

Review

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Review

# LncRNAs in Ovarian Cancer: Mechanistic Insights and Clinical Applications

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**Simple Summary:** Ovarian cancer is a highly fatal disease, often diagnosed at advanced stages due to non-specific symptoms. This review focuses on the role of long non-coding RNAs (lncRNAs) in ovarian cancer, highlighting their dual nature as oncogenes or tumor suppressors. These molecules regulate critical cancer processes, including cell growth, survival, metastasis, and therapy resistance. By exploring their complex structures and functions, this research emphasizes the potential of lncRNAs as diagnostic markers, prognostic indicators, and therapeutic targets. Integrating insights from cutting-edge technologies like bioinformatics and single-cell sequencing, this review aims to provide a comprehensive understanding of lncRNAs in ovarian cancer. The findings could significantly advance personalized cancer medicine, offering new strategies to improve detection, treatment, and patient outcomes.

**Abstract: Background/Objectives:** Ovarian cancer is a leading cause of gynecological cancer mortality worldwide, often diagnosed at advanced stages due to vague symptoms and lack of effective early detection methods. Long non-coding RNAs (lncRNAs) have emerged as key regulators in cancer biology, influencing cellular processes such as proliferation, apoptosis, and chemoresistance. This review explores the multifaceted roles of lncRNAs in ovarian cancer pathogenesis and their potential as biomarkers and therapeutic targets. **Methods:** A comprehensive literature review was conducted to analyze the structural and functional characteristics of lncRNAs and their contributions to ovarian cancer biology. This includes their regulatory mechanisms, interactions with signaling pathways, and implications for therapeutic resistance. Advanced bioinformatics and omics approaches were also evaluated for their potential in lncRNA research. **Results:** The review highlights the dual role of lncRNAs as oncogenes and tumor suppressors, modulating processes such as cell proliferation, invasion, and angiogenesis. Specific lncRNAs, such as HOTAIR and GAS5, demonstrate significant potential as diagnostic biomarkers and therapeutic targets. Emerging technologies, such as single-cell sequencing, provide valuable insights into the tumor microenvironment and the heterogeneity of lncRNA expression. **Conclusions:** LncRNAs hold transformative potential in advancing ovarian cancer diagnosis, prognosis, and treatment. Targeting lncRNAs or their associated pathways offers promising strategies to overcome therapy resistance and enhance personalized medicine. Continued research integrating omics and bioinformatics will be essential to unlock the full clinical potential of lncRNAs in ovarian cancer management.

**Keywords:** Ovarian cancer; Long non-coding RNA (lncRNA); Biomarkers; Therapeutic targets; Cancer pathogenesis; Chemoresistance; Tumor microenvironment; Epigenetic regulations; Gene expression; Personalized medicine

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## 1. Introduction

Ovarian cancer (OC) is recognized as the eighth most common cancer among women worldwide and a leading cause of female mortality, with approximately 207,000 deaths annually [1,2]. In the United States, it ranks fifth in cancer-related deaths amongst women with a predicted 611,720 OC-associated deaths for the year 2024 [3]. Predominantly originating from epithelial cells, OC presents significant challenges for early detection due to its non-specific symptoms [4,5], leading to its description as a “silent killer” [6]. The consequent late-stage diagnoses severely limit therapeutic options and contribute to poor patient outcomes. These outcomes are further complicated by the heterogeneity of OC, the lack of effective targeted therapy, and the development of resistance to existing therapies [7-9]. These challenges underscore the urgent need for newer personalized therapeutic strategies.

Long non-coding RNAs (lncRNAs), RNA molecules consisting of over 200 nucleotides that do not code for proteins, have emerged as critical players in the development and progression of various cancers, including OC [10-12]. Acting as oncogenes or tumor suppressors, lncRNAs are involved in a wide array of cellular processes, such as gene regulation, mRNA stabilization, molecular scaffolding, post-translational modifications, epigenetic regulation, and chromatin remodeling [13-15]. Their dysregulation is linked to the hallmarks of cancer including cellular proliferation, invasion, metastasis, resistance to chemotherapy, angiogenesis, cancer stemness, and alterations in epigenetic and transcriptional landscapes [11,12,16]. In OC, the aberrant expression of lncRNAs contributes to the disease's aggressive nature, making them promising candidates as biomarkers and targets of therapy [17,18].

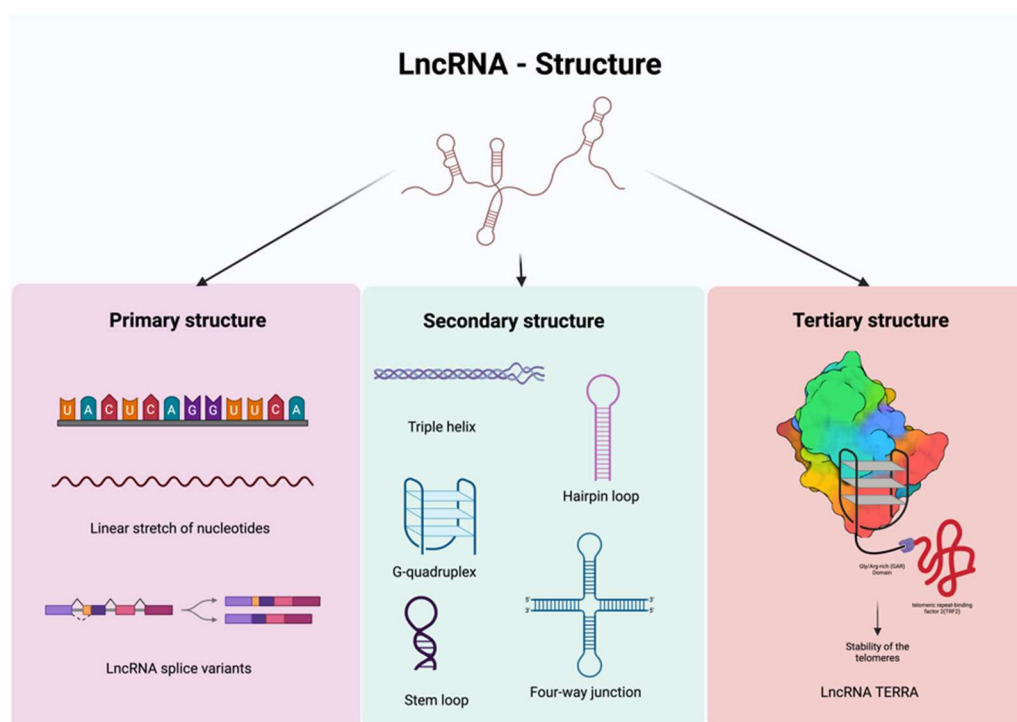
This review explores the multifunctional role of lncRNAs in OC, providing an in-depth analysis of how they regulate various cellular processes and contribute to OC pathogenesis. In addition, a detailed examination of lncRNAs as a novel class of signaling molecules, diagnostic and prognostic biomarkers and potential therapeutic targets in OC is discussed, emphasizing their potential in early detection, prognosis, and treatment.

## 2. LncRNAs: Structure and Function

LncRNAs form a distinct family different from other shorter non-coding RNA molecules such as micro-RNA (miRNA), piwi-interacting RNA (piRNA), small nuclear RNA (snRNA), and circular RNA (circRNA). Despite not being translated, they play a significant role in regulating gene expression and various cellular processes [19]. LncRNAs are involved in the regulation of chromosomal remodeling, transcription, post-transcriptional modifications, and diverse cell signaling pathways [20,21]. They also modulate the sub-cellular localisation of different proteins and RNAs within the cytoplasm [13,15,22]. The aberrant and asynchronous expression of lncRNAs is linked to a variety of cancers, including OC, making them potential biomarkers [23]. The functions and localization of lncRNAs, whether in the nucleus or cytoplasm, are highly tissue-specific and are influenced by their complex structures [24,25].

### 2.1. Primary, Secondary, and Tertiary Structures of lncRNAs

The regulatory capabilities of lncRNAs can be attributed to their structural configurations encompassing primary, secondary, and tertiary structures (Figure 1).



**Figure 1.** Structural differences in lncRNAs across the three levels: primary, secondary, and tertiary. The primary structure of lncRNA includes a linear stretch of nucleotides and splice variants of the same lncRNA, showcasing sequence diversity. The secondary structure includes a triple helix, hairpin loop, G-quadruplex, stem-loop, and four-way junction demonstrating the complex folding patterns of the primary lncRNA. The tertiary structure is depicted with an example of lncRNA TERRA which forms a complex G-quadruplex to interact with the telomeric-repeat binding factor 2 (TRF2) to confer stability to the telomeres.

### 2.1.1. Primary Structure

The primary structure of lncRNAs is a linear sequence of nucleotides, namely adenine, guanine, cytosine, and uracil. Typically transcribed by RNA Polymerase II, lncRNAs may sometimes be transcribed by RNA Polymerase III [26]. They often have multiple splice variants, leading to diverse transcripts with varying lengths and functions. Unlike protein-coding genes, lncRNAs generally exhibit poor evolutionary sequence conservation across species, although some conserved regions exist [27,28]. This primary sequence forms the backbone of the lncRNA, determining its basic properties and serving as the foundation for the more complex secondary and tertiary structures that dictate its functionality [11].

### 2.1.2. Secondary Structure

Secondary structures in lncRNAs arise from the folding and interactions among base pairs within the primary sequence through hydrogen bonds, forming structural elements such as pseudoknots, stem-loops, hairpins, triple helix structures, and kissing loop interactions [11,29]. These structures confer stability and provide a structural basis for the diverse functions of the lncRNAs [30]. For example, MALAT1, known for its role in the regulation of gene expression, forms a triple helix structure, which protects it from the 3'-5' exonucleases [31]. Similarly, a specific 24-nucleotide conserved region in lncRNA XIST forms a tetraloop structure, a stem-loop variant that involves four nucleotides for the formation of the loop, which allows XIST to interact with YTH N6-Methyladenosine RNA Binding Protein C1 (YTHDC1), facilitating XIST-mediated transcription silencing [32]. In fact, it has been inferred that XIST recruits over 80 distinct proteins through its structural motifs, enabling the efficient silencing of the X-chromosome through multiple mechanisms [33]. Certain lncRNAs such as Growth Arrest-Specific 5 (GAS5) exhibit multiple stable secondary structure conformations including a 3'-Serine and arginine (3' SR) binding short hairpin motif that acts as a scaffold to interact with steroid receptors to inhibit steroid-mediated cancer cell growth and survival [34].

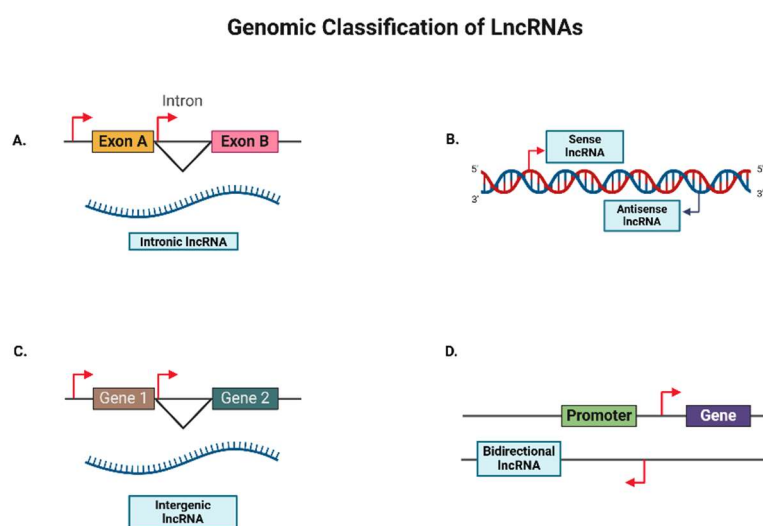
### 2.1.3. Tertiary Structure

The tertiary structures refer to the three-dimensional conformations of lncRNAs formed by further folding and interactions among secondary structural elements formed by both the classical Watson and Crick base pairing and the non-canonical interactions [16]. The resulting higher-order structures such as G-quadruplexes - which involve guanine-rich regions folding to form a stable, four-stranded structure - form specific docking sites for interactions with proteins, RNA, or DNA [30]. This is exemplified in the case of lncRNA HOTAIR, which relies on G-quadruplex structure for its interaction with Polycomb Repressive Complex 2 (PRC2) proteins in the epigenetic silencing of genes [35]. Likewise, the G-quadruplex motifs of MALAT1 are essential for its binding with the non-POU Domain containing Octamer Binding (NONO) protein, a canonical nuclear paraspeckle protein [36]. Similarly, NEAT1 forms a G-quadruplex, essential for the formation of paraspeckles nuclear bodies, through the interaction with NONO and Splicing factor proline and glutamine-rich (SPFQ) proteins [37-39]. In a similar vein, the complex stem-loop structures and G-quadruplex motifs of the lncRNA TERRA are essential for the regulation of the telomere function, which is often altered in OC [40,41]. Tertiary structures also contribute significantly to the stability of lncRNAs, protecting them from rapid degradation. This stability is crucial for lncRNAs to sustain their regulatory roles in eliciting specific cellular responses [42].

The intricate architecture of lncRNAs, spanning from basic primary sequences to complex tertiary structures enable lncRNA to participate in a broad spectrum of biological functions, from the regulation of gene expression to the maintenance of chromatin architecture.

### 2.2. Positional Diversity of lncRNAs

lncRNAs can be classified into various categories based on their genomic location, including intronic, antisense, sense, intergenic, and bidirectional, each with a distinct mode of action (Figure 2) [43].



**Figure 2.** Genomic classifications of lncRNAs. lncRNAs can be classified on the basis of their origin in the genome. A. Intronic lncRNA: transcribed from the intronic region of a transcript, B. Sense lncRNA, Antisense lncRNA: transcribed from the sense and antisense strand respectively, C. Intergenic lncRNA: transcribed from the region between two genes, D: Bidirectional lncRNA: transcribed from the promoters of coding genes but in an opposite direction.

#### 2.2.1. Intronic lncRNAs



Intronic lncRNAs are transcribed from the introns (non-coding regions) of coding genes. They often regulate the expression of gene from which they originate [13]. For example, the lncRNA *SPRY4-IT1*, originating from the *SPRY4* gene's intronic region, suppresses the expression of *SPRY4*, thus inhibiting epithelial-mesenchymal transition (EMT) and metastasis in OC [44].

### 2.2.2. Antisense lncRNAs

Antisense lncRNAs are complementary to the protein-coding gene and are transcribed from the opposite strand of coding sequences. They often regulate expression of the cognate sense mRNAs [45]. An example here is *CDKN2B-AS1* (ANRIL), an antisense lncRNA of the *CDKN2B* gene, which is overexpressed in OC cell lines, SKOV3, A2780, and HO-8910. ANRIL suppresses *CDKN2A* and *CDKN2B* expression to promote OC cell migration and invasion [46]. In some instances, antisense lncRNAs such as *RUNX1-IT1*, transcribed from the same promoter as *RUNX1* gene, does not suppress its expression. *RUNX1-IT1* promotes EMT in OC by acting as a scaffold linking STAT1 and NuRD complex, eventually leading to the activation of NF- $\kappa$ B [47]. Therefore, it is not necessary that an antisense lncRNA will be acting only on its adjacent gene, it can also have different regulatory mechanisms.

### 2.2.3. Intergenic lncRNAs

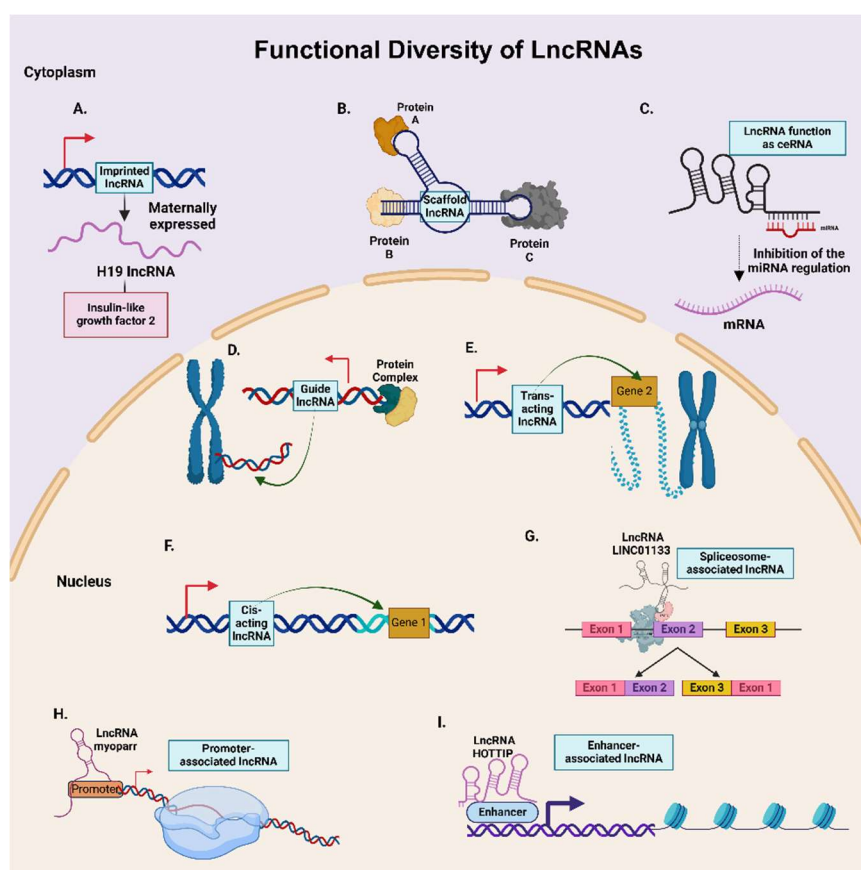
Intergenic lncRNAs are located between the coding genes. They have been shown to modulate the expression of nearby as well as distal genes through diverse regulatory mechanisms [48]. One example involves the regulation of gene expression by the lncRNA *GAS5*, an intergenic tumor suppressor lncRNA located on chromosome 1 [49,50]. *GAS5* has been shown to regulate the expression of *PARP1* gene, which is also present on chromosome 1 by recruiting the transcription factor E2F4 to its promoter, so as to increase the chemosensitivity in a panel of OC cell lines [51]. It has also been shown that *GAS5* can mediate tumor suppressor function by inhibiting the expression levels of the distal gene *hnrNPk1*, thereby inhibiting AKT pathway [52] and/or promoting the expression of the pro-apoptotic Bcl-2 family proteins, BAK and BAX in OC cells [53].

### 2.2.4. Bidirectional lncRNAs

Bidirectional lncRNAs are transcribed in the opposite directions of an adjacent coding gene, often sharing a bidirectional promoter and regulatory elements. For instance, the lncRNA known as ncRNA-RBI/RB1-DT/LINC00441 is a bidirectional RNA, which is transcribed from the promoter of retinoblastoma gene, *RB1* [54] and it facilitates the expression and translocation of calreticulin (CALR) from the endoplasmic reticulum to the cell surface, initiating an anticancer immune response [54].

## 2.3. Functional Diversity of lncRNAs

lncRNAs, with their structural and positional diversity, exhibit a remarkable functional diversity that allows them to play complex regulatory roles in modulating a wide array of oncogenic responses (Figure 3). The functional classification of lncRNAs includes the following categories:



**Figure 3.** Functional diversity of lncRNAs. In the cytoplasm, lncRNAs function as A. imprinted lncRNAs, B. scaffold lncRNAs, and C. ceRNA, showcasing their diverse regulatory mechanism throughout the cell. Within the nucleus, the lncRNAs can D. act as a guide lncRNA, function either as E. trans- and F. cis-regulatory elements or can be associated with G. spliceosome complex, H. promoters, or I. enhancers.

### 2.3.1. Cis- and Trans-acting LncRNAs

Cis-acting lncRNAs regulate genes on the same chromosome, often through chromatin modification, enhancer-like activity, and transcriptional interference [55]. For example, *KCNQ1OT1*, located at chromosome 11p15.5, regulates nearby genes like *SLC22A18* and *CDKN1C*, both of which are located in a nearby genomic location in Chr. 11p15.4, through histone methylation to suppress their expressions [56].

Trans-acting lncRNAs influence distally located genes, modulating cellular processes by either sequestering miRNAs, or interacting with RNA-protein complexes, or altering chromatin structure [55]. For instance, *RHPN1-AS1* promotes OC cell proliferation by sequestering miR-1299 [57]. In another example, *RUNX-IT1* acts as a scaffold for NuRD complex and STAT1 which allows the recruitment of several histone modifiers, eventually activating NF- $\kappa$ B and promoting OC [47].

### 2.3.2. Enhancer and Promoter-associated LncRNAs

Enhancer-associated lncRNAs are transcribed from enhancer regions of the gene and modulate gene expression by influencing the activity of enhancers of the cognate gene [13]. An example is the lncRNA *HOTTIP*, transcribed from the 5' end of the *HOXA* gene cluster enhancer, and regulates *HOXA* gene expression by binding to the WDR5 adaptor protein, facilitating H3 lysine 4 trimethylation [57].

Promoter-associated lncRNAs are transcribed from the promoter regions of coding genes and regulate the transcription of these genes. For example, the lncRNA *FOXCUT* is transcribed from the promoter region of the *FOXC1* gene and regulates its expression, essential for cancer progression in esophageal cancer [54]. Some promoter-associated lncRNAs, act as scaffolds for assembling transcriptional regulatory complexes, affecting the transcription of specific genes. LncRNA *KHPS1*,

transcribed from the *SPHK1-C* promoter, forms a triplex RNA-DNA structure, recruiting transcription factors and activating SPHK1 expression [58].

### 2.3.3. Competing Endogenous RNAs (ceRNAs)

Certain lncRNA act as ceRNAs, sequestering miRNAs to modulate gene expression of other coding genes [59]. For example, lncRNA UCA1 which is identified as an LPA-stimulated lncRNA sequesters the let-7 family of miRNAs, promoting OC progression by suppressing the tumor suppressor roles of let-7 miRNAs [60]. LncRNA LINC01123 contributes to increased angiogenesis in OC by sequestering miR-516b-5p, and upregulating vascular endothelial growth factor, VEGFA, expression [61].

### 2.3.4. Guide and Scaffold LncRNAs

Guide lncRNAs recruit regulatory proteins to the target regions of the chromatin or DNA to regulate gene expression [62]. UCA1, acting as a guide lncRNA, promotes YAP dephosphorylation and increased expression of its target genes in OC cell lines through its binding to AMOT, which guides and stimulates its interaction with YAP [63].

In a variation of the theme, scaffold lncRNAs facilitate the assembly of various proteins and RNAs to form functional ribonucleoprotein (RNP) complexes complex [64]. LINC00176 functions as a molecular scaffold, facilitating the interaction between BCL3 and p53 which binds to the promoter region of the ceruloplasmin gene, thereby activating its expression and promoting oncogenic pathways in OC cell lines via the NF- $\kappa$ B signaling pathway [65].

### 2.3.5. Imprinted LncRNAs

Imprinted lncRNAs are associated with genomic imprinting, expressing only one allele of paternal or maternal origin [66]. A well-studied lncRNA is H19, which is maternally expressed and found at high levels in carboplatin-resistant OC cell line, SKOV3, compared to its non-resistant counterparts. H19 acts as a ceRNA for miR-29b-3p and confers carboplatin resistance through the upregulation of drug-resistance-associated proteins MRP1, P-gp, and LRP and STAT3, which are the downstream targets of miR-29b-3p [67,68].

### 2.3.6. Spliceosome-associated LncRNAs

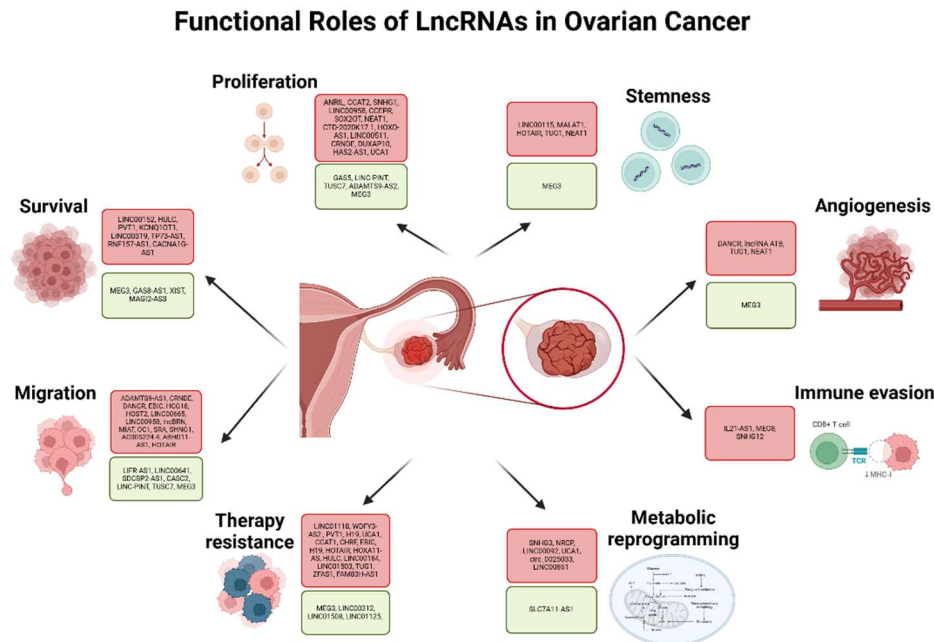
Spliceosome-associated lncRNAs interact with or modulate the expression of the spliceosomal complex, influencing alternative splicing and differential modulation of gene expression [69,70]. MALAT1, for instance, is associated with the expression of a host of splicing regulatory (SR) proteins including RNA binding protein fox-1 homolog 2 (RBFOX2) that regulates alternative splicing events in HEY and OVCA420 OC cells. This activity is correlated with the decreased expression of the pro-apoptotic splice variant Kinesin Family Member 1Bb (KIF1Bb) protein along with the increased expression of the non-apoptotic truncated splice variant KIF1Ba, both of which promote OC cell proliferation, invasion, anchorage-independent growth [71].

The remarkable structural and functional diversity of lncRNAs enable them to play critical roles in OC, impacting on cellular events ranging from chromatin remodeling to immune response modulation. Functional diversity, along with context-dependency, is crucial in many cancers, including OC. For instance, factors such as tumor hypoxia can alter the expression of specific lncRNAs and their target genes, channeling lncRNAs toward specific functional responses [72]. Aberrant expression of both oncogenic and tumor suppressor lncRNAs contributes to the genesis and progression of OC, with different lncRNAs playing distinct roles in either promoting or inhibiting cancer development [73]. The following section explores how these lncRNAs contribute to the development and progression of OC, emphasizing their roles as both oncogenic drivers and tumor suppressors.

## 3. LncRNAs in Ovarian Cancer



lncRNAs play diverse and crucial roles in gene expression, chromatin remodeling, and post-translational regulation, significantly impacting OC [74]. Acting as either oncogenes or tumor suppressors, lncRNAs are often differentially expressed compared to non-cancerous cells, engaging in complex regulatory mechanisms essential for OC progression (Figure 4) [75].



**Figure 4.** Functional roles of lncRNAs in Ovarian Cancer. lncRNAs are critically involved in cell proliferation, cell survival, cell migration, therapy resistance, metabolic reprogramming, immune evasion, angiogenesis and cancer cell stemness in ovarian cancer. Examples of lncRNAs that induce these processes and act as oncogenes in OC are highlighted in the red box whereas those that tend to reduce these processes are highlighted in the green box.

The discovery of their involvement in oncogenic pathways has spurred extensive research into the specific functions of lncRNAs in OC. Despite the vast number of lncRNAs expressed, only a small fraction has been characterized, with even fewer being definitively linked to OC. Tables 1 and 2 provide a summary of the key lncRNAs identified as oncogenes and tumor suppressors in OC, respectively. These identified lncRNAs have become the focus of detailed studies aimed at elucidating their roles in OC genesis and progression.

**Table 1.** LncRNAs that act as oncogenes in ovarian cancer.

	LncRNA	Function	Mechanism
1.	ADAMTS9-AS1	Inhibits ferroptosis resulting in increased cell proliferation and migration	Acts as a ceRNA to miR-587 downregulating the expression of SLC7A11 [76]
2.	ANRIL	Promotes cell proliferation and invasion.	Activation of Wnt/ $\beta$ -catenin pathway [77]
3.	ATB	Promotes tumorigenesis	Acts as a ceRNA towards miR-204-3p upregulating TGF $\beta$ R2 pathway [78]
4.	AWPPH	Promotes overall OC development	Up-regulates $\beta$ -catenin expression by activating the Wnt/ $\beta$ -catenin pathway [79]
5.	CCAT1	Confers cisplatin resistance	Acts as a ceRNA against miR-454, inducing the expression of survivin [80]
		Induces EMT of OC cells	Upregulates TGF $\beta$ R1 through sponging of miR-490-3p [81]
		Contributes to metastasis and progression in epithelial ovarian cancer (EOC)	Modulates the ADAM17/Wnt1/STAT3/ZEB1 regulatory network via miR-152 and miR-130b [82]
		Promotes proliferation of OC	Sequesters miR-1290 and suppresses its tumorigenic role [83]
6.	CCAT2	Acts as an oncogene	Sequesters to miR-424 resulting in its downregulation [84]
7.	CCEPR	Promotes cellular invasion and poor prognosis	Activation of Wnt/ $\beta$ -catenin pathway [85]
8.	CHRF	Confers cisplatin resistance	Acts as ceRNA to miR-10b activating STAT3 pathway [86]
9.	CRNDE	Promotes cell migration, invasion, and proliferation	Acts as a ceRNA against miR-423-5p resulting in its downregulation [87]
		Confers cisplatin resistance	Activation of SRSF1/TIA1 signaling pathway [88]
10.	DANCR	Promotes cell proliferation and migration	Negative regulation of TGF- $\beta$ by acting a ceRNA for miR-214 [89]
11.	DUXAP10	Promotes cell proliferation	Increased expression of DUXAP10 positively regulates the proliferation of OC cells [90]

12.	EBIC	Promotes cell proliferation, invasion and migration. Confers cisplatin resistance	Activation of Wnt/ $\beta$ -catenin pathway [91]
13.	ElncRNA1	Oncogenic role in overall EOC progression	E2 (estrogen) transcriptionally induces ElncRNA1, which modulates cyclin D1-CDK4/6 [92]
14.	FLVCR1-AS1	Promotes EMT	Acts as ceRNA to miR-513 upregulating YAP1 expression [93]
15.	H19	Promotes cisplatin-resistance	Glutathione metabolism [94]
16.	HAS2-AS1	Accelerates EOC tumorigenesis, facilitates invasion and proliferation	HAS2-AS1, induced by CREB1, sequesters miR-466, thus positively regulates RUNX2 gene [95]
17.	HCG18	Cell proliferation and migration	Acts as a ceRNA for miR-29a/b downregulating TRAF4/5, activating NF- $\kappa$ B pathway [96]
18.	HOST2	Promotes cell proliferation, migration and invasion	Activation of JAK2/STAT3 pathway [97]
19.	HOTAIR	Confers cisplatin resistance	Regulates Her2 expression by acting as a ceRNA against miR-138-5p [98]
20.	HOXA11-AS	Confers cisplatin resistance	Inhibits intracellular autophagy and cell cycle arrest [99]
21.	HOXD-AS1	Regulates cell migration, invasion, and EMT in EOC	Elevated HOXD-AS1 leads to increased levels of PIK3R3 by sequestering miR-186-5p (acts as a ceRNA) [100]
		Promotes cell proliferation, migration, and invasion and EMT in EOC cells	Activates the Wnt/ $\beta$ -catenin pathway by sequestering miR-133a-3p [101]
		Positively regulates proliferation, migration, and invasion in OC cells	HOXD-AS1 mediates this effect partially through the miR-608/FZD4 axis [102]
22.	HULC	Confers paclitaxel resistance	Acts as a ceRNA against miR-199a-3p upregulating the expression of ITGB8 [103]
23.	KCNQ1OT1	Enhances cell growth, migration, and invasion and inhibits cell apoptosis	Positively regulates LCN2 expression by repressing miR-212-3p [104]
24.	LINC-ROR	Promotes EMT	Suppresses miR-145, promoting the expression of FLNB [105]

25.	LINC00152	Confers cisplatin resistance in COC1/DDP cells	Modulates apoptosis and expression of MDR1, GSTn, and MRP1 [106]
		Increased levels facilitate invasion and tumor proliferation in EOC	Prevents ubiquitination of Bcl6 by binding to its Ser 333/Ser 343 site [107]
		Mediates cell proliferation and survival in OC	Affects MCL1- dependent mitochondrial apoptosis and acts as a ceRNA of miR-125b [108]
		Regulates cell cycle and cell proliferation in EOC cells	Modulates the Tumor Necrosis Factor (TNF) signaling pathway [109]
26.	LINC00184	Promotes cellular proliferation and confers cisplatin resistance	Promotes CNTN1 expression by acting as a ceRNA towards miR-1305 [110]
27.	LINC00319	Facilitates proliferation, migration, invasion, and tumor growth	Upregulates NACC1 by sequestering miR-423-5p [111]
28.	LINC00511	Promotes cell proliferation and invasion	Acts as a ceRNA against miR-424-5p and miR-370-5p which are responsible for anti-tumor effects [112]
29.	LINC00665	Promotes tumor progression	Regulates the miRNA-34a-5p/E2F3 axis [113]
		Facilitates cancer cell proliferation and inhibits apoptosis	Upregulates FHDC1 by sequestering miR-181a-5p [114]
		Promotes cancer cell proliferation and migration	Positively regulates KLF5 via sponging miR-148b-3p [115]
30.	LINC00857	Modulates OC progression and glycolysis	Regulates Hippo signaling Pathway through the miR-486-5p/YAP1 axis [116]
		Reduces the proliferative, invasive, and migratory capacity of OC cells and facilitates cell apoptosis	Reduces YAP-TEAD expression via Hippo signaling pathway [117]
31.	LINC00858	Contributes to the metastatic nature of OC	Acts as a ceRNA towards miR-134-5p, upregulating RAD18 expression [118]
32.	LINC00958	STAT1-induced over-expression promotes overall EOC progression (proliferation, invasion, and migration)	Epigenetic modulation of the Wnt/ $\beta$ -catenin pathway [119]

33.	LINC00968	Accelerates EOC progression	Arrests cell cycle in the G1 phase by inhibiting the MAPK and PI3K/Akt/mTOR pathways [120]
34.	LINC01503	Contributes to carboplatin resistance in OC	Up-regulates PD-L1 levels by sequestering miR-766-5p [121]
35.	lncARSR	Enhances EOC cells' proliferative and invasive property	Upregulates $\beta$ -catenin and ZEB1/2 via association with HuR and miR-200 family respectively [122]
36.	lncBRM	Facilitates migration, invasion, and proliferation in OC cells	Up-regulates SOX4 via sequestering miR-204 [123]
37.	MALAT1	Induces cell proliferation, migration and EMT-transition.	Activation of PI3K/AKT pathway [124]
38.	MIAT	Promotes EMT, migration, invasion and proliferation	Acts as a ceRNA towards resulting in its suppression [125]
39.	MIF-AS1	Promotes cell proliferation, migration and invasion	Acts as a ceRNA to miR-NA-31-5p downregulating PLCB1 expression [126]
40.	MNX1-AS1	Promotes overall OC carcinogenesis	Upregulates SOX12 by repressing miR-744-5p [127]
41.	NEAT1	Promotes cell proliferation and migration.	Acts as ceRNA binding to let-7g promoting MEST and inhibiting ATGL expression [128]
		Confers cisplatin resistance	Regulates the expression of PARP1 and acts as a ceRNA against miR-770-5p [129]
42.	OC1	Promotes cell proliferation and migration	Acts as a ceRNA to miR-34a and miR-34c which regulates tumorigenesis [130]
43.	PVT1	Promotes cell migration and survival	Activation of YAP1-mediated tumorigenesis [131]
44.	SNHG1	Promotes proliferation and migration in EOC	Activates downstream effectors of the Wnt/ $\beta$ -catenin pathway[132]
		Facilitates migration and invasion of OC cells	Modulates via SNHG1/miR-454/ZEB1 axis[133]
		Modulates chemoresistance in SOC cells and patients (paclitaxel)	Functions as a ceRNA for miR-216b-5p in conferring paclitaxel resistance in OC [134]
45.	SNHG25	Promotes overall EOC progression	Positively regulates COMP (cartilage oligomeric matrix



			protein) contributing to the more invasiveness nature of the tumor [135]
46.	SOX2OT	Facilitates OC progression	SOX2-OT contributed to OC malignancy through miR-181b-5p/SCD1 axis [136]
47.	SRA	Facilitates cell proliferation, migration, and tumor invasion	Via EMT and NOTCH signaling pathway [137]
48.	TP73-AS1	Contributes to EOC carcinogenesis	Epigenetically suppresses p21 via trimethylation of H3K27 by recruiting EZH2 [138]
		Positively regulates tumor growth and metastasis, and facilitates overall OC progression	Increased expression of TP73-AS1 enhances levels of MMP2 and MMP9 [139]
		Promotes proliferation and overall OC progression	Negatively regulates cellular apoptosis and cell cycle [140]
49.	TPT1-AS1	Contributed to EOC tumor development and metastasis, and inhibited cellular adhesion	Induces TPT1 expression and activates the PI3K/AKT pathway [141]
50.	TUG1	Facilitates angiogenesis of endothelial cells in OC cells	Regulates LRG1 secretion levels partially via the TGF- $\beta$ pathway [142]
		Promotes OC cell proliferation and malignancy	Acts as a ceRNA for miR-1299, thus positively regulating NOTCH3 expression levels [143]
		Affects OC progression and carcinogenesis	Works as an interacting component of the miR-582-3p/AKT/mTOR axis [144]
		Contributes to stemness, proliferation, and invasion of OC cells	TUG1 sequesters miR-186-5p to release ZEB1 [145]
		Confers autophagy-associated paclitaxel resistance in OC cells	Sequesters miR-29b-3p and consequently mediates paclitaxel resistance via autophagy induction [146]
51.	UCA1	Confers cisplatin resistance	Acts as ceRNA to miR-27a-5p regulating the expression of UBE2N [147] Acts as a ceRNA for miR-143 upregulating FOSL2 expression [148]

		Promotes proliferation, invasive migration, and therapy resistance	Sequesters a panel of the let-7 family of miRNAs negatively regulating their tumor suppressive roles [60]
52.	ZFAS1	Promotes cell proliferation and metastasis	Sequesters tumor suppressive roles of miR-548e [149]
		Confers cisplatin resistance	Suppresses the expression of let-7a further elevating BCL-XL/S levels [149]

**Table 2.** LncRNAs that act as tumor suppressors in ovarian cancer.

	LncRNA	Function	Mechanism
1.	ADAMTS9-AS2	Inhibits cell proliferation and invasion	Acts as a ceRNA against miR-182-5p modulating FOXF2 pathway [150]
2.	AS-SLC7A11	Reduced AS-SLC7A11 promotes EOC progression	AS-SLC7A11 mainly deregulates SLC7A11 to suppress EOC progression [151]
3.	CASC2	Inhibits migration, invasion and proliferation	Reduced expression can be linked with poor prognosis in patient samples [152]
4.	DUXAP8	Regulate the proliferation and apoptosis of OC cells	Mediates YAP1 regulation via the suppression of miR-590-5p[153]
5.	FER1L4	Higher levels of FER1L4 facilitate paclitaxel sensitivity of OC cells	Suppresses paclitaxel resistance via inhibition of the MAPK pathway [154]
6.	GAS5	Inhibition of cell proliferation, migration, and invasion.	Activation of AKT/PTEN pathway by sequestering miR-96-5p [155]
7.	LIFR-AS1	Deregulation in OC cells and subsequent patients correlates to poor prognosis and increased carcinogenesis	Overexpression of LIFR-AS1 is associated with decreased invasion, migration, proliferation and viability in SOC cells [156]
8.	LINC-PINT	Inhibits cell migration, invasion, EMT, and proliferation, and promotes cellular apoptosis (acts as a tumor suppressor)	Increased levels of LINC-PINT sequester miR-374a-5p (acts as an oncogene) [157]
9.	LINC00641	Suppresses the oncogenic role of miR-320a	Acts as a ceRNA for miR-320a which promotes cell migration and invasion [158]

10.	MAGI2-AS3	Suppresses the oncogenic role of miRNAs	Sequesters towards miR-15-5p, miR-374a-5p and miR-374b-5p [159]
11.	MEG3	Inhibits cellular proliferation and metastasis	Acts as a ceRNA against miR-885-5p increasing VASH1 expression [160]
12.	NBAT-1	Suppresses tumorigenesis	Mediates its effect by targeting the AKT and ERK pathway [161]
13.	RP11-190D6.2	Low levels of RP11-190D6.2 associates with increased proliferative, invasive, and migratory properties in EOC	RP11-190D6.2 acts like a tumor suppressor where it confers its effects partly by regulating the expression of the gene WWOX [162]
14.	SDCBP2-AS1	Inhibits cell migration, invasion and increased apoptotic rate	Sequesters miR-100-5p, upregulating its expression and downregulating EPDR1 expression [163]
15.	TUSC7	Low levels of TUSC7 mediate proliferation, migration, and invasion of OC cells	Regulates GSK3 $\beta$ / $\beta$ -catenin pathway through sponging of miR-616-5p [164]
16.	XIST	Reduces tumor growth by inducing apoptosis	Sequesters against miR-106a [165]

3.1. *LncRNAs in Ovarian Cancer Cell Proliferation*

OC cells, like other cancer cells, promote cancer growth by increasing cellular proliferation through dysregulated cell cycle machinery [166]. LncRNAs play diverse roles in this process, influencing key events such as cell cycle progression, resistance to apoptosis, and overall cellular proliferation.

3.1.1. Regulation of Cell Proliferation

Abnormal expression of some lncRNAs activates specific signaling pathways, creating favorable conditions for cancer cells to proliferate. LncRNA Colon cancer-associated Transcript 2 (CCAT2) has been shown to promote cell proliferation through the Wnt/ $\beta$ -catenin pathway in OC cell lines SKOV3 and A2780. Inhibition of the Wnt/ $\beta$ -catenin pathway prevents these cells from progressing from the G1 to the S phase. In addition, silencing of CCAT2 reduces the expression of c-MYC and MMP-7, which are critically involved in cell proliferation and metastasis [167]. Likewise, lncRNA SNHGI, LINC00958, CCEPR, and HOXD-AS1, activate the Wnt/ $\beta$ -catenin pathway, positively regulating OC cell proliferation [85,101,119,132]. LncRNA NEAT1, stabilized by the protein LIN28 promotes cellular proliferation *in vivo* which was detected by the increase in expression of Ki67, an essential proliferation index marker. Additionally, NEAT1 promotes metastasis in OVCAR3 and A2780 OC cell lines by sequestering miR-506, which positively regulates the expression of vimentin, ZEB1, and Snail2. However, the interaction of NEAT1 with both LIN28 and miR-506 has not been not completely elucidated [168]. In another study, NEAT1 has been reported to promote proliferation in OC by acting as ceRNA for miR-365 resulting in the upregulation of Fibroblast growth factor 9 (FGF9). FGF9 is a positive regulator of proliferation and angiogenesis in multiple cancer types. However, analysis of specific downstream effectors of FGF9 in OC requires further studies [169]. LncRNA CTD-2020K17.1 is highly upregulated in metastatic tissue and OC cell lines. SKOV3 cells highly expressing lncRNA

CTD-2020K17.1 is actively dividing, and their distribution is more in the S phase. CTD-2020K17.1 has been associated with the Caspase-associated recruitment domain (CARD11), a positive regulator of NF- $\kappa$ B pathway[170].

### 3.1.2. Regulation of Cell Cycle Progression

When lncRNAs interfere with cyclin-dependent kinases (CDKs), cyclin-dependent inhibitors (CDIs), and cyclins, they disrupt the mechanisms of cell cycle arrest, leading to uncontrolled cell proliferation. This interference disables the normal checks and balances that prevent excessive cell division. For instance, lncRNA ANRIL is upregulated in OC patient tissues, contributing to cellular proliferation by increasing Bcl-2 and downregulating the CDK-inhibitors, p15INK4a and p15INK4b. Knockdown of ANRIL restricts cell cycle transition in the S phase, inhibiting cell proliferation [171]. Another lncRNA, UCA1 acts as an oncogene in SKOV3 and OVCAR8 OC cell lines by modulating the expression of essential cell cycle regulators, CCND1, CCND3 and Ki67, eventually promoting cell proliferation [60]. LncRNA SOX2OT is highly upregulated in HO-8910PM OC cell line and its knockdown restricts the cell cycle progression in the G0/G1 phase and suppresses the expression of essential cell cycle regulators, Cdc25c and Cyclin B1 [172].

### 3.1.3. Tumor Suppression and Proliferation Inhibition

Conversely, some lncRNAs act as tumor suppressors and are often downregulated in OC cells. Their decreased expression contributes to the malignancy and progression of OC. LncRNA GAS5, for instance, functions as a tumor suppressor and serves as a prognostic marker in OC [173]. It binds to heterogeneous nuclear ribonucleoprotein K (hnRNP K), stabilizing it and inhibiting the downstream p-AKT pathway, thereby reducing OC cell proliferation [174]. Another tumor suppressor lncRNA, MEG3, sequesters miR-376a, which promotes cell proliferation by targeting Krüppel-like factor 15 (KLF15) and Caspase-8 [175]. The reduced expression of MEG3 in OC patient samples correlates with higher levels of miR-376a and increased cell proliferation [176]. Similarly, tumor suppressor lncRNAs such as LINC-PINT, lncRNA TUSC7, and ADAMTS9-AS2 downregulate the proliferation of OC cells through different mechanisms by modulating genes that regulate the cell cycle and proliferation [150,157,164].

## 3.2. LncRNAs in Ovarian Cancer Cell Survival

LncRNAs promote tumor cell survival through various mechanisms. Cancer cells adapt to hostile environments by evading or suppressing programmed cell death (apoptosis), and autophagy [177]. Aberrant regulation of signaling pathways such as mTOR, KRAS, and MAPK promotes cell survival and proliferation, the hallmarks of cancer cells [178]. In OC, lncRNAs alter gene expression to create a tumor microenvironment (TME) conducive to growth and survival.

### 3.2.1. Evasion of Apoptosis

LncRNAs can promote OC cell survival by inhibiting apoptosis, thus allowing cancer cells to evade programmed cell death. LncRNA LINC00152 is upregulated in HO-8910, A2780, and SVOV3 OC cell lines, where it enhances cell survival by stimulating the increased expression of myeloid cell leukemia (MCL-1), an anti-apoptotic protein. LINC00152 achieves this by sequestering miR-125b, which normally targets MCL-1. By preventing cytochrome C release from mitochondria, MCL-1 attenuates the activity of the apoptotic protein family, Bcl-2, thereby restricting apoptosis [108]. Highly upregulated lncRNA HULC increases tumorigenesis by decreasing the apoptotic rate in OVCAR3 and A2780 OC cell lines. HULC interacts with ATG7 to induce the reduction in expression of autophagy-related components LC3-II and LAMP1, reducing apoptosis and enhancing cell survival [179].

Although very few lncRNAs are known to induce apoptosis in OC, MEG3, a tumor suppressor lncRNA, acts as a ceRNA against miR-205-5p, a miRNA that regulates proliferation by suppressing

PTEN and SMAD4 in OC. Overexpression of MEG3 significantly downregulates miR-205-5p with an increase in apoptotic rate in SKOV3 and OVCAR8 OC cell lines [180].

### 3.2.2. Regulation of Ferroptosis

Ferroptosis is a distinct form of programmed cell death characterized by iron-dependent lipid peroxidation, and some lncRNAs play a key role in inhibiting this process, thereby supporting tumor cell survival. The lncRNA CACNA1G-AS1 has been identified as a key player in inhibiting ferroptosis, which supports the survival and growth of tumor cells. CACNA1G-AS1 achieves this by upregulating ferritin heavy chain 1 (FTH1), which in turn leads to a reduction in mitochondrial autophagy. This effect is further amplified by the increased expression of IGF2 mRNA Binding Protein 1 (IGF2BP1). Together, these actions enhance tumor cell survival in OC cell lines, specifically SKOV3 and A2780, providing evidence for its role in cancer cell survival and cancer progression [181].

### 3.2.3. Modulation of Autophagy

Autophagy serves dual roles in cancer, both suppressing and supporting tumor survival under stress conditions such as nutrient deprivation, hypoxia, and chemotherapy [182]. LncRNAs modulate autophagy in OC, either promoting or inhibiting this process to influence cell survival. LncRNA RNF157-AS1 acts as an oncogene by inhibiting autophagy in SKOV3 cells to promote cell survival. It functions as a molecular scaffold, tethering chromatin modifiers like Enhancer of Zeste Homolog 2 (EZH2) and High mobility AT-Hook 1 (HMGA1), which suppresses the mTOR pathway and key autophagy proteins Unc-51 like Autophagy Activating Kinase 1 (ULK1) and DIRAS Family GTPase 3 (DIRAS3) [183].

Conversely, overexpression of the tumor suppressor lncRNA GAS8-AS1 has been found to induce autophagy in SKOV3, and A2780 OC cell lines by increasing the level of LC3II expression. In addition, the binding of GAS8-AS1 with Beclin1, an essential component for the formation of autophagosomes, increases the apoptotic rate in OC [184].

## 3.3. LncRNAs in Ovarian Cancer Metabolic Reprogramming

Metabolic reprogramming refers to the alteration of cellular metabolism to meet the demands of cancer cells [185]. In cancer cells the metabolic pathways are reprogrammed to augment the biosynthesis of macromolecules, enhance the cellular ATP/energy levels and provide redox homeostasis within the cells to promote tumor genesis and progression and lncRNAs play an indispensable role in regulating these functions [186,187]. In OC cells, lncRNAs play a cardinal role in regulating major cellular metabolisms such as that of glucose, lipids and amino acids to promote cancer progression.

### 3.3.1. Regulation of Glucose Metabolism

Even under normoxic conditions, OC cells favor lactate production from glucose, promoting glycolysis and altering OXPHOS (oxidative phosphorylation) to augment energy supply to facilitate tumor cell proliferation, metastasis and therapy resistance [188]. LncRNAs play a key role in this process. In OC cells, lncRNA SNHG3 sequesters miR-186-5p, leading to the upregulation of the translation factor EIF4AIII and its downstream targets, such as PKM, PDHB, IDH2, and UQCRH. These targets enhance the tricarboxylic acid (TCA) cycle and OXPHOS, thereby meeting the energy demands of OC cells [189]. Similarly, the lncRNA NRCP has been shown to upregulate the expression of the glycolytic enzyme, glucose-6-phosphate isomerase (GPI), by promoting the interactions between STAT1 and RNA Pol II in *GPI* promoter to promote *GPI* transcription and tumor progression [190].

### 3.3.2. Regulation of Fatty Acid Metabolism

OC cells often prefer fatty acid metabolism for energy needs over glucose metabolism and hence metastasize to the lipid-enriched omental fat pad [191]. Despite the recognized importance of fatty



acid metabolism in OC, research on lncRNAs regulating these mechanisms in OC is still emerging. Recent studies involving bioinformatics predictive models and computational analysis based on the TCGA patient data have identified a candidate lncRNA, LINC00861, that regulate fatty acid metabolism in OC and can serve as prognostic signatures. However, detailed mechanistic studies are needed to understand their precise mechanisms in regulating fatty acid metabolism driving OC progression [192,193].

### 3.3.3. Regulation of Amino Acid Metabolism

lncRNAs also regulate amino acid metabolisms to promote OC progression. It has been shown that circ\_0025033 sequesters miR-370-3p to upregulate sodium-dependent neutral amino acid transporter, SLC1A5 expression to promote amino acid metabolism [194]. Conversely, tumor suppressor lncRNA, SLC7A11-AS1, which is downregulated in OC, normally acts as antisense to *SLC7A11*, a sodium-independent, anionic amino acid transporter [195]. In cancer cells, higher SLC7A11 promotes glutathione production and regulates glutamine metabolism as well as redox homeostasis that enhances OC progression [195].

### 3.3.4. Intercellular Metabolic Signaling in the Tumor Microenvironment

In addition to reprogramming cancer cell metabolism, lncRNAs are involved in intercellular signaling within the TME, influencing both cancer cells and stromal components such as cancer-associated fibroblasts (CAFs). In OC, CAFs within the pro-metastatic niche synthesize and release CXCL14, which stimulates OC cells through paracrine signaling to upregulate LINC00092. LINC00092 binds to PFKFB2 protein, stabilizing and upregulating PFKFB2 expression and promoting glycolysis in OC cells. This metabolic shift triggers the release of secretory signals from OC cells that, in turn, regulate CAFs, maintaining CAF-specific markers such as  $\alpha$ SMA and FAP, thereby promoting OC metastasis [196]. lncRNAs also play a role in the metabolic reprogramming of CAFs within the TME. For example, small extracellular vesicles (sEVs) containing UCA1, released from OC cells, are taken up by stromal fibroblasts, leading to enhanced glucose metabolism in peri-tumoral fibroblasts through the upregulation of HK2 and GLUT2 [197]. This intercellular signaling highlights how lncRNAs within sEVs contribute to tumor progression through metabolic reprogramming.

## 3.4. lncRNAs in Ovarian Cancer Cell Migration

Cellular migration is critical for the metastatic spread of OC, allowing cancer cells to spread from the primary site to distant locations in the body. This process involves the degradation of the extracellular matrix proteins like integrins, facilitating cellular migration and disrupting cellular adhesion. EMT is a key process in this process, where epithelial cells lose their polarity and adhesion properties and acquire mesenchymal characteristics, making them more mobile and invasive. This facilitates the escape of cancer cells from the primary tumor site into the blood vessels, disseminating to distant organs and forming metastases [198].

### 3.4.1. Promotion of EMT by Oncogenic lncRNAs

EMT is a fundamental process in cancer metastasis, and several lncRNAs play crucial roles in promoting this transition in OC [199]. lncRNA SNHG1 is overexpressed in A2780 and SKOV3 OC cells, where it promotes EMT by sequestering miR-454, leading to the upregulation of ZEB1. ZEB1 is a key transcription factor that suppresses E-cadherin, a marker of epithelial cells and promotes mesenchymal characteristics [133]. In a recent study, lncRNA AC005224.4 was shown to be highly upregulated and associated with EMT and metastasis in SKOV3, and CaOV3 OC cell lines. AC005224.4 sequesters miR-140-3p, allowing increased expression of the transcription factor SNAI2 which results in the increased expression of several EMT markers, Vimentin, Snail, And N-cadherin [200]. HOTAIR, a widely studied lncRNA in OC, plays multiple roles in OC progression including EMT [201]. In vitro and in vivo studies has shown that HOTAIR promotes pro-metastatic effects in OC through regulation of EMT-associated genes and MMPs [202].

### 3.4.2. Inhibition of EMT by Tumor Suppressor LncRNAs

Tumor suppressor lncRNAs often counteract EMT, thereby inhibiting cancer cell metastasis. LINC-PINT is a lncRNA that is downregulated in OC and acts as a ceRNA for miR-374a-5p. By sequestering miR-374a-5p, LINC-PINT upregulates FOXO1, a transcription factor that inhibits vimentin (a mesenchymal marker) and promotes E-cadherin expression (an epithelial marker), thereby suppressing EMT in OVCAR3 and A2780 cells [157,203]. LIFR-AS1 is another tumor suppressor lncRNA that inhibits EMT by downregulating Snail and N-cadherin, both of which are critical for mesenchymal transition, while upregulating E-cadherin in A2780 and SKOV3 cells [156].

### 3.4.3. Direct Regulation of Cell Migration

In addition to regulating EMT, lncRNAs directly influence the migration of OC cells, which is essential for metastasis. Several lncRNAs not only modulate the expression of the components of different signaling pathways such as Wnt/ $\beta$ -catenin, PI3K/AKT, and TGF- $\beta$  but also upregulate the expression of different cytoskeletal regulators and matrix-remodeling enzymes involved in cell migration and invasion [199,204]. LncRNA HOTAIR not only promotes EMT but also enhances cell migration by sequestering miR-206. This sequestration leads to increased expression of Cyclin D1 (CCND1) and Cyclin D2 (CCND2), which are involved in cell migration and invasion along with their role in cell proliferation in SKOV3, OVCAR3, COV362 and A2780 OC cell lines [205].

Conversely, tumor suppressor lncRNAs that inhibit cellular migration are often downregulated in OC. LINC-PINT, a lncRNA expressed at low levels in OC, acts as a ceRNA for miR-374a-5p which downregulates its target the Foxhead box O1 (FOXO1) gene which regulates cell migration by inhibiting vimentin and promoting E-cadherin expression in OVCAR3, and A2780 cells [157,203]. Similarly, lncRNA TUSC7 inhibits cellular migration in SKOV3 cells by sequestering miR-616-5p, which negatively regulates Glycogen Synthase Kinase 3 beta (GSK3 $\beta$ ), leading to the activation of the  $\beta$ -catenin pathway promoting OC cell migration [164]. LncRNA MEG3 which is a potential tumor suppressor lncRNA reduces the migration of SKOV3 OC cells through the induction of cell apoptosis. MEG3 positively regulates PTEN, present downstream of MEG3, and is found to be upregulated when MEG3 is overexpressed [206].

## 3.5. LncRNAs in Ovarian Cancer Angiogenesis

Angiogenesis, the formation of new blood vessels, is a crucial process by which cancer cells meet their increasing demands for nutrients and oxygen, facilitating their growth and progression. This process is tightly regulated by a balance of pro- and anti-angiogenic factors [207]. Aberrant expression of lncRNAs can disrupt this balance and promote tumor angiogenesis in the TME [208].

### 3.5.1. Promotion of Angiogenesis by Oncogenic LncRNAs

Oncogenic lncRNAs can enhance angiogenesis by modulating the expression of pro-angiogenic factors. For example, lncRNA DANCR promotes tumor angiogenesis by sequestering miR-145, which normally targets VEGF. By inhibiting miR-145, DANCR upregulates VEGF expression in SKOV3 and A2780 OC cell lines, contributing to increased tumor angiogenesis [209]. Another example is the sEV-packaged lncRNA ATB, which is released by OC cell lines SKOV3 and A2780. This lncRNA promotes angiogenesis in human umbilical vein endothelial cells (HUVECs) by sequestering miR-204-3p. This sequestration prevents miR-204-3p from downregulating Transforming Growth Factor  $\beta$  Receptor 2 (TGF $\beta$ R2), thereby altering the TME in HUVECs and enhancing angiogenesis [210]. LncRNA NEAT1 is associated with the upregulation of several angiogenesis-related genes, including Sema4D, Tiam1, Rac1, and Plexin B1, in SKOV3 and A2780 OC cell lines. Another study on NEAT1 has shown that it specifically promotes angiogenesis by sequestering miR-214-3p, which results in the increased expression of its target, SEMA4D, thereby enhancing malignancy and angiogenesis in OC [211]. LncRNA TUG1 promotes angiogenesis in SKOV3 and CaOV3 OC cell lines by the positive regulation of leucine-rich  $\alpha$ -2-glycoprotein-1 (LRG1).

LRG1 binds to TGF- $\beta$  receptor, additionally activating certain angiogenic factors, for example, VEGFA and Ang-1[142].

### 3.5.2. Inhibition of Angiogenesis by Tumor Suppressor LncRNAs

In contrast, tumor suppressor lncRNAs inhibit tumor angiogenesis. One such lncRNA is MEG3. It has been demonstrated that overexpression of the MEG3 in ovarian carcinoma-derived microvascular endothelial cells (ODMECs) resulted in the suppression of angiogenesis. MEG3 competitively binds with miR-376a, preventing it from targeting YBX1, and allowing the expression of RAS p21 protein activator 1 (RASA1), a known suppressor of angiogenesis [212]. This mechanism highlights the role of MEG3 in maintaining angiogenic balance within the TME and preventing tumor angiogenesis.

### 3.6. LncRNAs in Ovarian Cancer Stemness

Cancer stem cells (CSCs) within OC represent a subpopulation of OC cells with unique properties that enable them to withstand harsh environmental conditions such as hypoxia within the TME. CSCs can evade therapy by altering different signaling pathways including Wnt, Notch, KRAS, and PTEN, among others [213]. Several CSC markers have been identified in OC, including CD133, CD117, ALDH, EpCAM, SOX2, and Nanog Homeobox (NANOG), all of which play a critical role in the initiation and progression of the disease. These markers play a critical role in the initiation and progression of the disease and are used to identify and isolate CSCs responsible for tumor initiation, therapy resistance, EMT, and metastasis [214]. Several lncRNAs have been studied for their role in conferring stemness in OC cells. These lncRNAs function through several molecular mechanisms, including epigenetic modulation of different signaling pathways, sequestration of several TS miRNAs, and transcriptional regulation of different oncogenes [215].

#### 3.6.1. Transcriptional Regulation of Stemness by LncRNAs

LncRNAs play a crucial role in regulating the transcription of genes that confer stemness in OC cells. For instance, lncRNA HOTAIR positively regulates the transcription factor T-box transcription factor 3 (TBX3), which in turn transactivates the expression of SRY-box 2 (SOX2) and Octamer-binding transcription factor 4 (Oct4). These factors are essential for maintaining pluripotency and self-renewal in the CSC population in SKOV3, ES2, and OVCAR3 OC cell lines [216,217]. This regulation promotes EMT and sustains the stem-like properties of CSCs, which are key drivers of tumor progression and therapy resistance.

#### 3.6.2. Epigenetic Modulation of Stemness by LncRNAs

Epigenetic regulation by lncRNAs is another mechanism through which CSCs maintain their stemness. MALAT1 is a lncRNA that functions as both a transcriptional and epigenetic regulator, effectively stabilizing YAP protein expression to promote stemness in the cisplatin-resistant SKOV3 OC cell line. Overexpression of YAP can reverse the effects of MALAT1 knockdown, leading to increased expression of stemness markers such as aldehyde dehydrogenase 1 (ALDH1) and NANOG. However, the exact mechanisms through which YAP regulates stemness in OC remain to be fully defined [218].

#### 3.6.3. Regulation of CSC Signaling Pathways by LncRNAs

LncRNAs modulate key signaling pathways to enhance CSC properties and promote stemness in OC. LINC00115, for example, upregulates the expression of SOX9 by sequestering miR-30a-5p. This interaction results in an increased CSC population and decreased apoptosis in A2780 and CD133+ OC cells via the Wnt signaling pathway. Suppression of LINC00115 leads to decreased levels of CSC markers, including CD44, NANOG, and CD133, as well as SOX9, highlighting its role in promoting CSC-related traits and therapy resistance [219].

### 3.7. *LncRNAs in Ovarian Cancer associated with Immune Evasion*

Immune evasion is a critical mechanism that allows cancer cells to avoid detection and destruction by the body's immune system. This process can occur early in tumor development, with cancer cells adopting various strategies to evade immune surveillance. The human immune system consists of two main components: innate and adaptive immune responses. The innate immune response provides the initial defense against pathogens and includes physical barriers (such as skin, mucous membranes, and gastric juices) and immune cells such as macrophages, natural killer cells, and neutrophils [220]. In contrast, the adaptive immune response is highly specific and involves T-lymphocytes (T-cells) and B-lymphocytes (B-cells) [123]. LncRNAs play a significant role in manipulating these immune responses, thereby facilitating immune evasion in OC.

#### 3.7.1. Modulation of Innate Immunity

LncRNAs can modulate the innate immune response, enabling OC cells to evade initial immune detection. A prime example is lncRNA IL21-AS1, which is highly upregulated in both OC patient tumor samples and SKOV3 and A2780 OC cells. IL21-AS1 promotes immune evasion by upregulating CD24 expression through the sequestration of miR-561-5p. CD24 inhibits macrophage-mediated phagocytosis by binding to the Siglec-10 receptor on macrophages, thus preventing the immune system from effectively targeting the OC cells [221]. Another example involves lncRNA MEG8, which has been implicated in the downregulation of sine oculis-binding protein (SOBP) in OC. Bioinformatics analyses of OC patient databases (GSE36668, GSE12470, GSE14407, and GSE27651) suggest that MEG8 could sequester miR-378, leading to the upregulation of SOBP and associated cytokines, which are involved in immune pathways. This interaction highlights a potential role for MEG8 in facilitating immune evasion in OC cells [222].

#### 3.7.2. Modulation of Adaptive Immunity

LncRNAs also play a role in modulating adaptive immunity, allowing OC cells to evade more specific and targeted immune responses. One such lncRNA is SNHG12, which has been shown to suppress T-cell activity in OC. In patient samples, SNHG12 was found to induce the overexpression of IL-6-mediated PD-L1 expression in cancer cells. SNHG12 recruits the transcription factor NF- $\kappa$ B1 to the IL-6 promoter region, enhancing IL-6 expression and subsequently increasing PD-L1 levels, which suppresses T-cell function and contributes to immune evasion [223].

### 3.8. *LncRNAs in Ovarian Cancer Therapy Resistance*

Therapy resistance in OC is a multifaceted and complex phenomenon. LncRNAs contribute significantly to this process by modulating gene expression related to drug uptake, efflux, metabolism, and resistance to radiotherapy, thereby reducing the effectiveness of therapeutic interventions [224].

#### 3.8.1. Modulation of Drug Efflux and Uptake

LncRNAs play a crucial role in regulating the expression of genes involved in drug efflux and uptake, leading to reduced intracellular concentrations of therapeutic drugs. For example, LINC01118 is highly expressed in OC patient tissue samples and upregulates ATP-Binding Cassette C1 (ABCC1) drug efflux transporters by sequestering miR-134, a negative regulator of ABCC1. This leads to paclitaxel resistance in OC [225]. Similarly, lncRNA WDFY3-AS2 is overexpressed in cisplatin-resistant A2780 OC cells and sequesters miR-139-5p, which modulates the expression of Syndecan-4 (SDC4), a transmembrane heparan sulfate proteoglycan that upregulates drug efflux pumps. This contributes to cisplatin resistance in OC cells [226].

#### 3.8.2. Alteration of Drug Metabolism

Several other lncRNAs are involved in conferring therapy resistance by altering drug metabolism. Knocking down of lncRNA PVT1 lowered the levels of aldo-keto reductase (AKR) family



1 member C1 (AKR1C1), AKR1C2 and AKR1B10 in SKOV3 OC cell line, which plays a role in breaking down therapeutic agents such as paclitaxel, cisplatin, and doxorubicin into simpler non-toxic compounds [227]. Transcriptionally, the downregulation of PVT1 has been associated with doxorubicin sensitivity in the SKOV3 OC cell line. Although the regulation of AKR enzymes by lncRNA PVT1 is yet to be studied [131].

LncRNA H19 promotes cisplatin resistance through the activation of the glutathione synthesis pathway (GSH) in A2780 and A2780 cisplatin-resistant OC cells. It stabilizes Nrf2, a key factor in the activation of Glutathione S-transferase Pi 1 (GSTP1), which positively regulates the GSH pathway, leading to cisplatin inactivation [94]. It has also been shown that UCA1 acts as a ceRNA for miR-143, resulting in the upregulation of FOS Like 2, AP-1 Transcription Factor Subunit (FOSL2), in cisplatin-resistant A2780 and SKOV3 OC cell lines. However, the mechanism through which FOSL2 regulates cisplatin resistance in OC is yet to be studied [148].

### 3.8.3. Role of Tumor Suppressor LncRNAs in Therapy Sensitivity

In contrast to these resistance-inducing lncRNAs, the expression of a few tumor suppressor lncRNAs can be correlated with therapy sensitivity in OC. For example, curcumin-treated OC cells showed overexpression of the tumor suppressor lncRNA MEG3, both in OVCAR3 and SKOV3 cells as well as the sEVs derived from them. MEG3 sequesters and reduces the levels of miR-214 both in the cell lines and in the sEVs, which is known to confer chemoresistance in OC cells through the activation of the Akt pathway through its interaction with PTEN. The overexpression of MEG3 has been shown to enhance chemosensitivity in the cisplatin-resistant A2780 cell line [228]. LINC00312 is downregulated in SKOV3 cisplatin-resistant cell lines when compared to SKOV3 cells. Its overexpression induced sensitivity to the cisplatin-resistant SKOV3 cells through the activation of the caspase-3 apoptotic pathway and downregulated expression of MDR1 membrane proteins.[229]

In another instance, LINC01508 has been shown to sensitize OC cells to cisplatin by modulating the AKT pathway and downregulating the YAP-Hippo pathway. Studies with the syngeneic sensitive and resistant cell OV2008 cell lines have indicated that the overexpression of LINC01508 sensitizes the OC cells to cisplatin by inhibiting the Hippo-YAP signaling pathway. In these cells, LINC01508 inhibits YAP signaling through a yet to defined signaling mechanism [230]. It has also been shown that LINC01125, expressed at a lower level in cisplatin-resistant SKOV3 and A2780 OC cell lines, confers cisplatin sensitivity when overexpressed. Overexpression of LINC01125 sequesters miR-1972, a highly expressed miRNA both in OC patient samples and cell lines. Although the oncogenic properties of miR-1972 is yet to be studied, through the use of the TargetScan tool, it has been deduced that miR-1972 is involved in the regulation of targets involved in the apoptotic pathway [231].

### 3.8.4. LncRNAs and Radiotherapy Resistance

Although radiotherapy is not commonly used in OC, *in vitro* experiments have shown that lncRNAs can contribute to radiotherapy resistance. Radiotherapy resistance primarily involves the ability of cancer cells to enhance their DNA repair abilities via proteins such as ATM and BRCA1/2 [232]. In addition, cancer cells can evade radiotherapy-induced apoptosis by upregulating anti-apoptotic proteins such as BCL-2 [233]. The hypoxic TME further contributes to resistance by stabilizing hypoxia-inducible factors that promote cell survival [224]. Few lncRNAs have been studied for their role in conferring radiotherapy resistance in OC cells. Specifically, the lncRNA FAM83H-AS1 has been shown to interact with Human Antigen R (HuR), an RNA-binding protein, stabilizing it and thus contributing to radio-resistance in SKOV3, A2780, and SW626 OC cell lines. Knockdown of FAM83H-AS1 restores radiosensitivity in these cells [234].

## 4. Clinical Implications

LncRNAs are gaining greater importance owing to their pivotal roles in OC, functioning either as oncogenes or tumor suppressors. Their clinical relevance extends from early detection to



specialized therapeutic strategies, highlighting the transformative impact of lncRNA research in clinical settings. Differential expression of lncRNAs in cancer cells and tissues presents opportunities for early cancer detection, prognosis, and treatment optimization. Specific lncRNAs associated with aggressive tumor behavior can provide insights into optimizing therapeutic approaches [235,236]. The exploitation of lncRNA expression profiles for patient stratification represents a promising frontier in personalized medicine for OC. Identifying lncRNA signatures associated with specific subtypes, disease stages, or treatment responses could lead to tailored therapeutic approaches, ultimately enhancing therapeutic efficacy and patient outcomes.

#### 4.1. *lncRNAs as diagnostic biomarkers in Ovarian Cancer*

The differential expression of lncRNAs in cancer cells compared to normal cells makes them potential biomarkers for OC. For example, the lncRNA LOXL1-AS1 shows heightened expression in EOC patients and is linked to poor patient survival of the patients especially in advanced cancer stages [237]. In addition, the overexpression of lncRNA XIST in 98 EOC patient tissue samples support its role as an important diagnostic biomarker in OC. Further, the pro-tumorigenic role of XIST was validated in OV90, OVCAR3, SKOV3, and A2780 OC cell lines [238]. In another study, GSEA data from GSE10971, GSE29450, and GSE54388 datasets were analyzed and a panel of 4 lncRNAs, LINC00511, LINC01132, RP11-83A24.2, and MIR762AG were found to be highly expressed in OC patients and were correlated with low survival by cox regression analysis. Further intensive study of LINC00511 revealed that it interacts with EZHZ and mediates the H3K27me3 modification of the promoter p21, an essential regulator of CDKN1A [239]. The exploration of lncRNAs as diagnostic biomarkers is ongoing, with continuous research unraveling new biomarkers and their roles in disease progression. The use of lncRNAs as biomarkers holds great promise for early detection and personalized therapy in OC.

#### 4.2. *lncRNAs as prognostic indicators and predictors of treatment response*

Aberrant expression of lncRNAs can serve as prognostic indicators for patient survival, disease progression, and tumor recurrence. Studies utilizing the TCGA database have indicated that the increased expression of LOC101927151 in OC patients is associated with poor prognosis, while decreased expression of LINC00861 and LEMD1-AS1 correlates with unfavorable outcomes [240]. A similar TCGA database-based analysis has identified that the increased expression of lncRNA RP4-700P18.3, RP11-57P19.1, RP11-307C12.11, RP11-254I22.1, RP1-223E5.4, and GACAT3 is associated with better tumor survival while higher expression of lncRNA PTPRD-AS1 and RP11-80H5.7 is linked with poor survival of OC patients [241]. OC progression and recurrence are also tied to aberrant lncRNA expressions. A novel lncRNA LINC00565 is highly expressed in OC and its knockdown inhibited the metastatic nature of suggesting a strong prognostic potential for this lncRNA [242]. A LASSO regression analysis of GSE9891 and GSE30161 GSEA datasets indicated that a panel of six lncRNAs namely, RUNX1-IT1, MALAT1, H19, HOTAIRM1, LOC100190986, and AL132709.8 associated with OC recurrence. All these lncRNAs exhibited a heightened expression in late-stage OC patients and were shown to be associated with a higher risk of recurrence [243].

#### 4.3. *lncRNAs as Therapeutic Targets*

A study involving 266 OC patients revealed that overexpression of lncRNAs LINC00472, ASP1-IT1, and FAM215A is associated with early-stage disease and low-grade tumors. These lncRNAs were found to play a role in inhibiting cellular proliferation offering insights into potential therapeutic targets [244]. In another study, differentially expressed lncRNAs in EOC patient data from 22 cohorts including GEO datasets and GEPIA2 were analyzed. A total of eight noteworthy novel upregulated lncRNAs were discovered, that can serve as potential diagnostic targets, including ENSG00000187951, ENSG00000285756, LINC01297, LINC01770, LINC01977, MIR205HG, TFAP2A-AS1, ZNF232-AS1. Additionally, lncRNA MIR924HG and GUSBP11 were associated with unfavorable prognosis [245].

#### 4.4. Therapeutic potential of targeting lncRNAs in Ovarian Cancer

Targeting lncRNAs in OC holds significant promise as a novel therapeutic strategy. Unlike conventional therapies that focus on single signaling nodes, targeting lncRNAs offers the potential to disrupt complex networks of pathways involved in cancer genesis and progression. lncRNAs modulate multiple cellular processes, including chemoresistance, autophagy, EMT, DNA damage repair, and apoptosis, making them particularly attractive as therapeutic targets. This multifunctional role could lead to more effective and multi-targeted therapeutic strategies [235,246].

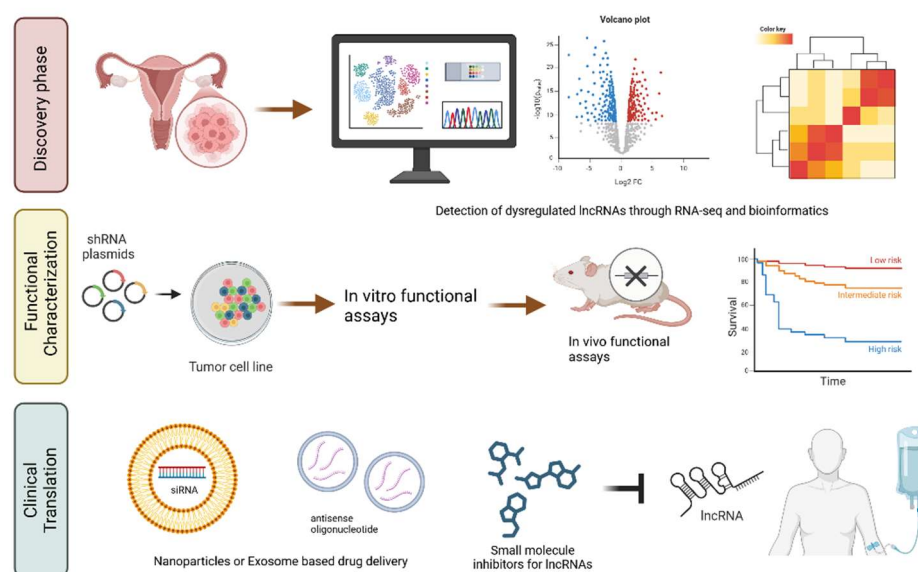
One key advantage of targeting lncRNAs is their ability to adapt and perform different functions under varying conditions, such as hypoxia or inflammation within the TME. This adaptability allows for a more dynamic and robust therapeutic approach [247]. Emerging strategies for targeting lncRNAs in OC include the use of antisense oligonucleotides (ASOs), LNAgapmers, RNA interference (RNAi) technologies, and small molecule inhibitors. These approaches aim to modulate lncRNA function by either inhibiting their expression or blocking their interactions with other biomolecules [248].

ASOs are short, synthetically designed nucleotide sequences that bind to specific lncRNAs, leading to their degradation or inhibition. LNAgapmers, which are ASOs modified with locked nucleic acids, provide greater stability and binding affinity, enhancing their ability to silence lncRNAs. RNAi technologies, including siRNA and shRNA, utilize small RNA molecules to interfere with specific lncRNAs, reducing their expression and altering cancer cell function. Small molecule inhibitors, on the other hand, disrupt lncRNA activity by interfering with their interactions with other proteins and signaling pathways [249]. Clinical trials involving RNA-targeting therapeutics have shown the feasibility of these strategies. For example, ASOs targeting survivin in prostate cancer [250] and c-Raf kinase in recurrent OC [251] demonstrate the potential for these approaches to be applied to lncRNA-targeted therapies in OC.

## 5. Summary and Perspectives

The review highlights the growing importance of lncRNAs as promising biomarkers and therapeutic targets in OC. Extensive research has provided valuable insights and revealed exciting opportunities for further exploration. Moving forward, validating lncRNA biomarkers across diverse patient cohorts and clinical settings is crucial. The variability in study designs, sample sizes, and analytical methods underscores the need for standardized protocols and rigorous validation frameworks to ensure the reliability and reproducibility of lncRNA biomarkers.

The complex roles and intricate molecular mechanisms of lncRNAs in OC pathogenesis offer rich opportunities for discovering novel diagnostic, prognostic, and therapeutic targets. Emerging technologies, such as advanced bioinformatics and single-cell sequencing, present unprecedented opportunities to identify these targets. The integration of lncRNA studies with other omics data (genomics, proteomics, metabolomics) could provide a more integrated view of the molecular landscape of OC. This network-based approach could uncover novel lncRNA-associated pathways and interactions, offering deeper insights into OC pathobiology and informing more effective treatment strategies (Figure 5).



**Figure 5.** Roadmap of lncRNA research in ovarian cancer. The roadmap can be divided in three main phases: The Discovery Phase involves identifying dysregulated lncRNAs through RNA sequencing (RNA-seq) and bioinformatics tools, as shown by volcano plots and clustering analyses. The Functional Characterization Phase includes validating lncRNAs as biomarkers and elucidating their roles through in vitro functional assays using tumor cell lines and in vivo studies in animal models, linking lncRNA expression to patient survival. Finally, the Clinical Translation Phase highlights therapeutic strategies, such as nanoparticle- or exosome-based delivery of antisense oligonucleotides (ASOs) and siRNAs, and the development of small-molecule inhibitors targeting specific lncRNAs for clinical applications.

Machine learning (ML) and artificial intelligence (AI) are poised to play transformative roles in the therapeutic targeting and clinical utility of lncRNAs. By analyzing large datasets, including multi-omics data, ML algorithms can identify patterns and predict lncRNA functions, interactions, and their roles in therapy resistance or disease progression. AI-driven models can also aid in the discovery of novel lncRNAs and predict their potential as therapeutic targets. Furthermore, AI can optimize personalized medicine by integrating lncRNA profiles with clinical data to predict patient responses to specific treatments, thereby enhancing treatment efficacy and minimizing adverse effects. As we move forward, these advancements are anticipated to open new avenues for the development of lncRNA-based diagnostics, prognostics, and therapeutic interventions. It can be envisioned that lncRNA-based personalized medicine becoming a cornerstone in the fight against OC, offering tailored precision cancer medicine therapies and significantly improving patient outcomes and quality of life.

**Author Contributions:** For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used “Conceptualization, D.N.D., S.B., and R.N.; formal analysis, S.B., and R.N.; data curation, S.B.; writing—original draft preparation, S.B.; writing—review and editing, R.N., and D.N.D.; supervision, D.N.D.; project administration, D.N.D.; funding acquisition, D.N.D. All authors have read and agreed to the published version of the manuscript.

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Abbreviations

The following abbreviations are commonly used in this manuscript:

OC	Ovarian Cancer
lncRNA	Long Non-Coding RNA
lincRNA	Long Intergenic Non-Coding RNA
ceRNA	Competing Endogenous RNA
miRNA	MicroRNA
piRNA	Piwi-Interacting RNA
snRNA	Small Nuclear RNA
circRNA	Circular RNA
siRNAs	Small Interfering RNAs
shRNA	Short Hairpin RNA
ASO	Antisense Oligonucleotide
RNA-seq	RNA Sequencing
CAF	Cancer Associated Fibroblasts
CSC	Cancer Stem Cells
TME	Tumor Micro-Environment
EMT	Epithelial-to-Mesenchymal Transition

References

1. Webb, P.M.; Jordan, S.J. Global epidemiology of epithelial ovarian cancer. *Nat Rev Clin Oncol* **2024**, 10.1038/s41571-024-00881-3, doi:10.1038/s41571-024-00881-3.
2. Tavares, V.; Marques, I.S.; de Melo, I.G.; Assis, J.; Pereira, D.; Medeiros, R. Paradigm Shift: A Comprehensive Review of Ovarian Cancer Management in an Era of Advancements. *Int J Mol Sci* **2024**, 25, 1845, doi:10.3390/ijms25031845.
3. Siegel, R.L.; Giaquinto, A.N.; Jemal, A. Cancer statistics, 2024. *CA: A Cancer Journal for Clinicians* **2024**, 74, 12-49, doi:10.3322/caac.21820.
4. Lheureux, S.; Braunstein, M.; Oza, A.M. Epithelial ovarian cancer: Evolution of management in the era of precision medicine. *CA: A Cancer Journal for Clinicians* **2019**, 69, 280-304, doi:10.3322/caac.21559.
5. Chan, J.K.; Tian, C.; Kesterson, J.P.; Monk, B.J.; Kapp, D.S.; Davidson, B.; Robertson, S.; Copeland, L.J.; Walker, J.L.; Wenham, R., et al. Symptoms of Women With High-Risk, Early-Stage Ovarian Cancer. *Obstet Gynecol* **2022**, 139, 157-162, doi:10.1097/AOG.0000000000004642.
6. Löhmußaar, K.; Kopper, O.; Korving, J.; Begthel, H.; Vreuls, C.P.H.; van Es, J.H.; Clevers, H. Assessing the origin of high-grade serous ovarian cancer using CRISPR-modification of mouse organoids. *Nat Commun* **2020**, 11, 2660, doi:10.1038/s41467-020-16432-0.
7. Marth, C.; Abreu, M.H.; Andersen, K.K.; Aro, K.M.; De Lurdes Batarda, M.; Boll, D.; Ekmann-Gade, A.W.; Haltia, U.M.; Hansen, J.; Haug, A.J., et al. Real-life data on treatment and outcomes in advanced ovarian cancer: An observational, multinational cohort study (<scp>RESPONSE</scp> trial). *Cancer* **2022**, 128, 3080-3089, doi:10.1002/cncr.34350.
8. Alatise, K.L.; Gardner, S.; Alexander-Bryant, A. Mechanisms of Drug Resistance in Ovarian Cancer and Associated Gene Targets. *Cancers (Basel)* **2022**, 14, 6246, doi:10.3390/cancers14246246.
9. Algethami, M.; Kulkarni, S.; Sadiq, M.T.; Tang, H.K.C.; Brownlie, J.; Jeyapalan, J.N.; Mongan, N.P.; Rakha, E.A.; Madhusudan, S. Towards Personalized Management of Ovarian Cancer. *Cancer Manag Res* **2022**, 14, 3469-3483, doi:10.2147/CMAR.S366681.
10. Nadhan, R.; Isidoro, C.; Song, Y.S.; Dhanasekaran, D.N. Long Non-coding RNAs in Cancer. In *Handbook of Oncobiology: From Basic to Clinical Sciences*, Sobti, R.C., Ganguly, N.K., Kumar, R., Eds. Springer Nature Singapore: Singapore, 2023; 10.1007/978-981-99-2196-6\_37-1pp. 1-45.
11. Nadhan, R.; Isidoro, C.; Song, Y.S.; Dhanasekaran, D.N. Signaling by LncRNAs: Structure, Cellular Homeostasis, and Disease Pathology. *Cells* **2022**, 11, 2517, doi:10.3390/cells11162517.

12. Nadhan, R.; Dhanasekaran, D.N. Decoding the Oncogenic Signals from the Long Non-Coding RNAs. *Onco* **2021**, *1*, 176-206.
13. Statello, L.; Guo, C.-J.; Chen, L.-L.; Huarte, M. Gene regulation by long non-coding RNAs and its biological functions. *Nature Reviews Molecular Cell Biology* **2021**, *22*, 96-118, doi:10.1038/s41580-020-00315-9.
14. Oo, J.A.; Brandes, R.P.; Leisegang, M.S. Long non-coding RNAs: novel regulators of cellular physiology and function. *Pflugers Arch* **2022**, *474*, 191-204, doi:10.1007/s00424-021-02641-z.
15. Noh, J.H.; Kim, K.M.; McClusky, W.; Abdelmohsen, K.; Gorospe, M. Cytoplasmic functions of lncRNAs. *Wiley Interdiscip Rev RNA* **2018**, *9*, e1471, doi:10.1002/wrna.1471.
16. Nadhan, R.; Dhanasekaran, D.N. Regulation of Tumor Metabolome by Long Non-Coding RNAs. **2022**, *16*, 1, doi:10.55233/1750-2187-16-1.
17. Nikpayam, E.; Tasharofi, B.; Sarrafzadeh, S.; Ghafouri-Fard, S. The Role of Long Non-Coding RNAs in Ovarian Cancer. *Iran Biomed J* **2017**, *21*, 3-15, doi:10.6091/21.1.3.
18. Zheng, M.; Hu, Y.; Gou, R.; Nie, X.; Li, X.; Liu, J.; Lin, B. Identification three lncRNA prognostic signature of ovarian cancer based on genome-wide copy number variation. *Biomedicine & Pharmacotherapy* **2020**, *124*, 109810, doi:10.1016/j.biopha.2019.109810.
19. Loganathan, T.; Doss, C. G.P. Non-coding RNAs in human health and disease: potential function as biomarkers and therapeutic targets. *Funct Integr Genomics* **2023**, *23*, 33, doi:10.1007/s10142-022-00947-4.
20. Qian, Y.; Shi, L.; Luo, Z. Long Non-coding RNAs in Cancer: Implications for Diagnosis, Prognosis, and Therapy. *Front Med (Lausanne)* **2020**, *7*, 612393, doi:10.3389/fmed.2020.612393.
21. Karakas, D.; Ozpolat, B. The Role of lncRNAs in Translation. *Noncoding RNA* **2021**, *7*, 16, doi:10.3390/ncrna7010016.
22. Gao, N.; Li, Y.; Li, J.; Gao, Z.; Yang, Z.; Li, Y.; Liu, H.; Fan, T. Long Non-Coding RNAs: The Regulatory Mechanisms, Research Strategies, and Future Directions in Cancers. *Front Oncol* **2020**, *10*, 598817, doi:10.3389/fonc.2020.598817.
23. Taniue, K.; Akimitsu, N. The Functions and Unique Features of lncRNAs in Cancer Development and Tumorigenesis. *Int J Mol Sci* **2021**, *22*, 632, doi:10.3390/ijms22020632.
24. Bridges, M.C.; Daulagala, A.C.; Kourtidis, A. LNCcation: lncRNA localization and function. *J Cell Biol* **2021**, *220*, e202009045, doi:10.1083/jcb.202009045.
25. Wei, C.; Xu, Y.; Shen, Q.; Li, R.; Xiao, X.; Saw, P.E.; Xu, X. Role of long non-coding RNAs in cancer: From subcellular localization to nanoparticle-mediated targeted regulation. *Molecular Therapy - Nucleic Acids* **2023**, *33*, 774-793, doi:10.1016/j.omtn.2023.07.009.
26. Kazimierczyk, M.; Kasproicz, M.K.; Kasprzyk, M.E.; Wrzesinski, J. Human Long Noncoding RNA Interactome: Detection, Characterization and Function. *Int J Mol Sci* **2020**, *21*, 1027, doi:10.3390/ijms21031027.
27. Ruan, X.; Li, P.; Chen, Y.; Shi, Y.; Pirooznia, M.; Seifuddin, F.; Suemizu, H.; Ohnishi, Y.; Yoneda, N.; Nishiwaki, M., et al. In vivo functional analysis of non-conserved human lncRNAs associated with cardiometabolic traits. *Nat Commun* **2020**, *11*, doi:10.1038/s41467-019-13688-z.
28. Huang, W.; Xiong, T.; Zhao, Y.; Heng, J.; Han, G.; Wang, P.; Zhao, Z.; Shi, M.; Li, J.; Wang, J., et al. Computational prediction and experimental validation identify functionally conserved lncRNAs from zebrafish to human. *Nature Genetics* **2024**, *56*, 124-135, doi:10.1038/s41588-023-01620-7.
29. Derrien, T.; Johnson, R.; Bussotti, G.; Tanzer, A.; Djebali, S.; Tilgner, H.; Guernec, G.; Martin, D.; Merkel, A.; Knowles, D.G., et al. The GENCODE v7 catalog of human long noncoding RNAs: Analysis of their gene structure, evolution, and expression. *Genome Res.* **2012**, *22*, 1775-1789, doi:10.1101/gr.132159.111.
30. Cruz, J.A.; Westhof, E. The Dynamic Landscapes of RNA Architecture. *Cell* **2009**, *136*, 604-609, doi:10.1016/j.cell.2009.02.003.
31. Wilusz, J.E.; JnBaptiste, C.K.; Lu, L.Y.; Kuhn, C.-D.; Joshua-Tor, L.; Sharp, P.A. A triple helix stabilizes the 3' ends of long noncoding RNAs that lack poly(A) tails. *Genes Dev.* **2012**, *26*, 2392-2407, doi:10.1101/gad.204438.112.
32. Jones, A.N.; Tikhiaia, E.; Mourao, A.; Sattler, M. Structural effects of m6A modification of the Xist A-repeat AUCG tetraloop and its recognition by YTHDC1. *Nucleic Acids Res* **2022**, *50*, 2350-2362, doi:10.1093/nar/gkac080.



33. Lu, Z.; Guo, J.K.; Wei, Y.; Dou, D.R.; Zarnegar, B.; Ma, Q.; Li, R.; Zhao, Y.; Liu, F.; Choudhry, H., et al. Structural modularity of the XIST ribonucleoprotein complex. *Nat Commun* **2020**, *11*, 6163, doi:10.1038/s41467-020-20040-3.
34. Frank, F.; Kavousi, N.; Bountali, A.; Dammer, E.B.; Mourtada-Maarabouni, M.; Ortlund, E.A. The lncRNA Growth Arrest Specific 5 Regulates Cell Survival via Distinct Structural Modules with Independent Functions. *Cell Reports* **2020**, *32*, 107933, doi:10.1016/j.celrep.2020.107933.
35. Somarowthu, S.; Legiewicz, M.; Chillón, I.; Marcia, M.; Liu, F.; Pyle, A.M. HOTAIR Forms an Intricate and Modular Secondary Structure. *Molecular Cell* **2015**, *58*, 353-361, doi:10.1016/j.molcel.2015.03.006.
36. Mou, X.; Liew, S.W.; Kwok, C.K. Identification and targeting of G-quadruplex structures in MALAT1 long non-coding RNA. *Nucleic Acids Research* **2022**, *50*, 397-410, doi:10.1093/nar/gkab1208.
37. Lin, Y.; Schmidt, B.F.; Bruchez, M.P.; McManus, C.J. Structural analyses of NEAT1 lncRNAs suggest long-range RNA interactions that may contribute to paraspeckle architecture. *Nucleic Acids Research* **2018**, *46*, 3742-3752, doi:10.1093/nar/gky046.
38. Simko, E.A.J.; Liu, H.; Zhang, T.; Velasquez, A.; Teli, S.; Haeusler, A.R.; Wang, J. G-quadruplexes offer a conserved structural motif for NONO recruitment to NEAT1 architectural lncRNA. *Nucleic Acids Research* **2020**, *48*, 10.1093/nar/gkaa475, doi:10.1093/nar/gkaa475.
39. Hirose, T.; Yamazaki, T.; Nakagawa, S. Molecular anatomy of the architectural NEAT1 noncoding RNA: The domains, interactors, and biogenesis pathway required to build phase-separated nuclear paraspeckles. *WIREs RNA* **2019**, *10*, e1545, doi:10.1002/wrna.1545.
40. Arora, R.; Lee, Y.; Wischniewski, H.; Brun, C.M.; Schwarz, T.; Azzalin, C.M. RNaseH1 regulates TERRA-telomeric DNA hybrids and telomere maintenance in ALT tumour cells. *Nat Commun* **2014**, *5*, 5220, doi:10.1038/ncomms6220.
41. Hirashima, K.; Seimiya, H. Telomeric repeat-containing RNA/G-quadruplex-forming sequences cause genome-wide alteration of gene expression in human cancer cells in vivo. *Nucleic Acids Research* **2015**, *43*, 2022-2032, doi:10.1093/nar/gkv063.
42. Uroda, T.; Chillón, I.; Annibale, P.; Teulon, J.-M.; Pessey, O.; Karuppasamy, M.; Pellequer, J.-L.; Marcia, M. Visualizing the functional 3D shape and topography of long noncoding RNAs by single-particle atomic force microscopy and in-solution hydrodynamic techniques. *Nat Protoc* **2020**, *15*, 2107-2139, doi:10.1038/s41596-020-0323-7.
43. Robinson, E.K.; Covarrubias, S.; Carpenter, S. The how and why of lncRNA function: An innate immune perspective. *Biochim Biophys Acta Gene Regul Mech* **2020**, *1863*, 194419, doi:10.1016/j.bbagr.2019.194419.
44. Yu, J.; Han, Q.; Cui, Y. Decreased long non-coding RNA SPRY4-IT1 contributes to ovarian cancer cell metastasis partly via affecting epithelial-mesenchymal transition. *Tumor Biology* **2017**, *39*, 101042831770912, doi:10.1177/1010428317709129.
45. Ma, L.; Bajic, V.B.; Zhang, Z. On the classification of long non-coding RNAs. *RNA Biol* **2013**, *10*, 924-933, doi:10.4161/rna.24604.
46. Wang, Y.; Huang, Y.; Liu, H.; Su, D.; Luo, F.; Zhou, F. Long noncoding RNA CDKN2B-AS1 interacts with miR-411-3p to regulate ovarian cancer *in vitro* and *in vivo* through HIF-1 $\alpha$ /VEGF/P38 pathway. *Biochemical and Biophysical Research Communications* **2019**, *514*, 44-50, doi:10.1016/j.bbrc.2019.03.141.
47. Yu, X.; Zhao, P.; Luo, Q.; Wu, X.; Wang, Y.; Nan, Y.; Liu, S.; Gao, W.; Li, B.; Liu, Z.; Cui, Z. RUNX1-IT1 acts as a scaffold of STAT1 and NuRD complex to promote ROS-mediated NF- $\kappa$ B activation and ovarian cancer progression. *Oncogene* **2024**, *43*, 420-433, doi:10.1038/s41388-023-02910-4.
48. Aliperti, V.; Skonieczna, J.; Cerase, A. Long Non-Coding RNA (lncRNA) Roles in Cell Biology, Neurodevelopment and Neurological Disorders. *Noncoding RNA* **2021**, *7*, 36, doi:10.3390/ncrna7020036.
49. Avgeris, M.; Tsilimantou, A.; Levis, P.K.; Tokas, T.; Sideris, D.C.; Stravodimos, K.; Ardavanis, A.; Scorilas, A. Loss of GAS5 tumour suppressor lncRNA: an independent molecular cancer biomarker for short-term relapse and progression in bladder cancer patients. *Br J Cancer* **2018**, *119*, 1477-1486, doi:10.1038/s41416-018-0320-6.
50. Lin, G.; Wu, T.; Gao, X.; He, Z.; Nong, W. Research Progress of Long Non-Coding RNA GAS5 in Malignant Tumors. *Front Oncol* **2022**, *12*, doi:10.3389/fonc.2022.846497.

51. Long, X.; Song, K.; Hu, H.; Tian, Q.; Wang, W.; Dong, Q.; Yin, X.; Di, W. Long non-coding RNA GAS5 inhibits DDP-resistance and tumor progression of epithelial ovarian cancer via GAS5-E2F4-PARP1-MAPK axis. *J Exp Clin Cancer Res* **2019**, *38*, 345, doi:10.1186/s13046-019-1329-2.
52. Zhang, T.; Leng, Y.; Duan, M.; Li, Z.; Ma, Y.; Huang, C.; Shi, Q.; Wang, Y.; Wang, C.; Liu, D., et al. LncRNA GAS5-hnRNPK axis inhibited ovarian cancer progression via inhibition of AKT signaling in ovarian cancer cells. *Discov Oncol* **2023**, *14*, 157, doi:10.1007/s12672-023-00764-6.
53. Gao, J.; Liu, M.; Zou, Y.; Mao, M.; Shen, T.; Zhang, C.; Song, S.; Sun, M.; Zhang, S.; Wang, B., et al. Long non-coding RNA growth arrest-specific transcript 5 is involved in ovarian cancer cell apoptosis through the mitochondria-mediated apoptosis pathway. *Oncol Rep* **2015**, *34*, 3212-3221, doi:10.3892/or.2015.4318.
54. Musahl, A.S.; Huang, X.; Rusakiewicz, S.; Ntini, E.; Marsico, A.; Kroemer, G.; Kepp, O.; Ørom, U.A. A long non-coding RNA links calreticulin-mediated immunogenic cell removal to RB1 transcription. *Oncogene* **2015**, *34*, 5046-5054, doi:10.1038/onc.2014.424.
55. Kopp, F.; Mendell, J.T. Functional Classification and Experimental Dissection of Long Noncoding RNAs. *Cell* **2018**, *172*, 393-407, doi:10.1016/j.cell.2018.01.011.
56. Pandey, R.R.; Mondal, T.; Mohammad, F.; Enroth, S.; Redrup, L.; Komorowski, J.; Nagano, T.; Mancini-DiNardo, D.; Kanduri, C. Kcnq1ot1 Antisense Noncoding RNA Mediates Lineage-Specific Transcriptional Silencing through Chromatin-Level Regulation. *Molecular Cell* **2008**, *32*, 232-246, doi:10.1016/j.molcel.2008.08.022.
57. Wang, K.C.; Yang, Y.W.; Liu, B.; Sanyal, A.; Corces-Zimmerman, R.; Chen, Y.; Lajoie, B.R.; Protacio, A.; Flynn, R.A.; Gupta, R.A., et al. A long noncoding RNA maintains active chromatin to coordinate homeotic gene expression. *Nature* **2011**, *472*, 120-124, doi:10.1038/nature09819.
58. Blank-Giwojna, A.; Postepska-Igielska, A.; Grummt, I. lncRNA KHPS1 Activates a Poised Enhancer by Triplex-Dependent Recruitment of Epigenomic Regulators. *Cell Reports* **2019**, *26*, 2904-2915.e2904, doi:10.1016/j.celrep.2019.02.059.
59. Niu, Z.-S.; Wang, W.-H.; Dong, X.-N.; Tian, L.-M.-L. Role of long noncoding RNA-mediated competing endogenous RNA regulatory network in hepatocellular carcinoma. *World J Gastroenterol* **2020**, *26*, 4240-4260, doi:10.3748/wjg.v26.i29.4240.
60. Ha, J.H.; Radhakrishnan, R.; Nadhan, R.; Gomathinayagam, R.; Jayaraman, M.; Yan, M.; Kashyap, S.; Fung, K.-M.; Xu, C.; Bhattacharya, R., et al. Deciphering a GPCR-lncrna-miRNA nexus: Identification of an aberrant therapeutic target in ovarian cancer. *Cancer Letters* **2024**, *591*, 216891, doi:10.1016/j.canlet.2024.216891.
61. Dong, B.; Li, C.; Xu, X.; Wang, Y.; Li, Y.; Li, X. LncRNA LINC01123 promotes malignancy of ovarian cancer by targeting hsa-miR-516b-5p/VEGFA. *Genes & Genomics* **2024**, *46*, 231-239, doi:10.1007/s13258-023-01440-3.
62. Zhang, X.; Wang, W.; Zhu, W.; Dong, J.; Cheng, Y.; Yin, Z.; Shen, F. Mechanisms and Functions of Long Non-Coding RNAs at Multiple Regulatory Levels. *Int J Mol Sci* **2019**, *20*, doi:10.3390/ijms20225573.
63. Lin, X.; Spindler, T.J.; De Souza Fonseca, M.A.; Corona, R.I.; Seo, J.-H.; Dezem, F.S.; Li, L.; Lee, J.M.; Long, H.W.; Sellers, T.A., et al. Super-Enhancer-Associated LncRNA UCA1 Interacts Directly with AMOT to Activate YAP Target Genes in Epithelial Ovarian Cancer. *iScience* **2019**, *17*, 242-255, doi:10.1016/j.isci.2019.06.025.
64. Mattick, J.S.; Amaral, P.P.; Carninci, P.; Carpenter, S.; Chang, H.Y.; Chen, L.-L.; Chen, R.; Dean, C.; Dinger, M.E.; Fitzgerald, K.A., et al. Long non-coding RNAs: definitions, functions, challenges and recommendations. *Nature Reviews Molecular Cell Biology* **2023**, *24*, 430-447, doi:10.1038/s41580-022-00566-8.
65. Dai, L.; Niu, J.; Feng, Y. Knockdown of long non-coding RNA LINC00176 suppresses ovarian cancer progression by BCL3-mediated down-regulation of ceruloplasmin. *Journal of Cellular and Molecular Medicine* **2020**, *24*, 202-213, doi:10.1111/jcmm.14701.
66. Wang, T.; Li, J.; Yang, L.; Wu, M.; Ma, Q. The Role of Long Non-coding RNAs in Human Imprinting Disorders: Prospective Therapeutic Targets. *Front. Cell Dev. Biol.* **2021**, *9*, doi:10.3389/fcell.2021.730014.
67. Monnier, P.; Martinet, C.; Pontis, J.; Stancheva, I.; Ait-Si-Ali, S.; Dandolo, L. H19 lncRNA controls gene expression of the Imprinted Gene Network by recruiting MBD1. *Proc Natl Acad Sci U S A* **2013**, *110*, 20693-20698, doi:10.1073/pnas.1310201110.

68. Tian, X.; Zuo, X.; Hou, M.; Li, C.; Teng, Y. LncRNA-H19 regulates chemoresistance to carboplatin in epithelial ovarian cancer through microRNA-29b-3p and STAT3. *J Cancer* **2021**, *12*, 5712-5722, doi:10.7150/jca.58979.
69. Wang, K.C.; Chang, H.Y. Molecular Cell Review Molecular Mechanisms of Long Noncoding RNAs. *Molecular Cell* **2011**, *43*, 904-914, doi:10.1016/j.molcel.2011.08.018.
70. Fang, Y.; Fullwood, M.J. Roles, Functions, and Mechanisms of Long Non-coding RNAs in Cancer. *Genomics, Proteomics & Bioinformatics* **2016**, *14*, 42-54, doi:10.1016/j.gpb.2015.09.006.
71. Gordon, M.A.; Babbs, B.; Cochrane, D.R.; Bitler, B.G.; Richer, J.K. The long non-coding RNA MALAT1 promotes ovarian cancer progression by regulating RBFOX2-mediated alternative splicing. *Molecular Carcinogenesis* **2019**, *58*, 196-205, doi:10.1002/mc.22919.
72. Zhang, Y.; Zhang, J.; Wang, F.; Wang, L. Hypoxia-Related lncRNA Prognostic Model of Ovarian Cancer Based on Big Data Analysis. *J Oncol* **2023**, *2023*, 6037121, doi:10.1155/2023/6037121.
73. Guzel, E.; Okyay, T.M.; Yalcinkaya, B.; Karacaoglu, S.; Gocmen, M.; Akcakuyu, M.H. Tumor suppressor and oncogenic role of long non-coding RNAs in cancer. *North Clin Istanb* **2019**, *7*, 81-86, doi:10.14744/nci.2019.46873.
74. Palazzo, A.F.; Lee, E.S. Non-coding RNA: what is functional and what is junk? *Frontiers in Genetics* **2015**, *6*.
75. Calanca, N.; Abildgaard, C.; Rainho, C.A.; Rogatto, S.R. The Interplay between Long Noncoding RNAs and Proteins of the Epigenetic Machinery in Ovarian Cancer. *Cancers (Basel)* **2020**, *12*, 2701, doi:10.3390/cancers12092701.
76. Cai, L.; Hu, X.; Ye, L.; Bai, P.; Jie, Y.; Shu, K. Long non-coding RNA ADAMTS9-AS1 attenuates ferroptosis by Targeting microRNA-587/solute carrier family 7 member 11 axis in epithelial ovarian cancer. *Bioengineered* **2022**, *13*, 8226-8239, doi:10.1080/21655979.2022.2049470.
77. Kong, Y.; Hsieh, C.-H.; Alonso, L.C. ANRIL: A lncRNA at the CDKN2A/B Locus With Roles in Cancer and Metabolic Disease. *Front Endocrinol (Lausanne)* **2018**, *9*, 405, doi:10.3389/fendo.2018.00405.
78. Yuan, D.; Guo, T.; Zhu, D.; Ge, H.; Zhao, Y.; Huang, A.; Wang, X.; Cao, X.; He, C.; Qian, H.; Yu, H. Exosomal lncRNA ATB Derived from Ovarian Cancer Cells Promotes Angiogenesis via Regulating miR-204-3p/TGF $\beta$ R2 Axis. *Cancer Manag Res* **2022**, *14*, 327-337, doi:10.2147/CMAR.S330368.
79. Yu, G.; Wang, W.; Deng, J.; Dong, S. LncRNA AWPPH promotes the proliferation, migration and invasion of ovarian carcinoma cells via activation of the Wnt/ $\beta$ -catenin signaling pathway. *Molecular Medicine Reports* **2019**, *49*, 3615-3621, doi:10.3892/mmr.2019.10029.
80. Wang, D.-Y.; Li, N.; Cui, Y.-L. Long Non-coding RNA CCAT1 Sponges miR-454 to Promote Chemoresistance of Ovarian Cancer Cells to Cisplatin by Regulation of Surviving. *Cancer Res Treat* **2020**, *52*, 798-814, doi:10.4143/crt.2019.498.
81. Mu, Y.; Li, N.; Cui, Y.L. The lncRNA CCAT1 upregulates TGF $\beta$ R1 via sponging miR-490-3p to promote TGF $\beta$ 1-induced EMT of ovarian cancer cells. *Cancer Cell International* **2018**, *18*, 1-12, doi:10.1186/S12935-018-0604-1/FIGURES/6.
82. Cao, Y.; Shi, H.; Ren, F.; Jia, Y.; Zhang, R. Long non-coding RNA CCAT1 promotes metastasis and poor prognosis in epithelial ovarian cancer. *Experimental Cell Research* **2017**, *359*, 185-194, doi:10.1016/j.YEXCR.2017.07.030.
83. Lai, X.J.; Cheng, H.F. LncRNA colon cancer-associated transcript 1 (CCAT1) promotes proliferation and metastasis of ovarian cancer via miR-1290. *European Review for Medical and Pharmacological Sciences* **2018**, *22*, 322-328, doi:10.26355/eurrev\_201801\_14175.
84. Hua, F.; Li, C.-H.; Chen, X.-G.; Liu, X.-P. Long Noncoding RNA CCAT2 Knockdown Suppresses Tumorous Progression by Sponging miR-424 in Epithelial Ovarian Cancer. *Oncol Res* **2018**, *26*, 241-247, doi:10.3727/096504017X14953948675412.
85. Chen, Z.; Zhu, Y.; Fan, X.; Liu, Y.; Feng, Q. Upregulation of long non-coding RNA CCEPR is associated with poor prognosis and contributes to the progression of ovarian cancer through regulating the Wnt/ $\beta$ -catenin signaling pathway. *Molecular Medicine Reports* **2020**, *21*, 1950-1958, doi:10.3892/mmr.2020.10979.

86. Tan, W.-X.; Sun, G.; Shangguan, M.-Y.; Gui, Z.; Bao, Y.; Li, Y.-F.; Jia, Z.-H. Novel role of lncRNA CHRF in cisplatin resistance of ovarian cancer is mediated by miR-10b induced EMT and STAT3 signaling. *Sci Rep* **2020**, *10*, 14768, doi:10.1038/s41598-020-71153-0.
87. Wang, Q.; Wang, L.-X.; Zhang, C.-Y.; Bai, N.; Feng, C.; Zhang, Z.-M.; Wang, L.; Gao, Z.-Z. LncRNA CRNDE promotes cell proliferation, migration and invasion of ovarian cancer via miR-423-5p/FSCN1 axis. *Mol Cell Biochem* **2022**, *477*, 1477-1488, doi:10.1007/s11010-022-04382-8.
88. Wu, J.; Ni, X.; Yu, Z.; Wu, S.; Liu, Z. CRNDE inducing cisplatin resistance through SRSF1/TIA1 signaling pathway in ovarian cancer. *Pathology - Research and Practice* **2022**, *235*, 153957, doi:10.1016/j.prp.2022.153957.
89. Huang, P.; Qi, B.; Yao, H.; Zhang, L.; Li, Y.; Li, Q. Knockdown of DANCER Suppressed the Biological Behaviors of Ovarian Cancer Cells Treated with Transforming Growth Factor- $\beta$  (TGF- $\beta$ ) by Sponging MiR-214. *Medical Science Monitor : International Medical Journal of Experimental and Clinical Research* **2020**, *26*, e922760, doi:10.12659/MSM.922760.
90. Zhang, Q.; Wang, W.W.; Xu, T.H.; Xu, Z.F. Highly expressed long non-coding RNA DUXAP10 promotes proliferation of ovarian cancer. *European Review for Medical and Pharmacological Sciences* **2018**, *22*, 314-321, doi:10.26355/eurev\_201801\_14174.
91. Xu, Q.F.; Tang, Y.X.; Wang, X. LncRNA EBIC promoted proliferation, metastasis and cisplatin resistance of ovarian cancer cells and predicted poor survival in ovarian cancer patients. *European Review for Medical and Pharmacological Sciences* **2018**, *22*, 4440-4447, doi:10.26355/eurev\_201807\_15495.
92. Qiu, J.J.; Zhang, X.D.; Tang, X.Y.; Zheng, T.T.; Zhang, Y.; Hua, K.Q. ElncRNA1, a long non-coding RNA that is transcriptionally induced by oestrogen, promotes epithelial ovarian cancer cell proliferation. *International Journal of Oncology* **2017**, *51*, 507-514, doi:10.3892/ijo.2017.4030.
93. Yan, H.; Li, H.; Silva, M.A.; Guan, Y.; Yang, L.; Zhu, L.; Zhang, Z.; Li, G.; Ren, C. LncRNA FLVCR1-AS1 mediates miR-513/YAP1 signaling to promote cell progression, migration, invasion and EMT process in ovarian cancer. *Journal of Experimental & Clinical Cancer Research* **2019**, *38*, 356, doi:10.1186/s13046-019-1356-z.
94. Zheng, Z.-G.; Xu, H.; Suo, S.-S.; Xu, X.-L.; Ni, M.-W.; Gu, L.-H.; Chen, W.; Wang, L.-Y.; Zhao, Y.; Tian, B.; Hua, Y.-J. The Essential Role of H19 Contributing to Cisplatin Resistance by Regulating Glutathione Metabolism in High-Grade Serous Ovarian Cancer. *Sci Rep* **2016**, *6*, 26093, doi:10.1038/srep26093.
95. Tong, L.; Wang, Y.; Ao, Y.; Sun, X. CREB1 induced lncRNA HAS2-AS1 promotes epithelial ovarian cancer proliferation and invasion via the miR-466/RUNX2 axis. **2019**, 10.1016/j.biopha.2019.108891, doi:10.1016/j.biopha.2019.108891.
96. Zhang, F.; Luo, B.-H.; Wu, Q.-H.; Li, Q.-L.; Yang, K.-D. LncRNA HCG18 upregulates TRAF4/TRAF5 to facilitate proliferation, migration and EMT of epithelial ovarian cancer by targeting miR-29a/b. *Mol Med* **2022**, *28*, 2, doi:10.1186/s10020-021-00415-y.
97. Shen, X.; Wang, D.; Chen, X.; Peng, J. Propofol inhibits proliferation, migration, invasion and promotes apoptosis by regulating HOST2/JAK2/STAT3 signaling pathway in ovarian cancer cells. *Cytotechnology* **2021**, *73*, 243-252, doi:10.1007/s10616-021-00462-7.
98. Zhang, Y.; Ai, H.; Fan, X.; Chen, S.; Wang, Y.; Liu, L. Knockdown of long non-coding RNA HOTAIR reverses cisplatin resistance of ovarian cancer cells through inhibiting miR-138-5p-regulated EZH2 and SIRT1. *Biological Research* **2020**, *53*, 18, doi:10.1186/s40659-020-00286-3.
99. Chen, Y.; Cui, Z.; Wu, Q.; Wang, H.; Xia, H.; Sun, Y. Long non-coding RNA HOXA11-AS knockout inhibits proliferation and overcomes drug resistance in ovarian cancer. *Bioengineered* **2022**, *13*, 13893-13905, doi:10.1080/21655979.2022.2086377.
100. Dong, S.; Wang, R.; Wang, H.; Ding, Q.; Zhou, X.; Wang, J.; Zhang, K.; Long, Y.; Lu, S.; Hong, T., et al. HOXD-AS1 promotes the epithelial to mesenchymal transition of ovarian cancer cells by regulating miR-186-5p and PIK3R3. *J Exp Clin Cancer Res* **2019**, *38*, 110, doi:10.1186/s13046-019-1103-5.
101. Zhang, Y.; Dun, Y.; Zhou, S.; Huang, X.H. LncRNA HOXD-AS1 promotes epithelial ovarian cancer cells proliferation and invasion by targeting miR-133a-3p and activating Wnt/ $\beta$ -catenin signaling pathway. *Biomedicine & Pharmacotherapy* **2017**, *96*, 1216-1221, doi:10.1016/J.BIOPHA.2017.11.096.
102. Wang, Y.; Zhang, W.; Wang, Y.; Wang, S. HOXD-AS1 promotes cell proliferation, migration and invasion through miR-608/FZD4 axis in ovarian cancer. *Am J Cancer Res* **2018**, *8*, 170-182.



103. Huang, B.; Wei, M.; Hong, L. Long noncoding RNA HULC contributes to paclitaxel resistance in ovarian cancer via miR-137/ITGB8 axis. *Open Life Sciences* **2021**, *16*, 667-681, doi:10.1515/biol-2021-0058.
104. Lu, X.; Wang, F.; Fu, M.; Li, Y.; Wang, L. Long Noncoding RNA KCNQ1OT1 Accelerates the Progression of Ovarian Cancer via MicroRNA-212-3/LCN2 Axis. *Oncol Res* **2020**, *28*, 135, doi:10.3727/096504019X15719983040135.
105. Li, J.; Zhang, S.; Wu, L.; Pei, M. Interaction between LncRNA-ROR and miR-145 contributes to epithelial-mesenchymal transition of ovarian cancer cells. | General Physiology & Biophysics | EBSCOhost. **2019**.
106. Zou, H.; Li, H. Knockdown of long non-coding RNA LINC00152 increases cisplatin sensitivity in ovarian cancer cells. *Experimental and Therapeutic Medicine* **2019**, *10*, 3892/etm.2019.8066, doi:10.3892/etm.2019.8066.
107. Wang, S.; Weng, W.; Chen, T.; Xu, M.; Wei, P.; Li, J.; Lu, L.; Wang, Y. LINC00152 Promotes Tumor Progression and Predicts Poor Prognosis by Stabilizing BCL6 From Degradation in the Epithelial Ovarian Cancer. *Front Oncol* **2020**, *10*, doi:10.3389/fonc.2020.555132.
108. Chen, P.; Fang, X.; Xia, B.; Zhao, Y.; Li, Q.; Wu, X. Long noncoding RNA LINC00152 promotes cell proliferation through competitively binding endogenous miR-125b with MCL-1 by regulating mitochondrial apoptosis pathways in ovarian cancer. *Cancer Medicine* **2018**, *7*, 4530-4541, doi:10.1002/cam4.1547.
109. Ni, H.; Niu, L.L.; Tian, S.C.; Jing, L.K.; Zhang, L.T.; Lin, Q.Q.; Cai, Y.H.; Liang, H.M.; Du, Q.; Li, H. Long non-coding RNA LINC00152 is up-regulated in ovarian cancer tissues and regulates proliferation and cell cycle of SKOV3 cells. *European Review for Medical and Pharmacological Sciences* **2019**, *23*, 9803-9813, doi:10.26355/eurrev\_201911\_19543.
110. Han, Y.; You, J.; Han, Y.; Liu, Y.; Huang, M.; Lu, X.; Chen, J.; Zheng, Y. LINC00184 Promotes Ovarian Cancer Cells Proliferation and Cisplatin Resistance by Elevating CNTN1 Expression via Sponging miR-1305. *OncoTargets and Therapy* **2021**, *14*, 2711-2726, doi:10.2147/OTT.S280490.
111. Du, W.; Feng, Z.; Sun, Q. LncRNA LINC00319 accelerates ovarian cancer progression through miR-423-5p/NACC1 pathway. *Biochemical and Biophysical Research Communications* **2018**, *507*, 198-202, doi:10.1016/j.bbrc.2018.11.006.
112. Wang, K.; Zhu, G.; Bao, S.; Chen, S. Long Non-Coding RNA LINC00511 Mediates the Effects of ESR1 on Proliferation and Invasion of Ovarian Cancer Through miR-424-5p and miR-370-5p. *Cancer Manag Res* **2019**, *11*, 10807-10819, doi:10.2147/CMAR.S232140.
113. Xu, D.; Song, Q.; Liu, Y.; Chen, W.; Xu, M.; Fang, X.; Zhao, W.; Zhou, H. LINC00665 promotes Ovarian Cancer progression through regulating the miRNA-34a-5p/E2F3 axis. *J Cancer* **2021**, *12*, 1755-1763, doi:10.7150/jca.51457.
114. Wang, S.; Wang, Y.; Lu, J.; Wang, J. LncRNA LINC00665 Promotes Ovarian Cancer Cell Proliferation and Inhibits Apoptosis via Targeting MiR-181a-5p/FHDC. **2021**, 10.21203/rs.3.rs-389237/v2, doi:10.21203/rs.3.rs-389237/v2.
115. Wang, S.; Liu, C.; Li, Y.; Qiao, J.; Chen, X.; Bao, J.; Li, R.; Xing, Y. LINC00665 affects the malignant biological behavior of ovarian cancer via the miR-148b-3p/KLF5. *Systems Biology in Reproductive Medicine* **2022**, *68*, 370-383, doi:10.1080/19396368.2022.2101961.
116. Lin, X.; Li, P.; Feng, D.; Zheng, J.; Chen, G.; Wu, X.; Dong, Z.; Lv, Y. Regulation of Transcription Factor YAP-TEAD by Non-coding RNA LINC00857 and the Inhibitory Effects on Ovarian Cancer Cell Proliferation. *Cellular and Molecular Biology* **2022**, *68*, 162-170, doi:10.14715/cmb/2022.68.2.23.
117. Lin, X.; Feng, D.; Li, P.; Lv, Y. LncRNA LINC00857 regulates the progression and glycolysis in ovarian cancer by modulating the Hippo signaling pathway. *Cancer Medicine* **2020**, *9*, 8122-8132, doi:10.1002/cam4.3322.
118. Xue, H.; Wu, Z.; Rao, D.; Zhuo, B.; Chen, Q. Long non-coding RNA LINC00858 aggravates the oncogenic phenotypes of ovarian cancer cells through miR-134-5p/RAD18 signaling. *Arch Gynecol Obstet* **2020**, *302*, 1243-1254, doi:10.1007/s00404-020-05722-z.
119. Xie, M.; Fu, Q.; Wang, P.P.; Cui, Y.L. STAT1-Induced Upregulation lncRNA LINC00958 Accelerates the Epithelial Ovarian Cancer Tumorigenesis by Regulating Wnt/ $\beta$ -Catenin Signaling. *Disease Markers* **2021**, *2021*, doi:10.1155/2021/1405045.



120. Yao, N.; Sun, J.Q.; Yu, L.; Ma, L.; Guo, B.Q. LINC00968 accelerates the progression of epithelial ovarian cancer via mediating the cell cycle progression. *European Review for Medical and Pharmacological Sciences* **2019**, *23*, 4642-4649, doi:10.26355/eurev\_201906\_18043.
121. Li, Y.; Zhai, Y.; Chen, Y. GATA1-induced upregulation of LINC01503 promotes carboplatin resistance in ovarian carcinoma by upregulating PD-L1 via sponging miR-766-5p. *Journal of ovarian research* **2021**, *14*, doi:10.1186/S13048-021-00856-3.
122. Shu, C.; Yan, D.; Mo, Y.; Gu, J.; Shah, N.; He, J. Long noncoding RNA lncARSR promotes epithelial ovarian cancer cell proliferation and invasion by association with HuR and miR-200 family. *Am J Cancer Res* **2018**, *8*, 981-992.
123. Xi, J.; Feng, J.; Zeng, S. Long noncoding RNA lncBRM facilitates the proliferation, migration and invasion of ovarian cancer cells via upregulation of Sox4. *Am J Cancer Res* **2017**, *7*, 2180-2189.
124. Qiao, F.-H.; Tu, M.; Liu, H.-Y. Role of MALAT1 in gynecological cancers: Pathologic and therapeutic aspects. *Oncol Lett* **2021**, *21*, 333, doi:10.3892/ol.2021.12594.
125. Zhou, S.; Xu, A.; Song, T.; Gao, F.; Sun, H.; Kong, X. lncRNA MIAT Regulates Cell Growth, Migration, and Invasion Through Sponging miR-150-5p in Ovarian Cancer. *Cancer Biotherapy and Radiopharmaceuticals* **2020**, *35*, 650-660, doi:10.1089/cbr.2019.3259.
126. Fan, Y.; Wang, L.; Han, X.C.; Ma, H.Y.; Zhang, N.; Zhe, L. LncRNA MIF-AS1 aggravates the progression of ovarian cancer by sponging miRNA-31-5p. *European Review for Medical and Pharmacological Sciences* **2020**, *24*, 2248-2255, doi:10.26355/eurev\_202003\_20490.
127. Shen, Y.; Lv, M.; Fang, Y.; Lu, J.; Wu, Y. LncRNA MNX1-AS1 promotes ovarian cancer process via targeting the miR-744-5p/SOX12 axis. *Journal of Ovarian Research* **2021**, *14*, 161, doi:10.1186/s13048-021-00910-0.
128. Yin, L.; Wang, Y. Long non-coding RNA NEAT1 facilitates the growth, migration, and invasion of ovarian cancer cells via the let-7 g/MEST/ATGL axis. *Cancer Cell International* **2021**, *21*, 437, doi:10.1186/s12935-021-02018-3.
129. Zhu, M.; Yang, L.; Wang, X. NEAT1 Knockdown Suppresses the Cisplatin Resistance in Ovarian Cancer by Regulating miR-770-5p/PARP1 Axis. *Cancer Manag Res* **2020**, *12*, 7277-7289, doi:10.2147/CMAR.S257311.
130. Tao, F.; Tian, X.; Lu, M.; Zhang, Z. A novel lncRNA, lnc-OC1, promotes ovarian cancer cell proliferation and migration by sponging miR-34a and miR-34c. *Journal of Genetics and Genomics* **2018**, *45*, 137-145, doi:10.1016/j.jgg.2018.03.001.
131. Tabury, K.; Monavarian, M.; Listik, E.; Shelton, A.K.; Choi, A.S.; Quintens, R.; Arend, R.C.; Hempel, N.; Miller, C.R.; Györrfy, B.; Myhre, K. PVT1 is a stress-responsive lncRNA that drives ovarian cancer metastasis and chemoresistance. *Life Sci. Alliance* **2022**, *5*, e202201370, doi:10.26508/lisa.202201370.
132. Wang, S.; Jiang, J.; Wang, Z.; Xie, Y.; Wu, X. Long non-coding RNA SNHG1 is an unfavorable prognostic factor and promotes cell proliferation and migration by Wnt/ $\beta$ -catenin pathway in epithelial ovarian cancer. *International Journal of Clinical and Experimental Pathology* **2017**, *10*, 9284.
133. Wu, Y.; Zhu, B.; Yan, Y.; Bai, S.; Kang, H.; Zhang, J.; Ma, W.; Gao, Y.; Hui, B.; Li, R., et al. Long non-coding RNA SNHG1 stimulates ovarian cancer progression by modulating expression of miR-454 and ZEB1. *Mol Oncol* **2021**, *15*, 1584-1596, doi:10.1002/1878-0261.12932.
134. Li Pei, M.; Xia Zhao, Z.; Shuang, T. Dysregulation of lnc-SNHG1 and miR-216b-5p correlate with chemoresistance and indicate poor prognosis of serous epithelial ovarian cancer. *Journal of Ovarian Research* **2020**, *13*, 144, doi:10.1186/s13048-020-00750-4.
135. Wang, Y.; Ding, M.; Yuan, X.; Jiao, R.; Zhu, D.; Huang, W.; Deng, W.; Liu, Y. lncRNA SNHG15 Promotes Ovarian Cancer Progression through Regulated CDK6 via Sponging miR-370-3p. *BioMed Research International* **2021**, *2021*, e9394563, doi:10.1155/2021/9394563.
136. Han, L.; Zhang, W.; Zhang, B.; Zhan, L. Long non-coding RNA SOX2OT promotes cell proliferation and motility in human ovarian cancer. *Experimental and Therapeutic Medicine* **2018**, *15*, 2182-2188, doi:10.3892/etm.2017.5618.
137. Kim, L.K.; Park, S.A.; Yang, Y.; Kim, Y.T.; Heo, T.H.; Kim, H.J. LncRNA SRA mediates cell migration, invasion, and progression of ovarian cancer via NOTCH signaling and epithelial-mesenchymal transition. *Bioscience Reports* **2021**, *41*, doi:10.1042/BSR20210565.

138. Li, Y.; Jiao, Y.; Hao, J.; Xing, H.; Li, C. Long noncoding RNA TP73-AS1 accelerates the epithelial ovarian cancer via epigenetically repressing p21. *Am J Transl Res* **2019**, *11*, 2447-2454.
139. Wang, X.; Yang, B.; She, Y.; Ye, Y. The lncRNA TP73-AS1 promotes ovarian cancer cell proliferation and metastasis via modulation of MMP2 and MMP9. *Journal of Cellular Biochemistry* **2018**, *119*, 7790-7799, doi:10.1002/JCB.27158.
140. Xiuyun, L.I.; Wang, X.; Li, M.A.O.; Zhao, S.; Haidong, W.E.I. LncRNA TP73-AS1 predicts poor prognosis and promotes cell proliferation in ovarian cancer via cell cycle and apoptosis regulation. *Molecular Medicine Reports* **2018**, *18*, 516-522, doi:10.3892/mmr.2018.8951.
141. Wu, W.; Gao, H.; Li, X.; Zhu, Y.; Peng, S.; Yu, J.; Zhan, G.; Wang, J.; Liu, N.; Guo, X. LncRNA TPT1-AS1 promotes tumorigenesis and metastasis in epithelial ovarian cancer by inducing TPT1 expression. *Cancer Science* **2019**, *110*, 1587-1598, doi:10.1111/cas.14009.
142. Fan, M.; Li, C.; He, P.; Fu, Y.; Li, M.; Zhao, X. Knockdown of long noncoding RNA-taurine-upregulated gene 1 inhibits tumor angiogenesis in ovarian cancer by regulating leucine-rich  $\alpha$ -2-glycoprotein-1. *Anti-Cancer Drugs* **2019**, *30*, 562-570, doi:10.1097/CAD.0000000000000734.
143. Pei, Y.; Li, K.; Lou, X.; Wu, Y.; Dong, X.; Wang, W.; Li, N.; Zhang, D.; Cui, W. MiR-1299/NOTCH3/TUG1 feedback loop contributes to the malignant proliferation of ovarian cancer. *Oncol Rep* **2020**, *44*, 438-448, doi:10.3892/or.2020.7623.
144. Dai, T.; Liang, J.; Liu, W.; Zou, Y.; Niu, F.; Li, M.; Zhang, H.; Li, C.; Fan, M.; Cui, G. The miRNA mir-582-3p suppresses ovarian cancer progression by targeting AKT/MTOR signaling via lncRNA TUG1. *Bioengineered* **2021**, *12*, 10771-10781, doi:10.1080/21655979.2021.2003662.
145. Zhan, F.-L.; Chen, C.-F.; Yao, M.-Z. LncRNA TUG1 facilitates proliferation, invasion and stemness of ovarian cancer cell via miR-186-5p/ZEB1 axis. **2020**, 10.1002/cbf.3544, doi:10.1002/cbf.3544.
146. Gu, L.; Li, Q.; Liu, H.; Lu, X.; Zhu, M. Long Noncoding RNA TUG1 Promotes Autophagy-Associated Paclitaxel Resistance by Sponging miR-29b-3p in Ovarian Cancer Cells. **2020**, 10.2147/OTT.S240434, doi:10.2147/OTT.S240434.
147. Wambecke, A.; Ahmad, M.; Morice, P.-M.; Lambert, B.; Weiswald, L.-B.; Vernon, M.; Vigneron, N.; Abeillard, E.; Brotin, E.; Figeac, M., et al. The lncRNA 'UCA1' modulates the response to chemotherapy of ovarian cancer through direct binding to miR-27a-5p and control of UBE2N levels. *Mol Oncol* **2021**, *15*, 3659-3678, doi:10.1002/1878-0261.13045.
148. Li, Z.; Niu, H.; Qin, Q.; Yang, S.; Wang, Q.; Yu, C.; Wei, Z.; Jin, Z.; Wang, X.; Yang, A.; Chen, X. lncRNA UCA1 Mediates Resistance to Cisplatin by Regulating the miR-143/FOSL2-Signaling Pathway in Ovarian Cancer. *Molecular Therapy - Nucleic Acids* **2019**, *17*, 92-101, doi:10.1016/j.omtn.2019.05.007.
149. Zhang, J.; Quan, L.-N.; Meng, Q.; Wang, H.-Y.; Wang, J.; Yu, P.; Fu, J.-T.; Li, Y.-J.; Chen, J.; Cheng, H., et al. miR-548e Sponged by ZFAS1 Regulates Metastasis and Cisplatin Resistance of OC by Targeting CXCR4 and let-7a/BCL-XL/S Signaling Axis. *Molecular Therapy - Nucleic Acids* **2020**, *20*, 621-638, doi:10.1016/j.omtn.2020.03.013.
150. Wang, A.; Jin, C.; Li, H.; Qin, Q.; Li, L. LncRNA ADAMTS9-AS2 regulates ovarian cancer progression by targeting miR-182-5p/FOXF2 signaling pathway. *International Journal of Biological Macromolecules* **2018**, *120*, 1705-1713, doi:10.1016/j.ijbiomac.2018.09.179.
151. Yuan, J.; Liu, Z.; Song, R. Antisense lncRNA As-SLC7A11 suppresses epithelial ovarian cancer progression mainly by targeting SLC7A11. *Pharmazie* **2017**, *72*, 402-407, doi:10.1691/ph.2017.7449.
152. Xue, Z.; Zhu, X.; Teng, Y. Long non-coding RNA CASC2 inhibits progression and predicts favorable prognosis in epithelial ovarian cancer. *Molecular Medicine Reports* **2018**, *18*, 5173-5181, doi:10.3892/mmr.2018.9550.
153. Meng, Q.; Li, Z.; Pan, J.; Sun, X. Long noncoding RNA DUXAP8 regulates proliferation and apoptosis of ovarian cancer cells via targeting miR-590-5p. *Human Cell* **2020**, *33*, 1240-1251, doi:10.1007/S13577-020-00398-8/METRICS.
154. Liu, S.; Zou, B.; Tian, T.; Luo, X.; Mao, B.; Zhang, X.; Lei, H. Overexpression of the lncRNA FER1L4 inhibits paclitaxel tolerance of ovarian cancer cells via the regulation of the MAPK signaling pathway. *Journal of Cellular Biochemistry* **2019**, *120*, 7581-7589, doi:10.1002/JCB.28032.

155. Dong, Q.; Long, X.; Cheng, J.; Wang, W.; Tian, Q.; Di, W. LncRNA GAS5 suppresses ovarian cancer progression by targeting the miR-96-5p/PTEN axis. *Ann Transl Med* **2021**, *9*, 1770, doi:10.21037/atm-21-6134.
156. Liu, F.; Cao, L.; Zhang, Y.; Xia, X.; Ji, Y. LncRNA LIFR-AS1 overexpression suppressed the progression of serous ovarian carcinoma. *Journal of Clinical Laboratory Analysis* **2022**, *36*, e25470, doi:10.1002/JCLA.24570.
157. Hao, T.; Huang, S.; Han, F. LINC-PINT suppresses tumour cell proliferation, migration and invasion through targeting miR-374a-5p in ovarian cancer. *Cell Biochemistry and Function* **2020**, *38*, 1089-1099, doi:10.1002/CBF.3565.
158. Li, Y.; Lv, M.; Wang, J.; Gao, C.; Wu, Y. LINC00641 inhibits the proliferation and invasion of ovarian cancer cells by targeting miR-320a. *Transl Cancer Res* **2021**, *10*, 4894-4904, doi:10.21037/tcr-21-2314.
159. Gokulnath, P.; de Cristofaro, T.; Manipur, I.; Di Palma, T.; Soriano, A.A.; Guarracino, M.R.; Zannini, M. Long Non-Coding RNA MAGI2-AS3 is a New Player with a Tumor Suppressive Role in High Grade Serous Ovarian Carcinoma. *Cancers (Basel)* **2019**, *11*, 2008, doi:10.3390/cancers11122008.
160. Li, Y.; Lou, S.; Zhang, J.; Zhao, S.; Lou, G. m6A methylation-mediated regulation of LncRNA MEG3 suppresses ovarian cancer progression through miR-885-5p and the VASH1 pathway. *J Transl Med* **2024**, *22*, 113, doi:10.1186/s12967-024-04929-x.
161. Yan, C.; Jiang, Y.; Wan, Y.; Zhang, L.; Liu, J.; Zhou, S.; Cheng, W. OncoTargets and Therapy Dovepress long noncoding rna nBaT-1 suppresses tumorigenesis and predicts favorable prognosis in ovarian cancer. *OncoTargets and Therapy* **2017**, *10*, 2147/OTT.S124645, 10-1993, doi:10.2147/OTT.S124645.
162. Tong, W.; Yang, L.; Yu, Q.; Yao, J.; He, A. A new tumor suppressor lncRNA RP11-190D6.2 inhibits the proliferation, migration, and invasion of epithelial ovarian cancer cells. *OncoTargets and Therapy* **2017**, *10*, 1227-1235, doi:10.2147/OTT.S125185.
163. Liu, X.; Liu, C.; Zhang, A.; Wang, Q.; Ge, J.; Li, Q.; Xiao, J. Long non-coding RNA SDCBP2-AS1 delays the progression of ovarian cancer via microRNA-100-5p-targeted EPDR1. *World J Surg Onc* **2021**, *19*, 199, doi:10.1186/s12957-021-02295-2.
164. Zhu, L.M.; Li, N. Downregulation of long noncoding RNA TUSC7 promoted cell growth, invasion and migration through sponging with miR-616-5p/GSK3 $\beta$  pathway in ovarian cancer. *European Review for Medical and Pharmacological Sciences* **2020**, *24*, 7253-7265, doi:10.26355/EURREV\_202007\_21880.
165. Guo, T.; Yuan, D.; Zhang, W.; Zhu, D.; Xiao, A.; Mao, G.; Jiang, W.; Lin, M.; Wang, J. Upregulation of long noncoding RNA XIST has anticancer effects on ovarian cancer through sponging miR-106a. *Human Cell* **2021**, *34*, 579-587, doi:10.1007/s13577-020-00469-w.
166. Nam, E.J.; Kim, Y.T. Alteration of cell-cycle regulation in epithelial ovarian cancer. *International Journal of Gynecologic Cancer* **2008**, *18*, doi:10.1111/j.1525-1438.2008.01191.x.
167. Wang, B.-D.; Jiang, J.; Liu, M.-M.; Zhuang, R.-J.; Wang, H.; Li, P.-L. Silencing CCAT2 inhibited proliferation and invasion of epithelial ovarian carcinoma cells by regulating Wnt signaling pathway. *International Journal of Clinical and Experimental Pathology* **2017**, *10*, 11771-11778.
168. Yong, W.; Yu, D.; Jun, Z.; Yachen, D.; Weiwei, W.; Midie, X.; Xingzhu, J.; Xiaohua, W. Long noncoding RNA NEAT1, regulated by LIN28B, promotes cell proliferation and migration through sponging miR-506 in high-grade serous ovarian cancer. *Cell Death & Disease* **2018**, *9*, doi:10.1038/s41419-018-0908-z.
169. Yuan, J.; Yi, K.; Yang, L. LncRNA NEAT1 promotes proliferation of ovarian cancer cells and angiogenesis of co-incubated human umbilical vein endothelial cells by regulating FGF9 through sponging miR-365. *Medicine* **2021**, *100*, e23423, doi:10.1097/md.00000000000023423.
170. Zhu, L.; Guo, Q.; Lu, X.; Zhao, J.; Shi, J.; Wang, Z.; Zhou, X. CTD-2020K17.1, a Novel Long Non-Coding RNA, Promotes Migration, Invasion, and Proliferation of Serous Ovarian Cancer Cells In Vitro. *Medical Science Monitor* **2018**, *24*, 1329-1339, doi:10.12659/msm.908456.
171. Qiu, J.-j.; Wang, Y.; Liu, Y.-l.; Zhang, Y.; Ding, J.-x.; Hua, K.-q. The long non-coding RNA ANRIL promotes proliferation and cell cycle progression and inhibits apoptosis and senescence in epithelial ovarian cancer. *Oncotarget* **2016**, *7*, 32478-32492, doi:10.18632/oncotarget.8744.
172. Han, L.; Zhang, W.; Zhang, B.; Zhan, L. Long non-coding RNA SOX2OT promotes cell proliferation and motility in human ovarian cancer. *Experimental and Therapeutic Medicine* **2017**, *10*, 3892/etm.2017.5618, doi:10.3892/etm.2017.5618.

173. Ma, N.; Li, S.; Zhang, Q.; Wang, H.; Qin, H.; Wang, S. Long non-coding RNA GAS5 inhibits ovarian cancer cell proliferation via the control of microRNA-21 and SPRY2 expression. *Experimental and Therapeutic Medicine* **2018**, *16*, 73-82, doi:10.3892/etm.2018.6188.
174. Zhang, T.; Leng, Y.; Duan, M.; Li, Z.; Ma, Y.; Huang, C.; Shi, Q.; Wang, Y.; Wang, C.; Liu, D., et al. LncRNA GAS5-hnRNPK axis inhibited ovarian cancer progression via inhibition of AKT signaling in ovarian cancer cells. *Discov Onc* **2023**, *14*, 157, doi:10.1007/s12672-023-00764-6.
175. Yang, L.; Wei, Q.-M.; Zhang, X.-W.; Sheng, Q.; Yan, X.-T. MiR-376a promotion of proliferation and metastases in ovarian cancer: Potential role as a biomarker. *Life Sciences* **2017**, *173*, 62-67, doi:10.1016/j.lfs.2016.12.007.
176. Li, Y.; Zhang, L.; Zhao, Y.; Peng, H.; Bai, W.; Zhang, N. MEG3 sponges miRNA-376a and YBX1 to regulate angiogenesis in ovarian cancer endothelial cells. *Heliyon* **2023**, *9*, doi:10.1016/j.heliyon.2023.e13204.
177. Chavez-Dominguez, R.; Perez-Medina, M.; Lopez-Gonzalez, J.S.; Galicia-Velasco, M.; Aguilar-Cazares, D. The Double-Edge Sword of Autophagy in Cancer: From Tumor Suppression to Pro-tumor Activity. *Front Oncol* **2020**, *10*, doi:10.3389/fonc.2020.578418.
178. Boroughs, L.K.; DeBerardinis, R.J. Metabolic pathways promoting cancer cell survival and growth. *Nat Cell Biol* **2015**, *17*, 351-359, doi:10.1038/ncb3124.
179. Chen, S.; Wu, D.-D.; Sang, X.-B.; Wang, L.-L.; Zong, Z.-H.; Sun, K.-X.; Liu, B.-L.; Zhao, Y. The lncRNA HULC functions as an oncogene by targeting ATG7 and ITGB1 in epithelial ovarian carcinoma. *Cell Death & Disease* **2017**, *8*, e3118-e3118, doi:10.1038/cddis.2017.486.
180. Tao, P.; Yang, B.; Zhang, H.; Sun, L.; Wang, Y.; Zheng, W. The overexpression of lncRNA MEG3 inhibits cell viability and invasion and promotes apoptosis in ovarian cancer by sponging miR-205-5p. *International Journal of Clinical and Experimental Pathology* **2020**, *13*, 869-879.
181. Jin, Y.; Qiu, J.; Lu, X.; Ma, Y.A.N.; Li, G. LncRNA CACNA1G-AS1 up-regulates FTH1 to inhibit ferroptosis and promote malignant phenotypes in ovarian cancer cells. *Oncol Res* **2023**, *31*, 169-179, doi:10.32604/or.2023.027815.
182. Nazio, F.; Bordi, M.; Cianfanelli, V.; Locatelli, F.; Cecconi, F. Autophagy and cancer stem cells: molecular mechanisms and therapeutic applications. *Cell Death & Differentiation* **2019**, *26*, 690-702, doi:10.1038/s41418-019-0292-y.
183. Xu, P.; Xu, S.; Pan, H.; Dai, C.; Xu, Y.; Wang, L.; Cong, Y.; Zhang, H.; Cao, J.; Ge, L.; Jia, X. Differential effects of the lncRNA RNF157-AS1 on epithelial ovarian cancer cells through suppression of DIRAS3- and ULK1-mediated autophagy. *Cell Death Dis* **2023**, *14*, 1-16, doi:10.1038/s41419-023-05668-5.
184. Fang, Y.-J.; Jiang, P.; Zhai, H.; Dong, J.-S. <p>LncRNA GAS8-AS1 Inhibits Ovarian Cancer Progression Through Activating Beclin1-Mediated Autophagy</p>. *OncoTargets and Therapy* **2020**, *Volume 13*, 10431-10440, doi:10.2147/ott.s266389.
185. Faubert, B.; Solmonson, A.; DeBerardinis, R.J. Metabolic reprogramming and cancer progression. *Science* **2020**, *368*, eaaw5473, doi:doi:10.1126/science.aaw5473.
186. Nadhan, R.; Dhanasekaran, D.N. Regulation of Tumor Metabolome by Long Non-Coding RNAs. *Journal of Molecular Signalling* **2022**, *10.55233/1750-2187-16-1*, doi:10.55233/1750-2187-16-1.
187. Nadhan, R.; Kashyap, S.; Ha, J.H.; Jayaraman, M.; Song, Y.S.; Isidoro, C.; Dhanasekaran, D.N. Targeting Oncometabolites in Peritoneal Cancers: Preclinical Insights and Therapeutic Strategies. *Metabolites* **2023**, *13*, doi:10.3390/metabo13050618.
188. Zhang, C.; Liu, N. Noncoding RNAs in the Glycolysis of Ovarian Cancer. *Frontiers in Pharmacology* **2022**, *13*, doi:10.3389/fphar.2022.855488.
189. Li, N.; Zhan, X.; Zhan, X. The lncRNA SNHG3 regulates energy metabolism of ovarian cancer by an analysis of mitochondrial proteomes. *Gynecol Oncol* **2018**, *150*, 343-354, doi:10.1016/j.ygyno.2018.06.013.
190. Rupaimoole, R.; Lee, J.; Haemmerle, M.; Ling, H.; Previs, Rebecca A.; Pradeep, S.; Wu, Sherry Y.; Ivan, C.; Ferracin, M.; Dennison, Jennifer B., et al. Long Noncoding RNA Ceruloplasmin Promotes Cancer Growth by Altering Glycolysis. *Cell Reports* **2015**, *13*, 2395-2402, doi:<https://doi.org/10.1016/j.celrep.2015.11.047>.
191. Nieman, K.M.; Kenny, H.A.; Penicka, C.V.; Ladanyi, A.; Buell-Gutbrod, R.; Zillhardt, M.R.; Romero, I.L.; Carey, M.S.; Mills, G.B.; Hotamisligil, G.S., et al. Adipocytes promote ovarian cancer metastasis and provide energy for rapid tumor growth. *Nat Med* **2011**, *17*, 1498-1503, doi:10.1038/nm.2492.



192. Li, M.; Yan, Y.; Liu, Y.; Zhao, J.; Guo, F.; Chen, J.; Nie, L.; Zhang, Y.; Wang, Y. Comprehensive analyses of fatty acid metabolism-related lncRNA for ovarian cancer patients. *Scientific Reports* **2023**, *13*, 14675, doi:10.1038/s41598-023-35218-0.
193. Ye, L.; Jiang, Z.; Zheng, M.; Pan, K.; Lian, J.; Ju, B.; Liu, X.; Tang, S.; Guo, G.; Zhang, S., et al. Fatty Acid Metabolism-Related lncRNA Prognostic Signature for Serous Ovarian Carcinoma. *Epigenomics* **2024**, *16*, 309-329, doi:10.2217/epi-2023-0388.
194. Ma, H.; Qu, S.; Zhai, Y.; Yang, X. circ\_0025033 promotes ovarian cancer development via regulating the hsa\_miR-370-3p/SLC1A5 axis. *Cellular & molecular biology letters* **2022**, *27*, 94, doi:10.1186/s11658-022-00364-2.
195. Yuan, J.; Liu, Z.; Song, R. Antisense lncRNA As-SLC7A11 suppresses epithelial ovarian cancer progression mainly by targeting SLC7A11. *Pharmazie* **2017**, *72*, 402-407, doi:10.1691/ph.2017.7449.
196. Zhao, L.; Ji, G.; Le, X.; Wang, C.; Xu, L.; Feng, M.; Zhang, Y.; Yang, H.; Xuan, Y.; Yang, Y., et al. Long Noncoding RNA LINC00092 Acts in Cancer-Associated Fibroblasts to Drive Glycolysis and Progression of Ovarian Cancer. *Cancer Research* **2017**, *77*, 1369-1382, doi:10.1158/0008-5472.Can-16-1615.
197. Nadhan, R.; Ha, J.H.; Jayaraman, M.; Kashyap, S.; Dhanasekaran, D.N. Abstract LB039: Ovarian cancer cell-derived exosomal UCA1 reprograms glucose metabolism in stromal fibroblasts. *Cancer Research* **2023**, *83*, LB039-LB039, doi:10.1158/1538-7445.Am2023-lb039.
198. Friedl, P.; Wolf, K. Tumour-cell invasion and migration: diversity and escape mechanisms. *Nat Rev Cancer* **2003**, *3*, 362-374, doi:10.1038/nrc1075.
199. Lampropoulou, D.I.; Papadimitriou, M.; Papadimitriou, C.; Filippou, D.; Kourlaba, G.; Aravantinos, G.; Gazouli, M. The Role of EMT-Related lncRNAs in Ovarian Cancer. *International Journal of Molecular Sciences* **2023**, *24*, 10079, doi:10.3390/ijms241210079.
200. Xiong, T.; Wang, Y.; Zhang, Y.; Yuan, J.; Zhu, C.; Jiang, W. lncRNA AC005224.4/miR-140-3p/SNAI2 regulating axis facilitates the invasion and metastasis of ovarian cancer through epithelial-mesenchymal transition. *Chinese Medical Journal* **2023**, *136*, 1098-1110, doi:10.1097/cm9.0000000000002201.
201. Li, J.; Wang, J.; Zhong, Y.; Guo, R.; Chu, D.; Qiu, H.; Yuan, Z. HOTAIR: a key regulator in gynecologic cancers. *Cancer Cell International* **2017**, *17*, 65, doi:10.1186/s12935-017-0434-6.
202. Qiu, J.J.; Lin, Y.Y.; Ye, L.C.; Ding, J.X.; Feng, W.W.; Jin, H.Y.; Zhang, Y.; Li, Q.; Hua, K.Q. Overexpression of long non-coding RNA HOTAIR predicts poor patient prognosis and promotes tumor metastasis in epithelial ovarian cancer. *Gynecol Oncol* **2014**, *134*, 121-128, doi:10.1016/j.ygyno.2014.03.556.
203. Gao, Z.; Liu, R.; Ye, N.; Liu, C.; Li, X.; Guo, X.; Zhang, Z.; Li, X.; Yao, Y.; Jiang, X. FOXO1 Inhibits Tumor Cell Migration via Regulating Cell Surface Morphology in Non-Small Cell Lung Cancer Cells. *Cellular Physiology and Biochemistry* **2018**, *48*, 138-148, doi:10.1159/000491670.
204. Zamaraev, A.V.; Volik, P.I.; Sukhikh, G.T.; Kopeina, G.S.; Zhivotovsky, B. Long non-coding RNAs: A view to kill ovarian cancer. *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer* **2021**, *1876*, 188584, doi:10.1016/j.bbcan.2021.188584.
205. Chang, L.; Guo, R.; Yuan, Z.; Shi, H.; Zhang, D. lncRNA HOTAIR Regulates CCND1 and CCND2 Expression by Sponging miR-206 in Ovarian Cancer. *Cellular Physiology and Biochemistry* **2018**, *49*, 1289-1303, doi:10.1159/000493408.
206. Wang, J.; Xu, W.; He, Y.; Xia, Q.; Liu, S. lncRNA MEG3 impacts proliferation, invasion, and migration of ovarian cancer cells through regulating PTEN. *Inflammation Research* **2018**, *67*, 927-936, doi:10.1007/s00011-018-1186-z.
207. Saman, H.; Raza, S.S.; Uddin, S.; Rasul, K. Inducing Angiogenesis, a Key Step in Cancer Vascularization, and Treatment Approaches. *Cancers (Basel)* **2020**, *12*, 1172, doi:10.3390/cancers12051172.
208. Teppan, J.; Barth, D.A.; Prinz, F.; Jonas, K.; Pichler, M.; Klec, C. Involvement of Long Non-Coding RNAs (lncRNAs) in Tumor Angiogenesis. *Noncoding RNA* **2020**, *6*, 42, doi:10.3390/ncrna6040042.
209. Lin, X.; Yang, F.; Qi, X.; Li, Q.; Wang, D.; Yi, T.; Yin, R.; Zhao, X.; Zhong, X.; Bian, C. lncRNA DANCR promotes tumor growth and angiogenesis in ovarian cancer through direct targeting of miR-145. *Molecular Carcinogenesis* **2019**, *58*, 2286-2296, doi:10.1002/mc.23117.



210. Yuan, D.; Guo, T.; Zhu, D.; Ge, H.; Zhao, Y.; Huang, A.; Wang, X.; Cao, X.; He, C.; Qian, H.; Yu, H. Exosomal lncRNA ATB Derived from Ovarian Cancer Cells Promotes Angiogenesis via Regulating miR-204-3p/TGF $\beta$ R2 Axis. *Cancer Management and Research* **2022**, Volume 14, 327-337, doi:10.2147/cmar.s330368.
211. Liu, Y.; Li, Y.; Wu, Y.; Zhao, Y.; Hu, X.; Sun, C. The long non-coding RNA NEAT1 promotes the progression of human ovarian cancer through targeting miR-214-3p and regulating angiogenesis. *Journal of Ovarian Research* **2023**, 16, doi:10.1186/s13048-023-01309-9.
212. Li, Y.; Zhang, L.; Zhao, Y.; Peng, H.; Bai, W.; Zhang, N. MEG3 sponges miRNA-376a and YBX1 to regulate angiogenesis in ovarian cancer endothelial cells. *Heliyon* **2023**, 9, e13204, doi:10.1016/j.heliyon.2023.e13204.
213. Kenda Suster, N.; Virant-Klun, I. Presence and role of stem cells in ovarian cancer. *World J Stem Cells* **2019**, 11, 383-397, doi:10.4252/wjsc.v11.i7.383.
214. Królewska-Daszczyńska, P.; Wendlocha, D.; Smycz-Kubańska, M.; Stępień, S.; Mielczarek-Palacz, A. Cancer stem cells markers in ovarian cancer: Clinical and therapeutic significance (Review). *Oncol Lett* **2022**, 24, 465, doi:10.3892/ol.2022.13585.
215. Yue, J.; Wu, Y.; Qiu, L.; Zhao, R.; Jiang, M.; Zhang, H. LncRNAs link cancer stemness to therapy resistance. *American Journal of Cancer Research* **2021**, 11, 1051-1068.
216. Zhang, Y.; Guo, J.; Cai, E.; Cai, J.; Wen, Y.; Lu, S.; Li, X.; Han, Q.; Jiang, J.; Li, T.; Wang, Z. HOTAIR maintains the stemness of ovarian cancer stem cells via the miR-206/TBX3 axis. *Experimental Cell Research* **2020**, 395, 112218, doi:10.1016/j.yexcr.2020.112218.
217. Mamun, M.A.; Mannoor, K.; Cao, J.; Qadri, F.; Song, X. SOX2 in cancer stemness: tumor malignancy and therapeutic potentials. *J Mol Cell Biol* **2018**, 12, 85-98, doi:10.1093/jmcb/mjy080.
218. Wu, X.; Wang, Y.; Zhong, W.; Cheng, H.; Tian, Z. The Long Non-Coding RNA MALAT1 Enhances Ovarian Cancer Cell Stemness by Inhibiting YAP Translocation from Nucleus to Cytoplasm. *Med Sci Monit* **2020**, 26, 0-0, doi:10.12659/MSM.922012.
219. Hou, R.; Jiang, L. LINC00115 promotes stemness and inhibits apoptosis of ovarian cancer stem cells by upregulating SOX9 and inhibiting the Wnt/ $\beta$ -catenin pathway through competitively binding to microRNA-30a. *Cancer Cell International* **2021**, 21, 360, doi:10.1186/s12935-021-02019-2.
220. Varier, K.M.; Dhandapani, H.; Liu, W.; Song, J.; Wang, C.; Hu, A.; Ben-David, Y.; Shen, X.; Li, Y.; Gajendran, B. An immunotherapeutic approach to decipher the role of long non-coding RNAs in cancer progression, resistance and epigenetic regulation of immune cells. *Journal of Experimental & Clinical Cancer Research* **2021**, 40, doi:10.1186/s13046-021-01997-5.
221. Liu, J.; Yan, C.; Xu, S. LncRNA IL21-AS1 facilitates tumour progression by enhancing CD24-induced phagocytosis inhibition and tumorigenesis in ovarian cancer. *Cell Death & Disease* **2024**, 15, doi:10.1038/s41419-024-06704-8.
222. Lei, J.; He, Z.Y.; Wang, J.; Hu, M.; Zhou, P.; Lian, C.L.; Hua, L.; Wu, S.G.; Zhou, J. Identification of MEG8/miR-378d/SOBP axis as a novel regulatory network and associated with immune infiltrates in ovarian carcinoma by integrated bioinformatics analysis. *Cancer Medicine* **2021**, 10, 2924-2939, doi:10.1002/cam4.3854.
223. Qian, M.; Ling, W.; Ruan, Z. Long non-coding RNA SNHG12 promotes immune escape of ovarian cancer cells through their crosstalk with M2 macrophages. *Aging* **2020**, 12, 17122-17136, doi:10.18632/aging.103653.
224. Yang, L.; Xie, H.-J.; Li, Y.-Y.; Wang, X.; Liu, X.-X.; Mai, J. Molecular mechanisms of platinum-based chemotherapy resistance in ovarian cancer (Review). *Oncol Rep* **2022**, 47, 1-11, doi:10.3892/or.2022.8293.
225. Shi, C.; Wang, M. LINC01118 Modulates Paclitaxel Resistance of Epithelial Ovarian Cancer by Regulating miR-134/ABCC1. *Med Sci Monit* **2018**, 24, 8831-8839, doi:10.12659/msm.910932.
226. Wu, Y.; Wang, T.; Xia, L.; Zhang, M. LncRNA WDFY3-AS2 promotes cisplatin resistance and the cancer stem cell in ovarian cancer by regulating hsa-miR-139-5p/SDC4 axis. *Cancer Cell International* **2021**, 21, 284, doi:10.1186/s12935-021-01993-x.
227. Penning, T.M.; Jonnalagadda, S.; Trippier, P.C.; Rižner, T.L. Aldo-Keto Reductases and Cancer Drug Resistance. *Pharmacological Reviews* **2021**, 73, 1150-1171, doi:10.1124/pharmrev.120.000122.
228. Zhang, J.; Liu, J.; Xu, X.; Li, L. Curcumin suppresses cisplatin resistance development partly via modulating extracellular vesicle-mediated transfer of MEG3 and miR-214 in ovarian cancer. *Cancer Chemother Pharmacol* **2017**, 79, 479-487, doi:10.1007/s00280-017-3238-4.

229. Zhang, C.; Wang, M.; Shi, C.; Shi, F.; Pei, C. Long non-coding RNA Linc00312 modulates the sensitivity of ovarian cancer to cisplatin via the Bcl-2/Caspase-3 signaling pathway. *BioScience Trends* **2018**, *12*, 309-316, doi:10.5582/bst.2018.01052.
230. Xiao, L.; Shi, X.-Y.; Li, Z.-L.; Li, M.; Zhang, M.-M.; Yan, S.-J.; Wei, Z.-L. Downregulation of LINC01508 contributes to cisplatin resistance in ovarian cancer via the regulation of the Hippo-YAP pathway. *Journal of Gynecologic Oncology* **2021**, *32*, doi:10.3802/jgo.2021.32.e77.
231. Guo, J.; Pan, H. Long Noncoding RNA LINC01125 Enhances Cisplatin Sensitivity of Ovarian Cancer via miR-1972. *Med Sci Monit* **2019**, *25*, 9844-9854, doi:10.12659/msm.916820.
232. Jurkovicova, D.; Neophytou, C.M.; Gašparović, A.Č.; Gonçalves, A.C. DNA Damage Response in Cancer Therapy and Resistance: Challenges and Opportunities. *International Journal of Molecular Sciences* **2022**, *23*, 14672, doi:10.3390/ijms232314672.
233. Hara, T.; Omura-Minamisawa, M.; Chao, C.; Nakagami, Y.; Ito, M.; Inoue, T. Bcl-2 inhibitors potentiate the cytotoxic effects of radiation in Bcl-2 overexpressing radioresistant tumor cells. *International Journal of Radiation Oncology\*Biophysics* **2005**, *61*, 517-528, doi:10.1016/j.ijrobp.2004.10.008.
234. Dou, Q.; Xu, Y.; Zhu, Y.; Hu, Y.; Yan, Y.; Yan, H. LncRNA FAM83H-AS1 contributes to the radioresistance, proliferation, and metastasis in ovarian cancer through stabilizing HuR protein. *European Journal of Pharmacology* **2019**, *852*, 134-141, doi:10.1016/j.ejphar.2019.03.002.
235. Salamini-Montemurri, M.; Lamas-Maceiras, M.; Barreiro-Alonso, A.; Vizoso-Vázquez, Á.; Rodríguez-Belmonte, E.; Quindós-Varela, M.; Cerdán, M.E. The Challenges and Opportunities of LncRNAs in Ovarian Cancer Research and Clinical Use. *Cancers (Basel)* **2020**, *12*, 1020, doi:10.3390/cancers12041020.
236. Chen, M.; Lei, N.; Tian, W.; Li, Y.; Chang, L. Recent advances of non-coding RNAs in ovarian cancer prognosis and therapeutics. *Ther Adv Med Oncol* **2022**, *14*, 17588359221118010, doi:10.1177/17588359221118010.
237. Liu, C.-N.; Zhang, H.-Y. Serum lncRNA LOXL1-AS1 is a diagnostic and prognostic marker for epithelial ovarian cancer. *The Journal of Gene Medicine* **2020**, *22*, e3233, doi:10.1002/jgm.3233.
238. Zuo, K.; Zhao, Y.; Zheng, Y.; Chen, D.; Liu, X.; Du, S.; Liu, Q. Long non-coding RNA XIST promotes malignant behavior of epithelial ovarian cancer. *OncoTargets and Therapy* **2019**, *12*, 7261-7267, doi:10.2147/OTT.S204369.
239. Wang, J.; Tian, Y.; Zheng, H.; Ding, Y.; Wang, X. An integrated analysis reveals the oncogenic function of lncRNA LINC00511 in human ovarian cancer. *Cancer Medicine* **2019**, *8*, 3026-3035, doi:10.1002/cam4.2171.
240. Chen, Y.; Bi, F.; An, Y.; Yang, Q. Identification of pathological grade and prognosis-associated lncRNA for ovarian cancer. *Journal of Cellular Biochemistry* **2019**, *120*, 14444-14454, doi:10.1002/JCB.28704.
241. Zhou, M.; Sun, Y.; Sun, Y.; Xu, W.; Zhang, Z.; Zhao, H.; Zhong, Z.; Sun, J. Comprehensive analysis of lncRNA expression profiles reveals a novel lncRNA signature to discriminate nonequivalent outcomes in patients with ovarian cancer. *Oncotarget* **2016**, *7*, 32433-32448, doi:10.18632/oncotarget.8653.
242. Gong, M.; Luo, C.; Meng, H.; Li, S.; Nie, S.; Jiang, Y.; Wan, Y.; Li, H.; Cheng, W. Upregulated LINC00565 Accelerates Ovarian Cancer Progression By Targeting GAS6. *OncoTargets and Therapy* **2019**, *12*, 10011-10022, doi:10.2147/OTT.S227758.
243. Yang, K.; Hou, Y.; Li, A.; Li, Z.; Wang, W.; Xie, H.; Rong, Z.; Lou, G.; Li, K. Identification of a six-lncRNA signature associated with recurrence of ovarian cancer. *Sci Rep* **2017**, *7*, 752, doi:10.1038/s41598-017-00763-y.
244. Fu, Y.; Biglia, N.; Wang, Z.; Shen, Y.; Risch, H.A.; Lu, L.; Canuto, E.M.; Jia, W.; Katsaros, D.; Yu, H. Long non-coding RNAs, *ASAP1-IT1*, *FAM215A*, and *LINC00472*, in epithelial ovarian cancer. *Gynecologic Oncology* **2016**, *143*, 642-649, doi:10.1016/j.ygyno.2016.09.021.
245. Salamini-Montemurri, M.; Lamas-Maceiras, M.; Lorenzo-Catoira, L.; Vizoso-Vázquez, Á.; Barreiro-Alonso, A.; Rodríguez-Belmonte, E.; Quindós-Varela, M.; Cerdán, M.E. Identification of lncRNAs Deregulated in Epithelial Ovarian Cancer Based on a Gene Expression Profiling Meta-Analysis. *International Journal of Molecular Sciences* **2023**, *24*, 10798, doi:10.3390/ijms241310798.
246. Kumar, A.; Girisa, S.; Alqahtani, M.S.; Abbas, M.; Hegde, M.; Sethi, G.; Kunnumakkara, A.B. Targeting Autophagy Using Long Non-Coding RNAs (LncRNAs): New Landscapes in the Arena of Cancer Therapeutics. *Cells* **2023**, *12*, 810, doi:10.3390/cells12050810.

247. Zhou, L.; Zhu, Y.; Sun, D.; Zhang, Q. Emerging Roles of Long non-coding RNAs in The Tumor Microenvironment. *Int J Biol Sci* **2020**, *16*, 2094-2103, doi:10.7150/ijbs.44420.
248. Fathi Dizaji, B. Strategies to target long non-coding RNAs in cancer treatment: progress and challenges. *Egypt J Med Hum Genet* **2020**, *21*, 41, doi:10.1186/s43042-020-00074-4.
249. Zhu, Y.; Zhu, L.; Wang, X.; Jin, H. RNA-based therapeutics: an overview and prospectus. *Cell Death & Disease* **2022**, *13*, doi:10.1038/s41419-022-05075-2.
250. Tanioka, M.; Nokihara, H.; Yamamoto, N.; Yamada, Y.; Yamada, K.; Goto, Y.; Fujimoto, T.; Sekiguchi, R.; Uenaka, K.; Callies, S.; Tamura, T. Phase I study of LY2181308, an antisense oligonucleotide against survivin, in patients with advanced solid tumors. *Cancer Chemother Pharmacol* **2011**, *68*, 505-511, doi:10.1007/s00280-010-1506-7.
251. Oza, A.M.; Elit, L.; Swenerton, K.; Faight, W.; Ghatage, P.; Carey, M.; McIntosh, L.; Dorr, A.; Holmlund, J.T.; Eisenhauer, E. Phase II study of CGP 69846A (ISIS 5132) in recurrent epithelial ovarian cancer: an NCIC clinical trials group study (NCIC IND.116)☆. *Gynecologic Oncology* **2003**, *89*, 129-133, doi:10.1016/s0090-8258(02)00144-0.

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