REVIEW PAPER

JMS Journal of Medical Science

Therapeutic *Targeting of Low-density lipoprotein receptor-related protein-1* (*LRP1*) gene in Ovarian Cancer: A Comprehensive Review

R.B. Devi Krishna
Department of Human Genetics, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0009-0000-3466-9800

Nandini Krishnamurthy
Department of Human Genetics, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0009-0000-2710-3577

Sanjana Murali
Department of Human Genetics, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0009-0006-3549-0080

Preet Agarwal
Department of Gynaecology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0000-0001-9907-5747

Elizabeth Rani Chellappan
Department of Biotechnology, Hindustan College of Arts & Science, Chennai, Tamil Nadu, India
https://orcid.org/0009-0000-6664-363X

Leena Dennis Joseph
Department of Pathology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0000-0002-9395-2961

Banu Keerthana
Department of Pathology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0000-0001-7858-8666

Andrea Mary Francis
Department of Human Genetics, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India
https://orcid.org/0000-0003-2260-7199

Corresponding author: andreamary@sriramachandra.edu.in

https://doi.org/10.20883/medical.e1221

Keywords: ovarian cancer, *LRP1*, proliferation, tumour, therapeutic target, clinical implication

Received 2025-02-04
Accepted 2025-08-28
Published 2025-09-22

How to Cite: Krishna RBD, Krishnamurthy N, Murali S, Agarwal P, Chellappan ER, Joseph LD, Keerthana B, Francis AM. Therapeutic Targeting of *Low-density lipoprotein receptor-related protein-1* (*LRP1*) gene in Ovarian Cancer: A Comprehensive Review. Journal of Medical Science. 2025 September;94(3);e1221. doi:10.20883/medical.e1221

ABSTRACT

Low-density lipoprotein receptor-related protein 1 (*LRP1*, also known as *CD91*) is a multifunctional endocytic and cell-signalling receptor widely expressed in various cell types, including neurons, fibroblasts, hepatocytes, muscle cells, astrocytes, and tumour cells. It maintains cellular homeostasis by mediating interactions with extracellular matrix proteins, growth factors, and proteases. These interactions enable *LRP1* to act as a co-receptor that modulates and influences signalling pathways associated with cell migration, survival, and proliferation. In ovarian cancer, LRP1 is frequently activated and contributes to tumour progression. Functional studies have demonstrated that LRP1 promotes these malignant traits through activation of PI3K/Akt and MAPK/ERK pathways, while its inhibition suppresses proliferation and invasion. This review aims to comprehensively examine the functional role of LRP1 in ovarian cancer, with particular emphasis on its capacity to regulate tumour cell migration and invasion through key molecular pathways. Understanding these mechanisms may provide insights into novel therapeutic strategies for ovarian cancer treatment.

Introduction

Ovarian cancer (OC) is one of the most lethal gynaecologic malignancies, primarily due to late-stage diagnosis [1]. It originates from ovarian tissue or, more commonly, from adjacent structures such as the fallopian tubes or the peritoneal lining, which are connected to the ovaries. The ovary consists of three distinct cell types: stromal, germ, and epithelial. When epithelial cells undergo abnormal growth, they can proliferate uncontrollably, leading to tumour formation [2,3]. According to the Global Cancer Observatory 2022, OC accounts for approximately 6.7 cases per 100,000 women globally, with an estimated 324,603 new cases reported in that year. In India, the incidence rate is around 6.6 cases per 100,000 women, totalling approximately 47,333 new cases. A major contributor to OC's high mortality is the lack of early, recognisable symptoms, resulting in delayed diagnosis [4]. However, vaginal ultrasound and serum Cancer Antigen 125 (CA125) testing are commonly used diagnostic tools; their low sensitivity and specificity limit early-stage detection [5]. The current standard of care involves cytoreductive surgery followed by platinum-based chemotherapy, often in combination with taxane agents. While these regimens initially induce remission in most patients, recurrence is frequent, and many eventually develop platinum-resistant ovarian cancer [6,7]. This therapeutic resistance underscores the urgent need for novel strategies that can overcome chemoresistance and improve long-term outcomes. Recent research efforts have focused on molecular targets, immune modulation, and receptor-mediated pathways, including the low-density lipoprotein receptor-related protein 1 (LRP1), which has emerged as a promising candidate for therapeutic intervention.

Initially identified as a receptor involved in lipid metabolism, LRP1 was subsequently shown to be a receptor for active a2-macroglobulin [8]. *LRP1* was once thought to function as a scavenger receptor. Still, an increasing amount of evidence points to the possibility that it may also control the activity of other membrane receptors, such as adhesion and tyrosine kinase receptors, and facilitate intracellular signalling [9]. *LRP1* influences tumour cell invasion and migration by regulating the expression of matrix metalloproteinases MMP2 and MMP9, which degrade the extracellular matrix and facilitate cancer cell movement. Additionally, *LRP1*-mediated activation of ERK signalling enhances tumour cell adhesion and motility, while its suppression of JNK signalling prevents apoptosis, further supporting invasive behaviour [9,10].

Among emerging molecular targets, *LRP1* has garnered significant interest due to its multifaceted role in cancer biology. *LRP1* is a transmembrane receptor involved in endocytosis and signal transduction, and its dysregulation has been associated with malignant behaviours such as enhanced cell motility, extracellular matrix remodelling, and reduced treatment efficacy. Notably, *LRP1* plays a key role in lipoprotein metabolism, facilitating the uptake of lipid-rich particles into cells. Tumours, including OC, often exploit these lipoprotein metabolic pathways to support rapid proliferation, with increased lipid intake and storage accelerating tumour growth and contributing to chemoresistance [11]. The viable therapeutic strategy for ovarian cancer involves inhibiting *LRP1* [12]. Inhibitors targeting LRP1 and related proteins are being researched as potential therapeutic agents since they have demonstrated promise in preclinical trials. It may be possible to prevent tumour growth and metastasis, as well as improve the efficiency of currently available ovarian cancer treatments, by impairing the functions of *LRP1* [12-15]. While *LRP1* shows potential as a therapeutic and diagnostic biomarker in ovarian cancer, its functional specificity and clinical utility remain to be fully elucidated.

Structure and Function of *LRP1*

LRP1 is a large endocytic receptor. During biosynthesis, the 600 kDa protein *LRP1* is cut into two polypeptides, which are permanently associated with the N-terminal extracellular domain (~515 kDa) and a transmembrane C-terminal fragment (~85 kDa) [13]. *LRP1* has a variety of biological functions that include lipid metabolism, cell proliferation, migration, inflammation, and death. *LRP1* functions as a key regulatory receptor in multiple physiological processes, including blood-brain barrier permeability, vascular tone modulation, and platelet-derived growth factor (PDGF) receptor signalling, which collectively

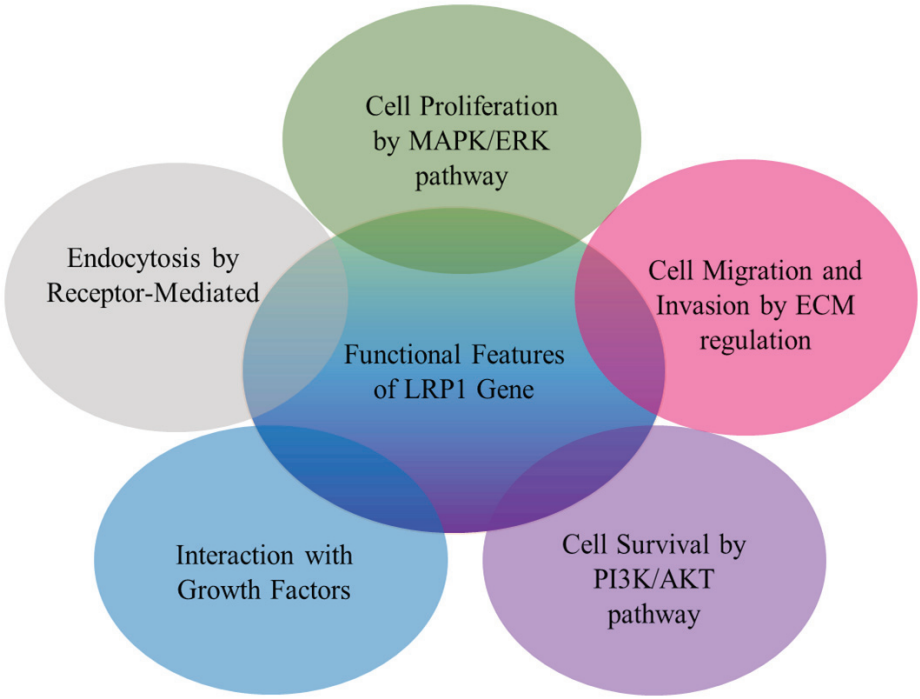

Figure 1. Low-density lipoprotein receptor-related protein 1 *(LRP1)* increases cell division by activating the Mitogen-Activated Protein Kinase/Extracellular Signal-Regulated Kinase (MAPK/ERK) pathway, and it improves cell survival by blocking the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt) pathway, which prevents apoptosis, or programmed cell death. The alteration of extracellular matrix (ECM) elements promotes the invasion and migration of cancer cells, aiding in the internalisation and degradation of signalling molecules, thereby inhibiting their access and activity. Interacting with several growth factors also affects the development and spread of cancer cells. Image created using Microsoft PowerPoint.

influence cellular migration and tissue remodelling. *LRP1* is also connected to diseases such as cancer, atherosclerosis, and neurological disorders [14,15]. *LRP1* may also affect several physiological processes by regulating cellular signalling and functioning as an endocytic receptor, according to earlier research. *LRP1* has been implicated in several cancers, including glioblastoma, breast cancer, and ovarian cancer, where it influences tumour progression through pathways involving vascular endothelial growth factor (VEGF). Studies suggest that *LRP1* can regulate VEGF expression, contributing to angiogenesis, tumour proliferation, and metastasis [8–10].

The function of this receptor is to regulate cell signalling pathways, such as the MAPK pathway (see **Figure.1**), which includes enzymes implicated in cancer invasion. It also participates in the metabolism of several external ligands, such as PDGF and MMP. By activating the MAPK/ERK pathway, *LRP1* promotes cell division. Several studies have examined *LRP1* gene expression and its function in various tumours. Additionally, LRP1 modulates the TGF-β signalling axis, which plays a dual role in OC, suppressing early tumorigenesis but promoting epithelial to mesenchymal transition (EMT) and metastasis in advanced stages. Through its interaction with urokinase-type plasminogen activator (uPA) and MMPs, LRP1 contributes to extracellular matrix (ECM) remodelling, facilitating tumour cell migration and invasion. The modification of ECM components facilitates the migration and invasion of tumour cells and helps internalise and degrade signalling molecules to regulate their exposure and activity. Tumours activate lipoprotein metabolic pathways, leading to increased lipid uptake and storage in various malignancies. This enhanced lipid metabolism supports rapid tumour growth and progression [16,17]. Several studies were conducted for the *LRP1* gene expression and functions in other tumours; however, its specific

involvement in the development of OC has not been thoroughly characterised [18].

Expression and localisation of *LRP1*

The *LRP1* gene is located on chromosome 12q13.14. There are 89 coding exons in the 85 kb gene. In addition, it has eight β-propeller domains, 22 EGF repeats, and 31 ligand-binding repeats. The endoplasmic reticulum synthesises *LRP1*, which is then cleaved into two subunits in the Golgi complex. *LRP1* is expressed in the cytoplasm of various cell types, including adipocytes, mesothelial cells, smooth muscle cells, fibroblasts, astrocytes, neurons, hepatocytes, macrophages, and malignant cells (see **Table 1**). It is essential for signalling pathways and endocytosis. It is found in the nucleoplasm and vesicles [19,20]. Amyloid-β (Aβ) peptide metabolism and lipid transport are regulated by *LRP1*, which is primarily present in the postsynaptic domain and the cell body of neurons [21].

The contribution of *LRP1* in ovarian cancer is complex, as both higher and lower expression have been implicated in tumour progression, depending on the cellular context. Elevated LRP1 expression has been associated with enhanced tumour invasion and metastasis, primarily through its regulation of MMP2/MMP9. Conversely, LRP1 downregulation has been linked to reduced tumour cell migration and proliferation, suggesting its involvement in maintaining tumour aggressiveness [22].

Role of *LRP1* in cancer progression and metastasis

In ovarian cancer, *LRP1* has been linked to both tumour growth and survival. It is capable of regulating several signalling pathways that are involved in cell survival, proliferation, and apoptosis resistance. The ability of ovarian tumour cells to spread is correlated with *LRP1* expression [22-24]. Through its modulation of processes such as extracellular matrix disintegration, cytoskeletal restructuring, and the EMT, it promotes invasion and metastasis [25,26].

Angiogenesis, which is essential for the development and spread of ovarian cancers, *LRP1* promotes angiogenesis, a key process in tumour growth and dissemination. It regulates the expression and activity of angiogenic mediators, including MMP and VEGF [27]. Chemotherapy resistance in OC has been linked to *LRP1* expression. It regulates the efflux of chemotherapeutic agents from cancer cells [28]. *LRP1* interacts with immune cells, extracellular matrix proteins, and stromal cells in the tumour microenvironment. This interaction affects immune suppression, inflammation, and the response to therapy, among other aspects of tumour growth [22,29].

Growth components, extracellular matrix proteins, toxins, protease inhibitor complexes, and viral proteins are examples of *ligands* for LRP1. *LRP1* maintains the integrity of the extracellular matrix and regulates the homeostasis of several secreted proteins by clearing proteases such as MMPs and extracellular proteins like coagula-

Table 1. *LRP1* plays distinct roles depending on its cellular localisation.

Localization	Function
Neurons	Regulates Aβ metabolism, lipid transport, and synaptic plasticity. Implicated in Alzheimer's disease due to its role in Aβ clearance.
Liver	Facilitates lipoprotein metabolism, including uptake of chylomicron remnants and regulation of cholesterol homeostasis.
Macrophages	Modulates inflammatory responses, phagocytosis, and clearance of apoptotic cells. Plays a role in atherosclerosis by influencing lipid uptake.
Cancer cells	Regulates tumor invasion and metastasis by regulating MMP2/MMP9 expression and interacting with PI3K/Akt and MAPK/ERK pathways.
Vascular Smooth Muscle Cells	Influences vascular remodeling, migration, and proliferation, contributing to atherosclerosis and vascular diseases.

Amyloid-β (Aβ), Extracellular signal-regulated kinase (ERK), Matrix Metalloproteinase (MMP), Mitogen-activated protein kinase (MAPK), Phosphatidylinositol 3-kinase (PI3K), Protein kinase B (Akt).

tion factor VIII [20]. *LRP1* may influence tumour growth by regulating the attachment and detachment of malignant cells. LRP1 promotes invasion and metastasis, as demonstrated by in vitro migration assays and in vivo mouse models showing enhanced metastatic potential via ERK-mediated MMP regulation [30]. It modulates focal adhesion dynamics through interactions with key proteins such as paxillin and focal adhesion kinase (FAK), which are involved in cell migration and invasion. This regulates integrin stimulation and the turnover of focal adhesions. The intricate nature of *LRP1*'s function in tumour cell invasion and migration is probably influenced by the type of tumour cell as well as the makeup and structure of the surrounding environment [31].

Researchers used short hairpin RNA (shRNA) to suppress *LRP1* expression in CL16 cells. This knockdown led to reduced VEGF expression and increased cell mortality under hypoxic conditions in vitro. In Severe Combined Immunodeficiency mice, *LRP1*-silenced cells created tumours and spread to the lungs, but the metastases did not expand, indicating a problem with cell proliferation or survival. These findings are supported by both in vitro and in vivo studies, which collectively validate the functional role of LRP1 in ovarian cancer progression, angiogenesis, and chemoresistance [32].

LRP1-Mediated tumour survival mechanisms in ovarian cancer

LRP1 significantly influences the regulation of cell apoptosis through its interactions with signalling pathways and apoptotic mediators. Through regulation of the expression of Caspase-3, the insulin receptor, the serine/threonine kinase signalling pathway, and *LRP1* has been shown to prevent cell apoptosis. The activation of caspase-3, an essential enzyme in cell death, is stimulated by *LRP1* [32]. AKT phosphorylation, insulin receptor signalling, apoptosis, and Caspase-3 activation were all markedly reduced in neurons upon *LRP1* knockdown. This implies that *LRP1* may inhibit Caspase-3 activation, hence preventing cancer cells from undergoing apoptosis [33]. The forebrain of mice lacking *LRP1* showed increased cell apoptosis, supporting LRP1's facilitation of insulin receptor signalling and AKT pathway activation, which regulates cell survival and metabolic regulation. The function of *LRP1* in apoptosis and its potential as a therapeutic target and its viability as a therapeutic target in the treatment of cancer require more investigation [34]. Apoptosis is orchestrated by a complex interplay of intracellular signalling pathways, including the insulin receptor, ERK, AKT, and JNK cascades. The insulin receptor activates downstream PI3K/AKT and MAPK/ERK pathways, which promote cell survival by inhibiting pro-apoptotic mediators such as BAD and caspase-9. AKT phosphorylation is particularly critical for suppressing apoptosis through modulation of transcription factors and metabolic regulators. ERK signalling, while primarily associated with proliferation, can exert anti-apoptotic effects depending on cellular context. In contrast, JNK activation is typically related to stress-induced apoptosis through c-Jun phosphorylation and the upregulation of death receptors [35].

Mechanisms of *LRP1* involvement in ovarian cancer

LRP1 was initially thought to have a tumour-suppressive function when multiple research groups reported lower *LRP1* expression in various tumour cell lines and tissues. It was recently demonstrated that *LRP1* acts as an internal suppressor of the melanoma aggressive phenotype in response to ApoE [36]. Nevertheless, conflicting data point to *LRP1*'s potential contribution to breast and ovarian cancer cell invasion and metastasis. Furthermore, it was discovered that elevated *LRP1* expression in endometrial carcinomas was linked to a higher histological grade and indicative of a more aggressive tumour behaviour. Since the extracellular portion of *LRP1* was initially discovered to be soluble in human plasma, *LRP1* shedders have been recognised as proteolytic enzymes belonging to various classes. These include BACE-1 and the serine proteinase tPA, MMP2 and MMP14, and others. The intracytoplasmic region of *LRP1* is capable of exiting the cytoplasmic membrane by γ-secretes after *LRP1* is shed, and this could serve as a mediator for signalling [36,37].

Early research on *LRP1*'s potential connection to cancer primarily used tumour cell lines

and hypothesised that the development of cancer is linked to a decrease in *LRP1* expression or, possibly, the gene's total deletion [38]. However, another study showed that hypoxic environments, which are typical of in vivo cancers, significantly boost *LRP1* expression. Therefore, the level of *LRP1* expression in cancer may not accurately reflect the expression of the protein in cancer cells grown under ambient conditions with abundant oxygen [39]. The involvement of *LRP1* in cancer, acting as both a promoter and suppressor of tumour progression, is regulated in a cellular context. On one hand, *LRP1* enhances tumour invasion and metastasis by regulating MMP2 and MMP9 and activating ERK signalling, which supports cancer cell migration.

On the other hand, *LRP1* has been shown to suppress tumour growth in specific conditions by modulating apoptotic pathways and immune responses, potentially limiting cancer cell survival [31,40]. Understanding these opposing functions is crucial for determining *the* therapeutic potential of LRP1 in ovarian cancer. It has been found that *LRP1* is increased in triple-negative breast cancer, malignant gliomas, and endometrial carcinomas. It is also associated with poor prognosis and tumour spread. *LRP1* is also an unfavourable prognostic factor for renal and urothelial cancers. It's interesting to note that tumour cell lines from ovarian, breast, and melanoma cancers all express *LRP1*, albeit to varying degrees, inhibiting the complexity of the link between *LRP1* expression and the development of cancer [41,42].

Proteomics research has demonstrated that the serum of OC patients contains higher levels of exosomal *LRP1* than that of healthy individuals [43]. Its function in the development of cancer has recently come into focus. OC progression is influenced by angiogenesis regulation, matrix metalloproteinase activity, and interactions with ERK signalling. These factors contribute to tumour invasion, metastasis, and resistance to apoptosis, highlighting key molecular mechanisms involved in OC pathophysiology. However, *LRP1* expression levels both low and high have been linked to worse prognosis in various cancer types (see **Figure 2**) [17]. Silencing *LRP1* disrupts cancer cell migration in a three-dimensional matrix by inhibiting FAK activation and increasing myosin light chain-2 (MLC-2) phosphorylation. This alteration in cytoskeletal dynamics reduces cell protrusion and motility, highlighting *LRP1*'s regulation in tumour invasion. In fact, despite a significant increase in pericellular proteolytic activity, *LRP1* knockdown limits cancer cell invasiveness. *LRP1* promotes cell invasion by precisely regulating the structure and adhesive properties of the actin network, facilitating cytoskeletal remodelling and dynamic cell movement. *LRP1* facilitates ovarian cancer cell invasion by regulating focal adhesion disassembly and activating key signalling cascades, notably the MAPK/JNK and ERK pathways [44]. It also modulates phosphatidylinositol 3-kinase signalling through adaptor protein interactions, contributing to enhanced cell survival [45]. Bioinformatics analyses have identified *LRP1* as a central node within the Notch signalling pathway's network, implicated in the dysregulation associated with various malignancies [46]. In both in vitro and in vivo models, *LRP1* has been shown to influence ovarian cancer migration through multiple pathways, including p-ERK/MMP2/MMP9 and Wnt signalling [47, 48].

LRP1 gene polymorphism

Cancer specimens were found to have mutations in the *LRP1* gene (see **Table 2**). The C766T polymorphism has been linked to an increased risk of breast carcinoma in Caucasian females. Despite being a silent variation that does not result in an amino acid change, it has also been associated with Alzheimer's disease and coronary artery disease [49]. The polymorphism 663 C>T (rs1800127) affects exon six and is linked to an increased likelihood of recurrent venous thromboembolism and coronary heart disease. Although the polymorphism's whole effect on the *LRP1* gene is unknown, it most certainly affects ligand binding. The exon 8 polymorphism rs1800137 results in a frameshift in exon 9, leading to a premature stop codon and potential mRNA instability and potential disruption of protein function [50].

Clinical implications of the *LRP1* gene as a key therapeutic target

A novel biomarker of OC cancer is necessary to enable early detection. While elevated carcinoembryonic antigen levels are considered a poor prog-

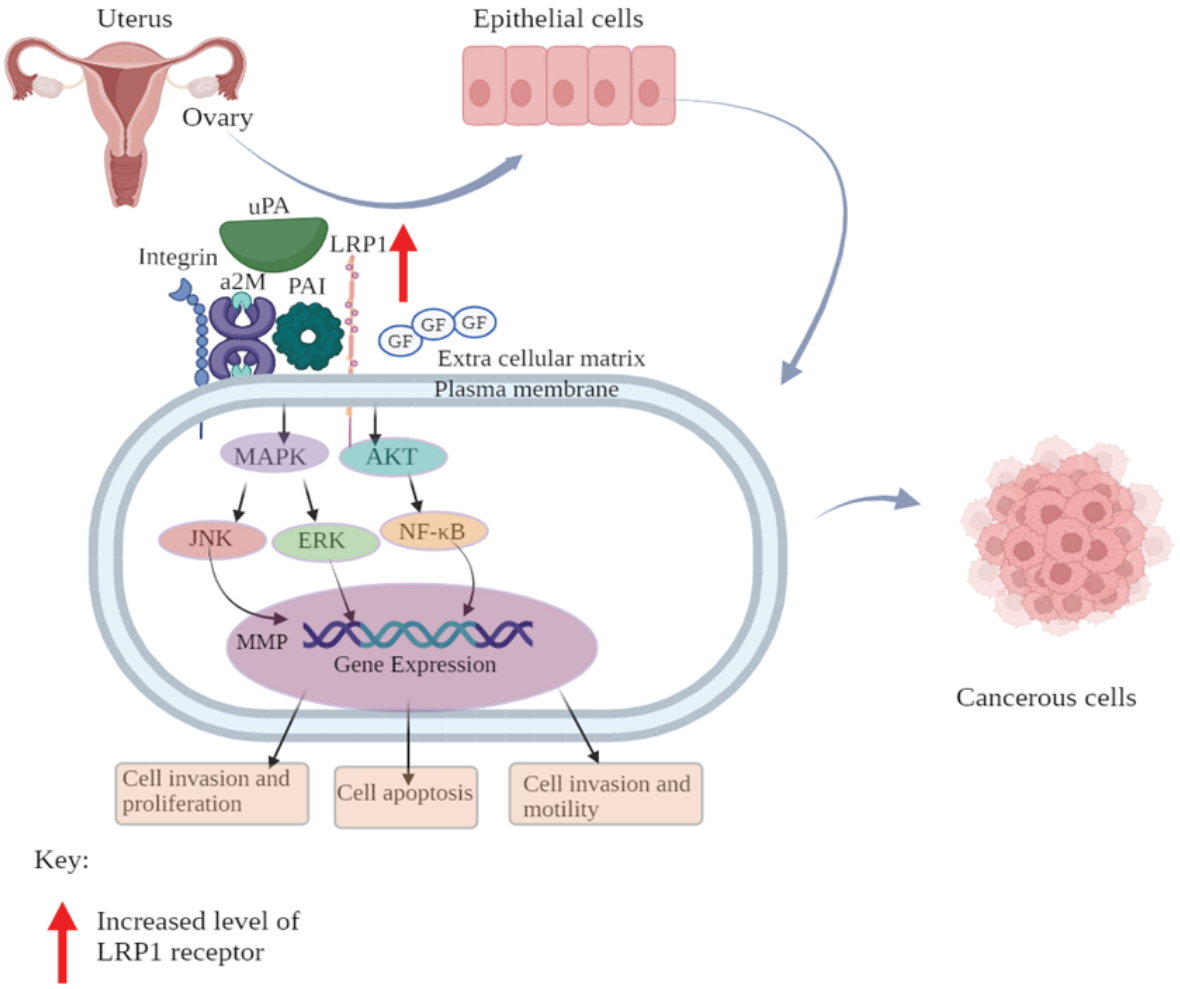

Figure 2. *LRP1*-mediated signalling pathways are involved in regulating various cellular processes, particularly those related to tumorigenesis and progression. *LRP1* modulates multiple signalling pathways in a manner regulated by phosphorylation. One such pathway is activated when *LRP1* binds to the growth factor (GF) receptor, triggering the mitogen-activated protein kinase (MAPK) signalling cascade. This activation eventually promotes the invasion and proliferation of cancer cells by activating the extracellular signal-regulated kinase (ERK) pathway and inhibiting c-jun N-terminal kinase (JNK). Furthermore, ERK promotes MMP2 and MMP9 gene expression patterns, which aid in the invasion of cancer cells. This figure was created using Microsoft PowerPoint.

Table 2. *LRP1* gene polymorphism and disease [23].

Known SNPs	Disease Association	Affect
rs1800127	Cardiovascular disease, obesity, cancer	*LRP1* expression and function
rs715948	Cancer	*LRP1* function
rs1799986	Hyperlipidemia and dyslipidemia, cancer, diabetes and metabolic syndrome	*LRP1* structure
rs138854007	Coronary atherosclerosis, familial hypercholesterolemia	*LRP1* expression
rs1800137	Obesity, hypertension, cancer	*LRP1* expression
rs1799986	Metabolic syndrome, cardiovascular disease, Alzheimer's disease	*LRP1* function
rs1800194	Cardiovascular disease, cancer, Alzheimer's disease	*LRP1* function
rs12814239	Unknown	*LRP1* function
rs34577247	Unknown	*LRP1* structure
rs7397167	Unknown	*LRP1* structure

c-Jun N-terminal Kinase (JNK), Extracellular Signal-Regulated Kinase (ERK), Low-Density Lipoprotein Receptor-Related Protein 1 (*LRP1*), Matrix Metalloproteinase (MMP), Mitogen-Activated Protein Kinase (MAPK).

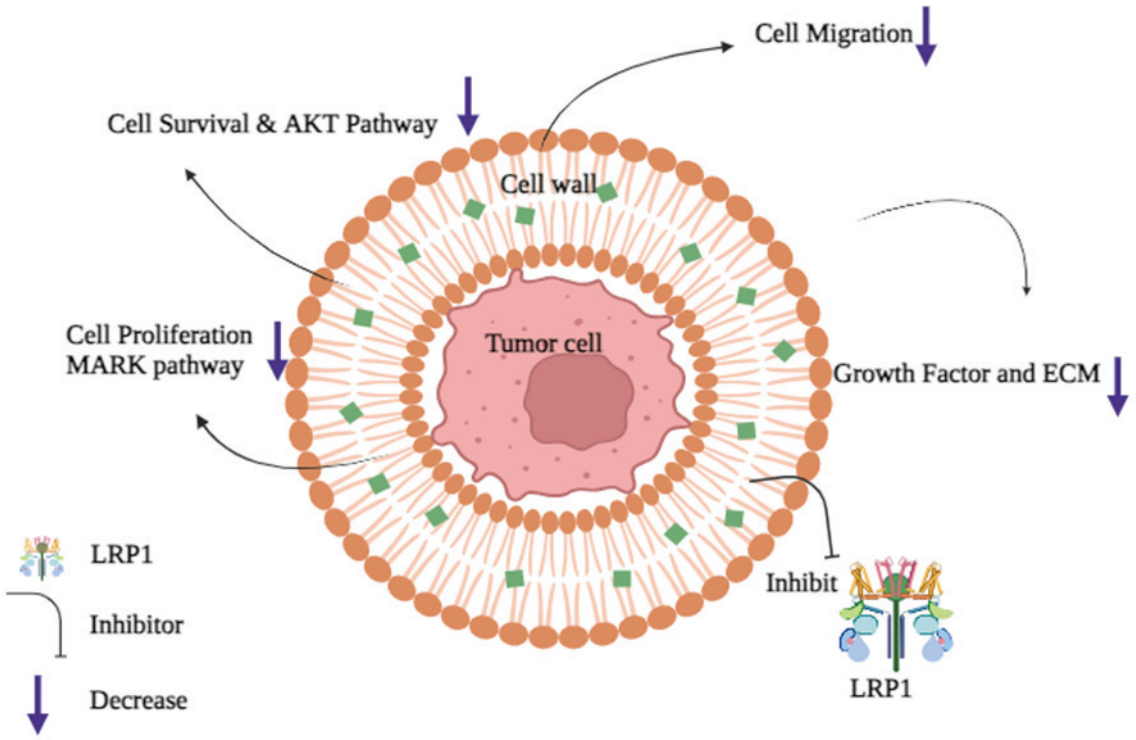

Figure 3. One particular inhibitor targets the ovarian cancer cell's surface *LRP1* receptor explicitly and blocks it. Signalling pathways like MAPK/ERK, which are essential for cell division and development, are disrupted by *LRP1*. The cancer cell's capacity to multiply is therefore reduced. Additionally, *LRP1* inhibition impacts the PI3K/AKT pathway, which often enables cancer cells to evade apoptosis. Inhibiting *LRP1* limits the cell's capacity for interaction with ECM, which in turn restricts the cell's ability to move around and invade other tissues—two essential processes in the metastasis of cancer—created using Microsoft PowerPoint.

nostic indicator in early-stage ovarian cancer, the favourable detection rates of α-fetoprotein and CA19-9 are comparatively low. However, CA125 and HE4 remain the most reliable biomarkers for ovarian cancer detection, with HE4 demonstrating higher specificity in differentiating malignant from benign pelvic masses. In OC tissues with downregulated *LRP1*, there was a decrease in the levels of MMP2, MMP9, and p-ERK (see **Figure 3**). Meanwhile, following *LRP1* knockdown, the MMP agonist 4-aminophenylmercuric acetate restored MMP2 and MMP9 expression. OC cells exposed to exosomes from healthy volunteers exhibited significantly higher levels of MMP9, MMP2, *LRP1*, and phosphorylated ERK (p-ERK) protein compared to OC cells treated with siRNA-mediated *LRP1* knockdown (SI-*LRP1*-Exos). Both exosomal and secreted forms of *LRP1* have been shown to influence ovarian cancer cell motility, primarily through activation of downstream signalling cascades such as p-ERK and matrix metalloproteinases [MMP2/MMP9]. The secreted *LRP1* and exosomal *LRP1* had a comparable mechanism influencing OC migration. Exosomes produced from tumour cells have been shown in accumulating data to facilitate cancer spread potentially. It was also demonstrated that the serum exosomes of OC patients encouraged the migration of OC cells.

Recent studies (see **Table 3**) have explored various strategies to inhibit LRP1, including receptor-associated protein, monoclonal antibodies, and siRNA-mediated knockdown. These approaches primarily function by blocking ligand binding, disrupting endocytic trafficking, or attenuating downstream signalling cascades such as ERK/MAPK and PI3K/AKT pathways known to regulate cell survival, migration, and chemoresistance [3,56]. Inhibiting the proliferation of tumour cells was observed in pancreatic cancer PANC-1 cells with the knockdown of *LRP1*. In pancreatic cancer, *LRP1* overexpression is linked to both cell invasion and a poor prognosis. *LDLR* is upregulated in tumour cells, and cholesterol levels rise as a result of the lipoprotein metabolic pathway in pancreatic cancer. High-grade gliomas, such as glioblastoma multiforme, are distinguished from low-grade astrocytomas by significantly

Table 3. Overview of in vitro and in vivo approaches targeting *LRP1* inhibition.

Author Name and reference	Place and study year	Study type	Sample Size	Description of the study	Finding
Wei Zhou et al. [3]	China, 2023	Experimental studies	Case-5 Control-5	Serum exosome proteomics analysis. Comparison of exosomal *LRP1* levels between ovarian cancer patients and healthy individuals. In-vitro and in-vivo migration assays to assess *LRP1*'s role in MMP2/MMP9 regulation via ERK signaling.	Exosomal *LRP1* levels were significantly higher in ovarian cancer patients compared to healthy individuals. *LRP1* influenced MMP2/MMP9 production via ERK signaling, affecting cell migration
Mengying Zhu et al. [24]	China, 2023	Experimental studies	Cell line	Bioinformatics analysis of *LRP1* expression in GI cancer. Western blot validation of *LRP1* protein presence in HepG2, BxPC-3, and HGC-27 cells. Lentivirus-mediated shRNA knockdown of *LRP1*. Functional assays to evaluate migration, invasion, and proliferation.	*LRP1* knockdown in gastrointestinal cancer cells reduced CD36 expression, inhibiting migration, invasion, and proliferation.
Aline Appert--Collin et al. [20]	France, 2017	Experimental studies	3D Cell line	FTC-133 thyroid cancer cell model. 3D collagen type I matrix experiments. Analysis of morphological changes, actin-cytoskeleton reorganization, and cell-matrix interactions. Assessment of FAK activation, RhoA activity, and MLC-2 phosphorylation.	*LRP1* suppression altered cell morphology, inhibited FAK activation, and increased RhoA activity, leading to reduced migration.
Océane Campion et al. [23]	France, 2021	Experimental studies	Cell line	RNA interference to silence *LRP1* in MDA-MB-231 cells. In-vivo tumor growth assessment using angiogenic assays and orthotopic xenograft models. DCE-MRI, FMT, and IHC for vascular structure and function analysis. Proteomic analysis of *LRP1*-regulating signaling pathways.	*LRP1* suppression in TNBC models delayed tumor growth by 60%, disrupted vascular structures, and inhibited angiogenesis via plasminogen/ TGF signaling
Cao Cuong Le et al. [58]	France, 2020	Experimental studies	Cell line	3D collagen matrix experiments. Analysis of *LRP1*-DDR1 molecular interactions at the plasma membrane. Endocytosis studies to assess DDR1 expression regulation. Cell cycle progression and apoptosis assays.	*LRP1*-mediated DDR1 endocytosis enhanced colon cancer cell proliferation, reduced apoptosis, and regulated tumor microenvironment interactions

Cluster of Differentiation 36 (CD36), Discoidin Domain Receptor 1 (DDR1), Dynamic contrast enhanced MRI (DCE-MRI), Extracellular Signal-Regulated Kinase (ERK), Faecal Microbiota Transplantation (FMT), Focal Adhesion Kinase (FAK), Gastrointestinal Cancer (GI cancer), Immunohistochemistry (ICH), Low Density Lipoprotein Receptor-related Protein 1 (*LRP1*), Matrix Metalloproteinase (MMP), Myosin Light Chain 2 (MLC-2), Ras homolog gene A (RhoA), Triple-Negative Breast Cancer (TNBC)

elevated levels of *LRP1* protein and mRNA. Low hepatocellular carcinoma metastatic potential is associated with high *LRP1* expression.

In contrast to similar normal tissues, *LRP1* was found at increased levels in cancer cells, such as pancreatic, ovarian, renal, and breast malignancies, among others [51,52]. The effect of *LRP1* inhibition is a marked decrease in the aggressive characteristics of ovarian cancer cells, including their capacity for unchecked proliferation, survival in harsh environments, and metastasis to other bodily regions. This highlights the potential therapeutic benefits of targeting *LRP1* in the treatment of ovarian cancer.

Challenges and future directions

Exploring how *LRP1* contributes to ovarian cancer remains challenging due to its complex involvement in tumour initiation, progression, and therapy response. Overcoming these obstacles is

essential to elucidating its specific functions in cancer biology fully. Scientists are attempting to determine if mutations in or levels of *LRP1* expression can act as predictive or prognostic indicators for ovarian cancer. Patient classification and personalised treatment plans may benefit from this. Another crucial avenue to pursue is the investigation of *LRP1* targeting's therapeutic potential in ovarian cancer. This involves creating antibodies, small-molecule inhibitors, or other targeted treatments that can successfully block *LRP1*-mediated pathways linked to tumour growth and metastasis [53,54].

There are several obstacles to overcome to comprehend the function of *LRP1* in ovarian cancer, especially when considering tumour genesis, development, and treatment resistance. Their unintentional contribution to drug resistance may compromise the effectiveness of treatments targeting LRP1-related pathways. Essential processes that inhibit *LRP1* expression and affect cancer cell survival include epigenetic changes, such as DNA methylation and histone alterations, as well as noncoding RNA activity. Additionally, microRNAs (miRNAs) modulate *LRP1* levels, influencing response to therapy. Beyond genetic regulation, *LRP1*-expressing ovarian cancer cells interact with extracellular matrix components, immune cells, and stromal cells, shaping tumour progression and resistance pathways. Investigating these interactions is crucial for predicting disease trajectory and therapeutic response. Translating preclinical findings into clinical trials is another challenge, as assessing the safety and efficacy of *LRP1*-targeted therapies requires extensive validation. Furthermore, identifying *LRP1* as a biomarker for therapy prediction could enhance precision medicine approaches, improving patient outcomes. Addressing these complexities will be essential for advancing ovarian cancer research and treatment strategies [55-57].

Conclusion

Although bioinformatics analyses have suggested that *LRP1* may serve as a prognostic indicator in OC, direct clinical validation remains limited, and further studies are required to establish its diagnostic significance. High *LRP1* expression correlates with advanced disease stage, poor differentiation, and worse clinical outcomes. *LRP1* is being explored as a therapeutic target in ovarian cancer. Strategies targeting *LRP1* signalling or its downstream effectors have shown encouraging outcomes in preclinical research, including the reversal of chemotherapy resistance and the prevention of tumour growth and metastasis. Prior research indicates that *LRP1* inhibited MMP2 and MMP9 expression via ERK signalling pathways. Enhancing the prognosis and survival of individuals with OC is contingent upon the timely identification of OC genesis. Although vaginal ultrasonography and blood CA125 testing are widely used for ovarian cancer diagnosis, their low sensitivity and specificity limit early-stage detection. Given these challenges, recent studies have explored alternative biomarkers, including *LRP1*, which has been found at elevated levels in ovarian cancer patients. This review highlights the role of *LRP1* in modulating the p-ERK/MMP2/MMP9 signalling axis, which facilitates ovarian cancer cell motility and invasion. Based on current evidence, we propose that LRP1 expression holds potential as a diagnostic and prognostic biomarker in ovarian cancer. However, its clinical relevance remains to be fully elucidated, and further validation through comprehensive in vitro and in vivo studies is warranted.

Glossary

OC: Ovarian Cancer, LRP1: Low-density lipoprotein receptor-related protein-1, MMP: Matrix metalloproteinases, LDL-R: Low-density lipoprotein receptor, ECM: Extracellular matrix, EMT: Epithelial-to-mesenchymal transition, VEGF: Vascular endothelial growth factor, shRNA: Short hairpin RNA, PDGF: Platelet-derived growth factor, FAK: Focal adhesion kinase.

Disclosures

Acknowledgements
We are grateful to our department for the facilities and to our Biochemical Genetics lab mates and staff for their support and encouragement.

Conflict of interest
The Authors do not have any competing interests.

Funding
This study received no external funding.

Authors' contributions
Devi Krishna RB was responsible for conceptualisation, methodology design, data analysis, and preparation of the original draft, including figures and tables. Nandini Krishnamurthy and Sanjana Murali contributed to data curation and literature investigation. Dr. Andrea Mary F and Dr. Preet Agarwal provided supervision and project administration throughout the study. Dr. Elizabeth Rani Junieus, Dr. Leena Joseph, and Dr. Banukeerthana participated in manuscript review, editing, and validation of the final content. All authors contributed to the development of the manuscript and approved its final version for submission.

Availability of data and materials
Not applicable

Ethics approval and consent to participate
Not applicable

Patient consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

References

1. Moch H. Female genital tumours: WHO Classification of Tumours, Volume 4. WHO classification of tumours. 2020.
2. Committee on the State of the Science in Ovarian Cancer Research; Board on Health Care Services; Institute of Medicine; National Academies of Sciences, Engineering, and Medicine. Ovarian Cancers: Evolving Paradigms in Research and Care. Washington (DC): National Academies Press (US); 2016 Apr 25.
3. Zhou W, Ma J, Zhao H, Wang Q, Guo X, Chen L, Cao Z, Xu J, Zhang B, Zhou X. Serum exosomes from epithelial ovarian cancer patients contain LRP1, which promotes the migration of epithelial ovarian cancer cells. Mol. Cell. Proteom. 2023 Apr 1;22(4):100520. https://doi.org/10.1016/j.mcpro.2023.100520.
4. International Agency for Research on Cancer. Global Cancer Observatory: Cancer Today. Lyon, France: IARC. Retrieved from GLOBOCAN 2022.
5. Bian W, Tang M, Jiang H, Xu W, Hao W, Sui Y, Hou Y, Nie L, Zhang H, Wang C, Li N. Low-density-lipoprotein-receptor-related protein 1 mediates Notch pathway activation. Dev. Cell. 2021 Oct 25;56(20):2902-19. https://doi.org/10.1016/j.devcel.2021.09.015.
6. Ortiz M, Wabel E, Mitchell K, Horibata S. Mechanisms of chemotherapy resistance in ovarian cancer. Cancer Drug Resist. 2022 Apr 3;5(2):304. https://doi.org/10.20517/cdr.2021.147.
7. Wang L, Wang X, Zhu X, Zhong L, Jiang Q, Wang Y, Tang Q, Li Q, Zhang C, Wang H, Zou D. Drug resistance in ovarian cancer: from mechanism to clinical trial. Mol. Cancer. 2024 Mar 28;23(1):66. https://doi.org/10.1186/s12943-024-01967-3.
8. Guo X, Yang F, Liu T, Chen A, Liu D, Pu J, Jia C, Wu Y, Yuan J, Ouyang N, Herz J. Loss of LRP1 Promotes Hepatocellular Carcinoma Progression via UFL1-Mediated Activation of NF-κB Signaling. Adv. Sci. 2024 Dec;11(45):2401672. https://doi.org/10.1002/advs.202401672.
9. Herz J, Strickland DK. LRP: a multifunctional scavenger and signaling receptor. J. Clin. Invest. 2001 Sep 15;108(6):779-84. https://doi.org/10.1172/JCI13992.
10. Vormittag R, Bencur P, Ay C, Tengler T, Vukovich T, Quehenberger P, Mannhalter C, Pabinger I. Low-density lipoprotein receptor-related protein 1 polymorphism 663 C> T affects clotting factor VIII activity and increases the risk of venous thromboembolism. J. Thromb. Haemost. 2007 Mar;5(3):497-502. https://doi.org/10.1111/j.1538-7836.2007.02337.x.
11. Vitols S, Peterson C, Larsson O, Holm P, Åberg B. Elevated uptake of low density lipoproteins by human lung cancer tissue in vivo. Cancer Res. 1992 Nov 15;52(22):6244-6247.
12. Herz J, Hamann U, Rogne S, Myklebost O, Gausepohl H, Stanley KK. Surface location and high affinity for calcium of a 500-kd liver membrane protein closely related to the LDL-receptor suggest a physiological role as lipoprotein receptor. EMBO J. 1988 Dec 20;7(13):4119-27. https://doi.org/10.1002/j.1460-2075.1988.tb03306.x.
13. Kang HS, Kim J, Lee HJ, Kwon BM, Lee DK, Hong SH. LRP1-dependent pepsin clearance induced by 2'-hydroxycinnamaldehyde attenuates breast cancer cell invasion. Int. J. Biochem. Cell Biol. 2014 Aug 1;53:15-23. https://doi.org/10.1016/j.biocel.2014.04.021.
14. Coleman RL, Monk BJ, Sood AK, Herzog TJ. Latest research and treatment of advanced-stage epithelial ovarian cancer. Nat. Rev. Clin. Oncol. 2013 Apr;10(4):211-24. https://doi.org/10.1038/nrclinonc.2013.5.
15. Zhang W, Ou X, Wu X. Proteomics profiling of plasma exosomes in epithelial ovarian cancer: A potential role in the coagulation cascade, diagnosis and prognosis. Int. J. Oncol. 2019 Mar 7;54(5):1719-33. https://doi.org/10.3892/ijo.2019.4742.
16. Spuch C, Ortolano S, Navarro C. LRP-1 and LRP-2 receptors function in the membrane neuron. Trafficking mechanisms and proteolytic processing in Alzheimer's disease. Front. Physiol. 2012 Jul 16;3:269. https://doi.org/10.3389/fphys.2012.00269.
17. Czekay RP, Wilkins-Port CE, Higgins SP, Freytag J, Overstreet JM, Klein RM, Higgins CE, Samarakoon R, Higgins PJ. PAI-1: an inte-

grator of cell signaling and migration. Int. J. Cell Biol. 2011;2011(1):562481. https://doi.org/10.1155/2011/562481.
18. Vos MC, van der Wurff AA, van Kuppevelt TH, Massuger LF. The role of MMP-14 in ovarian cancer: a systematic review. J. Ovarian Res. 2021 Dec;14:1-3. doi.org/10.1186/s13048-021-00852-7.
19. Boucher P, Herz J. Signaling through LRP1: Protection from atherosclerosis and beyond. Biochem. Pharmacol. 2011 Jan 1;81(1):1-5. https://doi.org/10.1016/j.bcp.2010.09.018.
20. Appert-Collin A, Bennasroune A, Jeannesson P, Terryn C, Fuhrmann G, Morjani H, Dedieu S. Role of LRP-1 in cancer cell migration in 3-dimensional collagen matrix. Cell Adhes. Migr. 2017 Jul 4;11(4):316-26. https://doi.org/10.1080/19336918.2016.1215788.
21. Feng C, Ding G, Ding Q, Wen H. Overexpression of low-density lipoprotein receptor-related protein 1 (LRP1) is associated with worsened prognosis and decreased cancer immunity in clear-cell renal cell carcinoma. Biochem. Biophys. Res. Commun. 2018 Sep 10;503(3):1537-1543. https://doi.org/10.1016/j.bbrc.2018.07.076.
22. Montel V, Gaultier A, Lester RD, Campana WM, Gonias SL. The low-density lipoprotein receptor–related protein regulates cancer cell survival and metastasis development. Cancer Res. 2007 Oct 15;67(20):9817-9824. https://doi.org/10.1158/0008-5472.CAN-07-0683.
23. Campion O, Al Khalifa T, Langlois B, Thevenard-Devy J, Salesse S, Savary K, Schneider C, Etique N, Dedieu S, Devy J. Contribution of the low-density lipoprotein receptor family to breast cancer progression. Front. Oncol. 2020 Jul 30;10:882. doi.org/10.3389/fonc.2020.00882.
24. Zhu M, Shen H, Wang B, He Y, Chen J, Ren J, Zhang Z, Jian X. LRP1 as a promising therapeutic target for gastrointestinal tumors: Inhibiting proliferation, invasion and migration of cancer cells. Oncol. Lett. 2023 Aug 2;26(4):1-12. https://doi.org/10.3892/ol.2023.14019.
25. May P, Woldt E, Matz RL, Boucher P. The LDL receptor-related protein (LRP) family: An old family of proteins with new physiological functions. Ann. Med. 2007 Jan 1;39(3):219-28. doi.org/10.1080/07853890701214881.
26. Jusić A, Avdić A, Hadžiavdić V, Junuzović I, Kurtčehajić D. Identification of 677C> T Polymorphism of LRP1 Gene by PCR-RFLP Method. TEM J. 2018 Nov;7(4):803-807. https://doi.org/10.18421/TEM74-17.
27. Fields BN. Genetic Polymorphisms in LRP1, a Newly Identified Receptor for Emerging Bunyaviruses. Doctoral dissertation. University of Pittsburgh, 2023.
28. Vučinić N, Stokić E, Djan I, Obreht D, Veličković N, Stankov K, Djan M. The gene polymorphism is associated with increased risk of metabolic syndrome prevalence in the Serbian population. Balkan J. Med. Genet. 2017 Jun 30;20(1):51-58. https://doi.org/10.1515/bjmg-2017-0004.
29. Shinohara M, Tachibana M, Kanekiyo T, Bu G. Role of LRP1 in the pathogenesis of Alzheimer's disease: evidence from clinical and preclinical studies. J. Lipid Res. 2017 Jul;58(7):1267. https://doi.org/10.1194/jlr.R075796.
30. Lee JD, Hsiao KM, Chang PJ, Chen CC, Kuo YW, Huang YC, Hsu HL, Lin YH, Wu CY, Huang YC, Lee M, Hsu CY, Pan YT, Kuo CY, Lin CH. A common polymorphism decreases LRP1 mRNA stability and is associated with increased plasma factor VIII levels. Biochim. Biophys. Acta Mol. Basis Dis. 2017 Jun;1863(6):1690-1698. https://doi.org/10.1016/j.bbadis.2017.04.015.
31. Xing P, Liao Z, Ren Z, Zhao J, Song F, Wang G, Chen K, Yang J. Roles of low-density lipoprotein receptor-related protein 1 in tumors. Chin. J. Cancer. 2016 Jan 6;35:6. https://doi.org/10.1186/s40880-015-0064-0.
32. Actis Dato V, Chiabrando GA. The role of low-density lipoprotein receptor-related protein 1 in lipid metabolism, glucose homeostasis and inflammation. Int. J. Mol. Sci. 2018 Jun 15;19(6):1780. https://doi.org/10.3390/ijms19061780.
33. Gan M, Jiang P, McLean P, Kanekiyo T, Bu G. Low-density lipoprotein receptor-related protein 1 (LRP1) regulates the stability and function of GluA1 α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor in neurons. PloS One. 2014 Dec 12;9(12):e113237. https://doi.org/10.1371/journal.pone.0113237.
34. Fuentealba RA, Liu Q, Kanekiyo T, Zhang J, Bu G. Low density lipoprotein receptor-related protein 1 promotes anti-apoptotic signaling in neurons by activating Akt survival pathway. J. Biol. Chem. 2009 Dec 4;284(49):34045-34053. https://doi.org/10.1074/jbc.M109.021030.
35. Mantuano E, Inoue G, Li X, Takahashi K, Gaultier A, Gonias SL, Campana WM. The hemopexin domain of matrix metalloproteinase-9 activates cell signaling and promotes migration of schwann cells by binding to low-density lipoprotein receptor-related protein. J. Neurosci. 2008 Nov 5;28(45):11571-11582. https://doi.org/10.1523/JNEUROSCI.3053-08.2008.
36. Yancey PG, Blakemore J, Ding L, Fan D, Overton CD, Zhang Y, Linton MF, Fazio S. Macrophage LRP-1 controls plaque cellularity by regulating efferocytosis and Akt activation. Arterioscler. Thromb. Vasc. Biol. 2010 Apr;30(4):787-795. https://doi.org/10.1161/ATVBAHA.109.202051.
37. Van Leuven F, Cassiman JJ, Van Den Berghe H. Demonstration of an alpha2-macroglobulin receptor in human fibroblasts, absent in tumor-derived cell lines. J. Biol. Chem. 1979 Jun 25;254(12):5155-5160.
38. Gonias SL, Campana WM. LDL receptor–related protein-1: a regulator of inflammation in atherosclerosis, cancer, and injury

to the nervous system. Am. J. Pathol. 2014 Jan;184(1):18-27. https://doi.org/10.1016/j.ajpath.2013.08.029.
39. Pires LA, Hegg R, Freitas FR, Tavares ER, Almeida C, Baracat EC, Maranhão RC. Effect of neoadjuvant chemotherapy on low-density lipoprotein (LDL) receptor and LDL receptor-related protein 1 (LRP-1) receptor in locally advanced breast cancer. Braz. J. Med. Biol. Res. 2012 Jun;45:557-564. https://doi.org/10.1590/S0100-879X2012007500068.
40. Sizova O, John LS, Ma Q, Molldrem JJ. Multi -faceted role of LRP1 in the immune system. Front. Immunol. 2023 Mar 20;14:1166189. doi.org/10.3389/fimmu.2023.1166189.
41. Jin HR, Wang J, Wang ZJ, Xi MJ, Xia BH, Deng K, Yang JL. Lipid metabolic reprogramming in tumor microenvironment: From mechanisms to therapeutics. J. Hematol. Oncol. 2023 Sep 12;16(103). doi.org/10.1186/s13045-023-01498-2.
42. Mathews SG, Krishna RD, Lavanya M, Nandini K, Murali S, Agarwal P, Rani E. The Role of the Plasminogen Activator Inhibitor 1 (PAI1) in Ovarian Cancer: Mechanisms and Therapeutic Implications. Glob. Med. Genet. 2024 Dec;11(04):358-65. https://doi.org/10.1055/s-0044-1791734.
43. Bourazopoulou E, Kapsogeorgou EK, Routsias JG, Manoussakis MN, Moutsopoulos HM, Tzioufas AG. Functional expression of the alpha 2-macroglobulin receptor CD91 in salivary gland epithelial cells. J. Autoimmun. 2009 Sep 1;33(2):141-6. https://doi.org/10.1016/j.jaut.2009.06.004.
44. Lillis AP, Van Duyn LB, Murphy-Ullrich JE, Strickland DK. LDL receptor-related protein 1: unique tissue-specific functions revealed by selective gene knockout studies. Physiol. Rev. 2008 Jul;88(3):887-918. https://doi.org/10.1152/physrev.00033.2007.
45. Timilsina S, Amara AR, Abu R, Spring BQ. Identification of potential cell surface targets in patient-derived cultures toward photoimmunotherapy of high-grade serous ovarian cancer. Photochem. Photobiol. 2025 Apr 9. https://doi.org/10.1111/php.14091.
46. Datta A, Deng S, Gopal V, Yap KC, Halim CE, Lye ML, Ong MS, Tan TZ, Sethi G, Hooi SC, Kumar AP. Cytoskeletal dynamics in epithelial-mesenchymal transition: insights into therapeutic targets for cancer metastasis. Cancers. 2021 Apr 14;13(8):1882. https://doi.org/10.3390/cancers13081882.
47. Duffy AM, Bouchier-Hayes DJ, Harmey JH. Vascular endothelial growth factor (VEGF) and its role in non-endothelial cells: autocrine signalling by VEGF. In: Madame Curie Bioscience Database. Austin (TX): Landes Bioscience; 2000-2013.
48. Seager RJ, Hajal C, Spill F, Kamm RD, Zaman MH. Dynamic interplay between tumour, stroma and immune system can drive or prevent tumour progression. Converg. Sci. Phys. Oncol. 2017 Jul 28;3(3):034002. https://doi.org/10.1088/2057-1739/aa7e86.
49. Van Gool B, Dedieu S, Emonard H, Roebroek AJ. The matricellular receptor LRP1 forms an interface for signaling and endocytosis in modulation of the extracellular tumor environment. Front. Pharmacol. 2015 Nov 10;6:271. doi.org/10.3389/fphar.2015.00271.
50. Qu L, Wang F, Wang Y, Li Z. The regulation of LRPs by miRNAs in cancer: influencing cancer characteristics and responses to treatment. Cancer Cell Int. 2025 Dec;25(1):1-22. doi.org/10.1186/s12935-025-03804-z.
51. Xing P, Liu H, Xiao W, Zhang G, Zhang C, Liao Z, Li T, Yang J. The fusion gene LRP1—SNRNP25 drives invasion and migration by activating the pJNK/37LRP/MMP2 signaling pathway in osteosarcoma. Cell Death Discov. 2024 Apr 27;10(1):198. https://doi.org/10.1038/s41420-024-01962-z.
52. NR S, Behera MM, Naik SK, Das SK, Gopan S, Ghosh A, Sahu RN, Patra S, Purkait S. Elevated expression of cholesterol transporter LRP-1 is crucially implicated in the pathobiology of glioblastoma. Front. Neurol. 2022 Oct 4;13:1003730. https://doi.org/10.3389/fneur.2022.1003730.
53. Pencheva N, Tran H, Buss C, Huh D, Drobnjak M, Busam K, Tavazoie SF. Convergent multi-miRNA targeting of ApoE drives LRP1/LRP8-dependent melanoma metastasis and angiogenesis. Cell. 2012 Nov 21;151(5):1068-82. https://doi.org/10.1016/j.cell.2012.10.028.
54. Dai W, Zhou J, Chen T. Unraveling the extracellular vesicle network: insights into ovarian cancer metastasis and chemoresistance. Mol. Cancer. 2024 Sep 16;23(1):201. doi.org/10.1186/s12943-024-02103-x.
55. Wang Y, Zhu N, Liu J, Chen F, Song Y, Ma Y, Yang Z, Wang D. Role of tumor microenvironment in ovarian cancer metastasis and clinical advancements. J. Transl. Med. 2025 Dec;23(1):1-63. doi.org/10.1186/s12967-025-06508-0.
56. Xie W, Sun H, Li X, Lin F, Wang Z, Wang X. Ovarian cancer: epigenetics, drug resistance, and progression. Cancer Cell Int. 2021 Dec;21:1-6. doi.org/10.1186/s12935-021-02136-y.
57. Fu R, Hu R, Li W, Lv X, Zhao H, Li F. Unveiling drug resistance pathways in high-grade serous ovarian cancer (HGSOC): recent advances and future perspectives. Front. Immunol. 2025 Apr 30;16:1556377. doi.org/10.3389/fimmu.2025.1556377.
58. Le CC, Bennasroune A, Collin G, Hachet C, Lehrter V, Rioult D, Dedieu S, Morjani H, Appert-Collin A. LRP-1 promotes colon cancer cell proliferation in 3D collagen matrices by mediating DDR1 endocytosis. Front. Cell Dev. Biol. 2020 Jun 3;8:412. https://doi.org/10.3389/fcell.2020.00412.