Review Article

Research progress of long non-coding RNA in ovarian cancer: a narrative review

Jinxin Qiu[1,2#^], Yanjun Sun[1,2#^], Huihua Ni[1], Li Li[1], Qinghua Xi[1], Haiyan Jiang[3]

[1]Department of Obstetrics and Gynecology, Affiliated Hospital of Nantong University, Nantong, China; [2]Medical School of Nantong University, Nantong, China; [3]Department of Emergency Medicine, Affiliated Hospital of Nantong University, Nantong, China

Contributions: (I) Conception and design: Q Xi, H Jiang; (II) Administrative support: Q Xi; (III) Provision of study materials or patients: H Ni, L Li; (IV) Collection and assembly of data: J Qiu, Y Sun; (V) Data analysis and interpretation: J Qiu, Y Sun; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Qinghua Xi. Department of Obstetrics and Gynecology, Affiliated Hospital of Nantong University, 20 West Temple Road, Nantong 226001, China. Email: ntdxfsyyxqh@163.com; Haiyan Jiang. Department of Emergency Medicine, Affiliated Hospital of Nantong University, 20 West Temple Road, Nantong 226001, China. Email: jhy@ntu.edu.cn.

Background and Objective: Ovarian cancer (OC) is one of the most lethal malignancies of women around the world. Among all gynecological malignant tumours, most OC patients are diagnosed at advanced stages with a low 5-year survival rate and dim prognosis. Long non-coding RNAs (lncRNAs) are a class of noncoding RNA over 200 nucleotides without protein coding capacity. LncRNAs are involved in different biological processes and form various regulatory networks in different type of cancers. Their aberrant expression plays an important role in the neoplasm and development of OC.

Methods: In this paper, literature reports related to lncRNA in OC in the past 10 years were searched on "PubMed" and they were classified and summarized. Keywords can be targeted as "epithelial ovarian cancer", "long non-coding RNA", "mechanism".

Key Content and Findings: In this paper, lncRNAs are divided into three categories, namely, those related to proliferation, invasion and migration of OC, those related to occurrence, development and prognosis of OC, and those related to targeted therapy of OC. The expression of lncRNAs is closely related to the above processes of OC cells, and participates in the occurrence, development, prognosis and targeted therapy of the disease.

Conclusions: This review mainly focuses on the research progress of lncRNAs in OC of recent years, which may provide us with potential therapeutic targets and lay a foundation for early diagnosis, and prognostic evaluation of o-OC.

Keywords: Ovarian cancer (OC); long non-coding RNA (lncRNA); therapeutic target

Received: 28 June 2022; Accepted: 21 January 2023; Published online: 15 February 2023.

doi: 10.21037/biotarget-22-3

View this article at: https://dx.doi.org/10.21037/biotarget-22-3

^ ORCID: Jinxin Qiu, 0000-0003-1580-854X; Yanjun Sun, 0000-0002-9099-6037.

Introduction

Ovarian cancer (OC) is one of the most fatal gynecologic malignant tumors worldwide, the morbidity of OC is ranked at the eighth among the most common women malignancies (1). Among all the female reproductive cancers, OC patients suffer from the worst prognosis with the highest mortality (2). Based on 2018 data, it is estimated that the number of new OC cases worldwide is about 300,000 per year, and more than 180,000 OC patients die for this disease per year (3). Due to its heterogeneities, 90% of ovarian carcinoma are epithelial ovarian cancer (EOC), while the rest could be classified as non-EOC, including asexual cell tumor, ovarian yolk cystic tumor, granulosa cell tumor, metastatic OC, etc. EOC are further divided into five categories: high-grade serous ovarian cancer (HHS-OVCA, about 70%), endometrioid carcinoma (about 10%), clear cell carcinoma (about 10%), mucinous OC (about 3%), and low-grade serous OC (<5%) (4). Since ovaries are located at the deep part of the pelvic cavity, the onset of OC is concealed. As lack of the effective early diagnostic methods, most patients are diagnosed at advanced stages (FIGO stage: III–IV), with a 5-year survival rate of less than 50% (5).

Long non-coding RNAs (lncRNAs) are a class of RNA over 200 nucleotides with no protein coding capacity. They have been reported to participate in various biologic and pathologic processes. And in addition, they form a variety of regulatory networks to regulate diverse pathophysiological processes *in vivo* (6). It has been confirmed that the regulation of lncRNA expression is related to the biological behavior of OC. This review mainly focuses on the research progress of lncRNAs related to the occurrence and development of OC in recent years, laying a foundation for the study of early diagnosis, therapeutic drugs and prognosis assessment of human OC. We present the following article in accordance with the Narrative Review reporting checklist (available at https://biotarget.amegroups.com/article/view/10.21037/biotarget-22-3/rc).

Methods

PubMed was searched for literature reports on lncRNA in OC, and the key words were "epithelial ovarian cancer", "long non-coding RNA", "mechanism". The time range was from 2012 to 2022. Then we categorized and summarized the literatures. We preliminarily divided lncRNAs into three categories: lncRNAs mainly related to the proliferation, migration and invasion of OC, lncRNAs mainly related to the occurrence, development and prognosis of OC, and lncRNAs mainly related to targeted therapy of OC. The specific strategy was listed in *Table 1*.

Discussion

Research progress of lncRNAs

LncRNAs are involved in epigenetic processes such as histone modification and genomic imprinting by binding to cellular biomolecules such as nucleic acids, miRNAs, and mRNAs, affecting specific transcription factors and polymerase activities to regulate mRNA production, and regulating mRNA expression through splicing, transport, and translation (7). Previous studies found that lncRNAs play an important role in the pathophysiology of breast cancer, cervical cancer, colon cancer, prostate cancer and other malignant tumors. In recent years, more and more studies have found that lncRNAs are related to the pathological physiological process of OC.

Expression of lncRNAs in OC

LncRNAs are associated with proliferation, invasion, migration, apoptosis, chemoresistance and other cell events of OC, and are involved in occurrence and development of the disease, prognosis and targeted therapy. Akrami *et al.* (8) demonstrated that the expression of 455 lncRNAs was specifically induced or inhibited in the four subtypes of high-grade serous OC (immunoreactive, differentiated, proliferative and mesenchymal).

LncRNAs related to proliferation, invasion and migration

Aberrant expression of lncRNAs is associated with the proliferation, invasion and migration of OC. Epithelial mesenchymal transformation (EMT) plays a crucial role in the invasion and metastasis of OC (9). Cell invasion, migration, and metastasis are the hallmarks of cancer, which lead to secondary tumor formation and high risks of death. Therefore, it is important for us to profoundly understand the involvement and mechanism between lncRNAs and invasion, migration and metastasis of OC cells. It may provide us with early diagnostic insights of OC.

HOX transcript antisense interRNA (HOTAIR)

Previous studies have proved that HOTAIR was an

Table 1 The search strategy summary

Items	Specification
Date of search	2022.04.01
Databases and other sources searched	PubMed
Search terms used	epithelial ovarian cancer, long non-coding RNA, mechanism
	First, we screened "epithelial ovarian cancer" from PubMed database, and then we performed a secondary screening with key words "lncRNA" and "mechanism of action"
Timeframe	2012.01.01–2022.04.01
Inclusion and exclusion criteria	All the quoted articles are in English
	Articles related to keywords in recent 10 years are selected, and the research articles with complete experimental procedures and conclusions are selected from the database
Selection process	Qiu and Sun conducted the selection cooperatively
	We selected the articles related to epithelial ovarian cancer and the mechanism of LncRNAs in the recent 10 years from PubMed database, and selected the research articles with complete experimental procedures and conclusions

oncogene. Dong *et al.* (10) found that miR-214 and miR-217 mediate the interaction between HOTAIR and PIK3R3, thereby regulating the expression of OC cells. Qiu *et al.* (11) found that the proliferation of SOC cells was inhibited after the silencing of HOTAIR. Chang *et al.* (12) found that the aberrant expression of HOTAIR and its related factors play roles in the proliferation, invasion and migration of OC via different pathways.

Metastasis associated lung adenocarcinoma transcript 1 (MALAT1)

MALAT1 is regulated by the tumor suppressor gene P53 and is located on human chromosome 11 (13). Gordon *et al.* (14) found that MALAT1 was overexpressed in OC tissues and cell lines, and low expression of MALAT1 inhibited the expression of RBFOX2, which was conducive to reducing the proliferation and invasion ability of OC cells. Lei *et al.* (15) first revealed the regulatory effect of MALAT1 on miR-506. As a tumor-inhibiting miRNA, miR-506 was negatively correlated with MALAT1 expression. MALAT1 can regulate OC progression by regulating the miR-506-IASPP axis. Therefore, MALAT1 may be a potential target for the early diagnosis of OC.

H19

H19 is a lncRNA associated with malignancies detected in early stages. Studies have shown that H19 plays an important role in proliferation, invasion and migration of OC. In a study conducted by Medrzycki *et al.* (16), H19 was an oncogene which is synergistic with histone H1.3 inhibiting proliferation of OC cells. Yan *et al.* (17) showed that Let-7 was a tumor suppressor, and the overexpression of H19 reduced the bioavailability of Let-7, which contributed to the occurrence and development of cancer to a certain extent. Sajadpoor *et al.* (18) found that valproic acid could reduce the expression of H19 in OC tissues, thus inhibiting cell proliferation. Therefore, H19 may play key roles in the early diagnosis of OC and may be a novel therapeutic target.

Colon cancer-associated transcript 1 (CCAT1) and colon cancer-associated transcript 2 (CCAT2)

CCAT1 and CCAT2 are located at 8q.24.2 near the MYC proto-oncogene region of human chromosome (19). Lai *et al.* (20) showed that CCAT1 expression was obviously higher in OC tissue than that in normal ovarian tissue. MiR-1290 is commonly recognized as a tumor suppressor in gynecological malignancies, and inhibiting expression of miR-1290 will obversely promote progression of OC. CCAT1 promotes the proliferation, invasion and migration of OC cells by targeting miR-1290 expression. Hua *et al.* (21) found that in EOC, CCAT2 knockout could promote cell apoptosis, while the expression of miR-424 in EOC cell lines was negatively correlated with CCAT2. Therefore, CCAT1 and CCAT2 are both involved in the occurrence and development of OC through the targeted regulation of miRNA-related molecules.

LncRNAs related to occurrence, development and prognosis

Urothelial carcinoma associated 1 (UCA1)

UCA1 is a lncRNA of 1,442 bp length. Investigators have demonstrated that overexpression of UCA1 is associated with lymph node metastasis of digestive system malignancies, leading to poor overall survival and disease-free survival. Therefore, UCA1 can be used as a prognostic marker (22). Wang *et al.* (23) found that UCA1 is overexpressed in OC and abnormal expression of UCA1 was involved in cell apoptosis. Wambecke *et al.* (24) found that in OC tissues, the median progression-free survival was negatively correlated with UCA1 expression, and UCA1 suggested poor prognosis of ovarian carcinoma. Further experiments demonstrated that down-regulation of UCA1 could enhance chemoresistant OC cells sensitive to cisplatin. Lin *et al.* (25) demonstrated that UCA1 influenced the progression and prognosis of OC by integrating lncRNA interaction groups and functional proteomics analysis. In addition, the role of UCA1-AMOTP130-YAP signal axis in the development of EOC is also clarified. Therefore, UCA1 can be used as a driving factor for the occurrence, development and prognosis of OC.

Antisense non-coding RNA in the INK4 locus (ANRIL)

ANRIL is a 3,800 nt lncRNA located on human chromosome 9P21. Qiu *et al.* (26) found that ANRIL played a carcinogenic role in SOC and ANRIL expression was positively correlated with advanced stages, high histological grades and poor prognosis. Further analysis suggested that the overall survival of SOC patients could be predicted by ANRIL, indicating that ANRIL could be a key biomarker for the prognosis of SOC patients. These data highlight the significance of ANRIL in evaluating the prognosis of patients with SOC, suggesting that ANRIL may be a potential therapeutic target for SOC.

Growth arrest specific transcript 5 (GAS5)

Previous studies have demonstrated that GAS5 inhibits cancer progression in other cancers. Low expression of GAS5 in OC tissues and cell lines is associated with poor disease-free survival in patients with OC. Zhao *et al.* (27) found that the expression of miR-196a-5p was up-regulated in OC tissues, and GAS5 regulated the OC progression and apoptosis of OC cells by targeting the expression of miR-196a-5p. Another study found that the survival time of OC patients with high GAS5 expression was longer than those with low GAS5 expression patients. Therefore, further study of GAS5 is conducive to effective evaluation of prognosis of OC patients.

LINC00858

Hitherto, few studies of LINC00858 have been conducted. LINC00858 is up-regulated in human OC tissue and is recognized as an oncogene. Inhibiting LINC00858 expression can accelerate cell apoptosis. Studies have shown that miR-134-5p was a target gene of LINC00858 and has been proved to be a tumor suppressor gene involved in the regulation of OC cell progression along with LINC00858 (28,29). LINC00858 may be a diagnostic and prognostic marker of OC.

Taurine up-regulated gene 1 (TUG1)

TUG1 is located on human chromosome 22q12.2 with 7,598 nt in length. The expression of TUG1 was increased in OC cells compared with normal ovarian cells. It was found that TUG1 affected the apoptosis level of OC cells by specifically regulating the expression of miR-196b-5p, thus affecting the prognosis of patients. Further study of TUG1 may be of significance for the prognostic assessment of OC.

X inactive specific transcript (XIST)

Hu *et al.* (30) found that the expression of XIST was decreased in OC tissue and overexpressed in normal ovarian tissue, and the overexpression of XIST predicted a good prognosis for OC patients. Research found that XIST was down-regulated in OC tissues by OC expression profiling chip analysis. Further experimental analysis showed that the overall survival, post-progression survival and progression-free survival were worse in the group with low XIST expression. Therefore, the in-depth study of XIST is conducive to the prognosis assessment of OC.

LncRNAs related to targeted therapy

As an antineoplastic drug, paclitaxel has been widely used in the treatment of ovarian tumors. No matter what type of OC, the treatment principle is mainly surgery, chemotherapy as a supplement. Chemotherapy for OC includes neoadjuvant chemotherapy, initial chemotherapy after surgery, maintenance therapy after remission and relapse rescue therapy. LncRNAs are not only involved in the proliferation, invasion and migration of ovarian tumors, but also in chemoresistance and targeted therapy of ovarian tumors.

Plasmacytoma variant translocation 1 (PVT1)

Existing studies have shown that PVT1 can induce cisplatin resistance and may be a potential therapeutic target for OC. Liu *et al.* (31) pretreated OC 3AO cells with

carboplatin-docetaxel and then found lncRNA PVT1 was abnormally expressed after treatment. Further experiments demonstrated that PVT1 regulated by carboplatin-docetaxel gained anti-tumorpotency, and upregulation of PVT1 would increase expression of tumor suppressor genes p53 and TIMP1, thus inhibiting disease progression. El-Khazragy *et al.* (32) noted that overexpression of PVT1 was associated with poor overall survival and cisplatin resistance. PVT1 can induce cisplatin resistance by inhibiting apoptosis. Chen *et al.* (33) found that the expression of PVT1 in EOC tissues resistant to cisplatin was higher than that in normal ovarian tissues. When JAK2/STAT3/PD-L1 signaling pathway was blocked, PVT1 expression in EOC resistant to cisplatin was inhibited. Therefore, PVT1 may be a potential therapeutic target for OC associated with cisplatin resistance.

Maternally expressed gene 3 (MEG3)

MEG3 is known as a tumor suppressor. El-Khazragy *et al.* (32) found that down-regulation of MEG3 was significantly correlated with poor survival rate and chemoresistance of OC patients. Zhang *et al.* (34) revealed for the first time that curcumin can be used as a demethylating agent to restore the expression level of MEG3 in cells and extracellular vesicles of OC cells. The restored MEG3 reduces cisplatin resistance through inhibiting expression of miR-214. Further study of MEG3 relative signaling pathways will be beneficial for improving sensitivity of chemoresistance in OC.

Fer-1-like protein 4 (FER1L4)

FER1L4 is located on human chromosome 20q11 and is 6.7 KB long. FER1L4 is one of the key factors involved in tumor development with good application prospects in different types of tumors. Liu *et al.* (35) showed that works as a tumor suppressor and its expression was decreased in chemotherapy-resistant OC cell lines compared to normal OC cell lines. FER1L4 enhanced sensitivity of OC cells to paclitaxel (PTX) via MAPK signaling pathway. Therefore, the FER1L4/MAPK signaling pathway is expected to improve the efficacy of PTX in treatment of OC.

Nuclear paraspeckle assembly transcript 1 (NEAT1)

NEAT1, a3.2 KB length lncRNA, is an oncogene that promotes the progression of OC. Zhu *et al.* (36) found that NEAT1 was overexpressed in cisplatin resistant OC cells, and the elimination of NEAT1 can inhibit cisplatin resistance through targeted regulation of miR-770-5p/PARP1 pathway. Jia *et al.* (37) found that overexpression of NEAT1 induced cisplatin-resistance in OC cells, and miR-491-5p was down-regulated in cisplatin-resistant OC cells. Studies have shown that NEAT1 can regulate chemoresistance in OC by targeting miR-491-5p /SOX3 pathway. These findings implied that NEAT1 may provide us with a novel target for chemoresistance of OC.

Zine finger antisense 1 (ZFAS1)

Xia *et al.* (38) found that overexpression of ZFAS1 promoted the proliferation, invasion and migration expression of EOC cells, resulting in poor prognosis and chemotherapy resistance of PATIENTS with EOC. MiR-150-5p is regulated by ZFAS1 and down-regulated in EOC cells. ZFAS1 promotes the progression and chemoresistance of EOC by regulating miR-150-5p/Sp1 axis. Liu *et al.* (39) demonstrated that ZFAS1 expression was up-regulated by cisplatin in HGS-OVCA cells in vitro, indicating that ZFAS1 may be involved in the process of cisplatin resistance in HGS-OVCA. Zhang *et al.* (40) found that miR-548e was down-regulated and was negatively correlated with ZFAS1 in OC tissues and was targeted by ZFAS1. ZFAS1 promotes OC progression and cisplatin resistance by regulating miR-548E/CXCR4 axis. In conclusion, the study of ZFAS1 signaling pathway is beneficial for targeted therapy of OC.

More lncRNAs with an implicated role in OC are summarized in *Table 2*, including therapeutic targets and prognostic markers. More detailed information on lncRNAs, including their interaction mechanisms with other factors or target genes, and their roles and functions in cellular processes (including proliferation, migration, invasion, prognosis, drug resistance) are detailed in *Table 2*.

Conclusions

Due to the unclear pathogenesis of OC, the lack of specific clinical symptoms or even no symptoms, the lack of effective diagnosis and treatment methods, and chemotherapy resistance, the prognosis of OC is poor and the mortality is high. Existing studies have proved that lncRNAs are involved in the regulation of the occurrence, development, prognosis and treatment of OC. However, due to the diversity of different lncRNAs in different types of malignancies, lncRNAs have become a hot issue in oncology research. Therefore, further studies are deserved to perform to delve into the mechanism of lncRNAs in OC. In this review, we presented several important lncRNAs related to OC, which may provide us with new insights to profoundly understand the role of lncRNAs in OC. Additionally, this review may help us to find novel therapeutic targets or prognostic markers for OC.

Table 2 Analysis of lncRNAs associated with ovarian cancer and related expression in ovarian cancer

LncRNA	Expression	Mechanism	miRNA	Function	Reference
HOTAIR	↑	HOTAIR inhibits miR-206 and enhances the expression of CCND1 and CCND2	miR-206	Proliferation, migration, invasion	(12)
		Overexpression of miR200c down-regulates the expression of HOTAIR	miR-200c	Invasion	(41)
		HOTAIR recruits EZH2 and affects 35H3K27 methylation	–	Migration, invasion, drug resistance	(42)
		HOTAIR prevents miR-138-5p from binding to EZH2 and SIRT1	miR-138-5p	Drug resistance	(43)
		HOTAIR increases CHEK1 protein levels	–	Drug resistance	(44)
MALAT1	↑	The MALAT1-miR-506-iASP axis	miR-506	Proliferation	(15)
		The MALAT1-miR-211-HF19 axis	miR-211	Proliferation, migration, prognosis	(45)
		MALAT1 down-regulates the expression of miR-503-5p	miR-503-5p	Proliferation, prognosis	(46)
		MALAT1 inhibits the activation of Wnt/β-catenin signaling pathway	–	Proliferation, invasion, migration, prognosis	(47)
		MALAT1 inhibits Notch1 signaling	–	Drug resistance	(48)
		The MALAT1-miR-1271-5p-E2F5 axis	miR-1271-5p	Proliferation, migration, invasion, prognosis, drug resistance	(49)
H19	↑	The H19-miR-140-Wnt1axis	miR-140	Proliferation ,migration	(50)
		H19-miR-140-5p-pi3k/AKT signaling pathway	miR-140-5p	Proliferation, invasion, migration	(51)
		The H19-miR-29b-3p-STAT3 axis	miR-29b-3p	Drug resistance	(52)
CCAT1	↑	The CCAT1-miR-4903p-TGFR1 axis	miR-4903p	Migration, invasion	(53)
		CCAT1 regulates the expression of miR-1290	miR-1290	Proliferation, metastasis, prognosis	(20)
		The CCAT1-miR-454-survivin axis	miR-454	Drug resistance	(54)
UCA1	↑	The UCA1-miR-27a-5p-UBE2N axis	miR-27a-5p	Drug resistance	(24)
		The UCA1-miR-654-5p-SIK2 axis	miR-654-5p	Drug resistance	(55)
		The UCA1-AMOTp130-YAP axis	–	Drug resistance	(25)
TUG1	↑	The TUG1-miR-186-5p-ZEB1 axis	miR-186-5p	Proliferation, invasion	(56)
		The TUG1-miR-582-3p-AKT-mTOR axis	miR-582-3p	Prognosis	(57)
		TUG1 targets the expression of miR-29b-3p	miR-29b-3p	Prognosis, drug resistance	(58)
PVT1	↑	The PVT1-JAK2-STAT3-PD-L1 axis	–	Proliferation, invasion, prognosis	(33)
		The PVT1-EZH2-p57 axis	–	Proliferation, prognosis	(59)
		The PVT1-miR-543-SERPINI1 axis	miR-543	Proliferation, migration, invasion, prognosis	(60)
		Foxo4-pvt1-miR-140 signaling pathway	miR-140	Proliferation, prognosis	(61)
MEG3	↓	MEG3-miR-205-5p	miR-205-5p	Migration, invasion, prognosis	(62)
		The MEG3-miR-219a-5p-EGFR axis	miR-219a-5p	Proliferation, migration, invasion, prognosis	(63)
		MEG3 targets the expression of miR-214	miR-214	Drug resistance	(34)

Table 2 *(continued)*

Table 2 *(continued)*

LncRNA	Expression	Mechanism	miRNA	Function	Reference
NEAT1	↑	The NEAT1-let-7g-MEST-ATGL axis	–	Migration, invasion	(64)
		The NEAT1-miR-4500-BZW1 axis	miR-4500	Proliferation, migration, invasion, prognosis	(65)
		The NEAT1-miR-491-5p-SOX3 axis	miR-491-5p	Prognosis, drug resistance	(37)
		The NEAT1-miR-770-5p-PARP1 axis	miR-770-5p	Drug resistance	(36)
ZFAS1	↑	The ZFAS1-miR-150-5p-Sp1 axis	miR-150-5p	Proliferation, migration, invasion, drug resistance	(38)
		The ZFAS1-miR-548e-CXCR4 axis	miR-548e	Proliferation, migration, drug resistance	(40)
FER1L4	↓	FER1L4 overexpression inhibits MAPK signaling	–	Drug resistance	(35)
XIST	↓	The XIST-miR-335-BCL2L2 axis	miR-335	Proliferation, invasion, migration	(66)
		The XIST-miR-106a axis	miR-106a	Proliferation, prognosis	(67)
		The XIST-miR-149-3p-FOXP3 axis	miR-149-3p	Proliferation, invasion, migration, prognosis	(68)
ANRIL	↑	ANRIL-miR-125a-3p-p38 MAPK signaling pathway	miR-125a-3p	Proliferation, migration, prognosis	(69)
		The ANRIL-let-7a-HMGA2 axis	–	Drug resistance	(70)
GAS5	↓	The GAS5-miR-31-5p-ARID1A axis	miR-31-5p	Proliferation, invasion	(71)
		Gas5-mir-21-spry2 signaling pathway	miR-21	Proliferation	(72)
		The GAS5-miR-96-5p-PTEN axis	miR-96-5p	Proliferation, migration	(73)
		The GAS5-miR-196a-5p-HOXA5 axis	miR-196a	Proliferation, prognosis	(27)
		The GAS5-E2F4-PARP1-MAPK axis	–	Drug resistance	(74)

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://biotarget.amegroups.com/article/view/10.21037/biotarget-22-3/rc

Peer Review File: Available at https://biotarget.amegroups.com/article/view/10.21037/biotarget-22-3/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://biotarget.amegroups.com/article/view/10.21037/biotarget-22-3/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Coburn SB, Bray F, Sherman ME, et al. International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. Int J Cancer 2017;140:2451-60.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018.

CA Cancer J Clin 2018;68:7-30.
4. Prat J; FIGO Committee on Gynecologic Oncology. Abridged republication of FIGO's staging classification for cancer of the ovary, fallopian tube, and peritoneum. Cancer 2015;121:3452-4.
5. Matz M, Coleman MP, Carreira H, et al. Worldwide comparison of ovarian cancer survival: Histological group and stage at diagnosis (CONCORD-2). Gynecol Oncol 2017;144:396-404.
6. Sun T. Long noncoding RNAs act as regulators of autophagy in cancer. Pharmacol Res 2018;129:151-5.
7. Kazimierczyk M, Kasprowicz MK, Kasprzyk ME, et al. Human Long Noncoding RNA Interactome: Detection, Characterization and Function. Int J Mol Sci 2020;21:1027.
8. Akrami R, Jacobsen A, Hoell J, et al. Comprehensive analysis of long non-coding RNAs in ovarian cancer reveals global patterns and targeted DNA amplification. PLoS One 2013;8:e80306.
9. López-Camarillo C, Ruíz-García E, Salinas-Vera YM, et al. Deciphering the Long Non-Coding RNAs and MicroRNAs Coregulation Networks in Ovarian Cancer Development: An Overview. Cells 2021;10:1407.
10. Dong L, Hui L. HOTAIR Promotes Proliferation, Migration, and Invasion of Ovarian Cancer SKOV3 Cells Through Regulating PIK3R3. Med Sci Monit 2016;22:325-31.
11. Qiu JJ, Wang Y, Ding JX, et al. The long non-coding RNA HOTAIR promotes the proliferation of serous ovarian cancer cells through the regulation of cell cycle arrest and apoptosis. Exp Cell Res 2015;333:238-48.
12. Chang L, Guo R, Yuan Z, et al. LncRNA HOTAIR Regulates CCND1 and CCND2 Expression by Sponging miR-206 in Ovarian Cancer. Cell Physiol Biochem 2018;49:1289-303.
13. Ji P, Diederichs S, Wang W, et al. MALAT-1, a novel noncoding RNA, and thymosin beta4 predict metastasis and survival in early-stage non-small cell lung cancer. Oncogene 2003;22:8031-41.
14. Gordon MA, Babbs B, Cochrane DR, et al. The long non-coding RNA MALAT1 promotes ovarian cancer progression by regulating RBFOX2-mediated alternative splicing. Mol Carcinog 2019;58:196-205.
15. Lei R, Xue M, Zhang L, et al. Long noncoding RNA MALAT1-regulated microRNA 506 modulates ovarian cancer growth by targeting iASPP. Onco Targets Ther 2017;10:35-46.
16. Medrzycki M, Zhang Y, Zhang W, et al. Histone h1.3 suppresses h19 noncoding RNA expression and cell growth of ovarian cancer cells. Cancer Res 2014;74:6463-73.
17. Yan L, Zhou J, Gao Y, et al. Regulation of tumor cell migration and invasion by the H19/let-7 axis is antagonized by metformin-induced DNA methylation. Oncogene 2015;34:3076-84.
18. Sajadpoor Z, Amini-Farsani Z, Teimori H, et al. Valproic Acid Promotes Apoptosis and Cisplatin Sensitivity Through Downregulation of H19 Noncoding RNA in Ovarian A2780 Cells. Appl Biochem Biotechnol 2018;185:1132-44.
19. Ozawa T, Matsuyama T, Toiyama Y, et al. CCAT1 and CCAT2 long noncoding RNAs, located within the 8q.24.21 'gene desert', serve as important prognostic biomarkers in colorectal cancer. Ann Oncol 2017;28:1882-8.
20. Lai XJ, Cheng HF. LncRNA colon cancer-associated transcript 1 (CCAT1) promotes proliferation and metastasis of ovarian cancer via miR-1290. Eur Rev Med Pharmacol Sci 2018;22:322-8.
21. Hua F, Li CH, Chen XG, et al. Long Noncoding RNA CCAT2 Knockdown Suppresses Tumorous Progression by Sponging miR-424 in Epithelial Ovarian Cancer. Oncol Res 2018;26:241-7.
22. Sun XD, Huan C, Qiu W, et al. Clinical Significance of UCA1 to Predict Metastasis and Poor Prognosis of Digestive System Malignancies: A Meta-Analysis. Gastroenterol Res Pract 2016;2016:3729830.
23. Wang F, Zhou J, Xie X, et al. Involvement of SRPK1 in cisplatin resistance related to long non-coding RNA UCA1 in human ovarian cancer cells. Neoplasma 2015;62:432-8.
24. Wambecke A, Ahmad M, Morice PM, 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;15:3659-78.
25. Lin X, Spindler TJ, de Souza Fonseca MA, et al. Super-Enhancer-Associated LncRNA UCA1 Interacts Directly with AMOT to Activate YAP Target Genes in Epithelial Ovarian Cancer. iScience 2019;17:242-55.
26. Qiu JJ, Lin YY, Ding JX, et al. Long non-coding RNA ANRIL predicts poor prognosis and promotes invasion/metastasis in serous ovarian cancer. Int J Oncol 2015;46:2497-505.
27. Zhao H, Yu H, Zheng J, et al. Lowly-expressed lncRNA GAS5 facilitates progression of ovarian cancer through targeting miR-196-5p and thereby regulating HOXA5. Gynecol Oncol 2018;151:345-55.
28. Xue H, Wu Z, Rao D, et al. Long non-coding RNA

LINC00858 aggravates the oncogenic phenotypes of ovarian cancer cells through miR-134-5p/RAD18 signaling. Arch Gynecol Obstet 2020;302:1243-54.
29. Li P, Huang G. Long noncoding RNA LINC00858 promotes the progression of ovarian cancer via regulating the miR-134-5p/TRIM44 axis. J Recept Signal Transduct Res 2022;42:382-9.
30. Hu Y, Mei XQ, Tang D. Long non-coding RNA XIST is down-regulated and correlated to better prognosis in ovarian cancer. Math Biosci Eng 2020;17:2070-81.
31. Liu E, Liu Z, Zhou Y. Carboplatin-docetaxel-induced activity against ovarian cancer is dependent on up-regulated lncRNA PVT1. Int J Clin Exp Pathol 2015;8:3803-10.
32. El-Khazragy N, Mohammed HF, Yassin M, et al. Tissue-based long non-coding RNAs "PVT1, TUG1 and MEG3" signature predicts Cisplatin resistance in ovarian Cancer. Genomics 2020;112:4640-6.
33. Chen Y, Li F, Li D, et al. Atezolizumab and blockade of LncRNA PVT1 attenuate cisplatin resistant ovarian cancer cells progression synergistically via JAK2/STAT3/PD-L1 pathway. Clin Immunol 2021;227:108728.
34. Zhang J, Liu J, Xu X, et al. Curcumin suppresses cisplatin resistance development partly via modulating extracellular vesicle-mediated transfer of MEG3 and miR-214 in ovarian cancer. Cancer Chemother Pharmacol 2017;79:479-87.
35. Liu S, Zou B, Tian T, et al. Overexpression of the lncRNA FER1L4 inhibits paclitaxel tolerance of ovarian cancer cells via the regulation of the MAPK signaling pathway. J Cell Biochem 2019;120:7581-9.
36. 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;12:7277-89.
37. Jia X, Wei L, Zhang Z. NEAT1 Overexpression Indicates a Poor Prognosis and Induces Chemotherapy Resistance via the miR-491-5p/SOX3 Signaling Pathway in Ovarian Cancer. Front Genet 2021;12:616220.
38. Xia B, Hou Y, Chen H, et al. Long non-coding RNA ZFAS1 interacts with miR-150-5p to regulate Sp1 expression and ovarian cancer cell malignancy. Oncotarget 2017;8:19534-46.
39. Liu R, Zeng Y, Zhou CF, et al. Long noncoding RNA expression signature to predict platinum-based chemotherapeutic sensitivity of ovarian cancer patients. Sci Rep 2017;7:18.
40. Zhang J, Quan LN, Meng Q, 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. Mol Ther Nucleic Acids 2020;20:621-38.
41. Yang C, Li H, Zhang T, et al. miR-200c overexpression inhibits the invasion and tumorigenicity of epithelial ovarian cancer cells by suppressing lncRNA HOTAIR in mice. J Cell Biochem 2020;121:1514-23.
42. Dai ZY, Jin SM, Luo HQ, et al. LncRNA HOTAIR regulates anoikis-resistance capacity and spheroid formation of ovarian cancer cells by recruiting EZH2 and influencing H3K27 methylation. Neoplasma 2021;68:509-18.
43. Zhang Y, Ai H, Fan X, et al. Knockdown of long non-coding RNA HOTAIR reverses cisplatin resistance of ovarian cancer cells through inhibiting miR-138-5p-regulated EZH2 and SIRT1. Biol Res 2020;53:18.
44. Jiang J, Wang S, Wang Z, et al. HOTAIR promotes paclitaxel resistance by regulating CHEK1 in ovarian cancer. Cancer Chemother Pharmacol 2020;86:295-305.
45. Tao F, Tian X, Ruan S, et al. miR-211 sponges lncRNA MALAT1 to suppress tumor growth and progression through inhibiting PHF19 in ovarian carcinoma. FASEB J 2018. [Epub ahead of print]. doi: 10.1096/fj.201800495RR.
46. Sun Q, Li Q, Xie F. LncRNA-MALAT1 regulates proliferation and apoptosis of ovarian cancer cells by targeting miR-503-5p. Onco Targets Ther 2019;12:6297-307.
47. Guo C, Wang X, Chen LP, et al. Long non-coding RNA MALAT1 regulates ovarian cancer cell proliferation, migration and apoptosis through Wnt/β-catenin signaling pathway. Eur Rev Med Pharmacol Sci 2018;22:3703-12.
48. Bai L, Wang A, Zhang Y, et al. Knockdown of MALAT1 enhances chemosensitivity of ovarian cancer cells to cisplatin through inhibiting the Notch1 signaling pathway. Exp Cell Res 2018;366:161-71.
49. Wang Y, Wang X, Han L, et al. LncRNA MALAT1 Regulates the Progression and Cisplatin Resistance of Ovarian Cancer Cells via Modulating miR-1271-5p/E2F5 Axis. Cancer Manag Res 2020;12:9999-10010.
50. Wang Y, Gao WJ. Long non-coding RNA-H19 promotes ovarian cancer cell proliferation and migration via the microRNA-140/Wnt1 axis. Kaohsiung J Med Sci 2021;37:768-75.
51. Xu H, Ding Y, Yang X. Overexpression of Long Noncoding RNA H19 Downregulates miR-140-5p and Activates PI3K/AKT Signaling Pathway to Promote Invasion, Migration and Epithelial-Mesenchymal Transition of Ovarian Cancer Cells. Biomed Res Int

2021;2021:6619730.
52. Tian X, Zuo X, Hou M, et al. LncRNA-H19 regulates chemoresistance to carboplatin in epithelial ovarian cancer through microRNA-29b-3p and STAT3. J Cancer 2021;12:5712-22.
53. Mu Y, Li N, Cui YL. The lncRNA CCAT1 upregulates TGFβR1 via sponging miR-490-3p to promote TGFβ1-induced EMT of ovarian cancer cells. Cancer Cell Int 2018;18:145.
54. Wang DY, Li N, Cui YL. 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.
55. Li ZY, Wang XL, Dang Y, et al. Long non-coding RNA UCA1 promotes the progression of paclitaxel resistance in ovarian cancer by regulating the miR-654-5p/SIK2 axis. Eur Rev Med Pharmacol Sci 2020;24:591-603.
56. Zhan FL, Chen CF, Yao MZ. LncRNA TUG1 facilitates proliferation, invasion and stemness of ovarian cancer cell via miR-186-5p/ZEB1 axis. Cell Biochem Funct 2020;38:1069-78.
57. Dai T, Liang J, Liu W, et al. The miRNA mir-582-3p suppresses ovarian cancer progression by targeting AKT/MTOR signaling via lncRNA TUG1. Bioengineered 2021;12:10771-81.
58. Gu L, Li Q, Liu H, et al. Long Noncoding RNA TUG1 Promotes Autophagy-Associated Paclitaxel Resistance by Sponging miR-29b-3p in Ovarian Cancer Cells. Onco Targets Ther 2020;13:2007-19.
59. Li T, Yang J, Yang B, et al. Ketamine Inhibits Ovarian Cancer Cell Growth by Regulating the lncRNA-PVT1/EZH2/p57 Axis. Front Genet 2020;11:597467.
60. Qu C, Dai C, Guo Y, et al. Long non-coding RNA PVT1-mediated miR-543/SERPINI1 axis plays a key role in the regulatory mechanism of ovarian cancer. Biosci Rep 2020;40:BSR20200800.
61. Ding Y, Fang Q, Li Y, et al. Amplification of lncRNA PVT1 promotes ovarian cancer proliferation by binding to miR-140. Mamm Genome 2019;30:217-25.
62. Tao P, Yang B, Zhang H, et al. The overexpression of lncRNA MEG3 inhibits cell viability and invasion and promotes apoptosis in ovarian cancer by sponging miR-205-5p. Int J Clin Exp Pathol 2020;13:869-79.
63. Wang L, Yu M, Zhao S. lncRNA MEG3 modified epithelial-mesenchymal transition of ovarian cancer cells by sponging miR-219a-5p and regulating EGFR. J Cell Biochem 2019;120:17709-22.
64. 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 Int 2021;21:437.
65. Xu H, Sun X, Huang Y, et al. Long non-coding RNA NEAT1 modifies cell proliferation, colony formation, apoptosis, migration and invasion via the miR-4500/BZW1 axis in ovarian cancer. Mol Med Rep 2020;22:3347-57.
66. Meng Q, Wang N, Duan G. Long non-coding RNA XIST regulates ovarian cancer progression via modulating miR-335/BCL2L2 axis. World J Surg Oncol 2021;19:165.
67. Guo T, Yuan D, Zhang W, et al. Upregulation of long noncoding RNA XIST has anticancer effects on ovarian cancer through sponging miR-106a. Hum Cell 2021;34:579-87.
68. Jiang R, Zhang H, Zhou J, et al. Inhibition of long non-coding RNA XIST upregulates microRNA-149-3p to repress ovarian cancer cell progression. Cell Death Dis 2021;12:145.
69. Wang W, Kong S, Xu A. LncRNA ANRIL suppresses proliferation and promotes apoptosis of ovarian cancer cells by regulating MiR-125a-3p/MAPK signaling pathway. Minerva Med 2022;113:581-2.
70. Miao JT, Gao JH, Chen YQ, et al. LncRNA ANRIL affects the sensitivity of ovarian cancer to cisplatin via regulation of let-7a/HMGA2 axis. Biosci Rep 2019;39:BSR20182101.
71. Zhang J, Yang ZM, Huang Y, et al. LncRNA GAS5 inhibits the proliferation and invasion of ovarian clear cell carcinoma via the miR-31-5p/ARID1A axis. Kaohsiung J Med Sci 2021;37:940-50.
72. Ma N, Li S, Zhang Q, et al. Long non-coding RNA GAS5 inhibits ovarian cancer cell proliferation via the control of microRNA-21 and SPRY2 expression. Exp Ther Med 2018;16:73-82.
73. Dong Q, Long X, Cheng J, et al. LncRNA GAS5 suppresses ovarian cancer progression by targeting the miR-96-5p/PTEN axis. Ann Transl Med 2021;9:1770.
74. Long X, Song K, Hu H, et al. 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: 10.21037/biotarget-22-3
Cite this article as: Qiu J, Sun Y, Ni H, Li L, Xi Q, Jiang H. Research progress of long non-coding RNA in ovarian cancer: a narrative review. Biotarget 2023;6:1.