Proceedings of the 3rd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/85/2025.20121

Function of circRNA in Ovarian Cancer and As a Potential Therapeutic Target

Xiaoen Huang[1,a,*]

[1]*Youjiang Medical University for Nationalities, Guangxi, China*
a. h2939158454@outlook.com
**corresponding author*

Abstract: As a common malignant tumor of female reproductive system, ovarian cancer has a high morbidity and mortality, and most patients have reached the advanced stage when diagnosed. In recent years, circular RNA (circRNA) has attracted much attention in ovarian cancer research due to its unique structural and functional properties. This study focused on the expression profile, function (covering cell proliferation, apoptosis, migration, invasion, drug resistance, etc.) and regulatory molecular mechanisms (including and.) of circRNA in ovarian cancer miRNA, protein interactions, and regulation of gene transcription) and prospects as potential therapeutic targets (such as interfering expression, enhancing function, combination therapy and other strategies and advantages). Through high-throughput sequencing, bioinformatics analysis and a variety of experimental verification methods, the role of ovarian cancer in the occurrence and development of ovarian cancer is deeply explored, aiming to provide a basis for the analysis of the pathogenesis of ovarian cancer, and to develop a new direction for the development of novel treatment strategies and improve the prognosis of patients.

Keywords: Ovarian cancer, circular RNA (circRNA), expression profile, mechanism of action.

1. Introduction

Ovarian cancer (OC) is one of the most common malignant tumors of the female reproductive system, with high morbidity and mortality. According to statistics, there are about 310,000 new cases and about 210,000 deaths worldwide every year. In China, the incidence of OC also shows an increasing trend year by year. Most patients are in the advanced stage at the time of diagnosis, mainly because the ovaries are located deep in the pelvic cavity, and early lesions are difficult to detect and often have no obvious symptoms.

In recent years, with the continuous development of molecular biology technology, the role of non-coding RNA (ncRNA) in the development of tumor has been paid more and more attention. Among them, circRNA stands out for its unique structural and functional characteristics. Circrnas are a special class of ncRNAs that form a closed ring structure through covalent bonds, unlike linear RNA. This unique structure makes circRNA have high stability and is not easily degraded by nucleases in the cell. It has been found in the studies of various tumors that the expression level of circRNA shows abnormal changes, which plays an important role in the occurrence, development, metastasis and drug

DOI: 10.54254/2753-8818/85/2025.20121

resistance of tumors. This provides a new direction for the study of ovarian cancer, and its special stability and potential function in tumors make it possible to develop novel targeted therapies.

The regulatory mechanisms of circRNA are as follows: 1) Interaction with miRNA 2) Interaction with proteins 3) Regulation of gene transcription. This paper mainly studied the expression profile and function of circRNA in OC (including its effects on cell proliferation, apoptosis, migration, invasion, and drug resistance), its mechanism of action as a regulatory molecule, and its prospects as a potential therapeutic target (including strategies and advantages of interfering expression, enhancing function, and combination therapy). The significance of this study lies in the in-depth analysis of the role of circRNA.

2. Expression and function of circRNA in ovarian cancer

2.1. Analysis of expression profile of circRNA in OC

First, RNA sequencing was performed on OC tissue and normal ovarian tissue using high-throughput sequencing techniques such as RNA-SEQ. The sequencing data need to be preprocessed, including the removal of low-quality sequences, pruning of splice sequences, and removal of contaminated sequences, to obtain high-quality RNA sequence data. Then, bioinformatics methods were used to identify and screen circRNA from pre-treated RNA sequence data. By comparing known genome sequences, RNA molecules with circular structures, known as circrnas, were identified. Furthermore, differentially expressed circRNA between OC tissue and normal ovarian tissue was screened by differential expression analysis. In order to verify the accuracy of bioinformatics analysis results, it is necessary to adopt experimental methods for verification. Common validation methods include real-time fluorescence quantitative PCR (qRT-PCR) and RNA fluorescence in situ hybridization (RNA-FISH). Through these methods, the expression of circRNA in OC tissues can be further confirmed. After confirming the expression of circRNA, the next step is to study its mechanism of action in the occurrence and development of diseases. This usually involves cell experiments, animal experiments and other methods, as well as the construction of cell models to observe the effects of circRNA on the biological behaviors of OC cells such as proliferation, migration and invasion.

The researchers first used high-throughput sequencing to detect circRNAs with differential expression in 3 cases of high-grade ovarian serous carcinoma (HGSOC) tissue and 3 cases of normal ovarian tissue. Combined with the differential multiple, P value, FDR, fpkm, etc. of circRNA, 8 circRNAs were selected in H The qRT-PCR verification and sequencing results were carried out in GSOC and ovarian benign lesion tissues, and the hsa-circ-0002755 with the highest differential multiple was screened for further verification and clinical pathological biological characteristics analysis in the HGSOC tissue and OC cell line [1]. Then construct hsa-circ-0002755-siRNA plasmids and overexpressed plasmids to transfect egg OC cells, and explore their biology of ovarian cancer through CCK-8, scratch experiment, Transwell experiment, flow cytometry, Western Blot and other experimental methods. The influence of function. Finally, the miRNA and target genes directly bound to hsa-circ-0002755 are predicted by bioinformatics software, and verified by bifluorescein enzyme experiments. At the same time, the expression of hsa-miR-211-3p in the HGSOC tissue and with hsa-circ-000 were detected. The correlation of 2755 expressions. Finally, the conclusion is that high-throughput sequencing found that 710 circRNAs were differently expressed in the HGSOC tissue. hsa-circ-0002755 was consistent with the sequencing results and had the highest number of differences after qRT-PCR verification. It was lowly expressed in HGSOC tissues and cell lines and Tumor FIGO is related to staging. Functional experiments show that hsa-circ-0002755 can inhibit the proliferation, migration, invasion and EMT of ovarian cancer cells, and promote cell apoptosis. It regulates the expression of the target gene CDKN1B by competitively inhibiting hsa-miR-211-3p.

DOI: 10.54254/2753-8818/85/2025.20121

By collecting ovarian cancer tissue and normal ovarian tissue samples, the researchers used high-throughput sequencing, qRT-PCR and other technologies to detect and compare the expression difference of circRNA in ovarian cancer tissue and normal tissue. Meanwhile, combined with clinicopathological data, the relationship between circRNA expression level and clinicopathological characteristics of ovarian cancer patients was analyzed. The effects of circRNA on biological behavior of ovarian cancer cells and its mechanism of action were also explored through functional experiments such as cell experiments and animal experiments [2]. Draw a conclusion: Hsa circ 0049116 and Hsa circ 0001806 were the main promoting factors of ovarian cancer, and Hsa circ 101057 and Hsa circ 0001095 were the inhibiting factors. Among them, circ ABCB10 and circ MAN1A2 can be used as potential diagnostic markers. The low expression of circ EXOC6B and circ N4BP2L2 is closely related to the prognosis of patients. These circrnas can affect the occurrence and development of ovarian cancer by adsorption of miRNA or by interaction with mRNA to regulate gene transcription or translation process.

2.2. Function of circRNA in OC

2.2.1. Effect on proliferation and apoptosis of OC cells

Overexpression of circ 0001649 in OCSKOV3 cells can inhibit the glycolysis, proliferation, migration and invasion of OC cells by down-regulating the expression of miR-223, and may promote the apoptosis of OC cells (since apoptosis was not directly mentioned in the study, However, inhibition of cell proliferation, migration, and invasion is usually associated with increased apoptosis or decreased cell activity [3]. This study suggests that specific circRNA molecules play an important regulatory role in OC cells, and may participate in the occurrence and development of OC by influencing biological processes such as proliferation and apoptosis.

2.2.2. Effect on migration and invasion of OC cells

CircRNA can influence the migration and invasion ability of OC tissues by regulating the expression of genes associated with OC cell migration and invasion. For example, CDR1as, as a kind of circRNA, has a special ring structure and multiple miRNA binding sites [4]. It can competitively bind specific mirnas (such as mir-7), thereby affecting the regulatory effects of these mirnas on their downstream target genes. This regulatory effect, in turn, affects gene expression related to OC cell migration and invasion, thereby altering the biological behavior of OC cells. The abnormal expression of CDR1as in OC, especially in high-grade serous OC (HGSOC), is closely related to the migration and invasion ability of OC cells. Specifically, high expression of CDR1as may inhibit OC cell migration and invasion, while low expression may promote these processes.

2.2.3. Effect on drug resistance of OC cells

One of the characteristics of OC is its drug resistance. Studies have shown that some circRNAs may be related to the resistance of OC. Li et al. found that the circrNA hsa circ 0010467, which is most upregulated in OC-platinum-resistant tissues, could mediate OC-platinum-resistant tissues by regulating the miR-637/LIF/STAT3 signaling axis [5]. High expression of hsa circ 0010467 can promote the proliferation of OC cells, tumor dry characteristics and platinum resistance.

DOI: 10.54254/2753-8818/85/2025.20121

3. Mechanism of action of circRNA as regulatory molecule

3.1. Interaction between circRNA and miRNA

CircRNA is a class of circular endogenous RNA molecules produced by special selective splicing and widely expressed in eukaryotic cells. They are rich in miRNA binding sites and can act as competitive endogenous RNA (ceRNA), acting as a miRNA "sponge" to unblock the inhibitory effects on their target genes. This interaction mechanism provides a new perspective for understanding gene expression regulation. Specifically, circRNA can reduce the inhibitory effect of miRNA on its target genes by binding to miRNA, thereby regulating the expression level of target genes. This interaction plays an important role in a variety of biological processes, including cell proliferation, differentiation, apoptosis, and the onset and progression of diseases.

Studies have shown that circLONP2 plays an important role in colorectal cancer (CRC) [6]. circLONP2 acts as a key metastasis initiation molecule during CRC development by regulating the intracellular maturation and intercellular transfer of miR-17. circLONP2 binds to miR-17 and reduces the inhibitory effect of miR-17 on its target gene TIAM1, thus promoting the invasion and metastasis of CRC cells. The results showed that the expression level of circLONP2 in CRC tissues was significantly higher than that in normal tissues. High expression of circLONP2 is associated with poor prognosis in CRC patients. Inhibition of circLONP2 expression can significantly reduce the invasion and metastasis ability of CRC cells.

3.2. Interaction between circRNA and Protein

Various ways of interaction between circRNA and proteins have been investigated, including physical binding and functional regulation. These interactions are realized through specific binding sites and sequence recognition, which can stabilize complex formation and regulate the function of circRNA and proteins [7]. CircRNAs can act as "Bridges" to connect proteins, changing interactions between proteins, or they can bind or isolate proteins, preventing them from interacting with other molecules. In addition, circRNA can also act as a "recruitment platform" to recruit proteins to chromatin and participate in the regulation of gene expression. These interactions play an important role in cellular physiological and pathological processes, providing new potential targets for the treatment and diagnosis of diseases.

3.3. Regulation of gene transcription by circRNA

Researchers conducted a study on the transcription of genes regulated by circRNA [8]: First, full transcriptomic sequencing was performed on laryngeal squamous cell carcinoma tissues and paired para-cancerous normal mucosal tissues to establish circRNA, miRNA and mRNA expression profiles of the tissues, so as to identify and screen out differentially expressed circRNAs and obtain circCORO1C. Then, the effects on cell proliferation, migration and apoptosis of laryngeal squamous cell carcinoma (LSCC) were observed by knockout experiment. Then, the interaction between circCORO1C and miRNA was explored by software prediction and molecular experiments, and the downstream target genes were predicted and verified. The results showed that circCORO1C could act as a miRNA sponge and directly interact with let-7c-5p in LSCC cells, eliminating the inhibition of let-7c-5p on the target gene pbx3, leading to the accumulation of pbx3, and then promoting the proliferation, migration and invasion ability of LSCC cells. It is suggested that circCORO1C has the potential as a biomarker and therapeutic target for laryngeal cancer.

DOI: 10.54254/2753-8818/85/2025.20121

4. The prospect of circRNA as a potential therapeutic target

4.1. Therapeutic strategies based on circRNA

4.1.1. Interferes with the expression of circRNA

Interfering the expression of circRNA is a promising direction in the treatment of ovarian cancer. Various bioinformatics tools were used to predict the circrnas associated with gastric cancer and the mirnas that may interact with them, and circ 0001946 and its potential target miRNA miR-142-3p were screened. The circ0001946 siRNA was transfected into gastric cancer cell lines to interfere with the expression of circ0001946 [9]. Then, real-time quantitative PCR was used to detect the expression level of circ 0001946 in cells after transfection to confirm the interference effect. At the same time, CCK-8 assay was used to detect cell viability to evaluate the change of cell proliferation ability, and Transwell assay was used to detect cell invasion ability. Luciferase reporter gene experiment was used to verify the targeting relationship between circ 0001946 and miR-142-3p, and further clarify its mechanism of action. The results were as follows: 1. After interfering the expression of circ 0001946, the expression level of circ 0001946 in gastric cancer cells was significantly reduced, and the proliferation and invasion ability of cells were also significantly inhibited. Luciferase reporter gene experiments confirmed that circ 0001946 could directly target miR-142-3p to regulate the biological behavior of gastric cancer cells. This study suggests that interference with the expression of circ 0001946 has potential value in the treatment of gastric cancer, providing new targets and ideas for the treatment of gastric cancer.

4.1.2. Enhance the function of circRNA

Gene therapy and other techniques were used to enhance the function of specific anticancer circRNA, which brings hope for the treatment of ovarian cancer. First, LAC patients paired with cancer and normal tissues were selected for circRNAs/mRNA co-expression chips to screen and verify circPRKCI, and then samples were expanded to verify its clinical expression characteristics and correlation with prognosis. Secondly, circPRKCI was silenced and overexpressed in vitro. A variety of cell experiments were carried out to evaluate the effects on malignant behavior of lung adenocarcinoma. The subcutaneous tumor carrying model and PDTX model of nude mice were constructed in vivo, and the effect of intratumoral injection of shRNA on the malignant progression of lung adenocarcinoma was evaluated [10]. This study showed that circPRKCI is a potential LAC "oncogene" that can promote the malignant progression of LAC in vivo and in vitro, and its expression is influenced by the expansion of host gene PRKCI. The transcription factor E2F7 is regulated by the ceRNA mechanism. That is, by enhancing the function of circPRKCI, the malignant progression of lung adenocarcinoma can be promoted.

4.1.3. Combined treatment

The combination therapy model of circRNA targeting strategy combined with traditional chemotherapy has achieved remarkable results. Studies have shown that circKDM4B is stably expressed in liver cancer cytoplasm, which can promote the proliferation, invasion and migration of liver cancer cells, and inhibit the apoptosis of liver cancer cells, suggesting that circKDM4B is expected to be a therapeutic target for liver cancer [11].

DOI: 10.54254/2753-8818/85/2025.20121

4.2. The advantage of circRNA as a therapeutic target

4.2.1. High stability

CircRNA has special structure, high intracellular stability and long half-life. This property makes circRNA-based therapeutics unique. Cell experiments have shown that siRNA or antisense oligonucleotides (ASO) targeting circRNA act longer in cells than linear RNA-like drugs. It can maintain an effective concentration in cells for a long time, continuously regulate the target circRNA, and ensure the lasting therapeutic effect.

From the clinical point of view, it can reduce the frequency of patient administration. Frequent administration of drugs in OC patients not only increases pain and medical costs, but also affects the efficacy due to compliance issues. CircRNA therapy has a long drug action time, reduces the number of administration, improves patient compliance, and is conducive to long-term stable treatment.

4.2.2. Tissue specificity

The expression specificity of circRNAs is strong in different tissues. Many circRNAs that are highly expressed in OC tissues have low or no expression in normal tissues such as liver, kidney and lung. This provides an ideal target for specific therapy.

Therapeutic drugs designed for OC-specific circRNA can accurately act on OC cells and reduce adverse effects on normal tissues. In animal model experiments, siRNA treatment for OC-specific circRNA was used to monitor the function indicators of liver, kidney and other important organs, and it was found that they fluctuated in the normal range, indicating that there was no significant impact on organ function.

Traditional chemotherapy drugs lack tissue specificity, kill cancer cells and often damage normal tissue cells, cause adverse reactions, and limit clinical application and efficacy. Tissue-specific treatment strategies for circRNA reduce the risk of side effects while improving efficacy, providing safer and more effective treatment options for patients with OC.

4.2.3. Multi-target role

The treatment strategy based on circRNA has a multi-target mechanism of action, which is superior to the traditional single-target therapy. Circrnas can interact with various molecules such as mirnas and proteins to form complex regulatory networks and affect multiple signaling pathways at the same time to achieve multi-target synergistic therapy. For example, circ ABC circRNA can interact with multiple mirnas and participate in the regulation of key OC signaling pathways. The malignant biological behavior of OC cells was completely inhibited by multi-target action. The cell experiment observed that the proliferation, migration and invasion ability of cancer cells were inhibited, and the resistance rate to chemotherapy drugs was reduced, effectively overcoming the problem of resistance to single target therapy, and improving the comprehensiveness and effectiveness of treatment.

In OC clinical treatment, drug resistance is one of the main causes of treatment failure. Single target therapy is easy to cause drug resistance in cancer cells, resulting in poor therapeutic effect. CircRNA multi-target therapy strategy can act on multiple key molecules and signaling pathways at the same time, making it difficult for cancer cells to escape treatment, and providing a strong guarantee for long-term treatment and cure of OC.

5. Conclusion

CircRNA plays a key role in the occurrence and development of ovarian cancer. It can deeply participate in the regulatory network of biological behaviors such as proliferation, apoptosis,

DOI: 10.54254/2753-8818/85/2025.20121

migration, invasion and drug resistance of ovarian cancer cells by interacting with miRNA and protein and regulating gene transcription in various ways, thus having a significant impact on the progression of ovarian cancer. As a potential therapeutic target, circRNA has significant advantages such as high stability, tissue-specific and multi-target action, which brings a new concept and opportunity for the treatment of ovarian cancer. Looking forward to the future, it is still necessary to invest heavily in research to elaborate the fine molecular mechanism of circRNA affecting ovarian cancer, make full efforts to develop precise diagnostic markers and innovative treatment schemes based on circRNA, and actively promote the transformation and application of relevant research results into clinical practice. Only in this way can the treatment level of ovarian cancer be effectively improved. The quality of life and prognosis of patients were significantly improved.

References

[1] *Gao, Y. (2019). Effect of Hsa-circ-0002755 on biological behavior and mechanism of high-grade ovarian serous carcinoma (Ph.D. Dissertation, China Medical University). Learned scholar. https://link.cnki.net/doi/10.27652/d.cnki.gzyku.2019.000050doi:10.27652/d.cnki.gzyku.2019.000050.*

[2] *Ye, S., Lin, Y., & NA. (2024). Overview of circular RNA and its role in ovarian cancer.* Guangdong Medicine, 11*, 1–9. https://doi.org/10.13820/j.carolcarrollnki.gdyx.20241934*

[3] *Cheng, S. Q., Li, H. B., & Yan, L. U. (2022). Inhibition of cyclic RNA0001649 on glycolysis, proliferation, migration, and invasion of SKOV3 cells in ovarian cancer.* Chinese Journal of Health Inspection, 23*, 2879–2882.*

[4] *Guo, Q. X. (2020). Expression of circular RNA CDR1as in high-grade serous ovarian cancer and its effect on invasion and migration of ovarian cancer cells (Master's Thesis, China Medical University). Master. https://link.cnki.net/doi/10.27652/d.cnki.gzyku.2020.000912doi:10.27652/d.cnki.gzyku.2020.000912.*

[5] *Wu, Y., Xu, M., Feng, Z., Wu, H., Wu, J., Ha, X., ... & Wu, X. (2023). AUF1-induced circular RNA hsa_circ_0010467 promotes platinum resistance of ovarian cancer through the miR-637/LIF/STAT3 axis.* Cellular and Molecular Life Sciences, 80*(9), 256.*

[6] *Han, K., Wang, F. W., Cao, C. H., Ling, H., Chen, J. W., Chen, R. X., ... & Xie, D. (2020). CircLONP2 enhances colorectal carcinoma invasion and metastasis through modulating the maturation and exosomal dissemination of microRNA-17.* Molecular Cancer, 19*, 1–18.*

[7] *Zhou, W. Y., Cai, Z. R., Liu, J., Wang, D. S., Ju, H. Q., & Xu, R. H. (2020). Circular RNA: metabolism, functions and interactions with proteins.* Molecular Cancer, 19*, 1–19.*

[8] *Wu, Y., Zhang, Y., Zheng, X., Dai, F., Lu, Y., Dai, L., ... & Gao, W. (2020). Circular RNA circCORO1C promotes laryngeal squamous cell carcinoma progression by modulating the let-7c-5p/PBX3 axis.* Molecular Cancer, 19*, 1–18.*

[9] *Cheng, Z., Liu, G., Huang, C., & Zhao, X. (2021). Upregulation of circRNA_100395 sponges miR-142-3p to inhibit gastric cancer progression by targeting the PI3K/AKT axis.* Oncology Letters, 21*(5), 419. https://doi.org/10.3892/ol.2021.12680*

[10] *Xia, W. J. (2017). Function and mechanism of circPRKCI in promoting malignant progression of lung adenocarcinoma (Master's Thesis, Nanjing Medical University). Master. https://link.cnki.net/doi/10.27249/d.cnki.gnjyu.2017.000405doi:10.27249/d.cnki.gnjyu.2017.000405.*

[11] *Ma, X., Tan, W., Yang, L., Xie, Z., Wang, Q., Chen, Y., & Shang, C. (2021). Experimental study on regulation of proliferation, invasion, and migration of hepatocellular carcinoma cells by circular RNA circKDM4B.* Lingnan Modern Clinical Surgery Department, 6*, 614–619+624.*