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Pathological Diagnostic Efficacy and Influencing Factors of Ovarian Tumour Using Cytological Smears Combined with Frozen Sections

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FL, NZ and DW conducted the experiments in this study. JH and YP contributed to the design and interpretation of the current study and wrote the article. All authors read, revised, and approved the final manuscript.

Key words
Ovarian tumor, Cytological smear, Frozen section, Paraffin section, Influencing factors

ABSTRACT

The objective of this study was to investigate the pathological diagnostic efficacy of applying cytological smears (CytS) combined with frozen sections (FroS) in patients with ovarian tumour (OT), and to study the relevant factors affecting the pathological diagnostic efficacy of CytS combined with FroS. A total of 106 patients admitted for OT surgery from May 2022 to May 2023 were selected as study subjects using simple random sampling method. FroS, CytS and paraffin sections were performed on all tumour tissue specimens during and after surgery. In the univariate analysis, tumour diameter and whether metastasis was a relevant factor affecting the diagnostic efficacy of cytology smear combined with frozen section, and in the multivariate logistic regression analysis, tumour diameter and whether metastasis was an independent risk factor affecting the pathological diagnostic efficacy of cytology smear combined with frozen section. The application value of cytology smear combined with frozen section diagnosis in OT patients is high, and its diagnostic effect is good. In order to ensure the accuracy of the diagnostic results of cytology smear combined with frozen section diagnostic results, the size of the diameter of the patient's tumour and whether metastasis occurs should be taken into account during the actual test, so as to improve the diagnostic accuracy of the case and provide a strong basis for clinical treatment.

INTRODUCTION

Ovarian tumour (OT) is one of the most common gynaecological tumours in women worldwide. According to statistics, in 2020, there will be about 9.2 million new cancer cases in women globally, of which ovarian cancer (OC) accounts for about 3.4%, and there will be about 4.4 million deaths due to cancer, of which OC accounts for 4.7%, which poses a serious threat to women's life and health (Sung *et al*., 2021). Family history is one of the important risk factors for OT, and about 10% to 15% of patients with OC have a family history, of which about 5% to 10% are associated with mutations in the *BRCA1* and *BRCA2* genes (Yun *et al*., 2022). OC can be classified into different subtypes, including epithelial OC, sexually cued neoplasms, and germ cell tumours. These subtypes differ in incidence, clinical manifestations and prognosis, presenting a diverse and multimorbid insidious disease (Ordulu *et al*., 2021).

In recent years, international research on OT mainly involves early screening and diagnosis, pathology, and new treatment methods. Since OC is often detected at a late stage, early screening and diagnosis have become the focus of research. cytological smear (CytS) and frozen section (FroS) are commonly used techniques in the diagnosis and surgical treatment of OT. Such diagnostic techniques play an important role in the classification, pathological diagnosis and surgical decision-making of OT. Therefore, it is particularly important to improve the efficacy of OT diagnosis.

CytS is a method by which suspected tumour cells are collected and coated, then observed and analyzed under a microscope. In the diagnosis of OT, CytS can be used to assess the cytological features of fluid within an ovarian cyst or an ovarian mass, and can help to identify the benign or malignant nature of ovarian cysts (Azami *et al*.,

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2018). FroS is a method of rapidly freezing, cutting, and staining suspected tumour tissues during surgery, followed by immediate pathological diagnosis under a microscope. FroS is usually used during surgery and can provide rapid pathological diagnostic results that help surgeons make decisions during surgery. For OT, FroS can be used to assess the nature of the tumour, the state of the margins and the presence of infiltration. However, due to the speed of sample processing, FroS may have limited assessment of tissue structure and cytological features (Buza, 2019; Mahadevappa *et al*., 2017).

Based on this, OT surgical patients admitted to our hospital during the period from May 2022 to May 2023 were selected as the study subjects to investigate the value of CytS combined with FroS in the diagnosis of OT patients as well as the factors affecting them.

MATERIALS AND METHODS

General information

A total of 106 OT patients treated from May 2022 to May 2023 were selected, with ages ranging from 21 to 64 years, median age (45.65±7.32) years, 70 premenopausal and 36 postmenopausal. Body mass index (BMI) of the patients was 19.2-27.6 kg/m^2, median BMI (23.11±2.69) kg/m^2, OT diameter: 2.5-13.3 cm and median diameter of 6.69±1.02 cm.

Patients were eligible to join the present study if they met the following inclusion criteria: (a) patients treated with OT resection or excision; (b) patients with complete intraoperative cell pictures, FroS and fresh tumour tissue in the specimen; (c) patients who underwent postoperative paraffin section (PaS) with a confirmed pathological diagnosis of OT; and (d) patients with complete and unabsent pathological diagnosis. Patients with comorbidities of other tumour diseases, those who were intolerant to OT resection or debulking and those who underwent preoperative radiotherapy or chemotherapy were excluded from the present study.

Diagnostic methods for CytS pathology

When the patient underwent surgery, the intraoperatively excised or rejected tissue was placed in a specimen bag and sent to the laboratory. Fresh tissue samples cut from OT lesions were prepared into CytS by scraping or printing method. CytS was placed in cryo-fixing solution, fixed for 30 s, stained with conventional hematoxylin-eosin (HE) staining method, and placed under an ordinary trinocular microscope (manufacturer: Leica Microsystems (Shanghai) Trading Co. Ltd; Model: DM3000) for pathological tissue observation.

Diagnostic methods for FroS pathology

Two to three pieces of fresh tissue samples of OT lesions excised or rejected intraoperatively were taken, with a sample size of approximately 20 mm × 20 mm × 2 cm, and the bloody components on the surface of the samples were drained with filter paper, and then the samples were placed in a tissue supporter, which was added with a water-soluble mixture of polyethylene glycol and polyethylene glycol coated around it (Optimal Cutting Temperature Compound; OTC), quickly placed in the low temperature (-25 ℃) quick-freezing table for tissue freezing, and then through the frozen sectioning machine on the frozen tissue for 6-8 μm continuous sectioning, after sectioning, it will be placed in cryofixing solution for 30s, stained with HE, dehydrated by alcohol gradient locks, dried and sealed by neutral gum, and then placed in a light microscope for pathology and tissue observation.

Pathological methods of diagnosis of PaS

In the remaining excised or rejected OT lesion fresh tissue in the specimen bag to take the size of about 20mm × 20mm × 2cm tissue block, after washing the surface with saline, filter dry surface water, fixed with 4% formaldehyde for 24h, after fixation, the sample was washed with water, low dehydration with alcohol, xylene transparent and get rid of the transparent agent, conventional paraffin embedded, correction of the tissue block, to the thickness of 5 μm to perform PaS, and then Conventional HE staining was performed, and finally they were placed under a light microscope for observation.

CytS, FroS, and PaS pathology diagnoses were performed by the same 2 pathologists with high seniority to ensure the accuracy of the diagnostic results.

Observation indicators and evaluation criteria

In this study, the diagnostic results of PaS were used as the gold standard. (a) the diagnostic results of CytS, FroS single diagnosis and combined diagnosis, i.e., the number of benign cases, the number of malignant cases, the number of diagnostic conformity rate (true positive+true negative)/total number of cases×100% were observed. (b) Receiver Operating Characteristic (ROC) curve analysis was used to compare the AUC value, sensitivity, and specificity of CytS, FroS single diagnosis and combined diagnosis. (c) Single-factor and multifactor binary logistic regression analyses were used to analyse the relevant factors affecting the efficacy of CytS combined with FroS pathology diagnosis.

Statistical analysis

Statistical analysis was performed with SPSS 26.0, Excel and other research tools, and the Kolmogorov-

Smirnov test verified that the measurements of this study conformed to the normal distribution, and the measurements (±S) were tested by t-test, and the counts [n(%)] were tested. The efficacy of CytS combined with FroS pathology diagnosis was assessed using the ROC curve, and the influencing factors were analysed by using CytS combined with FroS pathology diagnosis as the dependent variable, and the single factors were compared and analysed, and the indicators with statistical significance (P<0.05) in their results were set up as the independent variables, and analysed by using the Logistic regression model was used to analyse the results. P<0.05 difference was statistically significant, test level α=0.05.

RESULTS

Taking the diagnostic results of PaS as the "gold standard", in the single CytS diagnosis, 45 cases were malignant and 61 cases were benign, with a diagnostic compliance rate of 89.62% (95/106). In the single FroS diagnosis, 41 cases were malignant and 65 cases were benign, with a diagnostic compliance rate of 85.85% (91/106). In CytS combined FroS diagnosis, there were 49 cases of malignant and 57 cases of benign, with a diagnostic compliance rate of 93.40% (99/106) (Table I).

Comparison of the efficacy of CytS, FroS Single Diagnosis and combined diagnosis are shown in Table II. Based on the OT benign and malignant diagnostic results of PaS, ROC curve analysis was performed with the tumour benign and malignant of the included subjects as the categorical variable, and the results showed that the AUC of CytS, FroS, and CytS combined with FroS were all 0.700 (P<0.05). The sensitivity of CytS combined with FroS was the highest, 87.50%, followed by single CytS, 80.36%, and the sensitivity of single FroS was the lowest, 73.21%. The two-by-two comparisons of ROC curves of CytS, FroS, and CytS combined with FroS were all statistically significant (P<0.05) (Table III).

Table I. Comparison of CytS, FroS single and combined diagnostic results (n).

Diagnostic methods	Diagnostic results	Gold standards		Total
		Malignant	Benign	
CytS (n=106)	Malignant	45	0	45
	Benign	11	50	61
	Total	56	50	106
FroS (n=106)	Malignant	41	0	41
	Benign	15	50	65
	Total	56	50	106
CytS combined with FroS (n=106)	Malignant	49	0	49
	Benign	7	50	57
	Total	56	50	106

The results of univariate analysis illustrated that age, tumour type, number of pregnancies, number of cystic cavities, number of miscarriages, family history of OT, and multiple foci were not statistically significant (P>0.05), while tumour diameter and whether or not it metastasized were statistically significant (P<0.05) (Table IV).

In order to further clarify the independent risk factors affecting the diagnostic efficacy of CytS combined with FroS pathology, this study conducted logistic regression analysis with whether CytS combined with FroS pathology meets the gold standard (PaS) as the dependent variable,

Table II. ROC curve analysis of CytS combined with FroS pathology for diagnosis of OT patients.

Methods	AUC	SE	95% CI	Youden index J	P	Sensitivity	Idiosyncrasy
CytS	0.902	0.027	0.829~0.951	0.804	<0.001	80.36%	100.00%
FroS	0.866	0.030	0.786~0.924	0.732	<0.001	73.21%	100.00%
CytS combined with FroS	0.938	0.022	0.873~0.975	0.875	<0.001	87.50%	100.00%

Table III. Comparison of CytS, FroS single diagnosis and combined diagnosis ROC curves.

Methods	AUC differential	SE	95% CI	Z	P
CytS ~ Frozen Smear	0.036	0.017	0.002~0.070	2.057	0.040
FroS ~ CytS combined FroS	0.071	0.024	0.025~0.118	3.028	0.003
CytS to CytS combined with FroS	0.036	0.017	0.002~0.070	2.057	0.040

Table IV. One-way analysis of factors affecting the diagnostic efficacy of CytS combined with FroS pathology (n).

Element		Compliance with gold standard (n=99)	Non-compliance with gold standard (n=7)	χ2 value	P value
Epithelial tumour		45(45.45)	5(5.05)	1.943	0.584
Germ cell tumour		28(28.28)	1(1.01)		
Gonadal mesenchymal tumours		20(20.20)	1(1.01)		
Metastatic tumour		6(6.06)	0(0.00)		
Age (Years)	<50	49(49.49)	3(3.03)	0.003	0.959
	≥50	50(50.51)	4(4.04)		
Pregnancies n(time)	≤1	80(80.81)	6(6.06)	0.032	0.858
	>1	19(19.19)	1(1.01)		
Cystic cavities (pcs)	<10	90(90.91)	7(7.07)	0.018	0.895
	≥10	9(9.09)	0(0.00)		
Abortions n (time)	≤1	70(70.71)	5(5.05)	0.152	0.697
	>1	29(29.29)	2(2.02)		
OT family history	Yes	13(13.13)	1(1.01)	0.241	0.624
	No	86(86.87)	6(6.06)		
Tumour diameter	<5	66(66.67)	1(1.01)	5.625	0.018
	≥5	33(33.33)	6(6.06)		
Transferred	Yes	37(37.37)	6(6.06)	4.490	0.034
	No	62(62.63)	1(1.01)		
Multilocular	Yes	32(32.32)	0(0.00)	1.889	0.169
	No	53(53.54)	7(7.07)		

and tumour diameter, whether it is metastatic or not, and multiple foci as the independent variables, and the assigned values (Table V). The results showed that tumour diameter and whether it was metastatic or not were independent risk factors affecting the diagnostic efficacy of CytS combined with FroS pathology (Table VI).

Table V. Variable assignment.

Variant		Assignment
Dependent variable	Does CytS combined with FroS pathology meet the "gold standard"?	0=No; 1=Yes
Independent variable	Tumour diameter	0=<5↑; 1=≥5↑
	Transferred or not	0=No; 1=Yes

DISCUSSION

Pathological diagnosis is of great significance in patients with OT, and it can determine the type of OT, such as epithelial tumours, gonadal mesenchymal tumours or germ cell tumours (Zhu *et al*., 2022; Saldanha *et al*., 2022). Different types of tumours have different biological behaviours and prognoses, so pathological diagnosis can provide a basis for selecting appropriate treatment options. Pathological diagnosis can determine the degree of malignancy of OT, i.e., the heterogeneity and proliferative activity of the tumour cells. This is essential for predicting the patient's prognosis and selecting appropriate treatment. Often, malignant tumours require more aggressive treatment strategies such as surgical resection, radiotherapy and chemotherapy. In addition, diagnostic pathology can provide detailed information about the OT tissue, such as tumour size, depth of infiltration, vascular invasion, and lymph node metastasis. This information can help doctors determine the best treatment strategy, such as the extent and method of surgery, the dose and area of radiotherapy, and the choice of chemotherapeutic agents.

Table VI. Multifactorial logistic regression analysis affecting the diagnostic efficacy of CytS combined with FroS pathology.

Independent variables	B	SE	Wald χ^2	P	OR	95%CI
Constant	-5.848	1.422	16.924	<0.001	0.003	/
Tumour diameter	2.630	1.126	5.449	0.020	13.868	1.525 ~ 126.144
Transferred	2.463	1.129	4.763	0.029	11.744	1.285 ~ 107.302

The commonly used pathological diagnostic methods in the clinic are frozen section, CytS, PaS, etc. Among them, CytS is relatively easy to operate. Among them, CytS is relatively easy to operate, and it is easy for pathologists to observe the clearer contours of the tumour tissue cells under the optical microscope, and the structures such as papillae and glands can be observed in the cell prints, which is beneficial to clinical diagnosis. By making multiple scrapings and prints of the tumour section, the defects in the sampling of FroS can be effectively compensated for, but a single CytS diagnosis lacks the histological structure, and the diagnostic misdiagnosis rate is relatively high if the tumour is infiltrative (Nomura *et al*., 2021; Mahadevappa *et al*., 2017). For FroS, histological structures can be clearly observed under light microscopy for histological features (Shah *et al*., 2019; Basaran *et al*., 2014). However, compared with PaS, this diagnostic method is affected by the preparation, which can result in swollen cells, oversized tissues that are not easily or unevenly frozen, and blurred cytoplasmic background with anisotropy, which can be

easily confused with OTs of different natures, and pseudo-infiltration, leading to misdiagnosis (Kumar *et al*., 2021; Kennedy *et al*., 2019; Tranoulis *et al*., 2018). Therefore, whether it is a single frozen section or a single CytS, each has its own shortcomings, while the combined diagnosis of frozen section and CytS can not only clearly observe the tumour cytology, but also the tumour cytological structure, and its diagnostic accuracy is better.

The results of this study showed that the combined diagnostic accuracy (93.40%) was higher compared to the diagnostic accuracy of single frozen section (85.85%) and single CytS (89.62%). After ROC curve analysis, CytS combined with FroS had the highest diagnostic efficacy, with a sensitivity of 87.50%, which was statistically significant compared with single frozen section and single CytS diagnosis ($P<0.05$). It is fully demonstrated that the combined diagnosis of frozen section and CytS has high sensitivity and its diagnostic accuracy is high, and its findings are consistent with the findings of Ferdous *et al*. (2019). From the results of the study, it can be seen that there were seven cases of false-negative CytS combined with FroS diagnosis, and after multifactorial logistic regression analysis, it was found that the diameter of the tumour and the presence of metastasis were the independent risk factors affecting the combined diagnosis of the two. The reason for this analysis was that tumours with larger diameters were more likely to be detected during surgery and larger specimens were obtained. In contrast, tumours with smaller diameters may be easily overlooked or incompletely resected during surgery. This may lead to differences in the quantity and quality of specimens, which in turn may affect the accuracy and comprehensiveness of pathological diagnosis (Chen *et al*., 2021). There may be a correlation between the diameter and metastasis of a tumour and its histological features. Larger diameter tumours may exhibit more pronounced histological changes, such as higher cellular heterogeneity, proliferative activity or areas of necrosis (Yoshida *et al*., 2021). In addition, metastatic tumours may present different histological features at the site of metastasis. These changes may affect the pathologist's judgement and diagnosis of the tumour (Hu *et al*., 2018). Moreover, larger diameter tumours and metastatic tumours are usually associated with a poorer prognosis.

CONCLUSION

Pathological diagnosis of tumours with these features may be more inclined to emphasise their malignancy and a more aggressive treatment approach. In contrast, tumours with smaller diameters and no metastases may be considered to have a better prognosis, and therefore pathological diagnoses may result in a greater focus on their benign or less malignant degree.

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IRB approval

This study was approved by the Advanced Studies Research Board of Peking University First Hospital Ningxia Women and Children's Hospital, Yinchuan, China.

Ethical approval

The study was carried out in compliance with guidelines issued by Ethical Review Board Committee of Peking University First Hospital Ningxia Women and Children's Hospital, China. Before the study was initiated, the case information was sent to our Ethics Committee to complete the ethical approval in accordance with the Declaration of Helsinki (Shrestha and Dunn, 2019) Ethical principles. The patient and guardian agreed to participate in the study and signed the consent form. The official letter would be available on fair request to corresponding author.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Azami, S., Aoki, Y., Iino, M., Sakaguchi, A., Ogura, K., Ogishima, D. and Matsumoto, T., 2018. Useful aspects of diagnosis of imprint cytology in intraoperative consultation of ovarian tumors: comparison between imprint cytology and frozen sections. *Diagn. Cytopathol.*, **46**: 28-34. https://doi.org/10.1002/dc.23844

Basaran, D., Salman, M.C., Calis, P., Ozek, A., Ozgul, N., Usubütün, A. and Yuce, K., 2014. Diagnostic accuracy of intraoperative consultation (frozen section) in borderline ovarian tumours and factors associated with misdiagnosis. *J. Obstet. Gynaecol.*, **34**: 429-434. https://doi.org/10.3109/01443615.2014.902043

Buza, N., 2019. Frozen section diagnosis of ovarian epithelial tumors: Diagnostic pearls and pitfalls. *Arch. Pathol. Lab. Med.*, **143**: 47-64. https://doi.

org/10.5858/arpa.2018-0289-RA

Chen, Y.Y., Lin, H., Wu, C.H., Lan, J., Tsai, C.C., Fu, H.C. and Ou, Y.C., 2021. Factors associated with the inconsistent diagnosis between frozen section and permanent pathologic examination in borderline ovarian tumors. *J. Obstet. Gynaecol. Res.*, **47**: 2729-2736. https://doi.org/10.1111/jog.14831

Ferdous, J., Chowdhury, S., Begum, F., Akhter, S., Khatun, S. and Faika, J., 2019. Intraoperative consultation (frozen section) in the diagnosis of ovarian tumour. *Bangladesh med. J.*, **48**: 34-38. https://doi.org/10.3329/bmj.v48i3.51795

Hu, J., Khalifa, R.D., Roma, A.A. and Fadare, O., 2018. The pathologic distinction of primary and metastatic mucinous tumors involving the ovary: A re-evaluation of algorithms based on gross features. *Annls Diagn. Pathol.*, **37**: 1-6. https://doi.org/10.1016/j.anndiagpath.2018.07.001

Kennedy, N.T., Sebastian, A., Thomas, D.S., Thomas, A., Gupta, M., Kumar, R.M. and Peedicayil, A., 2019. Diagnostic accuracy of frozen section and its influence on intraoperative management of indeterminate epithelial ovarian tumors. *Indian J. Surg. Oncol.*, **10**: 268-273. https://doi.org/10.1007/s13193-018-00869-3

Kumar, A.S., Chander, V. and Parthasarathy, J., 2021. Diagnostic accuracy of intraoperative frozen section analysis in correlation with histopathological diagnosis of ovarian tumors in a tertiary care center–a retrospective study. *Cancer Invest.*, **39**: 153-158. https://doi.org/10.1080/07357907.2020.1865395

Mahadevappa, A., Nisha, T.G. and Manjunath, G.V., 2017. Intra-operative diagnosis of breast lesions by imprint cytology and frozen section with histopathological correlation. *J. clin. Diagn. Res.,* **11**: EC01-EC06. https://doi.org/10.7860/JCDR/2017/24454.9323

Nomura, N., Sugiyama, T., Tajiri, T., Fujita, H., Hiraiwa, S., Toguchi, S., Machida, T., Itoh, H., Kajiwara, H., Muramatsu, T. and Nakamura, N., 2021. Accuracy of imprint cytology and frozen section histology for intraoperative diagnosis of ovarian epithelial tumors: A comparative study and proposed algorithm. *Diagn. Cytopathol.*, **49**: 682-690. https://doi.org/10.1002/dc.24722

Ordulu, Z., Watkins, J. and Ritterhouse, L.L., 2021. Molecular pathology of ovarian epithelial neoplasms: Predictive, prognostic, and emerging biomarkers. *Surg. Pathol. Clin.*, **14**: 415-428. https://doi.org/10.1016/j.path.2021.05.006

Saldanha, E., Desai, S.M., Patel, D.G., Dhakad, V., Joseph, B., Ghosh, S., Prakash, V., Deepti, H. and Monteiro, A., 2022. NIPEC with single-dose intraperitoneal cisplatin and paclitaxel in stage III Epithelial ovarian cancer. *South Asian J. Cancer*, **12**: 74-80. https://doi.org/10.1055/s-0042-1751098

Shah, J.S., Mackelvie, M., Gershenson, D.M., Ramalingam, P., Kott, M.M., Brown, J., Gauthier, P., Nugent, E., Ramondetta, L.M. and Frumovitz, M., 2019. Accuracy of intraoperative frozen section diagnosis of borderline ovarian tumors by hospital type. *J. Minim. Invasive Gynecol.*, **26**: 87-93. https://doi.org/10.1016/j.jmig.2018.04.005

Shrestha, B. and Dunn, L., 2019. The declaration of Helsinki on medical research involving human subjects: A review of seventh revision. *J. Nepal Hlth. Res. Counc.*, **17**: 548-552. https://doi.org/10.33314/jnhrc.v17i4.1042

Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A. and Bray, F., 2021. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: Cancer J. Clin.*, **71**: 209-249. https://doi.org/10.3322/caac.21660

Tranoulis, A., Thomakos, N., Sotiropoulou, M. and Rodolakis, A., 2018. What is the accuracy of frozen section in the diagnosis of mucinous ovarian tumours? A 9-year review of performance in a Greek tertiary referral centre. *Arch. Gynecol. Obstet.*, **297**: 185-191. https://doi.org/10.1007/s00404-017-4582-7

Yoshida, H., Tanaka, H., Tsukada, T., Abeto, N., Kobayashi-Kato, M., Tanase, Y., Uno, M., Ishikawa, M. and Kato, T., 2021. Diagnostic discordance in intraoperative frozen section diagnosis of ovarian tumors: A literature review and analysis of 871 cases treated at a Japanese cancer center. *Int. J. Surg. Pathol.*, **29**: 30-38. https://doi.org/10.1177/1066896920960518

Yun, H., Han, G.H., Cho, H., Kim, S. and Kim, J.H., 2022. NANOG regulates tumor metastasis via AMPK/mTOR signaling pathway in patients with epithelial ovarian cancer (252). *Gynecol. Oncol.*, **166**: S135-S136. https://doi.org/10.1016/S0090-8258(22)01474-3

Zhu, S., Zhang, C., Cao, D., Bai, J., Yu, S., Chen, J., Wang, J., Ren, T., Yang, J., Yu, M. and Xiao, X., 2022. Genomic and TCR profiling data reveal the distinct molecular traits in epithelial ovarian cancer histotypes. *Oncogene*, **41**: 3093-3103. https://doi.org/10.1038/s41388-022-02277-y