Journal of Biosciences and Medicines, 2025, 13(6), 142-155
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Research Progress on Signaling Pathways of LGALS1 in Malignant Tumors

Cheng Feng[1,2], Zizhao Ye[1,2], Shixin Wei[1,2], Fuyi Wei[2], Kaiyan Yang[2*]

[1]Graduate School, Youjiang Medical College for Nationalities, Baise, China
[2]Department of Otorhinolaryngology—Head and Neck Surgery, Southwest Hospital Affiliated to Youjiang Medical University for Nationalities, Baise, China
Email: *2493176206@qq.com

How to cite this paper: Feng, C., Ye, Z.Z., Wei, S.X., Wei, F.Y. and Yang, K.Y. (2025) Research Progress on Signaling Pathways of LGALS1 in Malignant Tumors. *Journal of Biosciences and Medicines*, **13**, 142-155.
https://doi.org/10.4236/jbm.2025.136013

Received: May 18, 2025
Accepted: June 16, 2025
Published: June 19, 2025

Abstract

LGALS1 is a protein belonging to the lectin family, widely distributed across immune and non-immune tissues. Characterized by high evolutionary conservation, LGALS1 specifically binds β-galactosides and functions as a multifunctional bioactive protein. It plays pivotal roles in immune regulation, cell migration, and tumor microenvironment remodeling. In malignant tumors, LGALS1 exhibits complex and context-dependent activities. This review systematically examines the downstream signaling pathways modulated by LGALS1—including NF-κB, PI3K/AKT/mTOR, MAPK, Hedgehog, TGF-β, and Wnt—highlighting its dual regulatory roles (promoting or inhibiting tumorigenesis) across cancer types. By synthesizing recent findings, we elucidate the molecular mechanisms underlying LGALS1's context-specific effects and its influence on key signaling cascades. These insights aim to provide a theoretical framework and research directions for future studies targeting LGALS1 in cancer therapy.

Keywords

LGALS1, Signaling Pathways, Malignant Tumors, Multifunctional Bioactive Protein

1. Introduction

Malignant tumors, commonly referred to as cancer, pose a significant global threat to human life and health. The incidence and mortality rates of malignant tumors have been steadily increasing each year. According to statistics, in 2020, there were 19.3 million new cancer cases worldwide, resulting in nearly 10 million deaths. Projections indicate that by 2040, the number of new cancer cases will rise

to 28.4 million, reflecting a rapid escalation in both the global incidence and mortality rates of cancer [1]-[4]. In China, the incidence and mortality rates of malignant tumors are also rising annually, with cancer now being the leading cause of death among the population [2] [5]. Currently, approximately 80% of cancer patients require surgical intervention for either curative treatment or palliative care. However, only 25% of cancer patients worldwide have access to safe, affordable, and timely surgical treatment [4].

Signal pathways play a critical role in fundamental cellular processes such as growth, differentiation, and apoptosis. Dysregulation of these pathways is a key factor contributing to the survival and progression of tumor cells [6]. In recent years, extensive research has highlighted LGALS1, a multifunctional bioactive protein, as an emerging focus in the study of malignant tumors. A growing body of evidence demonstrates that LGALS1 is intimately involved in regulating multiple key signaling pathways and is closely associated with tumor cell proliferation, invasion, metastasis, and immune evasion. This review aims to comprehensively summarize recent advances in understanding the downstream signaling pathways linked to LGALS1 and to elucidate the mechanisms through which LGALS1 influences various cancers. These insights provide a foundation for future studies.

2. Structure and Molecular Functions of LGALS1

LGALS1 is the first identified member of the galectin family and exhibits a high affinity for β-galactosides. Encoded by the LGALS1 gene located on chromosome 22q13.1, it is a 14.5 kDa homodimeric protein composed of four exons. This protein generates a 0.6 kb transcript capable of encoding a 135-amino acid protein [7]-[11]. In humans, LGALS1 exists as a dimer, with its structure stabilized by hydrophobic interactions at the monomer interface and a central hydrophobic core. The dimer features two carbohydrate recognition domains (CRDs) located at opposite ends of the quaternary structure, approximately 5 nm apart. Each CRD can bind a tetrasaccharide, facilitating cell recognition and signal transduction [12]. The LGALS1 sequence contains six cysteine residues, which are sensitive to oxidation. This oxidation sensitivity limits its physiological activity but does not impair its β-galactoside binding capacity [8]. LGALS1 synthesized on ribosomes can be processed for storage within the cell membrane or secreted extracellularly. Inside the cell, it receives regulatory signals through non-carbohydrate binding interactions and participates in mRNA splicing [9]. Extracellularly, LGALS1 binds to glycoproteins in the extracellular matrix or cell surface receptors (e.g., laminin, fibronectin, and integrins), influencing various cellular activities and promoting tumor cell metastasis [8].

LGALS1 is overexpressed in various human cancers, including lung cancer [13], gastric cancer [14]-[16], esophageal cancer [17], cervical cancer [18], bladder cancer [19] where it exerts its multifunctional biological activities. As a glycoprotein, LGALS1 regulates key signaling pathways—including NF-κB, PI3K/AKT/mTOR, MAPK, Hedgehog, TGF-β, and Wnt/β-catenin—by binding β-galactoside ligands

on the cell surface or in the extracellular matrix. This regulation influences tumor cell proliferation, invasion, metastasis, and immune evasion.

Additionally, LGALS1 modulates immune cell infiltration and angiogenesis within the tumor microenvironment, creating conditions favorable for tumor growth. Its overexpression is often associated with tumor malignancy and poor prognosis, making it a valuable biomarker for cancer diagnosis and prognosis assessment [20] [21]. These findings highlight LGALS1 as both a potential biomarker for malignant tumors and a promising therapeutic target. Strategies targeting LGALS1 or its related pathways may offer new directions for cancer treatment (Table 1).

Table 1. Signaling pathways related to malignant tumors regulated by LGALS1.

Signaling Pathway	Role of LGALS1 in Tumors	Examples of Related Tumors
NF-κB Signaling Pathway	Promotes progression in epithelial ovarian cancer [22]; acts as a negative regulator and inhibits cell proliferation in colorectal cancer; regulates the tumor microenvironment in pancreatic ductal adenocarcinoma [12]; promoting growth, metastasis, and exacerbating inflammation; and promotes cell cycle progression in esophageal squamous cell carcinoma [23].	Epithelial ovarian cancer [22]; colorectal cancer [24]; pancreatic ductal adenocarcinoma [12]; esophageal squamous cell carcinoma [23].
PI3K/AKT/mTOR Signaling Pathway	Enhances cell migration in bladder cancer [25]; mediates tumor metastasis and invasion in urothelial carcinoma [26]; inhibits cell proliferation in intrahepatic cholangiocarcinoma [27]; where metformin alleviates pathway activation by suppressing LGALS1.	Bladder cancer [25], urothelial carcinoma [26], intrahepatic cholangiocarcinoma [27]
MAPK Signaling Pathway	Mediates cancer cell metastasis in oral cancer [28]; inhibits cell growth, invasion, and induces apoptosis in osteosarcoma [29]; promotes metastasis and epithelial-mesenchymal transition (EMT) in ovarian cancer [30]; promotes metastasis and epithelial-mesenchymal transition (EMT) in ovarian cancer [31]; and suppresses cell proliferation, migration, and invasion while promoting apoptosis in lung adenocarcinoma [7]	Oral cancer [28], osteosarcoma [29], ovarian cancer [30], cervical cancer [31], lung adenocarcinoma [7]
Wnt/β-catenin Signaling Pathway	Enhances the immune complex characteristics of cancer cells in colorectal cancer [32], thereby promoting metastasis, tumor dissemination, and clinical recurrence	Colorectal cancer [32]
Hedgehog Signaling Pathway	Promotes cell invasion and epithelial-mesenchymal transition (EMT) in gastric cancer [14] and induces vascular mimicry; facilitates signal transduction in pancreatic ductal adenocarcinoma [33]	Gastric cancer [14], pancreatic ductal adenocarcinoma [33]
TGF-β Signaling Pathway	Promotes cell migration and invasion in gastric cancer [34], Promotes cell migration and invasion in gastric cancer [35] inhibits cancer metastasis	Gastric cancer [34], breast cancer [35]

3. Relationship between LGALS1 and the NF-κB Signaling Pathway

Nuclear factor kappa B (NF-κB) is a crucial transcriptional regulatory factor, first discovered in the nuclear extract of B lymphocytes in 1986 [36]. The activation of NF-κB primarily occurs through two pathways: the classical signaling pathway and the non-classical signaling pathway [37]-[40]. In the classical pathway, external stimuli—such as growth factors and cytokines—bind to cell surface receptors, activating the IκB kinase (IKK) complex. This leads to the phosphorylation and degradation of inhibitory IκB proteins, allowing the NF-κB dimer to translocate into the nucleus and activate the transcription of target genes [22]. In the non-classical pathway, specific receptor-induced kinases phosphorylate IKKα, which processes p100 into p52, thereby promoting gene transcription [41]. NF-κB plays a pivotal role in inflammatory responses, immune regulation, and tumorigenesis, and its dysregulation is implicated in various diseases. Therefore, a comprehensive understanding of NF-κB's regulatory mechanisms is essential for elucidating disease pathogenesis and developing effective therapeutic strategies.

The NF-κB signaling pathway is an important intracellular signal transduction pathway closely related to cell growth and differentiation, inflammatory responses, apoptosis, immune response regulation, and stress responses [36]. In various tumors, the abnormal activation of the NF-κB pathway and the oncogenic activities driven by NF-κB components are widely recognized as playing important roles in tumorigenesis and development, serving as key players in many steps [42].

LGALS1 exerts various biological functions in cells and participates in the regulation of multiple signaling pathways, among which the NF-κB signaling pathway is particularly prominent. In epithelial ovarian cancer, Le Chen *et al.* [22] downregulated LGALS1 in epithelial ovarian cancer cells and detected a significant decrease in the levels of p65, p-IKKα/β, MMP-2, and MMP-9, indicating that galectin-1 promotes the progression of epithelial ovarian cancer (EOC) through the activation of the NF-κB pathway. However, in colorectal cancer, LGALS1 affects the NF-κB signaling pathway in a way that interferes with cell proliferation. Its expression leads to the loss of activated IKKα/β and p65, acting as a negative regulator of NF-κB [24]. In pancreatic ductal adenocarcinoma, LGALS1 mainly enhances the production of chemokines such as monocyte chemoattractant protein-1 and cytokine-induced neutrophil chemoattractant-1 through the NF-κB signaling pathway, thereby regulating the tumor microenvironment, promoting tumor growth and metastasis, and exacerbating the degree of inflammation [12]. Previous studies have elucidated that the abnormal activation of the NF-κB signal is related to the progression of esophageal squamous cell carcinoma. The study by Yuanbo Cui *et al.* [23] showed that esophageal squamous cell carcinoma-specific associated fragment non-coding RNA transcript 1 may promote the cell cycle progression of esophageal squamous cell carcinoma cells through LGALS1-dependent NF-κB activation.

In-depth analysis reveals that the bidirectional effects of LGALS1 may be influenced by cytokines and metabolic products in the tumor microenvironment. In the

ovarian cancer microenvironment, high concentrations of pro-inflammatory cytokines may promote LGALS1 binding to specific receptors, thereby activating the NF-κB pathway and driving tumor cell proliferation and metastasis. Conversely, in colorectal cancer, local metabolic changes in the tumor microenvironment may alter the glycosylation state of LGALS1, impairing its ability to effectively activate the NF-κB pathway. Instead, LGALS1 exerts a negative regulatory effect through interactions with other factors. Additionally, differences in the expression or activity of upstream and downstream molecules within the NF-κB signaling pathway may vary across tumor types, further modulating LGALS1's regulatory role in this context.

4. Relationship between LGALS1 and the PI3K/AKT/mTOR Pathway

The PI3K/AKT/mTOR signaling pathway plays a critical role in cellular responses and adaptations by integrating extracellular and intracellular signals [43]. This pathway primarily involves three key components: phosphatidylinositol-3-kinase (PI3K), protein kinase B (AKT), and mammalian target of rapamycin (mTOR). PI3K is typically activated by receptor tyrosine kinases (RTKs) and G-protein-coupled receptors (GPCRs), driving processes such as autophagy, cell migration, and angiogenesis, in addition to initiating this signaling cascade [43]-[48]. mTOR is a family of serine/threonine protein kinases that exist in two distinct complexes: mTOR complex 1 (mTORC1) and mTOR complex 2 (mTORC2). mTORC1 regulates cell metabolism, controlling protein synthesis and autophagy, and promoting cell growth when energy is abundant; whereas mTORC2 is involved in cell proliferation, cytoskeletal organization, and cell survival. This signaling pathway (**Figure 1**) is primarily negatively regulated by the tumor suppressor protein PTEN, which inhibits downstream signaling mediated by AKT [44].

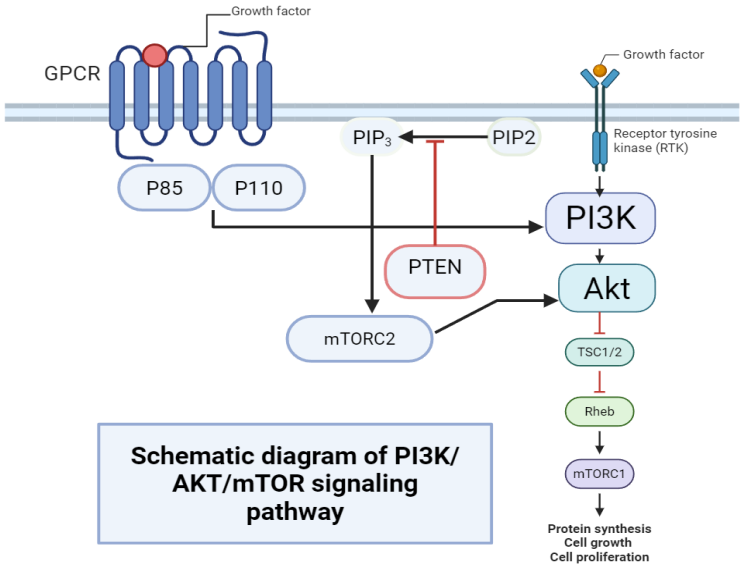

Figure 1. Schematic diagram of the PI3K/Akt/mTOR signaling pathway. Created in https://BioRender.com (Accessed on March 18, 2025).

The PI3K/AKT/mTOR signaling pathway plays a pivotal role in cell differentiation, proliferation, energy and glucose metabolism, apoptosis, the cellular response to oxidative stress, and angiogenesis [43]. This pathway has also been implicated in various human cancers, where it contributes to cancer progression, angiogenesis, chemotaxis, and invasiveness [44].

Bladder cancer, a common malignancy in the urogenital system, has seen limited research on the mechanisms and signaling pathways involving LGALS1. Wu Longxiang *et al.* [25] demonstrated that LGALS1 may enhance the migration ability of bladder cancer cells by promoting AKT signaling pathway phosphorylation, providing initial insights into the relationship between LGALS1 and bladder cancer, as well as the AKT signaling pathway. Yu-Li Su *et al.* [26], in a study of 86 patients with urothelial carcinoma, identified multiple key signaling pathways associated with LGALS1 expression changes. Their findings revealed that LGALS1 regulates downstream proteins in the FAK/PI3K/AKT/mTOR signaling pathway, mediating tumor metastasis and invasion, thus elucidating the connection between LGALS1 and UTUC (urothelial carcinoma) pathways. Intrahepatic cholangiocarcinoma, a highly aggressive tumor, has also been studied in the context of LGALS1. Bioinformatics and molecular biology techniques have been employed to explore metformin's role in inhibiting intrahepatic cholangiocarcinoma cell proliferation. These studies showed that metformin reduces LGALS1 expression, thereby decreasing PI3K/AKT signaling pathway activation and suppressing tumor cell proliferation [27].

Further research indicates that LGALS1 may directly bind to the regulatory subunit of PI3K, stabilizing its activity and promoting AKT phosphorylation. Additionally, LGALS1 regulates the assembly and activity of mTORC1 and mTORC2 complexes, influencing cell metabolism and proliferation. In certain tumor cells, LGALS1 enhances protein synthesis and cell growth by activating mTORC1, while in others, it modulates cell survival and migration by inhibiting mTORC2 activity. This bidirectional effect is thought to be influenced by factors such as the tumor microenvironment's nutritional status, growth factor levels, and intracellular signaling molecule interactions.

5. Relationship between LGALS1 and MAPK and Wnt/β-Catenin Signaling Pathways

The mitogen-activated protein kinase (MAPK) signaling pathway is a crucial eukaryotic pathway for transmitting extracellular signals into cells and regulating gene expression. This pathway comprises four main cascade phosphorylation reactions: extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), p38, and ERK5 [49]. It primarily involves a series of three-tier phosphorylation-dependent kinases: MAPK kinase kinase (MAPKKK), MAPK kinase (MAPKK), and MAPK [50]. Among these, the JNK and p38 MAPK signaling pathways are associated with cellular stress responses and apoptosis, whereas the ERK/MAPK signaling pathway is closely linked to cell proliferation and differen-

tiation [51]. ERK, a serine/threonine protein kinase located in the cytoplasm, primarily consists of ERK1 (p42) and ERK2 (p44) and is tightly connected to growth factor activation [49]. The MAPK signaling pathway collectively regulates a wide range of biological and pathological processes, including cell growth, differentiation, environmental stress adaptation, and inflammatory responses. Additionally, it plays a pivotal role in vascular endothelial cell proliferation and angiogenesis.

The Wnt signaling pathway is an ancient and evolutionarily conserved pathway comprising four key components: extracellular signaling, membrane components, cytoplasmic components, and nuclear components. Based on its characteristics, the Wnt pathway can be categorized into at least three distinct types: the canonical pathway, the planar cell polarity pathway, and the Wnt/Ca^{2+} pathway [52]. The Wnt signaling pathway is essential for cell differentiation and embryonic development and also regulates various other processes, such as cell proliferation, polarization, migration, apoptosis, asymmetric cell division, and the renewal and maintenance of stem cells [52]-[54].

LGALS1 is expressed in various human malignant tumors and influences these cancers through the MAPK signaling pathway. Ji-Min Li *et al.* [28] demonstrated that secretory LGALS1 mediates oral cancer cell metastasis by activating the p38 MAPK pathway. In osteosarcoma, LGALS1 is highly expressed in human osteosarcoma and is associated with distant metastasis in OS patients. Knocking down LGALS1 inhibits the growth and invasion of OS cells and induces apoptosis via the MAPK/ERK signaling pathway [29]. In ovarian cancer, studies have shown that LGALS1 promotes metastasis and enhances epithelial-mesenchymal transition (EMT) by activating the MAPK JNK/p38 signaling pathway [30]. In cervical cancer, LGALS1 has been reported to promote cell proliferation by activating the ERK/MAPK pathway, with its expression and that of vascular endothelial growth factor (VEGF) in cervical squamous cell carcinoma correlating with tumor malignancy and metastasis [31]. Research on lung adenocarcinoma suggests that LGALS1 may inhibit the proliferation, migration, and invasion of lung adenocarcinoma cells while promoting apoptosis through the ERK pathway [7]. In colorectal cancer, the Wnt/β-catenin signaling pathway is central to the disease's pathogenesis. Fibroblast-secreted LGALS1 enhances the immunocomplex characteristics of colorectal cancer cells *in vitro*, simultaneously promoting EMT and activating β-catenin. This leads to in vivo metastasis, tumor spread, and clinical recurrence [32].

The regulation of the MAPK signaling pathway by LGALS1 varies across different cancers, influenced by interactions among multiple molecules in the tumor microenvironment. For instance, in oral cancer, specific growth factors activate p38 MAPK, and LGALS1 interacts with these signaling molecules to further enhance p38 MAPK activity, thereby promoting cancer cell metastasis. In lung adenocarcinoma, LGALS1 may inhibit ERK activation by regulating upstream signaling molecules of ERK, thereby exerting an anti-cancer effect. Additionally, the binding modes of LGALS1 with MAPK pathway components differ, affecting its regulatory effects. Regarding the Wnt signaling pathway, LGALS1 binds to core

molecules such as Frizzled and LRP5/6, stabilizes β-catenin, and promotes its nuclear translocation, thereby activating the transcription of downstream target genes. LGALS1 also modulates the intracellular signal transduction network to influence Wnt pathway activity. Due to variations in cytokine and growth factor levels and states across different tumor cells, the regulatory effects of LGALS1 on the Wnt signaling pathway differ among cancers.

6. Relationship between LGALS1 and Hedgehog and TGF-β Signaling Pathways

The Hedgehog signaling pathway was initially discovered in Drosophila melanogaster and later confirmed in vertebrates. It represents a highly conserved evolutionary pathway responsible for signal transduction from the cell membrane to the nucleus and serves as a classic regulator of embryonic development [55] [56]. This pathway exerts its biological effects through a cascade of signals, governing cell growth, proliferation, and differentiation. Aberrant activation of the Hedgehog signaling pathway has been implicated in tumor onset and progression.

Transforming growth factor-β (TGF-β) is a pivotal cytokine ubiquitously present in cells, primarily orchestrating various cell behavior processes. The TGF-β superfamily encompasses key members such as TGF-β proteins, activins, bone morphogenetic proteins (BMPs), and growth differentiation factors (GDFs) [57]. The TGF-β signaling pathway constitutes a complex network comprising ligands, receptors, SMAD proteins, and transcription factors, which regulate target gene transcription through interactions with other pathways [58]. This pathway operates through two main routes: the canonical SMAD-dependent pathway and the non-SMAD-dependent pathway. TGF-β plays a critical role in regulating cell proliferation and differentiation, wound healing, immune responses, development, tissue repair, and the pathogenesis of numerous diseases [58]. Given its intimate association with tumorigenesis and immune system disorders, investigating the TGF-β signaling pathway holds significant scientific importance.

Yang Chong *et al.* [10] conducted in vivo and in vitro experiments using 162 gastric cancer tissue specimens and demonstrated that LGALS1 promotes the invasion and epithelial-mesenchymal transition (EMT) of gastric cancer cells by activating the non-canonical Hedgehog (Hh) pathway. Their findings also revealed that LGALS1 upregulates glioma-associated oncogene 1 (GLI1) signaling in gastric cancer, thereby inducing EMT. Additional studies have reported that LGALS1 facilitates angiogenesis mimicry in gastric adenocarcinoma through the Hedgehog/GLI signaling pathway [14]. In pancreatic ductal adenocarcinoma (PDAC), Neus Martínez-Bosch *et al.* [33] demonstrated that LGALS1 enhances Hedgehog signal transduction in PDAC cells, stromal fibroblasts, and tumor tissues within pancreatic cancer model. Furthermore, elevated LGALS1 expression in the gastric cancer microenvironment promotes cancer cell migration and invasion via EMT through the TGF-β1/Smad signaling pathway, correlating with a poor prognosis for gastric cancer patients [34]. In breast cancer, TGF-β signaling has been estab-

lished as a promoter of metastasis. LGALS1 serves as a marker for cancer-associated fibroblasts (CAFs). Xue Zhu *et al.* [35] demonstrated that TGF-β signaling drives metastasis, and silencing LGALS1 in CAFs reverses fibroblast activation, potentially inhibiting cancer metastasis.

Hedgehog Signaling Pathway: LGALS1 is thought to interact with Smoothened and Gli transcription factors to modulate Hedgehog signal transduction, thereby influencing tumor cell growth and invasion. However, these interactions are highly susceptible to modulation by other signaling molecules within the tumor microenvironment. Consequently, the regulatory effects of LGALS1 on the Hedgehog pathway vary across different tumor cells due to differential molecular interactions. TGF-β Signaling Pathway: LGALS1 likely binds to TGF-β receptors and Smad proteins to regulate TGF-β signaling, thereby affecting tumor cell migration and invasion. Similar to its role in the Hedgehog pathway, LGALS1's regulatory effects on TGF-β signaling are influenced by the tumor microenvironment, including varying levels and states of cytokines and growth factors, which result in context-dependent regulatory outcomes.

7. Exploration of the Bidirectional Effects of LGALS1 in Different Cancers

LGALS1 exhibits bidirectional effects in different cancers, which may be influenced by multiple factors. One key factor is differential glycosylation. The varying activities of glycosyltransferases in different tumor cells can alter the glycosylation status of LGALS1, thereby affecting its function. In some tumor cells, specific glycosylation modifications enable LGALS1 to readily bind to signaling pathway components and activate relevant pathways. Conversely, in other cells, changes in the glycosylation status may impair its normal function or even produce inhibitory effects.

The tumor microenvironment (TME) also plays a crucial role. The TME contains various cytokines, chemokines, and metabolic products that can interact with LGALS1 to regulate its activity and function. For instance, in an inflammatory microenvironment, high concentrations of pro-inflammatory cytokines prompt LGALS1 to bind to specific receptors, activate signaling pathways, and promote tumor cell proliferation and metastasis. In contrast, in an immunosuppressive microenvironment, certain immunosuppressive factors may interfere with the interactions between LGALS1 and other molecules, causing LGALS1 to exert an inhibitory effect.

Additionally, the states of upstream and downstream molecules in the signaling pathways vary among different tumor cells, which can also influence the regulatory effects of LGALS1 on these pathways.

8. Therapeutic Potential and Challenges of Targeting LGALS1

Given the critical role of LGALS1 in malignant tumors, therapeutic strategies targeting LGALS1 hold significant promise. Currently, several studies have focused on developing inhibitors or antibodies to block LGALS1 function in tumor cells.

However, targeted therapy for LGALS1 faces several challenges. For instance, ensuring the specificity and efficacy of inhibitors or antibodies is crucial to avoid off-target effects and minimize damage to normal cells. Additionally, overcoming tumor cell drug resistance and enhancing treatment efficacy remain key hurdles.

Although clinical trials targeting LGALS1 are ongoing, substantial results have yet to be achieved. Moving forward, it is imperative to further elucidate the mechanisms underlying LGALS1 function and develop more efficient and specific targeted therapeutic approaches.

9. Summary and Outlook

LGALS1, a multifunctional bioactive protein, plays a pivotal role in tumor progression by regulating signaling pathways across multiple dimensions in malignant tumors. Its mechanism of action is both complex and context-specific. Given its critical involvement in tumor initiation and development, therapeutic strategies targeting LGALS1 hold significant promise.

Currently, research efforts are focused on developing inhibitors or antibodies to block LGALS1 function in tumor cells. These studies not only enhance our understanding of LGALS1's mechanism of action but also elucidate its interactions with related signaling pathways in tumors. Future research should prioritize three key directions: Developing single-cell technology dynamic expression atlases to more precisely map LGALS1 expression patterns. Exploring interaction networks to design more effective inhibitors. Conducting organoid model precision medicine research to provide robust evidence for clinical applications. However, targeted LGALS1 therapy faces significant challenges. To ensure that inhibitors or antibodies are highly specific and effective while minimizing damage to normal cells, it is essential to thoroughly investigate the expression differences and mechanisms of action of LGALS1 in tumor versus normal cells. Additionally, the issue of tumor cell drug resistance must be addressed to improve therapeutic outcomes. Although relevant clinical trials have been conducted, no substantial results have been achieved thus far.

Moving forward, it is imperative to further explore the mechanism of action of LGALS1 and comprehensively analyze its characteristics across different tumor types and microenvironments. Based on these findings, the development of efficient and specific targeted therapies should be prioritized. With continued in-depth research, it is anticipated that new breakthroughs will emerge, offering renewed hope for the treatment of cancers and other diseases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Tuo, J.Y. and Xiang, Y.B. (2023) Research Progress on the Current Status of Cancer Epidemiology, Etiology, and Nutritional Epidemiology. *Tumor*, **43**, 359-366.

[2] Jiang, D., Wang, Z. and Liu, D.P. (2023) Current Prevalence and Distribution Char-

acteristics of Malignant Tumors in China. *Journal of Modern Urological and Genitourinary Oncology*, **15**, 374-375, 378.

[3] Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A., *et al.* (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA*: *A Cancer Journal for Clinicians*, **71**, 209-249. https://doi.org/10.3322/caac.21660

[4] Deo, S.V.S., Sharma, J. and Kumar, S. (2022) GLOBOCAN 2020 Report on Global Cancer Burden: Challenges and Opportunities for Surgical Oncologists. *Annals of Surgical Oncology*, **29**, 6497-6500. https://doi.org/10.1245/s10434-022-12151-6

[5] Wang, S.M. *et al.* (2024) Analysis of the Age Characteristics of Incidence and Mortality of Malignant Tumors in the Chinese Population in 2022. *China Oncology*, **33**, 165-174.

[6] Yip, H.Y.K. and Papa, A. (2021) Signaling Pathways in Cancer: Therapeutic Targets, Combinatorial Treatments, and New Developments. *Cells*, **10**, Article 659. https://doi.org/10.3390/cells10030659

[7] Astorgues-Xerri, L., Riveiro, M.E., Tijeras-Raballand, A., Serova, M., Neuzillet, C., Albert, S., *et al.* (2014) Unraveling Galectin-1 as a Novel Therapeutic Target for Cancer. *Cancer Treatment Reviews*, **40**, 307-319. https://doi.org/10.1016/j.ctrv.2013.07.007

[8] Cousin, J. and Cloninger, M. (2016) The Role of Galectin-1 in Cancer Progression, and Synthetic Multivalent Systems for the Study of Galectin-1. *International Journal of Molecular Sciences*, **17**, Article 1566. https://doi.org/10.3390/ijms17091566

[9] Camby, I., Le Mercier, M., Lefranc, F. and Kiss, R. (2006) Galectin-1: A Small Protein with Major Functions. *Glycobiology*, **16**, 137R-157R. https://doi.org/10.1093/glycob/cwl025

[10] Shi, Y., Tang, D., Li, X., Xie, X., Ye, Y. and Wang, L. (2022) Galectin Family Members: Emerging Novel Targets for Lymphoma Therapy? *Frontiers in Oncology*, **12**, Article 889034. https://doi.org/10.3389/fonc.2022.889034

[11] Qin, X.X., Sun, H.M., Zhao, H.P., Chu, W.H., Wang, D.T. and Li, C.Y. (2012) Galectin-1 Protein and Its Biological Functions. *Chinese Journal of Animal Husbandry and Veterinary Medicine*, **39**, 141-145.

[12] Bogut, A., Stojanovic, B., Jovanovic, M., Dimitrijevic Stojanovic, M., Gajovic, N., Stojanovic, B.S., *et al.* (2023) Galectin-1 in Pancreatic Ductal Adenocarcinoma: Bridging Tumor Biology, Immune Evasion, and Therapeutic Opportunities. *International Journal of Molecular Sciences*, **24**, Article 15500. https://doi.org/10.3390/ijms242115500

[13] Chen, W.B., *et al.* (2022) Galectin-1 Knockdown Inhibits Proliferation, Migration, Invasion and Promotes Apoptosis of Lung Adenocarcinoma Cells *in Vitro*. *Journal of Southern Medical University*, **42**, 1628-1637.

[14] You, X., Wu, J., Wang, Y., Liu, Q., Cheng, Z., Zhao, X., *et al.* (2020) Galectin-1 Promotes Vasculogenic Mimicry in Gastric Adenocarcinoma via the Hedgehog/GLI Signaling Pathway. *Aging*, **12**, 21837-21853. https://doi.org/10.18632/aging.104000

[15] Chong, Y., Tang, D., Xiong, Q., Jiang, X., Xu, C., Huang, Y., *et al.* (2016) Galectin-1 from Cancer-Associated Fibroblasts Induces Epithelial-Mesenchymal Transition through B1 Integrin-Mediated Upregulation of Gli1 in Gastric Cancer. *Journal of Experimental & Clinical Cancer Research*, **35**, Article No. 175. https://doi.org/10.1186/s13046-016-0449-1

[16] Chong, Y. (2017) The Role of Galectin-1 in the Invasion and Metastasis of Gastric Adenocarcinoma and the Effect of Dihydroartemisinin on Its Expression. Master's

Thesis, Yangzhou University.

[17] Bai, Y., Wang, Y.X., Yao, W.J. and Wang, Z.M. (2013) Effects of Downregulation of Galectin-1 Expression on the Proliferation of Esophageal Squamous Cell Carcinoma Cells. *Chinese Journal of Gerontology*, **33**, 365-366.

[18] Chetry, M., Song, Y., Pan, C., Li, R., Zhang, J. and Zhu, X. (2020) Effects of Galectin-1 on Biological Behavior in Cervical Cancer. *Journal of Cancer*, **11**, 1584-1595. https://doi.org/10.7150/jca.38538

[19] Wu, L.X., *et al.* (2018) Expression of Galectin-1 in Bladder Cancer Cells and Its Effect on the Proliferation and Migration Abilities of Bladder Cancer Cells. *Chinese Journal of Medical Engineering*, **26**, 6-11.

[20] Chou, F., Chen, H., Kuo, C. and Sytwu, H. (2018) Role of Galectins in Tumors and in Clinical Immunotherapy. *International Journal of Molecular Sciences*, **19**, Article 430. https://doi.org/10.3390/ijms19020430

[21] Huang, Y., Wang, H., Zhao, J., Wu, M. and Shih, T. (2021) Immunosuppressive Roles of Galectin-1 in the Tumor Microenvironment. *Biomolecules*, **11**, Article 1398. https://doi.org/10.3390/biom11101398

[22] Zhou, Y., Cui, C., Ma, X., Luo, W., Zheng, S.G. and Qiu, W. (2020) Nuclear Factor *κ*B (NF-*κ*B)-Mediated Inflammation in Multiple Sclerosis. *Frontiers in Immunology*, **11**, Artice 391. https://doi.org/10.3389/fimmu.2020.00391

[23] Cui, Y., Yan, M., Wu, W., Lv, P., Wang, J., Huo, Y., *et al.* (2022) ESCCAL-1 Promotes Cell-Cycle Progression by Interacting with and Stabilizing Galectin-1 in Esophageal Squamous Cell Carcinoma. *NPJ Precision Oncology*, **6**, Article No. 12. https://doi.org/10.1038/s41698-022-00255-x

[24] Satelli, A. and Rao, U.S. (2011) Galectin-1 Is Silenced by Promoter Hypermethylation and Its Re-Expression Induces Apoptosis in Human Colorectal Cancer Cells. *Cancer Letters*, **301**, 38-46. https://doi.org/10.1016/j.canlet.2010.10.027

[25] Bacigalupo, M.L., Carabias, P. and Troncoso, M.F. (2017) Contribution of Galectin-1, a Glycan-Binding Protein, to Gastrointestinal Tumor Progression. *World Journal of Gastroenterology*, **23**, 5266-5281. https://doi.org/10.3748/wjg.v23.i29.5266

[26] Su, Y., Luo, H., Huang, C., Liu, T., Huang, E., Sung, M., *et al.* (2020) Galectin-1 Overexpression Activates the FAK/PI3K/AKT/mTOR Pathway and Is Correlated with Upper Urinary Urothelial Carcinoma Progression and Survival. *Cells*, **9**, Article 806. https://doi.org/10.3390/cells9040806

[27] Shi, R., Mo, H.L., Li, Y.B., Zhang, Z.B. and Li, H. (2023) The Role and Mechanism of Galectin-1 in the Inhibition of Cholangiocarcinoma Cell Proliferation by Metformin. *Journal of Hunan Normal University* (*Medical Edition*), **20**, 18-23.

[28] Li, J., Tseng, C., Lin, C., Law, C., Chien, Y., Kuo, W., *et al.* (2018) Upregulation of LGALS1 Is Associated with Oral Cancer Metastasis. *Therapeutic Advances in Medical Oncology*, **10**, 1-20. https://doi.org/10.1177/1758835918794622

[29] Miao, J., Wang, S., Zhang, M., Yu, F., Zhang, L., Yu, Z., *et al.* (2014) Knockdown of Galectin-1 Suppresses the Growth and Invasion of Osteosarcoma Cells through Inhibition of the MAPK/ERK Pathway. *Oncology Reports*, **32**, 1497-1504. https://doi.org/10.3892/or.2014.3358

[30] Zhu, J., Zheng, Y., Zhang, H., Liu, Y., Sun, H. and Zhang, P. (2019) Galectin-1 Induces Metastasis and Epithelial-Mesenchymal Transition (EMT) in Human Ovarian Cancer Cells via Activation of the MAPK JNK/p38 Signalling Pathway. *American Journal of Translational Research*, **11**, 3862-3878.

[31] Deng, X.Y., Lin, H.Y. and Chen, W.G. (2018) Expression of Galectin-1 and VEGF in

Cervical Squamous Cell Carcinoma and Their Relationship with Clinical Characteristics. *Cancer Progress*, **16**, 1278-1280.

[32] Peng, K., Jiang, S., Lee, Y., Tsai, F., Chang, C., Chen, L., *et al.* (2021) Stromal Galectin-1 Promotes Colorectal Cancer Cancer-Initiating Cell Features and Disease Dissemination through SOX9 and β-Catenin: Development of Niche-Based Biomarkers. *Frontiers in Oncology*, **11**, Article 716055. https://doi.org/10.3389/fonc.2021.716055

[33] Martínez-Bosch, N., Fernández-Barrena, M.G., Moreno, M., Ortiz-Zapater, E., Munné-Collado, J., Iglesias, M., *et al.* (2014) Galectin-1 Drives Pancreatic Carcinogenesis through Stroma Remodeling and Hedgehog Signaling Activation. *Cancer Research*, **74**, 3512-3524. https://doi.org/10.1158/0008-5472.can-13-3013

[34] You, X., Wu, J., Zhao, X., Jiang, X., Tao, W., Chen, Z., *et al.* (2021) Fibroblastic Galectin-1-Fostered Invasion and Metastasis Are Mediated by TGF-β1-Induced Epithelial-Mesenchymal Transition in Gastric Cancer. *Aging*, **13**, 18464-18481. https://doi.org/10.18632/aging.203295

[35] Zhu, X., Wang, K., Zhang, K., Xu, F., Yin, Y., Zhu, L., *et al.* (2016) Galectin-1 Knockdown in Carcinoma-Associated Fibroblasts Inhibits Migration and Invasion of Human MDA-MB-231 Breast Cancer Cells by Modulating MMP-9 Expression. *Acta Biochimica et Biophysica Sinica*, **48**, 462-467. https://doi.org/10.1093/abbs/gmw019

[36] Kizilirmak, C., Bianchi, M.E. and Zambrano, S. (2022) Insights on the NF-κB System Using Live Cell Imaging: Recent Developments and Future Perspectives. *Frontiers in Immunology*, **13**, Article 886127. https://doi.org/10.3389/fimmu.2022.886127

[37] Cornice, J., Verzella, D., Arboretto, P., Vecchiotti, D., Capece, D., Zazzeroni, F., *et al.* (2024) NF-κB: Governing Macrophages in Cancer. *Genes*, **15**, Article 197. https://doi.org/10.3390/genes15020197

[38] Choi, M., Jo, J., Park, J., Kang, H.K. and Park, Y. (2019) NF-κB Signaling Pathways in Osteoarthritic Cartilage Destruction. *Cells*, **8**, Article 734. https://doi.org/10.3390/cells8070734

[39] Schrank, T.P., *et al.* (2022) NF-κB Over-Activation Portends Improved Outcomes in HPV-Associated Head and Neck Cancer. *Oncotarget*, **13**, 707-722.

[40] Barnabei, L., Laplantine, E., Mbongo, W., Rieux-Laucat, F. and Weil, R. (2021) Nf-κB: At the Borders of Autoimmunity and Inflammation. *Frontiers in Immunology*, **12**, Article 716469. https://doi.org/10.3389/fimmu.2021.716469

[41] Martin, M., Sun, M., Motolani, A. and Lu, T. (2021) The Pivotal Player: Components of NF-κB Pathway as Promising Biomarkers in Colorectal Cancer. *International Journal of Molecular Sciences*, **22**, Article 7429. https://doi.org/10.3390/ijms22147429

[42] Deka, K. and Li, Y. (2023) Transcriptional Regulation during Aberrant Activation of NF-κB Signalling in Cancer. *Cells*, **12**, Article 788. https://doi.org/10.3390/cells12050788

[43] Miricescu, D., Totan, A., Stanescu-Spinu, I., Badoiu, S.C., Stefani, C. and Greabu, M. (2020) PI3K/AKT/mTOR Signaling Pathway in Breast Cancer: From Molecular Landscape to Clinical Aspects. *International Journal of Molecular Sciences*, **22**, Article 173. https://doi.org/10.3390/ijms22010173

[44] Aguayo, F., Perez-Dominguez, F., Osorio, J.C., Oliva, C. and Calaf, G.M. (2023) PI3K/AKT/mTOR Signaling Pathway in HPV-Driven Head and Neck Carcinogenesis: Therapeutic Implications. *Biology*, **12**, Article 672. https://doi.org/10.3390/biology12050672

[45] Luo, Q., Du, R., Liu, W., Huang, G., Dong, Z. and Li, X. (2022) PI3K/AKT/mTOR Signaling Pathway: Role in Esophageal Squamous Cell Carcinoma, Regulatory Mechanisms and Opportunities for Targeted Therapy. *Frontiers in Oncology*, **12**, Article

852383. https://doi.org/10.3389/fonc.2022.852383

[46] Li, W.S., Wang, T.T. and He, W.Q. (2024) Relationship between the PI3K/Akt/mTOR Signaling Pathway and Autophagy Regulation and Related Diseases. *Chongqing Medicine*, **53**, 2047-2052.

[47] Dai, Y.Z., Li, Y.N. and Shang, R.Z. (2024) Research Progress on the Mechanism of Action of the PI3K/AKT/mTOR Signaling Pathway in Liver Cancer. *Journal of Hepatobiliary and Pancreatic Surgery*, **36**, 116-123.

[48] Yang, G.N. and Zhang, X.P. (2024) Research Progress on the PI3K/AKT/mTOR Signaling Pathway in Targeted Therapy for Triple-Negative Breast Cancer. *Chinese Medical Innovation*, **21**, 155-158.

[49] Kyosseva, S.V. (2016) Targeting MAPK Signaling in Age-Related Macular Degeneration. *Ophthalmology and Eye Diseases*, **8**, 23-30. https://doi.org/10.4137/oed.s32200

[50] Kurtzeborn, K., Kwon, H.N. and Kuure, S. (2019) MAPK/ERK Signaling in Regulation of Renal Differentiation. *International Journal of Molecular Sciences*, **20**, Article 1779. https://doi.org/10.3390/ijms20071779

[51] Guo, Y., Pan, W., Liu, S., Shen, Z., Xu, Y. and Hu, L. (2020) ERK/MAPK Signalling Pathway and Tumorigenesis (Review). *Experimental and Therapeutic Medicine*, **19**, 1997-2007. https://doi.org/10.3892/etm.2020.8454

[52] Colozza, G. and Koo, B. (2021) Wnt/β-Catenin Signaling: Structure, Assembly and Endocytosis of the Signalosome. *Development, Growth & Differentiation*, **63**, 199-218. https://doi.org/10.1111/dgd.12718

[53] Liu, J., Xiao, Q., Xiao, J., Niu, C., Li, Y., Zhang, X., *et al.* (2022) Wnt/β-Catenin Signaling: Function, Biological Mechanisms, and Therapeutic Opportunities. *Signal Transduction and Targeted Therapy*, **7**, Article No. 3. https://doi.org/10.1038/s41392-021-00762-6

[54] Yu, F., Yu, C., Li, F., Zuo, Y., Wang, Y., Yao, L., *et al.* (2021) Wnt/β-Catenin Signaling in Cancers and Targeted Therapies. *Signal Transduction and Targeted Therapy*, **6**, Article No. 307. https://doi.org/10.1038/s41392-021-00701-5

[55] Skoda, A.M., Simovic, D., Karin, V., Kardum, V., Vranic, S. and Serman, L. (2018) The Role of the Hedgehog Signaling Pathway in Cancer: A Comprehensive Review. *Bosnian Journal of Basic Medical Sciences*, **18**, 8-20. https://doi.org/10.17305/bjbms.2018.2756

[56] Gao, L., Zhang, Z., Zhang, P., Yu, M. and Yang, T. (2018) Role of Canonical Hedgehog Signaling Pathway in Liver. *International Journal of Biological Sciences*, **14**, 1636-1644. https://doi.org/10.7150/ijbs.28089

[57] Cellière, G., Fengos, G., Hervé, M. and Iber, D. (2011) The Plasticity of TGF-β Signaling. *BMC Systems Biology*, **5**, Article No. 184. https://doi.org/10.1186/1752-0509-5-184

[58] Morikawa, M., Derynck, R. and Miyazono, K. (2016) TGF-β and the TGF-β Family: Context-Dependent Roles in Cell and Tissue Physiology. *Cold Spring Harbor Perspectives in Biology*, **8**, a021873. https://doi.org/10.1101/cshperspect.a021873