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GOLM1 (Golgi membrane protein 1): A Key Culprit in Cancer Progression and Disease Pathogenesis

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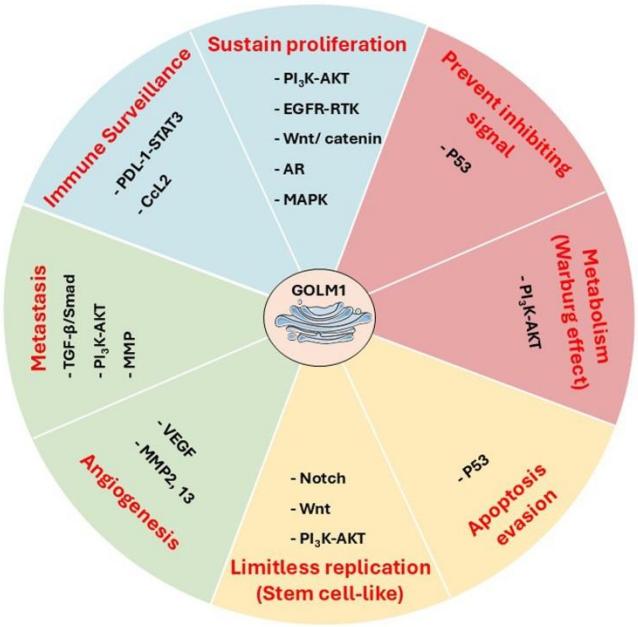
Abstract:

Since the initial discovery of the Golgi apparatus protein's role in normal cellular function and its association with malignancy, remarkable studies and findings on Golgi proteins have continuously emerged across various cancers. Among these proteins, GOLM1 was first identified by the American scholar Kladney and his colleagues in adult giant cell hepatitis. Over time, GOLM1 has been recognized as one of the most significant proto-oncogenes in multiple cancers. Its diagnostic role in both hepatocellular carcinoma and prostate cancer has yielded crucial results, positioning it as a strong competitor to traditional diagnostic markers in these tumors. Due to its secretory nature, GOLM1 levels can be detected in blood or urine, making it a potential non-invasive diagnostic tool for certain malignancies. Regarding its oncogenic role in cancers such as lung, colon, ovarian and breast cancer, multiple studies have highlighted its involvement in advanced resistant cases, suggesting its potential as a future target for therapy.

Keywords: Golgi apparatus; GOLM1; Cancer; Diagnosis; Prognosis.

Graphical Abstract: Hallmarks of cancers by GOLM1



Overview of GOLM1 protein:

Golgi membrane protein 1 (GOLM1), also known as GP73 (previously referred to as GOLPH2 or C9orf155), is a type II Golgi transmembrane protein consisting of 401 amino acids (73 kDa). In humans, it is encoded by the GOLM1 gene located on chromosome 9. Under normal conditions, GOLM1 is expressed by epithelial cells in various human tissues, including the intestinal columnar epithelial cells lining the glands,

ciliated columnar epithelium of lung bronchioles, epithelial cells lining the proximal and distal tubules as well as collecting ducts in the kidney, epithelial cells of the biliary system in the liver, and glandular prostatic epithelium. Conversely, GOLM1 expression is minimal or even absent in hepatocytes and glomeruli [1]. In 2000, Kladney and his colleagues were the first to demonstrate that GOLM1 is a Golgi-associated epithelial cell protein that becomes upregulated in response to viral infections [2].

Normal Structure:

GOLM1 is an integral transmembrane protein composed of a short hydrophobic cytoplasmic N-terminus, which is linked to a single transmembrane domain (TMD, 12-36 amino acids), and a long, highly hydrophilic luminal C-terminal domain. This luminal domain contains two α-helices forming coiled-coil domains (helix 1: 56–205 amino acids and helix 2: 206–401 amino acids) [3]. It also features a unique open reading frame consisting of two regions that together form 392 - 401 amino acids. The acidic amino acid composition plays a role in calcium sequestration [4]. The coiled-coil domains contribute to molecular transportation, dimerization, binding, trafficking, and interactions with extracellular chaperones. The cytoplasmic region (1–12 amino acids) interacts with substrates and is involved in their vesicular trafficking. GOLM1 contains three glycosylation sites (N109, N144, and N398) and two phosphorylation sites (S187 and S309), though their exact functions remain unknown [2,5,6]. At the R55 residue, the proteinase Furin cleaves the N-terminal of GOLM1, generating soluble GOLM1 (sGOLM1) (56–401 amino acids), which is secreted into extracellular spaces via exosomes. Due to this, sGOLM1 has been proposed as a potential serum biomarker for diagnosing certain tumors. In hepatocellular carcinoma (HCC), GOLM1 can be detected in blood serum. However, in prostate cancer, secretion occurs through a different mechanism where the full-length GOLM1 protein is secreted from shed prostatic cells [7]. **Figure (1)**.

Synthesis and Pathway of GOLM1:

The synthesis of GOLM1 begins in the endoplasmic reticulum, after which it is transported to the cis-Golgi and then to the cell membrane. Endosomal pathways also play a role in GOLM1 trafficking, as a small proportion of GOLM1 undergoes endocytosis and is subsequently returned to Golgi for recycling [1]. The primary function of GOLM1 is the sorting and modification of cellular proteins that are transferred from the endoplasmic reticulum after synthesis. Due to this essential role, GOLM1 is often described as the 'housekeeper' of the cell and is predominantly localized in the perinuclear region [5]. Figure **(1).**

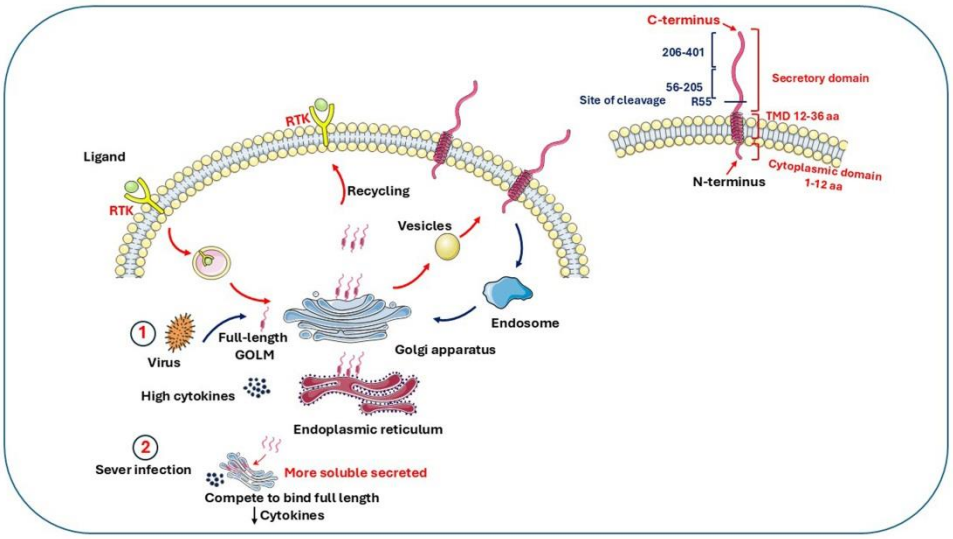


Figure (1): GOLM1 consists of three main domains: the cytoplasmic domain, the transmembrane domain, and the secretory domain. It is initially synthesized in the endoplasmic reticulum (ER) and then transported to the Golgi apparatus for further processing. During viral infections, the full-length GOLM1 stimulates cytokine

secretion, whereas its soluble form reduces cytokine release. Additionally, GOLM1 plays a role in EGFR-RTK recycling, leading to sustained cellular stimulation and signaling.

Function of GOLM1:

The Golgi apparatus is primarily involved in secretion, glycosylation, sorting, and modification of proteins and lipids that are synthesized and transported from the endoplasmic reticulum. It also plays a crucial role in membrane transformation. Through cooperation between Golgi proteins and mitochondria, the Golgi apparatus can regulate apoptosis signaling. Additionally, the Golgi apparatus is involved in various cellular processes, including migration, mitosis, apoptosis, inflammation, DNA repair, autophagy, and stress responses. It plays a vital role in maintaining cellular structure, differentiation, and functional performance [8]. Molecular alterations in Golgi apparatus proteins can contribute to carcinogenesis [6]. Among these proteins, GOLM1 has been identified as a key Golgi protein that helps maintain the integrity of the Golgi complex under cellular stress. Mutations in GOLM1 can lead to tumor development [2,9]. Recent studies have also found that GOLM1 plays a role in type 2 diabetes mellitus (DM), with elevated levels observed in DM patients. GOLM1 is involved in systemic and liver glucose homeostasis [10].

GOLM1 in Infection:

Several studies have shown that GOLM1 plays a role in infectious diseases caused by viruses such as adenovirus, SARS-CoV-2, Hepatitis B virus (HBV), and Hepatitis C virus (HCV) [11]. It has been found that GOLM1 stimulates the production of infectious HCV particles from infected cells while inhibiting the production of inflammatory cytokines such as IL-6, 12, TNF, and interferon-1. Conversely, it stimulates IFN-gamma and chemokines, including CCL2 (C-C motif chemokine ligand 2) and CXCL10 (C-X-C motif chemokine 10) [12]. The effects of GOLM1 on inflammatory mediators vary depending on the stimulus and cell type. GOLM1 can exert its effects directly through NOTCH signaling or indirectly by altering RTK and EGFR signaling. Autocrine signaling also contributes to this process [11]. Moreover, full-length GOLM1 functions as a chaperone, facilitating the trafficking of receptors and molecules such as cytokines, EGFR, RTK, MMP2, and MMP7. However, in cases of inflammation and cancer, overexpression of GOLM1 promotes the release of soluble GOLM1 (sGOLM1), which inhibits cytokine and chemokine production by competing for binding with full-length GOLM1 [13]. The relationship between GOLM1 and cytokine/chemokine production suggests its potential as a therapeutic target 11. In HBV and HCV infections, viral activation of GOLM1 occurs through IFN secretion, which suppresses innate immunity and facilitates mitochondrial protein degradation [14]. In 2019, Liu et al. found that GOLM1 levels in patients with hepatitis B e-antigen-positive, HBeAg-negative status, liver fibrosis, and hepatocellular carcinoma (HCC) were significantly higher than in healthy individuals [15].

GOLM1 and cancers:

The relationship between Golgi apparatus proteins and tumor development has recently gained significant attention. GOLM1, a Golgi protein, is upregulated in several malignancies, including hepatocellular carcinoma (HCC), as well as lung, breast, prostate, colon, and esophageal cancers. It functions as an oncogene by promoting malignant cell proliferation, migration, angiogenesis, and invasion while inhibiting therapy-induced apoptosis [16], Table **(1).**

Table (1): Oncogenic role of GOLM1 in cancers:

Cancers	Oncogenic pathways activation by GOLM1	Role	References
Hepatocellular carcinoma	EGFR/RTK TGF-B/smad CCL2 PDL1-STAT3 MMP2,13	Diagnostic/ prognostic	14,15,18,19,20, 21,22,23,24
Prostate cancer	PI3K/AKT AR	Diagnostic/ prognostic	7,27,28,29,30,3 1,32,33

	TGF-B/smad		
Breast cancer	MMP13 LINC01977	Poor prognosis	34,35,36,37
Lung cancer	P53 MAPK MMP13	Poor prognosis	38,39,40
Colon cancer	AKT/GSK3B CCL2	Poor prognosis	41,42
Glioma	WNT/B-catenin AKT PDGFA/PDGFR1	Poor prognosis	43,44
Esophageal carcinoma	WNT/B-catenin	Poor prognosis	45,46
Ovarian Carcinoma	Dysregulation of B7-H3 ASB16-AS1	Poor prognosis	47 48

1) **Hepatocellular carcinoma:**

Hepatocellular carcinoma (HCC) is one of the most prevalent liver malignancies and a leading cause of cancer-related deaths worldwide [17]. Most HCC patients are diagnosed at an advanced stage, where therapeutic options are limited, and effectiveness is poor. Several studies indicate that GOLM1 is a promising biomarker for the early diagnosis and prognosis of HCC [18]. Under normal conditions, GOLM1 protein levels in serum or tissue are minimal or undetectable compared to those in HCC patients. GOLM1 has demonstrated high sensitivity and specificity as a diagnostic marker for early-stage HCC, even in patients with negative AFP results [19].

Oncogenic Role of GOLM1 in HCC:

The oncogenic mechanisms of GOLM1 in hepatocellular carcinoma (HCC) can be summarized as follows:

- **Endoplasmic Reticulum (ER) Stress and ROS Generation:** Under ER stress, GOLM1 triggers the release of hydrogen peroxide and calcium ions into the cytosol, leading to mitochondrial stress and the generation of reactive oxygen species (ROS). This oxidative stress in the liver promotes STAT3 signaling, driving HCC development [14].
- **Activation of CREB-MMP13 Axis:** GOLM1 activates the cAMP-responsive element-binding protein (CREB) transcription factor, which elevates matrix metalloproteinase-13 (MMP13) levels, establishing a positive feedback loop between GOLM1 and MMP13 [20].
- **MMP-2 Mediated Cell Invasion:** Direct interaction between the cytoplasmic domain of GOLM1 and MMP-2 enhances tumor cell invasion [21].
- **EGFR/RTK Signaling and Metastasis:** GOLM1 supports epidermal growth factor receptor (EGFR) recycling while reducing its degradation, leading to sustained EGFR stimulation. This persistent activation enhances downstream signaling pathways, including AKT and S6 kinase, which increase MMP9 levels and reduce E-cadherin expression, thereby promoting invasion and metastasis [22,23].
- **TGF-β1-Induced EMT and Invasion:** GOLM1 facilitates epithelial-mesenchymal transition (EMT) and tumor invasion by enhancing TGF-β1 stimulation. This activation induces Smad2/3 signaling, leading to increased vimentin expression and reduced E-cadherin levels [24].
- **VEGF Pathway and Angiogenesis:** GOLM1 promotes angiogenesis and vascular invasion by activating the VEGF pathway. It achieves this by binding to E2F4 and PTBP1, an RNA-binding protein involved in RNA splicing [14].
- **Immune Suppression via CCL2 Recruitment:** Overexpression of GOLM1 promotes the transcription of CCL2, which recruits myeloid-derived suppressor cells (MDSCs), leading to immunosuppression and tumor progression [5].

- **PD-L1 Upregulation and Immune Evasion:** GOLM1 enhances programmed cell death ligand-1 (PD-L1) expression through the GOLM1–STAT3–PD-L1 axis or via the RTK pathway, enabling malignant cells to evade immune surveillance [1,5].

Several studies have investigated the diagnostic and prognostic roles of GOLM1 in hepatocellular carcinoma (HCC). Shaker et al. reported that GOLM1 could predict HCC with a sensitivity of 96.9% and specificity of 96.9% at a cutoff value of 17.5 ng/mL. In comparison, α-fetoprotein (AFP) demonstrated a sensitivity of 75% and specificity of 92% at a cutoff value of 9.4 ng/mL 25. A meta-analysis conducted by Zang et al., which included 36 studies with a total sample size of 8,314 cases, found that GOLM1 could detect HCC with a sensitivity of 79% and specificity of 85%. This meta-analysis also concluded that GOLM1 is highly effective for diagnosing HCC but has only moderate value in distinguishing HCC from liver cirrhosis [18]. Furthermore, GOLM1 is considered a poor prognostic marker, as its expression is associated with higher tumor grades, advanced stages, and reduced overall survival [14].

2) **Prostate cancer (PCa):** Prostate cancer (PCa) is a significant public health concern, ranking among the most common malignancies in males worldwide [17]. PCa progression is driven by various molecular mechanisms, including androgen receptor (AR) signaling and activation of the PI3K-AKT-mTOR pathway [26].

- **GOLM1 and AR Signaling in PCa:** Recent studies have identified GOLM1 as a pro-cancerous factor in PCa due to its involvement in AR signaling regulation. GOLM1 interacts with the proteasome 26S subunit, non-ATPase 1 (PSMD1), to enhance proteasome activity. A correlation has been observed between GOLM1 expression and key AR downstream genes, including KLK3, TMPRSS2, and NKX3-1, suggesting its role in resistance to androgen deprivation therapy (ADT) in some PCa patients [27].
- **PI3K-AKT-mTOR Signaling and PCa Progression:** The PI3K-AKT-mTOR pathway serves as a central hub connecting various upstream and downstream signals in PCa and is associated with poor clinical outcomes, recurrence, and therapy resistance. This pathway also contributes to epithelial-mesenchymal transition (EMT) by activating vimentin, N-cadherin, Snail1, Twist, and ZEB, while suppressing E-cadherin. Additionally, it promotes angiogenesis and cancer stem cell maintenance through downstream signaling [28]. Activation of matrix metalloproteinases (MMP-2 and MMP-9) via the AKT pathway enhances the invasive and metastatic potential of malignant cells. Furthermore, GOLM1 interacts with multiple signaling pathways, including AR, MAPK, and WNT [29].
- **GOLM1 and TGF-β1/Smad2 Signaling in PCa:** GOLM1 facilitates PCa progression by activating the TGF-β1/Smad2 pathway. In this signaling cascade, TGF-β binds to its receptor, leading to phosphorylation of Smad2 and Smad3. These proteins then form complexes with Smad4 to regulate target genes such as c-Jun, MAPK, mTOR, RAS, and c-Src, all of which contribute to EMT progression [30].
- **GOLM1 as a Diagnostic and Prognostic Marker in PCa:** Several studies have documented a significant difference in GOLM1 expression among normal, benign, and malignant prostate glands [7,27,28,30-33]. Kristiansen et al. reported a GOLM1 sensitivity of 92.3%, while Li et al. found a sensitivity of 92% but a lower specificity of 53% 31. In contrast, Varambally et al. observed a sensitivity of 75% and specificity of 72% using urine samples [7]. A large cohort study involving 614 cases demonstrated that GOLM1 expression is less heterogeneous than AMACR and could serve as a valuable diagnostic marker, particularly in AMACR-negative cases and small-core biopsies [31]. Furthermore, studies have shown that GOLM1 expression is associated with higher tumor stages, grades, and poor survival outcomes [27,30].
- **GOLM1 as a Therapeutic Target:** Given its role in PCa progression, GOLM1 presents a potential therapeutic target. Agents that inhibit the PI3K-AKT-mTOR signaling pathway could be particularly effective in PCa patients with GOLM1 upregulation [26].

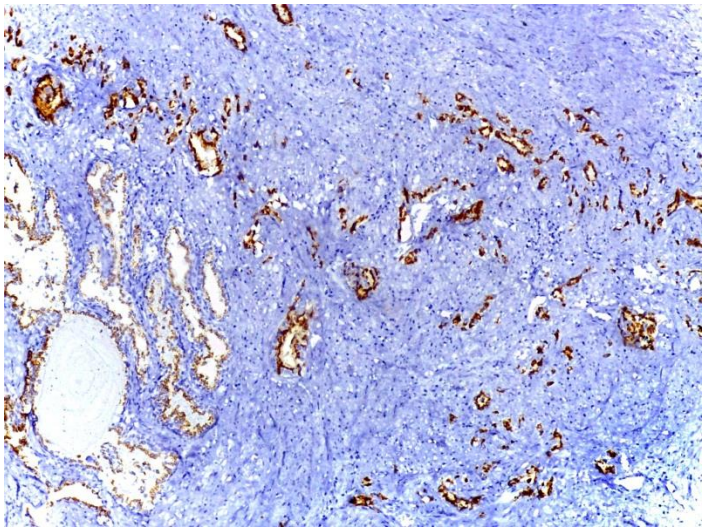


Figure (2): Immunohistochemical staining for GOLM1 in prostatic tissue: The left side of the image demonstrates benign prostatic glands with low GOLM1 expression, whereas the right side exhibits malignant glands with significantly higher GOLM1 expression. (Magnification: x100)

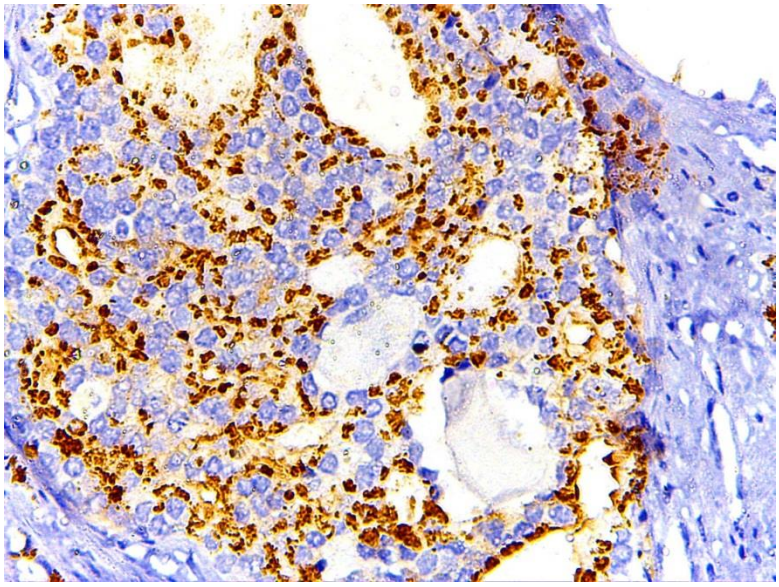


Figure (3): Immunohistochemical staining of GOLM1 in malignant tissue: The image demonstrates perinuclear granular expression of GOLM1, indicating its subcellular localization in malignancy. (Magnification: x400).

3) **Breast cancer:** Breast cancer (BC) remains one of the most significant health concerns for women worldwide [17]. Recent advancements in breast cancer research aim to reduce mortality rates by uncovering novel molecular targets and treatment strategies. GOLM1 has emerged as a key regulator in breast carcinogenesis, influencing tumor growth, metastasis, and therapy resistance [34].

- **GOLM1 and BC Progression:** Zhang et al. demonstrated that GOLM1 facilitates breast cancer cell growth and metastasis by activating matrix metalloproteinase-13 (MMP13). This highlights its role in BC progression and potential as a therapeutic target [34].
- **Targeting GOLM1 in BC Therapy:** Xie et al. (2021) introduced a breakthrough in breast cancer therapy, showing that the natural anti-tumor compound Epigallocatechin gallate (EGCG), found in green tea, can inhibit GOLM1 expression. EGCG achieves this by modulating the HGF/HGFR/AKT/GSK-3/β-catenin/-Myc signaling pathway. This discovery opens the door to potential plant-based therapies targeting GOLM1 in BC [35].

- **GOLM1 and BC Metastasis:** Metastasis remains a major challenge in breast cancer treatment. Chang et al. (2024) identified GOLM1 as one of the critical genes responsible for metastasis, even in small breast cancer tumors. This suggests that GOLM1 could serve as an early indicator of metastatic potential in BC patients [36].
- **GOLM1 and Chemoresistance in BC:** Chemoresistance is a common obstacle in BC therapy, reducing treatment effectiveness. Li et al. found that the long non-coding RNA LINC01977 acts as an oncogenic factor in BC by promoting proliferation, metastasis, and resistance to Doxorubicin. This occurs through the miR-212-3p/GOLM1 axis, presenting a novel therapeutic target for overcoming drug resistance in BC. Given its diverse roles in BC progression, metastasis, and therapy resistance, GOLM1 is an important biomarker and potential target for novel treatment strategies [37].

4) **Lung Cancer:** Lung cancer remains the leading cause of cancer-related deaths worldwide [17]. Early detection and effective management are critical, making the identification of novel biomarkers a major research focus. Recently, GOLM1 has emerged as a promising biomarker in lung cancer, playing a significant role in tumor progression and aggressiveness [38].

- **GOLM1 Expression in Lung Adenocarcinoma:** The role of GOLM1 in lung cancer was first identified by Zhang et al. (2010), who found that GOLM1 is highly expressed in lung adenocarcinoma [38].
- **Oncogenic Function of GOLM1 in Lung Cancer:** Song et al. later demonstrated that GOLM1 contributes to tumor progression by promoting p53 instability and affecting the MAPK signaling pathway. This finding suggests that GOLM1 plays a critical role in lung cancer pathogenesis through multiple oncogenic pathways [39].
- **GOLM1 and Lung Cancer Aggressiveness:** Further studies by Aruna and Li revealed that GOLM1 enhances the aggressiveness of non-small-cell lung carcinoma (NSCLC) by activating matrix metalloproteinase-13 (MMP13) signaling. This highlights its potential as both a diagnostic and therapeutic target in NSCLC. Given its role in lung cancer progression, GOLM1 represents a valuable biomarker for early detection and a potential target for novel therapeutic strategies [40].

5) **Colorectal cancer (CRC):** Colorectal cancer (CRC) is one of the most prevalent malignancies worldwide [17]. Recent studies have investigated the role of GOLM1 in CRC, particularly its involvement in tumor progression and potential therapeutic targeting [41].

- **Oncogenic Role in CRC:** GOLM1 plays a crucial role in CRC carcinogenesis by activating the AKT/GSK3β signaling pathway, which promotes malignant cell proliferation and metastasis [41].
- **Immune Evasion Mechanism:** GOLM1 contributes to CRC immune escape by upregulating CCL2, a key chemokine that recruits myeloid-derived suppressor cells (MDSCs). This recruitment helps suppress immune responses, allowing tumor cells to evade immune detection [42].
- **Impact on Tumor Microenvironment:** In addition to MDSCs, CCL2 also attracts monocytes and macrophages to the tumor microenvironment. These immune cells further support CRC progression by enhancing tumor cell survival and immune evasion. Given its significant role in CRC progression and immune modulation, GOLM1 is emerging as a potential biomarker for early detection and a target for immunotherapy [42].

6) **Glioma:** Glioma, particularly glioblastoma (GBM), is one of the most aggressive brain tumors with poor prognosis. Recent research has identified GOLM1 as a potential tumor biomarker and therapeutic target in glioblastoma [43].

- **Role in Proliferation and Metastasis:** In 2019, Ding et al. demonstrated that GOLM1 contributes to glioblastoma progression by activating the Wnt/β-catenin signaling pathway. This pathway is known to regulate tumor cell proliferation, invasion, and stemness [43].
- **Activation of the AKT Pathway:** Another study by Xu et al. (2017) revealed that GOLM1 promotes glioma progression by activating the AKT signaling pathway. The AKT pathway plays a critical role in tumor growth, survival, and resistance to therapy [44].
- **PDGFA/PDGFRα-Mediated Signaling:** GOLM1 is also a key element in platelet-derived growth factor A (PDGFA) and PDGF receptor alpha (PDGFRα)-mediated activation of AKT. This mechanism further supports glioblastoma cell proliferation and invasion, making GOLM1 a promising therapeutic target. Given

its involvement in multiple oncogenic pathways, GOLM1 could serve as a valuable biomarker for glioblastoma diagnosis and a potential target for novel therapeutic interventions [44].

7) **Esophageal Tumors:** Byrne et al. demonstrated that the subcellular localization of GOLM1 is altered throughout the progression of esophageal disease, from metaplasia to dysplasia and ultimately adenocarcinoma. In response to acid reflux, GOLM1 undergoes modification, cleavage, and subsequent secretion [45]. Additionally, Lui et al. found that GOLM1 is upregulated in esophageal squamous cell carcinoma (ESCC) through activation of the Wnt/β-catenin signaling pathway [46].
8) **Ovarian Cancer (OC):** Ovarian cancer is an aggressive tumor being the second leading cause of cancer-related deaths in women. Guan et al. exhibited that GOLM1 is a key regulator of B7-H3 protein formation and secretion; and reduced GOLM1 levels inhibit B7-H3 secretion, which is essential for tumor metastasis and invasion. These findings suggest that GOLM1 plays a crucial role in ovarian cancer development by regulating B7-H3 protein distribution, providing further insight into B7-H3-targeted therapy and its underlying mechanisms in ovarian cancer [47]. Experiments done by Fan et al. revealed that LncRNA ASB16 antisense RNA1 (ASB16-AS1) regulates the oncogenesis of ovarian cancer cells by regulating GOLM1. GOLM1 was identified as the target mRNA that competes with ASB16-AS1 for binding to miR-3918. Inhibition of miR-3918 restored the malignant behaviors suppressed by ASB16-AS1 depletion [48].

Role of GOLM1 in Diabetes: Type 1 diabetes results from the dysfunction of β-cells due to an autoimmune mechanism. PD-L1, a protein expressed in β-cells, plays a crucial role in suppressing the immune response. Inflammatory cytokines upregulate GOLM1 expression, leading to increased GOLM1 levels in the residual β-cells of diabetic patients. Notably, a relationship exists between GOLM1 and PD-L1 in diabetes, as GOLM1 stabilizes PD-L1 by protecting it from proteasomal degradation [49].

Conclusion:

GOLM1 has emerged as a unique biomarker in various tumors and diseases. Its diagnostic significance is particularly valuable in prostate cancer (PCa) and HCC, besides its pivotal role in tumor progression and metastasis. Additionally, in lung, breast, glioma, esophageal, ovarian and colorectal cancers, GOLM1 contributes to both primary tumor development and metastasis through distinct molecular pathways.

References:

1. Yan J, Zhou B, Li H, et al. Recent advances of GOLM1 in hepatocellular carcinoma. Hepatic oncology. 2020 May;7(2): HEP22. https://doi.org/10.2217/hep-2020-0006
2. Kladney RD, Bulla GA, Guo L, et al. GP73, a novel Golgi-localized protein upregulated by viral infection. Gene. 2000 May 16;249(1-2):53-65. https://doi.org/10.1016/S0378-1119(00)00136-0
3. Munro S. Localization of proteins to the Golgi apparatus. Trends Cell Biol. 1998 Jan 1;8(1):11-5. DOI: 10.1016/S0962-8924(97)01197-5
4. Farquhar MG, Palade GE. The Golgi apparatus: 100 years of progress and controversy. Trends Cell Biol. 1998 Jan 1;8(1):2-10. DOI: 10.1016/S0962-8924(97)01187-2
5. Liu Y, Hu X, Liu S, et al. Golgi Phosphoprotein 73: The driver of epithelial-mesenchymal transition in cancer. Front Oncol. 2021 Dec 7; 11:783860. https://doi.org/10.3389/fonc.2021.783860
6. Wright LM, Yong S, Picken MM, et al. Decreased survival and hepato-renal pathology in mice with C-terminally truncated GP73 (GOLPH2). Int J Clin Exp Pathol. 2008 Apr 24;2(1):34.
7. Varambally S, Laxman B, Mehra R, et al. Golgi protein GOLM1 is a tissue and urine biomarker of prostate cancer. Neoplasia. 2008 Nov 1;10(11):1285-IN35. PMCID: PMC2491393 PMID: 18830387
8. Makhoul C, Gosavi P, Gleeson PA. The Golgi architecture and cell sensing. Biochem Soc Trans. 2018 Oct 19;46(5):1063-72. https://doi.org/10.1042/BST20180323
9. Bachert C, Fimmel C, Linstedt AD. Endosomal trafficking and proprotein convertase cleavage of cis Golgi protein GP73 produces marker for hepatocellular carcinoma. Traffic. 2007 Oct;8(10):1415-23. **https://doi.org/10.1111/j.1600-0854.2007.00621.x**
10. Yang X, Fan X, Feng J, et al. GP73 blockade alleviates abnormal glucose homeostasis in diabetic mice. J. Mol. Endocrinol. 2023 Feb 1;70(2). **DOI:** https://doi.org/10.1530/JME-22-0103

11. Frans MT, Kuipers EM, Bianchi F, et al. Unveiling the impact of GOLM1/GP73 on cytokine production in cancer and infectious disease. Immunol. Cell Biol. 2023 Sep;101(8):727-34. **https://doi.org/10.1111/imcb.12664**
12. Zhang X, Zhu C, Wang T, et al. GP73 represses host innate immune response to promote virus replication by facilitating MAVS and TRAF6 degradation. PLoS Pathog. 2017 Apr 10;13(4): e1006321. https://doi.org/10.1371/journal.ppat.1006321
13. Li Y, Oosting M, Deelen P, et al. Inter-individual variability and genetic influences on cytokine responses to bacteria and fungi. Nat Med. 2016 Aug;22(8):952-60. https://doi.org/10.1038/nm.4139
14. Lin Y, He Z, Gao X, et al. Integrative analysis reveals the potential role and prognostic value of GOLM1 in hepatocellular carcinoma. Oxid. Med. Cell. Longev. 2022;2022(1):8284500. **https://doi.org/10.1155/2022/8284500**
15. Liu Y, Zhang X, Zhou S, et al. Knockdown of Golgi phosphoprotein 73 blocks the trafficking of matrix metalloproteinase-2 in hepatocellular carcinoma cells and inhibits cell invasion. J. Cell. Mol. Med. 2019 Apr;23(4):2399-409. **https://doi.org/10.1111/jcmm.14055**
16. Spano D, Colanzi A. Golgi complex: a signaling hub in cancer. Cells. 2022 Jun 21;11(13):1990. **https://doi.org/10.3390/cells11131990**
17. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May;74(3):229-63 **doi.org/10.3322/caac.21834**
18. Zhang X, Wu LN, Li XQ, et al. Whether the Golgi protein 73 could be a diagnostic serological marker in hepatocellular carcinoma: a meta-analysis. BMC Gastroenterol. 2023 Mar 24;23(1):85. https://doi.org/10.1186/s12876-023-02685-8
19. Zhou Y, Yin X, Ying J, et al. Golgi protein 73 versus alpha-fetoprotein as a biomarker for hepatocellular carcinoma: a diagnostic meta-analysis. BMC cancer. 2012 Dec; 12:1-8. https://doi.org/10.1186/1471-2407-12-17
20. Jin D, Tao J, Li D, et al. Golgi protein 73 activation of MMP-13 promotes hepatocellular carcinoma cell invasion. Oncotarget. 2015 Oct 10;6(32):33523. doi: 10.18632/oncotarget.5590
21. Liu Y, Zhang X, Zhou S, et al. Knockdown of Golgi phosphoprotein 73 blocks the trafficking of matrix metalloproteinase-2 in hepatocellular carcinoma cells and inhibits cell invasion. J. Cell. Mol. Med. 2019 Apr;23(4):2399-409. **https://doi.org/10.1111/jcmm.14055**
22. Ye QH, Zhu WW, Zhang JB, et al. GOLM1 modulates EGFR/RTK cell-surface recycling to drive hepatocellular carcinoma metastasis. Cancer cell. 2016 Sep 12;30(3):444-58. DOI: 10.1016/j.ccell.2016.07.017
23. Gai X, Tang B, Liu F, et al. mTOR/miR-145-regulated exosomal GOLM1 promotes hepatocellular carcinoma through augmented GSK-3β/MMPs. J. Genet. Genom. 2019 May 20;46(5):235-45. https://doi.org/10.1016/j.jgg.2019.03.013
24. Yang Y, Liu Q, Li Z, et al. GP73 promotes epithelial–mesenchymal transition and invasion partly by activating TGF-β1/Smad2 signaling in hepatocellular carcinoma. Carcinogenesis. 2018 Jul 3;39(7):900-10. https://doi.org/10.1093/carcin/bgy010
25. Shaker MK, Attia FM, Hassan AA, et al. Evaluation of Golgi Protein 73 (GP73) as Potential Biomarkers for Hepatocellular Carcinoma. Clin. Lab. 2020 Aug 1(8). DOI: 10.7754/ Clin.Lab.2020.190911
26. Tortorella E, Giantulli S, Sciarra A, et al. AR and PI3K/AKT in Prostate Cancer: A Tale of Two Interconnected Pathways. Int. J. Mol. Sci. 2023 Jan 20; 24(3): 2046. **https://doi.org/10.3390/ijms24032046**
27. Yan G, Zhu T, Zhou J, et al. GOLM1 promotes prostate cancer progression via interaction with PSMD1 and enhancing AR-driven transcriptional activation. J. Cell. Mol. Med. 2024 Oct; 28(20): e70186. **https://doi.org/10.1111/jcmm.70186**
28. Yan G, Ru Y, Wu K, et al. GOLM1 promotes prostate cancer progression through activating PI3K-AKT-mTOR signaling. The Prostate. 2018 Feb;78(3):166-77. **https://doi.org/10.1002/pros.23461**
29. Xu JI, Hao SH, Han KA, et al. How is the AKT/mTOR pathway involved in cell migration and invasion? Biocell. 2023 Jan 1;47(4):773-88. Doi: 10.32604/biocell.2023.026618

30. Qin X, Liu L, Li Y, et al. GOLM1 promotes epithelial-mesenchymal transition by activating TGFβ1/Smad2 signaling in prostate cancer. Technology in cancer research & treatment. 2023 Mar; 22:15330338231153618.
31. Kristiansen G, Fritzsche FR, Wassermann K, et al. GOLPH2 protein expression as a novel tissue biomarker for prostate cancer: implications for tissue-based diagnostics. Br J Cancer. 2008 Sep;99(6):939-48. DOIhttps://doi.org/10.1038/sj.bjc.6604614
32. Li W, Wang X, Li B, et al. Diagnostic significance of overexpression of Golgi membrane protein 1 in prostate cancer. Urology. 2012 Oct 1;80(4):952-e1. https://doi.org/10.1016/j.urology.2012.06.017
33. Wei S, Dunn TA, Isaacs WB, et al. GOLPH2 and MYO6: putative prostate cancer markers localized to the Golgi apparatus. The Prostate. 2008 Sep 15;68(13):1387-95. https://doi.org/10.1002/pros.20806
34. Zhang R, Zhu Z, Shen W, et al. Golgi Membrane Protein 1 (GOLM1) Promotes Growth and Metastasis of Breast Cancer Cells via Regulating Matrix Metalloproteinase-13 (MMP13). Med Sci Monit. 2019 Jan 29; 25:847-855. doi: 10.12659/MSM.911667. PMID: 30695018; PMCID: PMC6367891.
35. Xie L, Yi J, Song Y, et al. Suppression of GOLM1 by EGCG through HGF/HGFR/AKT/GSK-3β/β-catenin/c-Myc signaling pathway inhibits cell migration of MDA-MB-231. Food Chem Toxicol. 2021 Nov; 157:112574. doi: 10.1016/j.fct.2021.112574. Epub 2021 Sep 16. PMID: 34536514.
36. Chang YT, Hong ZJ, Tsai HH, et al. Hub metastatic gene signature and risk score of breast cancer patients with small tumor sizes using WGCNA. Breast Cancer. 2024 Nov;31(6):1114-1129. doi: 10.1007/s12282-024-01627-w. Epub 2024 Aug 27. PMID: 39190284; PMCID: PMC11489208.
37. Li Z, Li Y, Wang X, et al. LINC01977 Promotes Breast Cancer Progression and Chemoresistance to Doxorubicin by Targeting miR-212-3p/GOLM1 Axis. Front Oncol. 2021 Mar 31; 11:657094. doi: 10.3389/fonc.2021.657094. PMID: 33869063; PMCID: PMC8046671.
38. Zhang F, Gu Y, Li X, et al. Up-regulated Golgi phosphoprotein 2 (GOLPH2) expression in lung adenocarcinoma tissue. Clin. Biochem. 2010 Aug 1;43(12):983-91. https://doi.org/10.1016/j.clinbiochem.2010.05.010
39. Song Q, He X, Xiong Y, et al. The functional landscape of Golgi membrane protein 1 (GOLM1) phosphoproteome reveal GOLM1 regulating P53 that promotes malignancy. Cell Death Discov. 2021 Mar 1;7(1):42. https://doi.org/10.1038/s41420-021-00422-2
40. Aruna, Li LM. Overexpression of golgi membrane protein 1 promotes non-small-cell carcinoma aggressiveness by regulating the matrix metallopeptidase 13. Am. J Cancer Res. 2018 Mar 1;8(3):551-565. PMID: 29637008; PMCID: PMC5883103.
41. Mao Z, Wu Y, Yao P, et al. GOLM1 facilitates human colorectal cancer progression and metastasis via activating the AKT/GSK3β/EMT axis. Neoplasma. 2023 Feb 1;70(1):136-44. https://doi.org/10.4149/neo_2023_220816n835
42. Dang Y, Yu J, Zhao S, et al. GOLM1 drives colorectal cancer metastasis by regulating myeloid-derived suppressor cells. J. Cancer. 2021;12(23):7158. doi: 10.7150/jca.61567
43. Ding X, Deng G, Liu J, et al. GOLM1 silencing inhibits the proliferation and motility of human glioblastoma cells via the Wnt/β-catenin signaling pathway. Brain Res. 2019 Aug 15; 1717:117-126. doi: 10.1016/j.brainres.2019.03.035. Epub 2019 Mar 29. PMID: 30935831
44. Xu R, Ji J, Zhang X, et al. PDGFA/PDGFRα-regulated GOLM1 promotes human glioma progression through activation of AKT. J Exp Clin Cancer Res. 2017 Dec 28;36(1):193. doi: 10.1186/s13046-017-0665-3. PMID: 29282077; PMCID: PMC5745991.
45. Byrne AM, Bekiaris S, Duggan G, et al. Golgi phosphoprotein 2 (GOLPH2) is a novel bile acid-responsive modulator of oesophageal cell migration and invasion. Br J Cancer. 2015 Nov 3;113(9):1332-42. doi: 10.1038/bjc.2015.350. Epub 2015 Oct 13. PMID: 26461057; PMCID: PMC4815786
46. Liu Y, Zhang J, Xiao M, et al. GOLM1 affects proliferation, invasion, and migration by regulating Wnt pathway in esophageal squamous cell carcinoma cells. j. radiat. res. appl. sci. 2023 Jun 1;16(2):100532. https://doi.org/10.1016/j.jrras.2023.100532
47. Guan J, Qin Y, Deng G, Zhao H. GOLM1 as a Potential Therapeutic Target Modulates B7-H3 Secretion to Drive Ovarian Cancer Metastasis. Evid Based Complement Alternat Med. 2022 Jan 25; 2022:5151065. doi: 10.1155/2022/5151065. PMID: 35116068; PMCID: PMC8807037.

48. Fan Y, Wang L, Han X, et al. LncRNA ASB16-AS1 accelerates cellular process and chemoresistance of ovarian cancer cells by regulating GOLM1 expression via targeting miR-3918. Biochemical and Biophysical Research Communications. 2023 Oct 1; 675:1-9.
49. huang F, Nelson J, Muralidharan C, et al. SAT068 The Golgi Transmembrane Protein GOLM1 Maintains PD-L1 Protein Levels in Islet Beta Cells in Response to Type 1 Diabetic Inflammation. J Endocr Soc. 2023 Oct 5;7(Suppl 1): bvad114.935. doi: 10.1210/jendso/bvad114.935. PMCID: PMC10553690.