch, K., Delattre, O., & Grünewald, T. (2021). Systematic multi-omics cell line profiling uncovers principles of Ewing sarcoma fusion oncogene-mediated gene regulation. *Cell Reports*, *41*, 111761. https://doi.org/10.1101/2021.06.08.447518

Overman, M., Javle, M., Davis, R., Vats, P., Kumar-Sinha, C., Xiao, L., Mettu, N., Parra, E., Benson, A., Lopez, C., Munugalavadla, V., Patel, P., Tao, L., Neelapu, S., & Maitra, A. (2020). Randomized phase II study of the Bruton tyrosine kinase inhibitor acalabrutinib, alone or with pembrolizumab in patients with advanced pancreatic cancer. *Journal for Immunotherapy of Cancer*, *8*. https://doi.org/10.1136/jitc-2020-000587

Özturan, D., Morova, T., & Lack, N. (2022). Androgen Receptor-Mediated Transcription in Prostate Cancer. *Cells*, *11*. https://doi.org/10.3390/cells11050898

Ozturk, R. Y., Durasi, E., Çalik, H., Yuka, S. A., & Koç, R. Ç. (2025). Nitidine and Paclitaxel co-loaded lipid-chitosan hybrid nanoparticles overcome ABCB1-mediated multidrug resistance in ovarian cancer. *ChemMedChem*. https://doi.org/10.1002/cmdc.202500065

Page, K., Guttery, D., Fernandez-Garcia, D., Hills, A., Hastings, R., Luo, J., Goddard, K., Shahin, V., Woodley-Barker, L., Rosales, B., Coombes, R., Stebbing, J., & Shaw, J. (2017). Next Generation Sequencing of Circulating Cell-Free DNA for Evaluating Mutations and Gene Amplification in Metastatic Breast Cancer. *Clinical Chemistry*, *63 2*, 532–541. https://doi.org/10.1373/clinchem.2016.261834

Pan, H., Chai, W., Liu, X., Yu, T., Sun, L.-F., & Yan, M.-X. (2021). DYNC1H1 Regulates NSCLC Cell Growth and Metastasis by IFN-γ-JAK-STAT Signaling and Is Associated with an Aberrant Immune Response. *Experimental Cell Research*, 112897. https://doi.org/10.1016/j.yexcr.2021.112897

Pan, X., Hong, X., Li, S., Meng, P., & Xiao, F. (2021). METTL3 promotes adriamycin resistance in MCF-7 breast cancer cells by accelerating pri-microRNA-221-3p maturation in a m6A-dependent manner. *Experimental & Molecular Medicine*, *53*, 91–102. https://doi.org/10.1038/s12276-020-00510-w

Pandini, G., Mineo, R., Frasca, F., Roberts, C., Marcelli, M., Vigneri, R., & Belfiore, A. (2005). Androgens up-regulate the insulin-like growth factor-I receptor in prostate cancer cells. *Cancer Research*, *65 5*, 1849–1857. https://doi.org/10.1158/0008-5472.CAN-04-1837

Pappas, K., Martin, T., Wolfe, A., Nguyen, C., Su, T., Jin, J., Hibshoosh, H., & Parsons, R. (2021). NOTCH and EZH2 collaborate to repress PTEN expression in breast cancer. *Communications Biology*, *4*. https://doi.org/10.1038/s42003-021-01825-8

Parambil, S. T., Antony, G., Littleflower, A. B., & Subhadradevi, L. (2024). The molecular crosstalk of the hippo cascade in breast cancer: A potential central susceptibility. *Biochimie*. https://doi.org/10.1016/j.biochi.2024.03.008

Park, S.-M., Gönen, M., Vu, L., Minuesa, G., Tivnan, P., Barlowe, T. S., Taggart, J., Lu, Y., Deering, R. P., Hacohen, N., Figueroa, M. E., Paietta, E., Fernandez, H. F., Tallman, M. S., Melnick, A., Levine, R., Leslie, C., Lengner, C. J., &

Kharas, M. G. (2015). Musashi2 sustains the mixed-lineage leukemia-driven stem cell regulatory program. *The Journal of Clinical Investigation*, *125*(3), 1286–1298. https://doi.org/10.1172/JCI78440

Patel, M., Lu, L., Zander, D., Sreerama, L., Coco, D., & Moreb, J. (2008). ALDH1A1 and ALDH3A1 expression in lung cancers: correlation with histologic type and potential precursors. *Lung Cancer*, *59 3*, 340–349. https://doi.org/10.1016/J.LUNGCAN.2007.08.033

Pavăl, D., Patton, R., McDonald, J., Skipworth, R., Gallagher, I., & Laird, B. (2022). A systematic review examining the relationship between cytokines and cachexia in incurable cancer. *Journal of Cachexia, Sarcopenia and Muscle*, *13*, 824–838. https://doi.org/10.1002/jcsm.12912

Peng, D., Feng, L., & Li, H. (2022). Identification of Novel circRNA-Based ceRNA Network Involved in the Pathogenesis of Gastric Cancer. *International Journal of Genomics*, *2022*. https://doi.org/10.1155/2022/5281846

Peng, Y., Song, Y., Qin, C., Ding, M., Huang, Z., Wang, F., HuangFu, Y., Yu, L., Du, Y., & Xu, T. (2025). Genomic subtypes of non-muscle-invasive bladder cancer: guiding immunotherapy decision-making for patients exposed to aristolochic acid. *Molecular Medicine*, *31*. https://doi.org/10.1186/s10020-025-01199-1

Peñuelas, S., Anido, J., Prieto-Sánchez, R., Folch, G., Barba, I., Cuartas, I., Garcia-Dorado, D., Poca, M., Sahuquillo, J., Sahuquillo, J., Baselga, J., Baselga, J., & Seoane, J. (2009). TGF-beta increases glioma-initiating cell self-renewal through the induction of LIF in human glioblastoma. *Cancer Cell*, *15 4*, 315–327. https://doi.org/10.1016/j.ccr.2009.02.011

Pi, J., Wang, W., Ji, M., Wang, X., Wei, X., Jin, J., Liu, T., Qiang, J., Qi, Z., Li, F., Liu, Y., Yanni, Si, Y., Huo, Y., Gao, Y., Chen, Y., Dong, L., Su, R., Chen, J., … Yu, J. (2020). YTHDF1 Promotes Gastric Carcinogenesis by Controlling Translation of FZD7. *Cancer Research*, *81*, 2651–2665. https://doi.org/10.1158/0008-5472.CAN-20-0066

Ping, Q., Wang, C., Cheng, X., Zhong, Y., Yan, R., Yang, M., Shi, Y., Li, X., Li, X., Huang, W., Wang, L., Bi, X., Hu, L., Yang, Y., Wang, Y., Gong, R., Tan, J., Li, R., Li, H., … Li, R. (2023). TGF-β1 dominates stromal fibroblast-mediated EMT via the FAP/VCAN axis in bladder cancer cells. *Journal of Translational Medicine*, *21*. https://doi.org/10.1186/s12967-023-04303-3

Porporato, P. (2016). Understanding cachexia as a cancer metabolism syndrome. *Oncogenesis*, *5*. https://doi.org/10.1038/oncsis.2016.3

Poulia, K., Sarantis, P., Antoniadou, D., Koustas, E., Papadimitropoulou, A., Papavassiliou, A., & Karamouzis, M. (2020). Pancreatic Cancer and Cachexia—Metabolic Mechanisms and Novel Insights. *Nutrients*, *12*. https://doi.org/10.3390/nu12061543

Qi, M., Yu, B., Yu, H., & Li, F. (2020). Integrated analysis of a ceRNA network reveals potential prognostic lncRNAs in gastric cancer. *Cancer Medicine*, *9*, 1798–1817. https://doi.org/10.1002/cam4.2760

Qiu, W., Cai, X., Xu, K., Song, S., Xiao, Z., Hou, Y.-D., Qi, X., Liu, F., Chen, Y.-M., Yang, H., Chu, L., & Liu, J. (2021). PRL1 Promotes Glioblastoma Invasion and Tumorigenesis via Activating USP36-Mediated Snail2 Deubiquitination. *Frontiers in Oncology*, *11*. https://doi.org/10.3389/fonc.2021.795633

Radhi, M., Rowlinson, J., Halliday, N., Kim, D.-H., Deacon, S., Knight, H., & Smith, S. (2023). M6A RNA METHYLATION AS A THERAPEUTIC TARGET IN HIGH GRADE GLIOMA. *Neuro-Oncology*. https://doi.org/10.1093/neuonc/noad147.053

Rajbhandari, N., Hamilton, M., Quintero, C. M., Ferguson, L. P., Fox, R., Schürch, C. M., Wang, J., Nakamura, M., Lytle, N. K., McDermott, M., Diaz, E., Pettit, H., Kritzik, M., Han, H., Cridebring, D., Wen, K. W., Tsai, S., Goggins, M. G., Lowy, A. M., … Reya, T. (2023). Single-cell mapping identifies MSI+ cells as a common origin for diverse subtypes of pancreatic cancer. *Cancer Cell*, *41*(11), 1989-2005.e9.

https://doi.org/10.1016/J.CCELL.2023.09.008/ATTACHMENT/A09414B4-A132-4F45-83C6-DBC2213CFA7A/MMC2.PDF

Rangel, R., Jenkins, N., Kodama, M., Wu, H., Parsons, P., Newberg, J., Kodama, T., Tien, J., Yoshihara, K., Copeland, N., & Finegold, M. (2016). Transposon mutagenesis identifies genes and cellular processes driving epithelial-mesenchymal transition in hepatocellular carcinoma. *Proceedings of the National Academy of Sciences*, *113*. https://doi.org/10.1073/pnas.1606876113

Rebollido-Ríos, R., Venton, G., Sánchez-Redondo, S., Felip, C. I., Fournet, G., González, E., Fernández, W. R., Escuela, D. B., Di Stefano, B., Penarroche-Díaz, R., Martin, G., Ceylan, I., Costello, R., & Pérez-Alea, M. (2020). Dual disruption of aldehyde dehydrogenases 1 and 3 promotes functional changes in the glutathione redox system and enhances chemosensitivity in nonsmall cell lung cancer. *Oncogene*, *39*, 2756–2771. https://doi.org/10.1038/s41388-020-1184-9

Ren, Y., Liu, W., Zhu, X., Miao, X., Bei, C., Tan, S., Luo, W., Tang, F., Tang, G., & Qin, L. (2016). MYC associated zinc finger protein promotes the invasion and metastasis of hepatocellular carcinoma by inducing epithelial mesenchymal transition. *Oncotarget*, *7*, 86420–86432. https://doi.org/10.18632/oncotarget.13416

Ren, Z., Qiu, S., Wu, W.-Z., Zheng, S., Zhang, B.-H., Yin, X., & Gao, D. (2015). Coexpression of gene Oct4 and Nanog initiates stem cell characteristics in hepatocellular carcinoma and promotes epithelial-mesenchymal transition through activation of Stat3/Snail signaling. *Journal of Hematology & Oncology*, *8*. https://doi.org/10.1186/s13045-015-0119-3

Rivera, A., Pelloski, C., Gilbert, M., Colman, H., De La Cruz, C., Sulman, E., Bekele, B., & Aldape, K. (2010). MGMT promoter methylation is predictive of response to radiotherapy and prognostic in the absence of adjuvant alkylating chemotherapy for glioblastoma. *Neuro-Oncology*, *12 2*, 116–121. https://doi.org/10.1093/neuonc/nop020

Roussel-Gervais, A., Naciri, I., Kirsh, O., Kasprzyk, L., Velasco, G., Grillo, G., Dubus, P., & Defossez, P. (2017). Loss of the Methyl-CpG-Binding Protein ZBTB4 Alters Mitotic Checkpoint, Increases Aneuploidy, and Promotes Tumorigenesis. *Cancer Research*, *77 1*, 62–73. https://doi.org/10.1158/0008-5472.CAN-16-1181

Rustgi, A., Bakir, B., Pitarresi, J., & Chiarella, A. (2020). EMT, MET, Plasticity, and Tumor Metastasis. *Trends in Cell Biology*. https://doi.org/10.1016/j.tcb.2020.07.003

Sabater-Arcis, M., Bargiela, A., Moreno, N., Poyatos-García, J., Vílchez, J., & Artero, R. (2021). Musashi-2 contributes to myotonic dystrophy muscle dysfunction by promoting excessive autophagy through miR-7 biogenesis repression. *Molecular Therapy. Nucleic Acids*, *25*, 652–667. https://doi.org/10.1016/j.omtn.2021.08.010

Sabater-Arcis, M., Moreno, N., Sevilla, T., Perez Alonso, M., Bargiela, A., & Artero, R. (2024). Msi2 enhances muscle dysfunction in a myotonic dystrophy type 1 mouse model. *Biomedical Journal*, *47*(4), 100667. https://doi.org/10.1016/j.bj.2023.100667

Saini, A., Kumar, M., Bhatt, S., Saini, V., & Malik, A. (2020). *CANCER CAUSES AND TREATMENTS*.

Samart, P., Heenatigala Palliyage, G., Issaragrisil, S., Luanpitpong, S., & Rojanasakul, Y. (2023). Musashi-2 in cancer-associated fibroblasts promotes non-small cell lung cancer metastasis through paracrine IL-6-driven epithelial-mesenchymal transition. *Cell and Bioscience*, *13*(1), 1–18. https://doi.org/10.1186/S13578-023-01158-5/FIGURES/7

Sanzey, M., Rahim, S. A., Oudin, A., Dirkse, A., Kaoma, T., Vallar, L., Herold-Mende, C., Bjerkvig, R., Gołębiewska, A., & Niclou, S. (2015). Comprehensive Analysis of Glycolytic Enzymes as Therapeutic Targets in the Treatment of Glioblastoma. *PLoS ONE*, *10*. https://doi.org/10.1371/journal.pone.0123544

Schmidt, M., Poser, C., & Von Maltzahn, J. (2020). Wnt7a Counteracts Cancer Cachexia. *Molecular Therapy Oncolytics*, *16*, 134–146. https://doi.org/10.1016/j.omto.2019.12.011

Sethi, A., Mishra, S., Upadhyay, V., Dubey, P., Siddiqui, S., Singh, A. K., Chaowdhury, S., Srivastava, S., Srivasatava, P., Sahoo, P., Bhatt, M., Mishra, A., & Trivedi, A. K. (2024). USP10 deubiquitinates and stabilizes CD44 leading to

enhanced breast cancer cell proliferation, stemness and metastasis. *The Biochemical Journal*. https://doi.org/10.1042/BCJ20240611

Sethi, G., Zarrabi, A., Ashrafizadeh, M., Paskeh, M. D. A., & Mirzaei, S. (2021). Wnt/β-Catenin Signaling as a Driver of Hepatocellular Carcinoma Progression: An Emphasis on Molecular Pathways. *Journal of Hepatocellular Carcinoma*, *8*, 1415–1444. https://doi.org/10.2147/JHC.S336858

Setiawan, T., Sari, I. N., Wijaya, Y. T., Julianto, N. M., Muhammad, J. A., Lee, H., Chae, J. H., & Kwon, H. (2023). Cancer cachexia: molecular mechanisms and treatment strategies. *Journal of Hematology & Oncology*, *16*. https://doi.org/10.1186/s13045-023-01454-0

Shakeri, F., Mohamadynejad, P., & Moghanibashi, M. (2024). Identification of ASMTL-AS1 and LINC02604 lncRNAs as novel biomarkers for diagnosis of colorectal cancer. *International Journal of Colorectal Disease*, *39*(1), 1–12. https://doi.org/10.1007/S00384-024-04692-X/FIGURES/14

Shakya, S., Gromovsky, A., Hale, J., Knudsen, A., Prager, B., Wallace, L., Penalva, L., Ivanova, P., Brown, H., Kristensen, B., Rich, J., Lathia, J., Brown, J., & Hubert, C. (2019). Altered lipid metabolism marks glioblastoma stem and non-stem cells in separate tumor niches. *Acta Neuropathologica Communications*, *9*. https://doi.org/10.1101/2020.09.20.304964

Shao, L., Sun, W., Zhang, H., Zhang, P., Wang, Z., Dong, W., He, L., Zhang, T., & Qin, Y. (2020). Long non-coding RNA AGAP2-AS1 increases the invasiveness of papillary thyroid cancer. *Aging (Albany NY)*, *12*, 18019–18032. https://doi.org/10.18632/aging.103570

Shen, L., Zeng, J., Lin, Li, S., Chen, C., Jia, J., & Liang, X. (2020). Helicobacter pylori Induces a Novel NF-kB/LIN28A/let-7a/hTERT Axis to Promote Gastric Carcinogenesis. *Molecular Cancer Research*, *19*, 74–85. https://doi.org/10.1158/1541-7786.MCR-19-0678

Sheng, W., Dong, M., Chen, C., Li, Y., Liu, Q., Dong, Q., Sheng, W., Dong, M., Chen, C., Li, Y., Liu, Q., & Dong, Q. (2016). Musashi2 promotes the development and progression of pancreatic cancer by down-regulating Numb protein. *Oncotarget*, *8*(9), 14359–14373. https://doi.org/10.18632/ONCOTARGET.8736

Sheng, W., Dong, M., Chen, C., Wang, Z., Li, Y., Wang, K., Li, Y., & Zhou, J. (2017). Cooperation of Musashi-2, Numb, MDM2, and P53 in drug resistance and malignant biology of pancreatic cancer. *FASEB Journal : Official Publication of the Federation of American Societies for Experimental Biology*, *31*(6), 2429–2438. https://doi.org/10.1096/FJ.201601240R

Sheng, W., Shi, X., Lin, Y., Tang, J., Jia, C., Cao, R., Sun, J., Wang, G., Zhou, L., & Dong, M. (2020). Musashi2 promotes EGF-induced EMT in pancreatic cancer via ZEB1-ERK/MAPK signaling. *Journal of Experimental and Clinical Cancer Research*, *39*(1), 1–15. https://doi.org/10.1186/S13046-020-1521-4/FIGURES/11

Shi, X., Zheng, Y., Jiang, L., Zhou, B., Yang, W., Li, L., Ding, L., Huang, M., Gery, S., Lin, D., Koeffler, H., Municipal, G., & Key, G. P. (2020). EWS-FLI1 regulates and cooperates with core regulatory circuitry in Ewing sarcoma. *Nucleic Acids Research*, *48*, 11434–11451. https://doi.org/10.1093/nar/gkaa901

Shukla, A., Gupta, P., Singh, R., & Mishra, D. (2018). Glycolytic inhibitor 2-Deoxy-d-Glucose activates migration and invasion in glioblastoma cells through modulation of the miR-7-5p/TFF3 signaling pathway. *Biochemical and Biophysical Research Communications*, *499 4*, 829–835. https://doi.org/10.1016/j.bbrc.2018.04.001

Singh, A., & Figg William. (2004). Upregulation of the Androgen Receptor during Prostate Cancer Progression. *Cancer Biology & Therapy*, *3*, 284–285. https://doi.org/10.4161/CBT.3.3.785

Sloan, E., Watson, J., Ahn, P., Jay, A., Minor, M., & Komlodi-Pasztor, E. (2023). DNAR-10. HETEROGENEOUS MGMT PROMOTER METHYLATION IN A MULTIFOCAL GLIOBLASTOMA: A CASE REPORT. *Neuro-Oncology*. https://doi.org/10.1093/neuonc/noad179.0376

Stanke, K., Wilson, C., & Kidambi, S. (2021). High Expression of Glycolytic Genes in Clinical Glioblastoma Patients Correlates With Lower Survival. *Frontiers in Molecular Biosciences*, *8*. https://doi.org/10.3389/fmolb.2021.752404

Stover, D., Parsons, H., Ha, G., Freeman, S., Barry, W., Guo, H., Atish, D., Choudhury, Gydush, G., Reed, S., Rhoades, J., Rotem, D., Hughes, M., Deborah, A., Dillon, Partridge, A., Wagle, N., Krop, I., Getz, G., … Adalsteinsson, V. (2018). Association of Cell-Free DNA Tumor Fraction and Somatic Copy Number Alterations With Survival in Metastatic Triple-Negative Breast Cancer. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, *36 6*, 543–553. https://doi.org/10.1200/JCO.2017.76.0033

Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., Paulovich, A., Pomeroy, S. L., Golub, T. R., Lander, E. S., & Mesirov, J. P. (2005). Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles. *Proceedings of the National Academy of Sciences*, *102*(43), 15545–15550. https://doi.org/10.1073/pnas.0506580102

Sumi, S., Chen, Y., Ohki, R., Hiraoka, N., Capodanno, Y., Tomosugi, M., Schrader, J., & Yokoyama, A. (2021). Cross-talk among MEN1, p53 and Notch regulates the proliferation of pancreatic neuroendocrine tumor cells by modulating INSM1 expression and subcellular localization. *Neoplasia (New York, N.Y.)*, *23*, 979–992. https://doi.org/10.1016/j.neo.2021.07.008

Sun, C., Wang, X., Hui, Y.-Y., Fukui, H., Wang, B., & Miwa, H. (2021). The Potential Role of REG Family Proteins in Inflammatory and Inflammation-Associated Diseases of the Gastrointestinal Tract. *International Journal of Molecular Sciences*, *22*. https://doi.org/10.3390/ijms22137196

Sun, R., He, S.-L., Liu, H.-Y., Wang, X.-W., & Li, S.-H. (2024). Tumor Suppressor LINC02487 Inhibits the Progression of Cervical Cancer in Vitro by Regulating the PTEN/Akt/mTOR Pathway. *Discovery Medicine*, *36 187*, 1732–1742. https://doi.org/10.24976/Discov.Med.202436187.159

Sun, X., Huang, T., Liu, Z., Sun, M., & Luo, S. (2019). LncRNA SNHG7 contributes to tumorigenesis and progression in breast cancer by interacting with miR-34a through EMT initiation and the Notch-1 pathway. *European Journal of Pharmacology*, *856*, 172407. https://doi.org/10.1016/j.ejphar.2019.172407

Sun, X.-X., Chen, Y., Su, Y., Wang, X., Chauhan, K., Liang, J., Daniel, C., Sears, R., & Dai, M. (2018). SUMO protease SENP1 deSUMOylates and stabilizes c-Myc. *Proceedings of the National Academy of Sciences*, *115*, 10983–10988. https://doi.org/10.1073/pnas.1802932115

Szymura, S., Zaemes, J., Allison, D., Clift, S., D'Innocenzi, J., Gray, L., McKenna, B., Morris, B., Bekiranov, S., Legallo, R., Jones, D., & Mayo, M. (2019). NF-κB upregulates glutamine-fructose-6-phosphate transaminase 2 to promote migration in non-small cell lung cancer. *Cell Communication and Signaling : CCS*, *17*. https://doi.org/10.1186/s12964-019-0335-5

Tadros, S., Shukla, S., King, R., Gunda, V., Vernucci, E., Abrego, J., Chaika, N., Yu, F., Lazenby, A., Berim, L., Grem, J., Sasson, A., & Singh, P. (2017). De Novo Lipid Synthesis Facilitates Gemcitabine Resistance through Endoplasmic Reticulum Stress in Pancreatic Cancer. *Cancer Research*, *77 20*, 5503–5517. https://doi.org/10.1158/0008-5472.CAN-16-3062

Tian, Y., Sun, H., Yang, L., Lei, Y., Wang, J.-H., Xia, F., Wang, X., & Fu, Y. (2021). Association of Preoperative NANOG-Positive Circulating Tumor Cell Levels With Recurrence of Hepatocellular Carcinoma. *Frontiers in Oncology*, *11*. https://doi.org/10.3389/fonc.2021.601668

Topchu, I., Karnaukhov, N., Mazitova, A., Yugai, V., Voloshin, M., Tikhomirova, M., Kit, O., Frantsiyants, E., Kharin, L., Airapetova, T., Ratner, E., Sabirov, A., Abramova, Z., Serebriiskii, I., Boumber, Y., & Deneka, A. (2021). Musashi 2

(MSI2) expression as an independent prognostic biomarker in non-small cell lung cancer (NSCLC). *Journal of Thoracic Disease*, *13*(3), 1370–1379. https://doi.org/10.21037/JTD-20-2787

Trejo-Solís, C., Silva-Adaya, D., Serrano-García, N., Magaña-Maldonado, R., Jimenez-Farfan, D., Ferreira-Guerrero, E., Cruz-Salgado, A., & Castillo-Rodríguez, R. (2023). Role of Glycolytic and Glutamine Metabolism Reprogramming on the Proliferation, Invasion, and Apoptosis Resistance through Modulation of Signaling Pathways in Glioblastoma. *International Journal of Molecular Sciences*, *24*. https://doi.org/10.3390/ijms242417633

Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., Moher, D., Peters, M. D. J., Horsley, T., Weeks, L., Hempel, S., Akl, E. A., Chang, C., McGowan, J., Stewart, L., Hartling, L., Aldcroft, A., Wilson, M. G., Garritty, C., … Straus, S. E. (2018). PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of Internal Medicine*, *169*(7), 467–473. https://doi.org/10.7326/M18-0850

Troschel, F. M., Minte, A., Ismail, Y. M., Kamal, A., Abdullah, M. S., Ahmed, S. H., Deffner, M., Kemper, B., Kiesel, L., Eich, H. T., Ibrahim, S. A., Götte, M., & Greve, B. (2020). Knockdown of Musashi RNA Binding Proteins Decreases Radioresistance but Enhances Cell Motility and Invasion in Triple-Negative Breast Cancer. *International Journal of Molecular Sciences*, *21*(6). https://doi.org/10.3390/IJMS21062169

Tsujino, T., Sugito, N., Taniguchi, K., Honda, R., Komura, K., Yoshikawa, Y., Takai, T., Minami, K., Kuranaga, Y., Shinohara, H., Tokumaru, Y., Heishima, K., Inamoto, T., Azuma, H., & Akao, Y. (2019). MicroRNA-143/Musashi-2/KRAS cascade contributes positively to carcinogenesis in human bladder cancer. *Cancer Science*, *110*(7), 2189–2199. https://doi.org/10.1111/CAS.14035

Udawant, S., Litif, C., Lopez, A., Gunn, B., Schuenzel, E., & Keniry, M. (2021). PI3K Pathway Inhibition with NVP-BEZ235 Hinders Glycolytic Metabolism in Glioblastoma Multiforme Cells. *Cells*, *10*. https://doi.org/10.3390/cells10113065

Ullah, R., Yin, Q., Snell, A., & Wan, L. (2021). RAF-MEK-ERK pathway in cancer evolution and treatment. *Seminars in Cancer Biology*. https://doi.org/10.1016/j.semcancer.2021.05.010

Um, H., Bae, I., & Yoon, S. H. (2008). Abstract A3: Bcl-w-induced invasive pathways in gastric cancer cells. *Cancer Prevention Research*, *1*. https://doi.org/10.1158/1940-6207.PREV-08-A3

Vadhan, A., Hou, M., Vijayaraghavan, P., Wu, Y.-C., Hu, S. C., Wang, Y.-M., Cheng, T., Wang, Y.-Y., & Yuan, S. (2022). CD44 Promotes Breast Cancer Metastasis through AKT-Mediated Downregulation of Nuclear FOXA2. *Biomedicines*, *10*. https://doi.org/10.3390/biomedicines10102488

Valla, S., Hassan, N., Vitale, D. L., Madanes, D., Spinelli, F. M., Teixeira, F. C. O. B., Greve, B., Espinoza-Sánchez, N. A., Cristina, C., Alaniz, L., & Götte, M. (2021). Syndecan-1 depletion has a differential impact on hyaluronic acid metabolism and tumor cell behavior in luminal and triple-negative breast cancer cells. *International Journal of Molecular Sciences*, *22*(11), 5874. https://doi.org/10.3390/IJMS22115874/S1

Van De Worp, W., Schols, A., Theys, J., Van Helvoort, A., & Langen, R. (2020). Nutritional Interventions in Cancer Cachexia: Evidence and Perspectives From Experimental Models. *Frontiers in Nutrition*, *7*. https://doi.org/10.3389/fnut.2020.601329

Van Poelgeest, M., Sturm, G., Van Der Burg, S., Van Egmond, S., Santegoets, S., Kortekaas, K., Trajanoski, Z., Finotello, F., Welters, M., & Ehsan, I. (2020). CD39 Identifies the CD4+ Tumor-Specific T-cell Population in Human Cancer. *Cancer Immunology Research*, *8*, 1311–1321. https://doi.org/10.1158/2326-6066.CIR-20-0270

Van Riggelen, J., Buchwalter, G., Soto, U., Arce, D.-C., Hausen, H., Wasylyk, B., & Rösl, F. (2005). Loss of Net as Repressor Leads to Constitutive Increased c-fos Transcription in Cervical Cancer Cells*. *Journal of Biological Chemistry*, *280*, 3286–3294. https://doi.org/10.1074/JBC.M409915200

Veen, L., Skrabanja, T., Derks, S., De Gruijl, T., Bijlsma, M., & Van Laarhoven, H. (2021). The role of transforming growth factor β in upper gastrointestinal cancers: A systematic review. *Cancer Treatment Reviews*, *100*, 102285. https://doi.org/10.1016/j.ctrv.2021.102285

Velcheti, V., Schalper, K., Yao, X., Cheng, H., Kocoglu, M., Dhodapkar, K., Deng, Y., Gettinger, S., & Rimm, D. (2013). High SOX2 Levels Predict Better Outcome in Non-Small Cell Lung Carcinomas. *PLoS ONE*, *8*. https://doi.org/10.1371/journal.pone.0061427

Velho, R., Danielyan, I., Mechsner, S., & Götte, M. (2023). Sox-2 positive cells identified in lymph nodes from endometriosis patients may play a role in the disease pathogenesis. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, *288*, 124–129. https://doi.org/10.1016/j.ejogrb.2023.07.017

Verret, B., Cortés, J., Bachelot, T., André, F., André, F., & Arnedos, M. (2019). Efficacy of PI3K inhibitors in advanced breast cancer. *Annals of Oncology*, *30*. https://doi.org/10.1093/annonc/mdz381

Volz, C., Breid, S., Selenz, C., Zaplatina, A., Golfmann, K., Meder, L., Dietlein, F., Borchmann, S., Chatterjee, S., Siobal, M., Schöttle, J., Florin, A., Koker, M., Nill, M., Ozretić, L., Uhlenbrock, N., Smith, S., Büttner, R., Miao, H., … Ullrich, R. (2020). Inhibition of Tumor VEGFR2 Induces Serine 897 EphA2-Dependent Tumor Cell Invasion and Metastasis in NSCLC. *Cell Reports*, *31 4*, 107568. https://doi.org/10.1016/j.celrep.2020.107568

Wang, C., Cheng, L., Song, S., Wu, S., & Sun, G. (2020). Gli1 interacts with YAP1 to promote tumorigenesis in esophageal squamous cell carcinoma. *Journal of Cellular Physiology*, *235*, 8224–8235. https://doi.org/10.1002/jcp.29477

Wang, C., Li, J., Qu, L., Tang, X., Song, X., Yang, F., Chen, X., Lin, Q., Lin, W., Zhou, Y., Tu, Z.-C., Chen, Y., Zhang, Z., & Lu, X. (2022). Discovery of D6808, a Highly Selective and Potent Macrocyclic c-Met Inhibitor for Gastric Cancer Harboring MET Gene Alteration Treatment. *Journal of Medicinal Chemistry*. https://doi.org/10.1021/acs.jmedchem.2c00981

Wang, J., Lu, Y., Sun, G., Fang, Z., Xing, Z., Nong, W., Wei, Y., Wang, S., Shi, G., Dong, M., & Wang, J. (2023). Machine learning algorithms for a novel cuproptosis-related gene signature of diagnostic and immune infiltration in endometriosis. *Scientific Reports*, *13*. https://doi.org/10.1038/s41598-023-48990-w

Wang, L., Tuo, H., Song, Z., Li, W., & Peng, Y. (2021). Reg3A (regenerating family member 3 alpha) acts as a tumor suppressor by targeting DMBT1 (deleted in malignant brain tumors 1) in gastric cancer. *Bioengineered*, *12*, 7644–7655. https://doi.org/10.1080/21655979.2021.1981800

Wang, L., Wang, L., Yu, Y., Su, R., Zhang, Y.-T., Li, Y., & Zang, M. (2022). Aldehyde Dehydrogenase 1 in Gastric Cancer. *Journal of Oncology*, *2022*. https://doi.org/10.1155/2022/5734549

Wang, L., Xing, Q., Feng, T., He, M., Yu, W., & Chen, H. (2020). SNP rs710886 A>G in long noncoding RNA PCAT1 is associated with the risk of endometriosis by modulating expression of multiple stemness-related genes via microRNA-145 signaling pathway. *Journal of Cellular Biochemistry*, *121*(2), 1703–1715. https://doi.org/10.1002/JCB.29406

Wang, L., Zhou, X., Yan, H., Miao, Y., Wang, B., Gu, Y., Fan, W., Xu, K., Huang, S., & Liu, J. (2024). Deciphering the role of tryptophan metabolism-associated genes ECHS1 and ALDH2 in gastric cancer: implications for tumor immunity and personalized therapy. *Frontiers in Immunology*, *15*. https://doi.org/10.3389/fimmu.2024.1460308

Wang, M., Sun, X. Y., Zhou, Y. C., Zhang, K. J., Lu, Y. Z., Liu, J., Huang, Y. C., Wang, G. Z., Jiang, S., & Zhou, G. B. (2020). Suppression of Musashi-2 by the small compound largazole exerts inhibitory effects on malignant cells. *International Journal of Oncology*, *56*(5), 1274–1283. https://doi.org/10.3892/IJO.2020.4993

Wang, M.-H., Qin, S.-Y., Zhang, S.-G., Li, G.-X., Yu, Z.-H., Wang, K., Wang, B., Teng, M.-J., & Peng, Z.-H. (2015). Musashi-2 promotes hepatitis Bvirus related hepatocellular carcinoma progression via the Wnt/β-catenin pathway. *American Journal of Cancer Research*, *5*(3), 1089–1100.

Wang, Q., Zhang, Y., Yuan, X., Xu, K., Yu, J., Chen, Z., Beroukhim, R., Wang, H., Lupien, M., Wu, T., Regan, M., Meyer, C., Carroll, J., Manrai, A., Jänne, O., Balk, S., Mehra, R., Han, B., Chinnaiyan, A., … Brown, M. (2009). Androgen Receptor Regulates a Distinct Transcription Program in Androgen-Independent Prostate Cancer. *Cell*, *138*, 245–256. https://doi.org/10.1016/j.cell.2009.04.056

Wang, R., Liu, L., Jiao, J., & Gao, D. (2020). Knockdown of MIR4435-2HG Suppresses the Proliferation, Migration and Invasion of Cervical Cancer Cells via Regulating the miR-128-3p/MSI2 Axis in vitro. *Cancer Management and Research*, *12*, 8745–8756. https://doi.org/10.2147/CMAR.S265545

Wang, S., Li, N., Yousefi, M., Nakauka-Ddamba, A., Li, F., Parada, K., Rao, S., Minuesa, G., Katz, Y., Gregory, B. D., Kharas, M. G., Yu, Z., & Lengner, C. J. (2015). Transformation of the intestinal epithelium by the MSI2 RNA-binding protein. *Nature Communications 2015 6:1*, *6*(1), 1–15. https://doi.org/10.1038/ncomms7517

Wang, S., Li, Z., Li, P.-P., Li, L., Liu, Y., Feng, Y.-L., Li, R., & Xia, S. (2023). SOX2 Promotes Radioresistance in Non-small Cell Lung Cancer by Regulating Tumor Cells Dedifferentiation. *International Journal of Medical Sciences*, *20*, 781–796. https://doi.org/10.7150/ijms.75315

Wang, X., Wang, R., Bai, S., Xiong, S., Li, Y., Liu, M., Zhao, Z., Wang, Y., Zhao, Y., Chen, W., Billiar, T. R., & Cheng, B. (2019). Musashi2 contributes to the maintenance of CD44v6+ liver cancer stem cells via notch1 signaling pathway. *Journal of Experimental & Clinical Cancer Research : CR*, *38*(1). https://doi.org/10.1186/S13046-019-1508-1

Wang, Y., Zheng, L., Shang, W., Yang, Z., Li, T., Liu, F., Shao, W., Lv, L., Chai, L., Qu, L., Xu, Q., Du, J., Liang, X., Zeng, J., & Jia, J. (2022). Wnt/beta-catenin signaling confers ferroptosis resistance by targeting GPX4 in gastric cancer. *Cell Death and Differentiation*, *29*, 2190–2202. https://doi.org/10.1038/s41418-022-01008-w

Wang, Z. L., Wang, C., Liu, W., & Ai, Z. L. (2020). Upregulation of microRNA-143-3p induces apoptosis and suppresses proliferation, invasion, and migration of papillary thyroid carcinoma cells by targeting MSI2. *Experimental and Molecular Pathology*, *112*, 104342. https://doi.org/10.1016/J.YEXMP.2019.104342

Wang, Z., Wang, F., Ding, X., Li, T.-E., Wang, H.-Y., Gao, Y.-H., Wang, W.-J., Liu, Y., Chen, X.-S., & Shen, K. (2021). Hippo/YAP signaling choreographs the tumor immune microenvironment to promote triple negative breast cancer progression via TAZ/IL-34 axis. *Cancer Letters*. https://doi.org/10.21203/RS.3.RS-524972/V1

Wang, Z., Yang, C., Zhang, H., Gao, Y., Xiao, M., Wang, Z., Yang, L., Zhang, J., Ren, C., & Liu, J. (2022). In Situ Transformable Supramolecular Nanomedicine Targeted Activating Hippo Pathway for Triple-Negative Breast Cancer Growth and Metastasis Inhibition. *ACS Nano*. https://doi.org/10.1021/acsnano.2c05263

Wang, Z., Zhang, Q., Zhang, C., Yan, J., Yang, T., & Jiang, A. (2024). CADM2 participates in endometriosis development by influencing the epithelial-mesenchymal transition. *Reproductive Sciences*. https://doi.org/10.1007/s43032-024-01592-x

Wang, Z.-L., Cong, W., Wei, L., & Zhi-Long, A. (2022). Retraction: Emerging roles of the long non-coding RNA 01296/microRNA-143-3p/MSI2 axis in development of thyroid cancer. In *Bioscience reports* (Vol. 42, Issue 12). https://doi.org/10.1042/BSR-2018-2376_RET

Watanabe, H., Ichihara, E., Kayatani, H., Makimoto, G., Ninomiya, K., Nishii, K., Higo, H., Ando, C., Okawa, S., Nakasuka, T., Kano, H., Hara, N., Hirabae, A., Kato, Y., Ninomiya, T., Kubo, T., Rai, K., Ohashi, K., Hotta, K., … Kiura, K. (2021). VEGFR2 blockade augments the effects of tyrosine kinase inhibitors by inhibiting angiogenesis and oncogenic signaling in oncogene-driven non-small-cell lung cancers. *Cancer Science*, *112*, 1853–1864. https://doi.org/10.1111/cas.14801

Wei, F., Xu, X., Gao, C., Sun, Y., Zhao, Z., Cui, T., Zhang, H., & Zhou, Z. (2024). Wnt/β-Catenin signaling pathway in hepatocellular carcinoma: pathogenic role and therapeutic target. *Frontiers in Oncology*, *14*. https://doi.org/10.3389/fonc.2024.1367364

Wen, S., Hou, Y., Fu, L., Xi, L., Yang, D., Zhao, M., Qin, Y., Sun, K., Teng, Y., & Liu, M. (2019). Cancer-associated fibroblast (CAF)-derived IL32 promotes breast cancer cell invasion and metastasis via integrin β3-p38 MAPK signalling. *Cancer Letters*, *442*, 320–332. https://doi.org/10.1016/j.canlet.2018.10.015

Wu, Q., Liu, Z., Li, B., Liu, Y., & Wang, P. (2023). Immunoregulation in cancer-associated cachexia. *Journal of Advanced Research*, *58*, 45–62. https://doi.org/10.1016/j.jare.2023.04.018

Wu, W., Li, J., Dong, D., Dou, F., Lin, Y., Yang, X., Zhou, Y., & Xie, J. (2022). Prognostic value of MSI2 expression in human malignancies: A PRISMA-compliant meta-analysis. *Medicine*, *101*(52), e32064. https://doi.org/10.1097/MD.0000000000032064

Xia, Y., Wei, K., Yang, F., Hu, L.-Q., Pan, C., Pan, X., Wu, W., Wang, J., Wen, W., He, Z., Xu, J., Xu, X., Zhu, Q., & Chen, L. (2019). miR-1260b, mediated by YY1, activates KIT signaling by targeting SOCS6 to regulate cell proliferation and apoptosis in NSCLC. *Cell Death & Disease*, *10*. https://doi.org/10.1038/s41419-019-1390-y

Xiao, G., & Schmid, S. (2020). FCHSD2 controls oncogenic ERK1/2 signaling outcome by regulating endocytic trafficking. *PLoS Biology*, *18*. https://doi.org/10.1101/2020.01.29.924449

Xie, G., & Richard, H. (2024). m6A mRNA Modifications in Glioblastoma: Emerging Prognostic Biomarkers and Therapeutic Targets. *Cancers*, *16*. https://doi.org/10.3390/cancers16040727

Xie, H.-J., Yadong, Li, J., Chen, H., Xie, Y.-F., Chen, M.-Z., Zhao, X., Tang, S., Zhao, S., Zhang, Y., Du, J., Zhang, F., & Gu, L. (2020). WNT7A Promotes EGF-Induced Migration of Oral Squamous Cell Carcinoma Cells by Activating β-Catenin/MMP9-Mediated Signaling. *Frontiers in Pharmacology*, *11*. https://doi.org/10.3389/fphar.2020.00098

Xie, Y., Kong, W., Zhao, X., Luo, D., Chen, S., Zhang, H., & Ran, Y. (2023). Metformin Inhibits the Estrogen-mediated Epithelial-Mesenchymal Transition of Ectopic Endometrial Stromal Cells in Endometriosis. *In Vivo*, *37*, 2490–2497. https://doi.org/10.21873/invivo.13356

Xing, Z., Zhang, M., Wang, X., Liu, J., Liu, G., Feng, K., & Wang, X. (2021). Silencing of Nek2 suppresses the proliferation, migration and invasion and induces apoptosis of breast cancer cells by regulating ERK/MAPK signaling. *Journal of Molecular Histology*, *52*, 809–821. https://doi.org/10.1007/s10735-021-09979-9

Xiong, Y., Zu, X., Wang, L., Li, Y., Chen, M., He, W., & Qi, L. (2021). The VIM-AS1/miR-655/ZEB1 axis modulates bladder cancer cell metastasis by regulating epithelial–mesenchymal transition. *Cancer Cell International*, *21*. https://doi.org/10.1186/s12935-021-01841-y

Xu, H., Niu, M., Yuan, X., Wu, K., & Liu, A. (2020). CD44 as a tumor biomarker and therapeutic target. *Experimental Hematology & Oncology*, *9*. https://doi.org/10.1186/s40164-020-00192-0

Xu, J., Hu, S., Chen, Q., Shu, L., Wang, P., & Wang, J. (2023). Integrated bioinformatics analysis of noncoding RNAs with tumor immune microenvironment in gastric cancer. *Scientific Reports*, *13*. https://doi.org/10.1038/s41598-023-41444-3

Xu, J., Zhou, Y., Yang, J., Gu, Y., Zhang, E., Yuan, W., Wang, C., Jin, G., Hongxia, & Hu, Z. (2021). Hypomethylation-activated cancer-testis gene LIN28B promotes cell proliferation and metastasis in gastric cancer. *Gene*, 146115. https://doi.org/10.1016/j.gene.2021.146115

Xu, T., Yu, T., Xie, M., Fang, Y., Xu, T., Pan, Y.-T., Pei, & Shu, Y. (2022). LOC101929709 promotes gastric cancer progression by aiding LIN28B to stabilize c-MYC mRNA. *Gastric Cancer*, *26*, 169–186. https://doi.org/10.1007/s10120-022-01348-z

Xu, X., Hou, Y., Long, N., Jiang, L., Yan, Z., Xu, Y., Lv, Y., Xiang, X., Yang, H., Liu, J., Qi, X., & Chu, L. (2023). TPPP3 promote epithelial-mesenchymal transition via Snail1 in glioblastoma. *Scientific Reports*, *13*. https://doi.org/10.1038/s41598-023-45233-w

Xu, Y., Li, T., Shen, A., Bao, X., Lin, J.-F., Guo, L., Meng, Q., Ruan, D.-Y., Zhang, Q.-H., Zuo, Z.-X., & Zeng, Z.-L. (2023). FTO up-regulation induced by MYC suppresses tumour progression in Epstein–Barr virus-associated gastric cancer. *Clinical and Translational Medicine*, *13*. https://doi.org/10.1002/ctm2.1505

Yadav, A., Sata, T. N., Verma, D., Mishra, A., Sah, A., Hossain, M., Pant, K., & Venugopal, S. (2022). Free fatty acid-induced miR-181a-5p stimulates apoptosis by targeting XIAP and Bcl2 in hepatic cells. *Life Sciences*, 120625. https://doi.org/10.1016/j.lfs.2022.120625

Yaeger, R., & Corcoran, R. (2019). Targeting Alterations in the RAF-MEK Pathway. *Cancer Discovery*, *9 3*, 329–341. https://doi.org/10.1158/2159-8290.CD-18-1321

Yamamoto, T., Oshima, T., Yoshihara, K., Yamanaka, S., Nishii, T., Arai, H., Inui, K., Kaneko, T., Nozawa, A., Woo, T., Rino, Y., Masuda, M., & Imada, T. (2010). Reduced expression of claudin-7 is associated with poor outcome in non-small cell lung cancer. *Oncology Letters*, *1 3*, 501–505. https://doi.org/10.3892/OL_00000088

Yan, W., Di Magliano, P., Bischoff, A., & Bednar, F. (2024). Abstract PR-03: Canonical Notch signaling in cancer-associated fibroblasts supports an immunosuppressive pancreatic tumor microenvironment. *Cancer Research*. https://doi.org/10.1158/1538-7445.pancreatic24-pr-03

Yang, C., Zhang, W., Wang, L., Kazobinka, G., Han, X., Li, B., & Hou, T. (2016). Musashi-2 promotes migration and invasion in bladder cancer via activation of the JAK2/STAT3 pathway. *Laboratory Investigation*, *96*(9), 950–958. https://doi.org/10.1038/labinvest.2016.71

Yang, D., Dong, L., Qiu, Y.-B., & Luo, G.-Y. (2021). An oncogenic lncRNA, GLCC1, promotes tumorigenesis in gastric carcinoma by enhancing the c-Myc/IGF2BP1 interaction. *Neoplasma*. https://doi.org/10.4149/neo_2021_210121N100

Yang, H., Hu, J., Chen, J., Chen, Z., Jiao, F., Cui, J., Quan, M., & Wang, L. (2020). RNA-binding protein Musashi2 regulates Hippo signaling via SAV1 and MOB1 in pancreatic cancer. *Medical Oncology*, *37*(9), 1–13. https://doi.org/10.1007/S12032-020-01384-8/METRICS

Yang, H., Wang, L., Zhao, J., Chen, Y., Lei, Z., Liu, X., Xia, W., Guo, L.-L., & Zhang, H.-T. (2015). TGF-β-activated SMAD3/4 complex transcriptionally upregulates N-cadherin expression in non-small cell lung cancer. *Lung Cancer*, *87 3*, 249–257. https://doi.org/10.1016/j.lungcan.2014.12.015

Yang, Y., Zhao, M., Ding, T., Ni, C., Zheng, Q., & Li, X. (2022). [Advances in research of Musashi2 in solid tumors]. *Nan fang yi ke da xue xue bao = Journal of Southern Medical University*, *42*(3), 448–456. https://doi.org/10.12122/j.issn.1673-4254.2022.03.20

Yang, Y.-M., & Yang, W.-X. (2017). Epithelial-to-mesenchymal transition in the development of endometriosis. *Oncotarget*, *8*, 41679–41689. https://doi.org/10.18632/oncotarget.16472

Yang, Z., Li, J., Shi, Y., Li, L., & Guo, X. (2019). Increased musashi 2 expression indicates a poor prognosis and promotes malignant phenotypes in gastric cancer. *Oncology Letters*, *17*(3), 2599–2606. https://doi.org/10.3892/ol.2019.9889

Yao, K., Zhan, X.-Y., Feng, M., Yang, K., Zhou, M.-S., & Jia, H. (2024). Furin, ADAM, and γ-secretase: Core regulatory targets in the Notch pathway and the therapeutic potential for breast cancer. *Neoplasia (New York, N.Y.)*, *57*. https://doi.org/10.1016/j.neo.2024.101041

Yao, S., Gan, C., Wang, T., Zhang, Q., Zhang, M., & Cheng, H. (2022). High ALDH2 expression is associated with better prognosis in patients with gastric cancer. *American Journal of Cancer Research*, *12 12*, 5425–5439. https://consensus.app/papers/high-aldh2-expression-is-associated-with-better-prognosis-yao-gan/2bec3e2ed2de5af9aa35b5fbd0ac17f7/

Ye, M., Zhao, L., Zhang, L., Wu, S., Li, Z., Qin, Y., Lin, F., & Pan, L. (2022). LncRNA NALT1 promotes colorectal cancer progression via targeting PEG10 by sponging microRNA-574-5p. *Cell Death & Disease*, *13*. https://doi.org/10.1038/s41419-022-05404-5

Yeh, D.-W., Zhao, X., Siddique, H. R., Zheng, M., Choi, H. Y., Machida, T., Narayanan, P., Kou, Y., Punj, V., Tahara, S. M., Feldman, D. E., Chen, L., & Machida, K. (2023). MSI2 promotes translation of multiple IRES-containing oncogenes and virus to induce self-renewal of tumor initiating stem-like cells. *Cell Death Discovery*, *9*(1), 141. https://doi.org/10.1038/s41420-023-01427-9

Yesharim, L., Talebi, S., Mojbafan, M., Alemrajabi, M., & Teimourian, S. (2022). An evaluation of gastric adenocarcinoma-associated CircRNAs based on microarray meta-analysis and ceRNA networks. *Translational Oncology*, *28*. https://doi.org/10.1016/j.tranon.2022.101611

Yiming, R., Takeuchi, Y., Nishimura, T., Li, M., Wang, Y., Meguro-Horike, M., Kohno, T., Horike, S. ichi, Nakata, A., & Gotoh, N. (2021). MUSASHI-2 confers resistance to third-generation EGFR-tyrosine kinase inhibitor osimertinib in lung adenocarcinoma. *Cancer Science*, *112*(9), 3810–3821. https://doi.org/10.1111/CAS.15036

Yin, Z., Wu, D., Shi, J., Wei, X., Jin, N., Lu, X., & Ren, X. (2020). Identification of ALDH3A2 as a novel prognostic biomarker in gastric adenocarcinoma using integrated bioinformatics analysis. *BMC Cancer*. https://doi.org/10.1186/s12885-020-07493-x

Yip, P. (2015). Phosphatidylinositol 3-kinase-AKT-mammalian target of rapamycin (PI3K-Akt-mTOR) signaling pathway in non-small cell lung cancer. *Translational Lung Cancer Research*, *4 2*, 165–176. https://doi.org/10.3978/j.issn.2218-6751.2015.01.04

Yousefi, H., Delavar, M. R., Piroozian, F., Baghi, M., Nguyen, K., Cheng, T., Vittori, C., Worthylake, D., & Alahari, S. (2022). Hippo signaling pathway: A comprehensive gene expression profile analysis in breast cancer. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *151*, 113144. https://doi.org/10.1016/j.biopha.2022.113144

Yu, J., Li, Y., Qu, J., Wang, W., & Zhou, Y. (2021). CASK regulates Notch pathway and functions as a tumor promoter in pancreatic cancer. *Archives of Biochemistry and Biophysics*, 108789. https://doi.org/10.1016/j.abb.2021.108789

Yu, J., Zhou, Z., Wei, Z.-W., Wu, J., Ouyang, J., Huang, W., He, Y., & Zhang, C. (2020). FYN promotes gastric cancer metastasis by activating STAT3-mediated epithelial-mesenchymal transition. *Translational Oncology*, *13*. https://doi.org/10.1016/j.tranon.2020.100841

Yu, L., Davis, I., & Liu, P. (2023). Regulation of EWSR1-FLI1 Function by Post-Transcriptional and Post-Translational Modifications. *Cancers*, *15*. https://doi.org/10.3390/cancers15020382

Yuan, F., Cai, X., Cong, Z., Wang, Y., Geng, Y., Aili, Y., Du, C., Zhu, J., Yang, J., Tang, C., Zhang, A., Zhao, S., & Chiyuan. (2022). Roles of the m6A Modification of RNA in the Glioblastoma Microenvironment as Revealed by Single-Cell Analyses. *Frontiers in Immunology*, *13*. https://doi.org/10.3389/fimmu.2022.798583

Zambon, C., Fadi, E., Bozzato, D., Plebani, M., Padoan, A., Navaglia, F., Semenzato, G., Pantano, G., Teolato, S., Greco, E., Facco, M., Basso, D., Pedrazzoli, S., Sanzari, M., & Fogar, P. (2011). Pancreatic Cancer Alters Human CD4+ T Lymphocyte Function: A Piece in the Immune Evasion Puzzle. *Pancreas*, *40*, 1131–1137. https://doi.org/10.1097/MPA.0b013e31822077b8

Zeng, F., Cao, J., Chen, Y., Tang, J., He, Q., Liao, S., Liang, L., Li, W., Liu, S., Luo, G., & Zhou, Y. (2024). Fra-1 affects chemotherapy sensitivity by inhibiting ferroptosis in gastric cancer cells. *Cancer Drug Resistance*, *7*. https://doi.org/10.20517/cdr.2024.101

Zeng, X., Xiao, J., Bai, X., Liu, Y., Zhang, M., Liu, J., Lin, Z., & Zhang, Z.-W. (2022). Research progress on the circRNA/lncRNA-miRNA-mRNA axis in gastric cancer. *Pathology, Research and Practice*, *238*, 154030. https://doi.org/10.1016/j.prp.2022.154030

Zepecki, J., Karambizi, D., Fajardo, J., Snyder, K., Guetta-Terrier, C., Tang, O., Chen, J.-S., Sarkar, A., Fiser, A., Toms, S., & Tapinos, N. (2020). miRNA-mediated loss of m6A increases nascent translation in glioblastoma. *PLoS Genetics*, *17*. https://doi.org/10.1371/journal.pgen.1009086

Zhan, Y., Chen, Z., Li, Y., He, A., He, S., Gong, Y., Li, X., & Zhou, L. (2018). Long non-coding RNA DANCR promotes malignant phenotypes of bladder cancer cells by modulating the miR-149/MSI2 axis as a ceRNA. *Journal of Experimental & Clinical Cancer Research : CR*, *37*(1), 273. https://doi.org/10.1186/s13046-018-0921-1

Zhang, J., Wang, F., Zhang, H., & Cao, M.-Z. (2021). A novel circular RNA circ_HN1/miR-628-5p/Ecto-5'-nucleotidase competing endogenous RNA network regulates gastric cancer development. *Bioengineered*, *12*, 9739–9752. https://doi.org/10.1080/21655979.2021.1989259

Zhang, K., Zhang, L., Mi, Y., Tang, Y., Reng, F., Liu, B., Zhang, Y., & Zheng, P. (2020). A ceRNA network and a potential regulatory axis in gastric cancer with different degrees of immune cell infiltration. *Cancer Science*, *111*, 4041–4050. https://doi.org/10.1111/cas.14634

Zhang, L., Hou, Y., Ashktorab, H., Gao, L., Xu, Y., Wu, K., Zhai, J., & Zhang, L. (2010). The impact of C-MYC gene expression on gastric cancer cell. *Molecular and Cellular Biochemistry*, *344*, 125–135. https://doi.org/10.1007/s11010-010-0536-0

Zhang, N., Hua, X., Tu, H., Li, J., Zhang, Z., & Max, C. (2021). Isorhapontigenin (ISO) inhibits EMT through FOXO3A/METTL14/VIMENTIN pathway in bladder cancer cells. *Cancer Letters*. https://doi.org/10.1016/j.canlet.2021.07.041

Zhang, P., Liu, L., Zhang, L., He, X., Xu, X., Lu, Y., & Li, F. (2020). Runx2 is required for activity of CD44+/CD24-/low breast cancer stem cell in breast cancer development. *American Journal of Translational Research*, *12 5*, 2305–2318. https://consensus.app/papers/runx2-is-required-for-activity-of-cd44cd24low-breast-zhang-liu/f284ec94e0525065a7bce1e1ed70dc65/

Zhang, W., Wu, Q., Liu, Y., Wang, X., Chengbin, & Zhu, W. (2021). LncRNA HOTAIR Promotes Chemoresistance by Facilitating Epithelial to Mesenchymal Transition through miR-29b/PTEN/PI3K Signaling in Cervical Cancer. *Cells Tissues Organs*, *211*, 16–29. https://doi.org/10.1159/000519844

Zhang, X., Su, K., Liu, Y., Zhu, D., Pan, Y., Ke, X., & Qu, Y. (2022). Small Molecule Palmatine Targeting Musashi-2 in Colorectal Cancer. *Frontiers in Pharmacology*, *12*, 793449. https://doi.org/10.3389/FPHAR.2021.793449/BIBTEX

Zhang, Z., Wu, L., Wang, J., Li, G., Feng, D., Zhang, B., Li, L., Yang, J.-D., Lianting, & Qin, H. (2014). Opposing Effects of PI3K/Akt and Smad-Dependent Signaling Pathways in NAG-1-Induced Glioblastoma Cell Apoptosis. *PLoS ONE*, *9*. https://doi.org/10.1371/journal.pone.0096283

Zhao, G., Li, H., Guo, Q., Zhou, A., Wang, X., Li, P., & Zhang, S. (2020). Exosomal Sonic Hedgehog derived from cancer-associated fibroblasts promotes proliferation and migration of esophageal squamous cell carcinoma. *Cancer Medicine*, *9*, 2500–2513. https://doi.org/10.1002/cam4.2873

Zhao, H., Ge, B., Yuan, Y., & Wang, G. (2020). Hyperbaric Oxygen Ameliorated Acute Pancreatitis in Rats via the Mitochondrial Pathway. *Digestive Diseases and Sciences*, 1–12. https://doi.org/10.1007/s10620-020-06070-3

Zhao, J., Zhang, Y., Liu, X. sheng, Zhu, F. ming, Xie, F., Jiang, C. yi, Zhang, Z. ye, Gao, Y. li, Wang, Y. chuan, Li, B., Xia, S. jie, & Han, B. min. (2020). RNA-binding protein Musashi2 stabilizing androgen receptor drives prostate cancer progression. *Cancer Science*, *111*(2), 369–382. https://doi.org/10.1111/CAS.14280

Zhao, L. W., Yu, A. J., Zhang, Y. J., Wang, X. C., Han, B., & Wang, X. H. (2020). MicroRNA-149 suppresses the malignant phenotypes of ovarian cancer via downregulation of MSI2 and inhibition of PI3K/AKT pathway. *European Review for Medical and Pharmacological Sciences*, *24*(1), 55–64. https://doi.org/10.26355/EURREV_202001_19895

Zhao, R., Ning, X., Lu, H., Xu, W., Jiaxin, Cheng, J., & Rong. (2024). XTP8 Promotes Ovarian Cancer Progression by Activating AKT/AMPK/mTOR Pathway to Regulate EMT. *Cell Biochemistry and Biophysics*. https://doi.org/10.1007/s12013-024-01246-4

Zhao, W., Cong, O., Huang, C., Zhang, J., Xiao, Q., Zhang, F., Wang, H., Lin, F., Wang, J., Wang, Z., Jiang, B., & Li, Q. (2023). ELP3 stabilizes c-Myc to promote tumorigenesis. *Journal of Molecular Cell Biology*, *15*. https://doi.org/10.1093/jmcb/mjad059

Zheng, P., Luo, Q., Wang, W., Li, J., Wang, T., Wang, P., Chen, L., Zhang, P., Chen, H., Liu, Y., Dong, P., Xie, G.-H., Yanhui, Jiang, L., Yuan, X., & Shen, L. (2018). Tumor-associated macrophages-derived exosomes promote the migration of gastric cancer cells by transfer of functional Apolipoprotein E. *Cell Death & Disease*, *9*. https://doi.org/10.1038/s41419-018-0465-5

Zheng, W., Peng, W., Qian, F., Zhang, M., Duan, B., Fan, Z., Xie, Y., & Fu, X. (2024). Vitamin D suppresses CD133+/CD44 + cancer stem cell stemness by inhibiting NF-κB signaling and reducing NLRP3 expression in triple-negative breast cancer. *Cancer Chemotherapy and Pharmacology*. https://doi.org/10.1007/s00280-024-04660-w

Zheng, W., Xiang, D., Wen, D., Luo, M., Liang, X., & Cao, L. (2023). Identification of key modules and candidate genes associated with endometriosis based on transcriptome data via bioinformatics analysis. *Pathology, Research and Practice*, *244*, 154404. https://doi.org/10.1016/j.prp.2023.154404

Zheng, X., Wang, X., Zheng, L., Zhao, H., Li, W., Wang, B., Xue, L., Tian, Y., & Xie, Y. (2020). Construction and Analysis of the Tumor-Specific mRNA-miRNA-lncRNA Network in Gastric Cancer. *Frontiers in Pharmacology*, *11*, 1112. https://doi.org/10.3389/fphar.2020.01112

Zhong, B.-H., Ma, Y.-T., Sun, J., Tang, J.-T., & Dong, M. (2024). Transcription factor FOXF2 promotes the development and progression of pancreatic cancer by targeting MSI2. *Oncology Reports*, *52*(1). https://doi.org/10.3892/or.2024.8752

Zhou, G., & Wang, S. (2023). YTHDC2 Retards Cell Proliferation and Triggers Apoptosis in Papillary Thyroid Cancer by Regulating CYLD-Mediated Inactivation of Akt Signaling. *Applied Biochemistry and Biotechnology*, *196*, 588–603. https://doi.org/10.1007/s12010-023-04540-8

Zhou, L., Sheng, W., Jia, C., Shi, X., Cao, R., Wang, G., Lin, Y., Zhu, F., Dong, Q., & Dong, M. (2020). Musashi2 promotes the progression of pancreatic cancer through a novel ISYNA1-p21/ZEB-1 pathway. *Journal of Cellular and Molecular Medicine*, *24*(18), 10560–10572. https://doi.org/10.1111/jcmm.15676

Zhu, D.-Y., Yu, Y., Wang, W., Wu, K., Liu, D., Yang, Y., Zhang, C., Qi, Y., & Zhao, S. (2019). Long noncoding RNA PART1 promotes progression of non-small cell lung cancer cells via JAK-STAT signaling pathway. *Cancer Medicine*, *8*, 6064–6081. https://doi.org/10.1002/cam4.2494

Zhu, H., Xu, W.-Y., Zhang, H., Liu, J., Xu, H., Lu, S.-Y., Dang, S., Kuang, Y., Jin, X., & Wang, Z. (2013). Targeted deletion of Kif18a protects from colitis-associated colorectal (CAC) tumors in mice through impairing Akt phosphorylation. *Biochemical and Biophysical Research Communications*, *438 1*, 97–102. https://doi.org/10.1016/j.bbrc.2013.07.032

Zhu, K., Wu, Y., He, P., Fan, Y., Zhong, X., Zheng, H., & Luo, T. (2022). PI3K/AKT/mTOR-Targeted Therapy for Breast Cancer. *Cells*, *11*. https://doi.org/10.3390/cells11162508

Zhu, Y., Zhou, B., Hu, X., Ying, S., Zhou, Q., Xu, W., Feng, L., Hou, T., Wang, X., Zhu, L., & Jin, H. (2022). LncRNA LINC00942 promotes chemoresistance in gastric cancer by suppressing MSI2 degradation to enhance c-Myc mRNA stability. *Clinical and Translational Medicine*, *12*(1), e703. https://doi.org/10.1002/ctm2.703

Zhuo, Z., Xian, H., Sun, Y.-J., Long, Y., Liu, C., Liang, B., & Zhao, X.-T. (2022). Long noncoding RNA ZNFX1-AS1 promotes the invasion and proliferation of gastric cancer cells by regulating LIN28 and CAPR1N1. *World Journal of Gastroenterology*, *28*, 4973–4992. https://doi.org/10.3748/wjg.v28.i34.4973

Zöllner, S., Amatruda, J., Bauer, S., Collaud, S., De Álava, E., DuBois, S., Hardes, J., Hartmann, W., Kovar, H., Metzler, M., Shulman, D., Streitbürger, A., Timmermann, B., Toretsky, J., Uhlenbruch, Y., Vieth, V., Grünewald, T., & Dirksen, U. (2021). Ewing Sarcoma—Diagnosis, Treatment, Clinical Challenges and Future Perspectives. *Journal of Clinical Medicine*, *10*. https://doi.org/10.3390/jcm10081685

Zong, Z., Zhou, T., Rao, L., Jiang, Z., Li, Y., Hou, Z., Yang, B., Han, F., & Chen, S. (2016). Musashi2 as a novel predictive biomarker for liver metastasis and poor prognosis in colorectal cancer. *Cancer Medicine*, *5*(4), 623–630. https://doi.org/10.1002/cam4.624

Zou, H., Luo, J., Guo, Y., Liu, Y., Wang, Y., Deng, L., & Li, P. (2022). RNA-binding protein complex LIN28/MSI2 enhances cancer stem cell-like properties by modulating Hippo-YAP1 signaling and independently of Let-7. *Oncogene*, *41*(11), 1657–1672. https://doi.org/10.1038/s41388-022-02198-w

Zou, M., Lin, M., Hu, K.-L., & Li, R. (2024). Cross-Tissue Regulatory Network Analyses Reveal Novel Susceptibility Genes and Potential Mechanisms for Endometriosis. *Biology*, *13*. https://doi.org/10.3390/biology13110871

Zou, Y., Lin, X., Bu, J., Lin, Z., Chen, Y., Qiu, Y., Mo, H., Tang, Y., Fang, W., & Wu, Z. (2020). Timeless-Stimulated miR-5188-FOXO1/β-Catenin-c-Jun Feedback Loop Promotes Stemness via Ubiquitination of β-Catenin in Breast Cancer. *Molecular Therapy : The Journal of the American Society of Gene Therapy*. https://doi.org/10.1016/j.ymthe.2019.08.015

Zubrzycka, A., Migdalska-Sęk, M., Jędrzejczyk, S., & Brzeziańska-Lasota, E. (2021). Circulating miRNAs Related to Epithelial–Mesenchymal Transitions (EMT) as the New Molecular Markers in Endometriosis. *Current Issues in Molecular Biology*, *43*, 900–916. https://doi.org/10.3390/cimb43020064

许万增. (2022). The Role of Platelets in the Pathogenesis of Endometriosis and New Therapeutic Ideas. *Advances in Clinical Medicine*. https://doi.org/10.12677/acm.2022.124367

SUPPLEMENTARY DATA

Supplementary Table 1.A. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. EWING'S SARCOMA.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
LncRNA TUG1 promotes Ewing's sarcoma cell proliferation, migration, and invasion via the miR-199a-3p-MSI2 signaling pathway	2021	DOI: 10.4149/neo_2021_201110N1198	In vitro	Ewing's sarcoma	TUG1/miR-199a-3p/MSI2	Upregulated	Indirect

Supplementary Table 1.B. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. GLIOBLASTOMA.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Exploring the role of m6A methylation regulators in glioblastoma multiforme and their impact on the tumor immune microenvironment.	2023	DOI: 10.1096/fj.202301343	In silico	Glioblastoma	m6A methylation PD1-PDL1	Upregulated	Indirect
Glioma glycolipid metabolism: MSI2-SNORD12B-FIP1L1-ZBTB4 feedback loop as a potential treatment target.	2021	doi: 10.1002/ctm2.411	In vitro In vivo In silico	Glioblastoma	Glycolytic pathway Lipid synthesis pathway Alternative polyadenylation (APA) pathway MSI2/SNORD12B/FIP1L1/ZBTB4 loop	Upregulated	Direct
MSI2-TGF-β/TGF-β R1/SMAD3 positive feedback regulation in glioblastoma.	2019	DOI: 10.1007/s00280-019-03892-5	In vitro In vivo	Glioblastoma	TGF-β/SMAD3 EMT activation Snail 1/2	Upregulated	Direct

Supplementary Table 1.C. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. THYROID CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Upregulation of microRNA-143-3p induces apoptosis and suppresses proliferation, invasion, and migration of papillary thyroid carcinoma cells by targeting MSI2.	2020	DOI: 10.1016/j.yexmp.2019.104342	In vitro	Thyroid cancer	MSI2/miR-143-3p BAX/BCL-2	Downregulated	Indirect
Emerging roles of the long non-coding RNA 01296/microRNA-143-3p/MSI2 axis in development of thyroid cancer	2019	DOI: 10.1042/BSR20182376	RETRACTED ON 2022	Thyroid cancer	RETRACTED ON 2022	RETRACTED ON 2022	RETRACTED ON 2022

Supplementary Table 1.D. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. ESOPHAGEAL CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Suppression of Musashi-2 by the small compound largazole exerts inhibitory effects on malignant cells	2020	https://doi.org/10.3892/ijo.2020.4993	In vitro In vivo In silico	Esophagueal Squamous Cell Carcinoma	Wnt/β-Catenin	Upregulated	Indirect
Msi2 plays a carcinogenic role in esophageal squamous cell carcinoma via regulation of the Wnt/β-catenin and Hedgehog signaling pathways	2017	https://doi.org/10.1016/j.yexcr.2017.10.016	In vitro In vivo	Esophagueal Squamous Cell Carcinoma	Wnt/β-Catenin Hedgehog	Upregulated	Indirect

Supplementary Table 1.E. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening.NSCLC.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Musashi-2 (MSI2) regulation of DNA damage response in lung cancer.	2023	DOI: 10.1101/2023.06.13.544756	In vitro In vivo In silico	Lung cancer (NSCLC)	DNA Damage Response Cell Cycle regulation (G2/M arrest) VEGFR2, SMAD3, SOX2	Upregulated	Direct
Musashi-2 (MSI2) supports TGF-β signaling and inhibits claudins to promote non-small cell lung cancer (NSCLC) metastasis	2016	DOI: 10.1073/pnas.1613616113	In vitro In vivo In silico	NSCLC	TGF-β/SMAD3 EMT (Claudins, SNAIL and SLUG) Tight junction integrity (TJ) Fibronectin (FN1 regulation	Upregulated	Direct
KLF4 suppresses the proliferation and metastasis of NSCLC cells via inhibition of MSI2 and regulation of the JAK/STAT3 signaling pathway.	2022	10.1016/j.tranon.2022.101396	In vitro	NSCLC	JAK2/STAT3	Upregulated	Indirect
Musashi-2 (MSI2) regulates epidermal growth factor receptor (EGFR) expression and response to EGFR inhibitors in EGFR-mutated non-small cell lung cancer (NSCLC).	2021	https://doi.org/10.1038/s41389-021-00317-y	In vivo xenografts In vitro cell lines In silico prediction of binding motifs on EGFR mRNA	NSCLC	EGFR/ERBB3/ERBB2 PI3KK/AK1/mTOR RAS/RAF/MEK/ERK TGF-β/SMAD3 Pathway	Upregulated	Direct
Musashi-2 in cancer-associated fibroblasts promotes non-small cell lung cancer metastasis through paracrine IL-6-driven epithelial-mesenchymal transition.	2023	https://doi.org/10.1186/s13578-023-01158-5	In vitro In vivo In silico	NSCLC	EMT pathway IL-6/JAK2/STAT3	Upregulated	Indirect
Musashi 2 (MSI2) expression as an independent prognostic biomarker in non-small cell lung cancer (NSCLC).	2020	doi. 10.21037/jtd-20-2787	Observational retrospective cohort study In silico	NSCLC	TGF-β/SMAD EGFR Wnt/β-catenin JAK/STAT	Upregulated	Direct
Suppression of Musashi-2 by the small compound largazole exerts inhibitory effects on malignant cells	2020	https://doi.org/10.3892/ijo.2020.4993	In vitro In vivo In silico	NSCLC	PI3K/Akt/mTOR TGF-β	Downregulated	Direct
Musashi RNA-Binding Proteins as Cancer Drivers and Novel Therapeutic Targets.	2017	10.1158/1078-0432.CCR-16-2728	In vitro In vivo	Lung cancer (NSCLC)	TGF-β/Smad tight junction	Upregulated	Direct
MUSASHI-2 confers resistance to third-generation EGFR-tyrosine kinase inhibitor osimertinib in lung adenocarcinoma.	2021	https://doi.org/10.1111/cas.15036	In vitro	Lung cancer	Nanog SOX2	Upregulated	Direct
Regulation of VEGFR2 and AKT Signaling by Musashi-2 in Lung Cancer	2023	DOI: 10.3390/cancers15092229	In vitro In silico	Lung cancer	VEGFR2 PTEN/AKT VEGF-A	Upregulated	Direct
Inhibition effect of miR-598 on migration and invasion of non-small cell lung cancer by targeting MSI2	2021	https://doi.org/10.1155/2021/9997806	In vitro In silico	NSCLC	miR-598/MSI2	Downregulated	Direct
Regulation of lung cancer initiation and progression by the stem cell determinant Musashi	2025	https://doi.org/10.7554/eLife.97021.2	In vitro In vivo	Lung cancer	Stemness/Developmental signaling (Prcn, Nupr1, Mbd3) DNA repair pathways (Brca1 and Atm) Metabolic regulators (Pck2, Cpt1 isoforms, Glud1) Oncogenic Signaling factors (Gli1, Tubb3, Ccr1) Novel effectors: Ptgds (prostaglandin D2 synthase), Arl2bp (binds and supports nuclear STAT3), Rnf157 (E3 ligase implicated in cell survival), Syt11 (vesicular trafficking protein).	Upregulated	Direct

Supplementary Table 1.F. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. BREAST CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Evaluation of cfDNA as an early detection assay for dense tissue breast cancer	2022	https://doi.org/10.1038/s41598-022-12457-1	Clnical Trial In silico	Breast cancer	TFGB/SMAD EMT	Upregulated	Direct
DBC2/RhoBTB2 functions as a tumor suppressor protein via Musashi-2 ubiquitination in breast cancer.	2016	https://doi.org/10.1038/onc.2016.441	In vitro	Breast cancer	p21/DBC2 BAX/Bcl-2 MAPK/ERK	Downregulated	Direct
RNA-binding protein MSI2 isoforms expression and regulation in progression of triple-negative breast cancer.	2020	https://doi.org/10.1186/s13046-020-01587-x	In vitro In vivo In silico	Breast cancer	TP53 signaling MAPK/ERK 1/2 p73/DUSP10 singnaling cascade	Upregulated	Direct
Knockdown of Musashi RNA Binding Proteins Decreases Radioresistance but Enhances Cell Motility and Invasion in Triple-Negative Breast Cancer.	2020	10.3390/ijms21062169	In vitro	Breast cancer	Notch signaling EGFR CD44/GBX42 and vimetin	Upregulated	Indirect
Syndecan-1 Depletion Has a Differential Impact on Hyaluronic Acid Metabolism and Tumor Cell Behavior in Luminal and Triple-Negative Breast Cancer Cells.	2021	https://doi.org/10.3390/ijms22115874	In vitro In silico	Breast cancer	PI3K/Akt/mTOR MYC APOPTOSIS EMT	Upregulated	Direct
Mapping genomic and transcriptomic alterations spatially in epithelial cells adjacent to human breast carcinoma.	2017	https://doi.org/10.1038/s41467-017-01357-y	In vitro	Breast cancer	Wnt β-catenin/TCF/LEF	Upregulated	Indirect
RNA-binding protein complex LIN28/MSI2 enhances cancer stem cell-like properties by modulating Hippo-YAP1 signaling and independently of Let-7.	2022	DOI: 10.1038/s41388-022-02198-w	In vitro In vivo In silico	Breast cancer	Hippo/YAP1	Upregulated	Direct
Prolonged DEHP exposure enhances the stemness and metastatic potential of TNBC cells in an MSI2-dependent manner	2025	DOI: 10.7150/ijbs.101598	In vitro In vivo	Breast cancer	PI3K/AKT NFκB Signaling Cascade MMP-9 mediated invasiveness Vimetin and EMT-related pathways Stemness pathways miR-155-5p/MSI2 axis	Upregulated	Direct

Supplementary Table 1.G. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. PANCREATIC CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Image-based detection and targeting of therapy resistance in pancreatic adenocarcinoma.	2016	https://doi.org/10.1038/nature17988	In vitro In vivo In silico	Pancreatic cancer	c-MET signaling Wnt/β-Catenin MSI2/ALDH1/LIN28 BRD4/HMGA2	Upregulated	Direct
Activating miRNA-mRNA network in gemcitabine-resistant pancreatic cancer cell associates with alteration of memory CD4(+) T cells.	2020	https://doi.org/10.21037/atm.2020.03.53	In vitro In silico	Pancreatic cancer	MSI2/CD4+ Ubiquitin-proteasome system IFN-γ/ IL-27 (indirect) IL-6/JAK/STAT3 (indirect)	Upregulated	Direct
The Novel KLF4/MSI2 Signaling Pathway Regulates Growth and Metastasis of Pancreatic Cancer.	2017	https://doi.org/10.1158/1078-0432.CCR-16-1064	In vitro In vivo	Pancreatic cancer	KLF4/MSI2 Wnt/β-Catenin MYC/Cyclin D1/CDK2 Notch	Upregulated	Direct
MSI2 regulates NLK-mediated EMT and PI3KK/AKT/mTOR pathway to promote pancreatic cancer progression.	2024	https://doi.org/10.1186/s12935-024-03444-9	In vitro In vivo In silico	Pancreatic cancer	EMT pathway PI3K/Akt/mTOR	Upregulated	Direct
Single-cell mapping identifies MSI(+) cells as a common origin for diverse subtypes of pancreatic cancer.	2023	https://doi.org/10.1016/j.ccell.2023.09.008	In vitro In vivo In silico	Pancreatic cancer	MAPK/KRAS/Notch MYC HMGB2/TOP2A SOX4/GATA6/OCT4/TEAD2	Upregulated	Indirect
Musashi2 promotes the development and progression of pancreatic cancer by down-regulating Numb protein.	2017	10.18632/oncotarget.8736	In vitro In vivo	Pancreatic cancer	Numb/Notch/p53/Gli1(Hedgehog) MSI2/SOX2 Ki-67	Upregulated	Direct
Cooperation of Musashi-2, Numb, MDM2, and P53 in drug resistance and malignant biology of pancreatic cancer.	2017	10.1096/fj.201601240R	In vitro In vivo	Pancreatic cancer	Numb/MDM2/p53	Upregulated	Direct
Musashi2 promotes EGF-induced EMT in pancreatic cancer via ZEB1-ERK/MAPK signaling.	2020	https://doi.org/10.1186/s13046-020-1521-4	In vitro In vivo	Pancreatic cancer	EGF/EGFR ZEB1-ERK/MAPK EMT MYC	Upregulated	Direct
RNA-binding protein Musashi2 regulates Hippo signaling via SAV1 and MOB1 in pancreatic cancer.	2020	https://doi.org/10.1007/s12032-020-01384-8	In vitro	Pancreatic cancer	Hippo pathway	Upregulated	Direct
Transcription factor FOXF2 promotes the development and progression of pancreatic cancer by targeting MSI2.	2024	DOI: 10.3892/or.2024.8752	In vitro In vivo In silico	Pancreatic cancer	FOXF2/MSI2/Numb Cell cycle and apoptotic pathways (indirect)	Upregulated	Direct
Musashi2 promotes the progression of pancreatic cancer through a novel ISYNA1-p21/ZEB-1 pathway.	2020	DOI: 10.1111/jcmm.15676	In vitro	Pancreatic cancer	MSI2/ISYNA1/p21 MSI2/ISYNA1/Zeb-1	Upregulated	Indirect

Supplementary Table 1.H. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. LIVER CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
ADAR1-dependent miR-3144-3p editing simultaneously induces MSI2 expression and suppresses SLC38A4 expression in liver cancer.	2023	https://doi.org/10.1038/s12276-022-00916-8	In vitro In vivo In silico	Liver Cancer	EMT signaling ADAR1/miR-2144-3p	Upregulated	Direct
Musashi2 contributes to the maintenance of CD44v6+ liver cancer stem cellsvia notch1 signaling pathway.	2019	10.1186/s13046-019-1508-1	In vivo In vitro In silico	Liver Cancer	Notch1/LFNG/Hes1/Hey1 Nanog/Oct4/Sox2 MMP7	Upregulated	Direct
Musashi 2 contributes to the stemness and chemoresistance of liver cancer stem cells via LIN28A activation.	2017	https://doi.org/10.1016/j.canlet.2016.10.007	In vitro In vivo	Liver Cancer	MSI2/LIN28A Reprogramming factors	Upregulated	Direct
Musashi-2 promotes hepatitis Bvirus related hepatocellular carcinoma progression via the Wnt/β-catenin pathway	2015	PMID: 26045988	In vitro In vivo	Liver cancer (HCC)	Wnt/β-catenin	Upregulated	Indirect
MSI2 promotes translation of multiple IRES-containing oncogenes and virus to induce self-renewal of tumor initiating stem-like cells	2023	https://doi.org/10.1038/s41420-023-01427-9	In vitro In vivo In silico	Liver cancer (HCC)	MYC pathway Oncogenesis, Self-Renewal, and Stemness RNA Metabolism	Upregulated	Direct

Supplementary Table 1.I. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. PROSTATIC CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
RNA-binding protein Musashi2 stabilizing androgen receptor drives prostate cancer progression.	2020	https://doi.org/10.1111/cas.14280	In vitro In vivo In silico	Prostaic cancer	Androgen receptor stabilization AR protein turnover AR-driven transcriptional cascade	Upregulated	Direct

Supplementary Table 1.J. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. BLADDER CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Suppression of Musashi-2 by the small compound largazole exerts inhibitory effects on malignant cells	2020	https://doi.org/10.3892/ijo.2020.4994	In vitro In vivo In silico	Bladder cancer	JAK2/STAT3	Upregulated	Indirect
MicroRNA-143/Musashi-2/KRAS cascade contributes positively to carcinogenesis in human bladder cancer.	2019	10.1111/cas.14035	In vitro In vivo In silico	Bladder cancer	KRAS/PI3K/AKT KRAS/MAPK MSI2/miR-143	Upregulated	Direct
Musashi-2 promotes migration and invasion in bladder cancer via activation of the JAK2/STAT3 pathway.	2016	https://doi.org/10.1038/labinvest.2016.71	In vitro	Bladder cancer	JAK2/STAT3 WASF3	Upregulated	Indirect
Long non-coding RNA DANCR promotes malignant phenotypes of bladder cancer cells by modulating the miR-149/MSI2 axis as a ceRNA	2018	https://doi.org/10.1186/s13046-018-0921-1	In vitro In vivo	Bladder cancer	EMT Cell proliferation and tumor growth	Upregulated	Indirect

Supplementary Table 1.K. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. COLORECTAL CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Integrated analysis of RNA-binding proteins in human colorectal cancer.	2020	https://doi.org/10.1186/s12957-020-01995-5	In silico	Colorectal cancer	PDK/AKT/mTORC1 axis	Upregulated	Indirect
Prognostic role and biologic features of Musashi-2 expression in colon polyps and during colorectal cancer progression.	2021	https://doi.org/10.1371/journal.pone.0252132	In vitro In silico	Colorectal cancer	TGF-β Signaling E-cadherin/ZO-1 translation EMTsignaling APC WNT PATHWAY	Upregulated	Direct
The Msi Family of RNA-Binding Proteins Function Redundantly as Intestinal Oncoproteins.	2015	https://doi.org/10.1016/j.celrep.2015.11.022	In vivo In vitro In silico	Colorectal cancer	PTEN/mTORC1/AKT MSI2/Bmpr1a Lrig1/ErbB Numb/Notch APC	Upregulated	Direct
Musashi-2 potentiates colorectal cancer immune infiltration by regulating the post-translational modifications of HMGB1 to promote DCs maturation and migration.	2024	https://doi.org/10.1186/s12964-024-01495-z	In vitro In vivo	Colorectal cancer	MSI2/P3000/HMGB1 TNF-α/IL-1β/IL-6/IFN-γ MCP-1/CCL5/CCL11	Upregulated	Direct
Musashi-2 Deficiency Triggers Colorectal Cancer Ferroptosis by Downregulating the MAPK Signaling Cascade to Inhibit HSPB1 Phosphorylation.	2023	https://doi.org/10.1186/s12575-023-00222-1	In vitro In vivo In silico	Colorectal cancer	MAPK/ERK/HSPB1 GPX4/FTH1/ACSL4 PCNA/Ki67 Oxidative phosphorylation and lipid metabolism	Upregulated	Direct
Increased Musashi-2 and Decreased NUMB Protein Levels Observed in Human Colorectal Cancer are reverted to Normal Levels by ATRA-Induced Cell Differentiation.	2018	10.33140/ijcrt/03/02/00003	In vitro	Colorectal cancer	MSI2/Numb/NOTCH ATRA treatment	Upregulated	Indirect
Identification of ASMTL-AS1 and LINC02604 lncRNAs as novel biomarkers for diagnosis of colorectal cancer.	2024	10.1007/s00384-024-04692-x	In vitro In silico	Colorectal cancer	Cell cycle progression and proliferation Apoptosis evasion Invasion and metastasis	Downregulated	Direct
Transformation of the intestinal epithelium by the MSI2 RNA-binding protein.	2015	https://doi.org/10.1038/ncomms7517	In vitro In vivo In silico	Colorectal cancer	PTEN/PDK/AKT/mTorc1 BMP signaling EGFR sifnaling CDKN1A/p21 Numb/Notch	Upregulated	Direct
Small Molecule Palmatine Targeting Musashi-2 in Colorectal Cancer.	2022	https://doi.org/10.3389/fphar.2021.793449	In vitro In vivo	Colorectal cancer	Splicesosome Nucleocytoplasmic transport MYC signaling TNFα–NFκB signaling KRAS signaling	Downregulated	Direct
Musashi2 as a novel predictive biomarker for liver metastasis and poor prognosis in colorectal cancer.	2016	DOI: 10.1002/cam4.624	In vitro	Colorectal cancer	PDK–AKT–mTORC1	Upregulated	Indirect

Supplementary Table 1.L. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. CERVICAL CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Musashi-2 is a prognostic marker for the survival of patients with cervical cancer.	2018	10.3892/ol.2018.8077	In vitro	Cervical cancer	Cell migration and invasive program	Upregulated	Indirect
Knockdown of MIR4435-2HG Suppresses the Proliferation, Migration and Invasion of Cervical Cancer Cells via Regulating the miR-128-3p/MSI2 Axis in vitro.	2020	https://doi.org/10.2147/CMAR.S265545	In vitro	Cervical cancer	miR-128-3p/MSI2 miR4435-2hg/MSI2 Cell proliferation, invasion and migration	Upregulated	Direct
Musashi-2, a novel oncoprotein promoting cervical cancer cell growth and invasion, is negatively regulated by p53-induced miR-143 and miR-107 activation	2017	https://doi.org/10.1186/s13046-017-0617-y	In vitro In silico	Cervical cancer	c-FOS PTEN EMT Cancer stemness	Upregulated	Direct

Supplementary Table 1.M. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. OVARIAN CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Musashi-2 is a novel regulator of paclitaxel sensitivity in ovarian cancer cells.	2016	https://doi.org/10.3892/ijo.2016.3683	In vitro	Ovarian cancer	MSI2/MDR1 p21 Numb	Upregulated	Indirect
Dual Knockdown of Musashi RNA-Binding Proteins MSI-1 and MSI-2 Attenuates Putative Cancer Stem Cell Characteristics and Therapy Resistance in Ovarian Cancer Cells.	2021	https://doi.org/10.3390/ijms222111502	In vitro In silico	Ovarian cancer	Numb/Notch1/3 Cell cycle p21 MYC ALDH-related mechanisms	Upregulated	Direct
SNP rs710886 A>G in long noncoding RNA PCAT1 is associated with the risk of endometriosis by modulating expression of multiple stemness-related genes via microRNA-145 signaling pathway.	2019	https://doi.org/10.1002/jcb.29406	In vitro In silico	Ovarian cancer	PCAT1/miR-145/MSI2 Stemness/proliferation miR-145/SOX2	Upregulated	Direct
MicroRNA-149 suppresses the malignant phenotypes of ovarian cancer via downregulation of MSI2 and inhibition of PI3K/AKT pathway.	2020	https://doi.org/10.26355/eurrev_202001_19895	In vitro	Ovarian cancer	PI3K/AKT EMT miR-149/MSI2	Upregulated	Direct

Supplementary Table 1.N. Operationalization of variables that were extracted for each article included in the scoping review after full-text screening. GASTRIC CANCER.

JOURNAL ARTICLE	YEAR	DOI	STUDY TYPE	SOLID TUMORS TYPE	ALTERED PATHWAY	MSI2 STATUS	EFFECT TYPE
Image-based detection and targeting of therapy resistance in pancreatic adenocarcinoma.	2016	https://doi.org/10.1038/nature17988	In vitro In vivo In silico	Gastrointestinal cacner	Reggenes	Upregulated	Direct
Increased musashi 2 expression indicates a poor prognosis and promotes malignant phenotypes in gastric cancer.	2019	https://doi.org/10.3892/ol.2019.9889	In vitro	Gastric cancer	Proliferation signaling Invasion and metasis Anglogenesis	Upregulated	Indirect
Construction and Analysis of the Tumor-Specific mRNA-miRNA-lncRNA Network in Gastric Cancer.	2020	https://doi.org/10.3389/fphar.2020.01112	In silico	Gastric cancer	KEGG on Cell cycle regulation, DNA repair, inmune-related pathways	Upregulated	Direct
LncRNA LINC00942 promotes chemoresistance in gastric cancer by suppressing MSI2 degradation to enhance c-Myc mRNA stability.	2021	DOI:10.1002/ctm2.703	In vitro In vivo In silico	Gastric cancer	LINC00942/Msi2/c-Myc SCF^β-TRCP–Ubiquitin Proteasome Pathway m6A Epitranscriptomic Regulation	Upregulated	Direct

Supplementary Table 2. Experimental model count of the papers included in the review after the full-text screening.

CATEGORY	Tumor_type	In_Vitro	In_Vivo	In_Silico	Total
BONE TUMORS	Ewing sarcoma	1	0	0	1
HEAD AND NECK TUMORS	Glioblastoma	2	2	2	3
HEAD AND NECK TUMORS	Thyroid cancer	2	0	0	2
GASTROINTESTINAL TUMORS	Esophagus cancer	2	2	1	2
CHEST TUMORS	NSCL	10	7	7	12
CHEST TUMORS	Breast cancer	7	3	4	8
GASTROINTESTINAL TUMORS	Pancreatic cancer	11	8	5	11
GASTROINTESTINAL TUMORS	Liver cancer	5	5	3	5
GASTROINTESTINAL TUMORS	Colorectal cancer	9	6	6	10
URINARY AND GENITAL SYSTEM	Prostatic cancer	1	1	1	1
URINARY AND GENITAL SYSTEM	Bladder cancer	4	4	2	4
URINARY AND GENITAL SYSTEM	Cervical cancer	3	0	1	3
URINARY AND GENITAL SYSTEM	Ovarian cancer	4	0	2	4
GASTROINTESTINAL TUMORS	Gastric cancer	4	2	3	4

Supplementary Table 3. Binary count of the Hallmarks affected by MSI2

	m6A methylation	LIN28/LET7 axis	Hippo pathway	Spliceosome Nucleocytoplasmic transport	Long non-coding and microRNAs*	HALLMARK_GLYCOLYSIS	HALLMARK_FATTY_ACID_METABOLISM	HALLMARK_PROTEIN_SECRETION	HALLMARK_TGF_BETA_SIGNALING	HALLMARK_EPITHELIAL_MESENCHYM/	HALLMARK_IL6_JAK_STAT3_SIGNALIN(	HALLMARK_KRAS_SIGNALING_UP	HALLMARK_PI3K_AKT_MTOR_SIGNALIN	HALLMARK_WNT_BETA_CATENIN_SIGN	HALLMARK_NOTCH_SIGNALING	HALLMARK_P53_PATHWAY	HALLMARK_ANGIOGENESIS	HALLMARK_APOPTOSIS	HALLMARK_HYPOXIA	HALLMARK_TNFA_SIGNALING_VIA_NFI	HALLMARK_MTORC1_SIGNALING	HALLMARK_MYC_TARGETS_V2	HALLMARK_APICAL_JUNCTION	HALLMARK_INFLAMMATORY_RESPONS	HALLMARK_REACTIVE_OXYGEN_SPECI	HALLMARK_E2F_TARGETS	HALLMARK_OXIDATIVE_PHOSPHORYL/	HALLMARK_NOTCH_SIGNALING	HALLMARK_G2M_CHECKPOINT	HALLMARK_HEDGEHOG_SIGNALING	HALLMARK_DNA_REPAIR	HALLMARK_MYC_TARGETS_V1	HALLMARK_UNFOLDED_PROTEIN_RESI	HALLMARK_INTERFERON_GAMMA_RES	HALLMARK_ANDROGEN_RESPONSE
Glioblastoma	1	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bladder cancer	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Breast cancer	0	0	1	0	-1	0	0	0	0	1	0	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cervical cancer	0	0	0	0	-1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Colorectal cancer	0	0	0	1	-1	0	1	0	1	1	0	1	1	1	0	0	1	1	0	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
Esophagueal Squamous Cell Carcinoma	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Ewing sarcoma	0	0	0	0	-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gastric cancer	1	0	0	0	-1	0	0	1	0	1	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0	0	1	0	1	1	1	0	0
Liver Cancer	0	1	0	0	0	0	0	0	0	1	1	1	1	1	0	0	1	1	1	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Lung Cancer (NSCLC)	0	0	0	0	-1	0	0	0	1	1	1	1	1	1	0	0	1	0	0	0	0	0	1	1	0	1	1	0	1	1	1	0	1	0	0
Ovarian cancer	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	1	0	0	0
Pancreatic cancer	0	1	1	0	-1	0	0	0	0	1	1	1	1	1	0	1	0	1	0	1	0	0	1	1	0	1	0	1	1	1	0	1	0	1	0
Prostatic cacner	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Thyroid cacner	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

*The Long non-coding and microRNAs group was assigned a "-1" regulatory status, which reflects its downregulated state.