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OC1

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2802

子宮頸黏液性腺癌:台北榮民總醫院的經驗
Mucinous adenocarcinoma of cervix: experience of a single institute

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論文發表方式：
口頭報告

論文歸類：
婦癌

Abstract

Objective: Mucinous adenocarcinoma of the uterine cervix is a rare form of cervical malignancy that carries a worse prognosis compared to more common types of cervical cancer. Furthermore, it is often not related to HPV. This is a case series describing the experience from a single institution.

Method: Newly diagnosed cervical cancer patients were enrolled using the pathology database at our hospital from January 2014 to October 2019.

Results: In total 16% (53/333) of the cases were adenocarcinoma of which 15% (8/53) were mucinous adenocarcinoma. Of the eight patients with mucinous adenocarcinoma of the cervix identified, two were gastric type, two intestinal type, one signet ring cell type and the rest were not specified. The overall average age was 55.6 years old. Four were advanced stage and four were early stage. Of the three patients tested for HPV, only one was positive. Of the 4 that have deceased, 3 (25%) lived less than 1 year which is significantly lower than the 92.1% 1-year survival at our hospital. For the other patients, three are relatively newly diagnosed and have just finished adjuvant treatment and one patient has been stable for over 4 years.

Conclusion: Mucinous adenocarcinoma of the uterine cervix is a rare and aggressive malignancy. Due to its rarity, there is little literature describing the disease course of the different subtypes or the response to therapy. More research is needed to better guide clinicians on its treatment.

台灣婦產科醫學會 109 年度年會暨擴大學術研討會

論 文 摘 要

稿件編號： OC2	**單一機構近 10 年早期惡性子宮平滑肌肉瘤之輔助性治療及預後**
臨時收件編號： 3332	劉承疆 黃琬珺 王功亮 張志隆 陳子健 陳楨瑞 台北馬偕紀念醫院婦產部
論文發表方式： 口頭報告	Objective: Uterine leiomyosarcoma (uLMS) is one of uterine sarcomas, it accounts 6% of all uterine corpus malignancies. The incidence of uLMS is rare but the behavior is aggressive. In patients with suspected uLMS, primary surgery (total hysterectomy + bilateral salpingo-oophorectomy) plays the leading role. In stage I uLMS, observation and systemic therapy after primary surgery is acceptable. In stage II uLMS, adjuvant systemic therapy or radiation therapy are used. However, no definite adjuvant therapy showed improvement in survival outcomes. We would like to know our experience in treating stage I and II uLMS in Mackay memorial hospital, therefore we conduct this retrospective study Materials and Methods: We reviewed medical charts, and enrolled patients who were diagnosed as LMS and confirmed by pathology in Mackay memorial hospital during January, 1st, 1998 – December, 31st, 2018. There were 24 patients with early-stage (stage I and II) LMS enrolled in our study. Progression free survival (PFS) and overall survival (OS) of these patients underwent different adjuvant therapy are analyzed by Kaplan-Meier method. All patients are divided into four groups as following, observation, adjuvant chemotherapy only, adjuvant radiotherapy only and adjuvant radiotherapy plus chemotherapy. Results: Mean PFS and mean OS of all patients were 55.6 months and 10.4 years respectively. Mean PFS were 26, 56.4, 55.7 and 57 months in group observation, adjuvant chemotherapy only, adjuvant radiotherapy only and adjuvant radiotherapy plus chemotherapy respectively. Mean OS in these groups were 2.4, 6.1, 8.5 and 12.9 years respectively, with statistically significant difference ($p<0.05$). Conclusions: There were few cases diagnosed as uLMS in our institute in these 10 years. Moreover, there were different adjuvant therapies. The sample size was too small to achieve statistically significant difference. In our opinion, patients with early-stage uLMS underwent adjuvant therapy had better outcome compared with patients under expectant treatment.
論文歸類： 婦癌	

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NKX6-1 促進平滑肌惡性肉瘤的癌症幹細胞特性並可用 SHH 訊息傳遞抑制劑治療

Leiomyosarcoma cells with NKX6-1 promoted cancer stem-like properties are susceptible to the sonic hedgehog signaling inhibitor

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論文發表方式：
口頭報告

論文歸類：
婦癌

Objective
Leiomyosarcoma (LMS) is a malignant neoplasm of smooth muscle and the most popular soft tissue sarcoma which frequently occurs in the uterus or retroperitoneum. LMS exhibits heterogeneous including highly complex genetic karyotypes, severe chromosomal instability and rearrangement. The NKX family is a homeodomain-containing transcription factor family involved in the development of various cancer, but the function of the NKX family in LMS has not yet been investigated. Here, we have investigated the role of the NKX family in LMS and its clinical relevance.
Materials and methods
The mRNA expression data of the NKX family in LMS patients was from The Cancer Genome Atlas. Functional studies of NKX6-1 were performed using uterine LMS cell lines and immunodeficient mice. Malignancy phenotypes were assayed by proliferation assay, anchorage-independent cell growth assay and drug resistance assay. NKX6-1-mediated stem ability was determined by sphere formation. Stem related genes and signaling were assessed by qPCR. Inhibitors of cancer stem signals were assessed for therapeutic potential in vitro.
Results
Among the 14 NKX genes, we found NKX6-1 is upregulated in human LMS tissues and correlated with poor overall survival. Functional studies showed NKX6-1 promotes cell proliferation, anchorage-independent growth, spheroid formation, cancer stemness, and tumorigenicity. The expression of cancer stem related genes, such as KLF8, MYC, and CD49f, and stem signals, including the SHH pathway and NOTCH pathway were corrected with NKX6-1 expression. In vitro drug resistance studies show NKX6-1 upregulates SHH signaling to sensitize LMS cells to an SHH signaling Inhibitor, RU-SKI43.
Conclusion
Our findings uncover the oncogenic and poor prognostic roles of NKX6-1 in LMS. The NKX6-1 mediated SHH signaling represents the new therapeutic targets for precision medicine of LMS.

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OC4

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2704

核磁共振預測子宮內膜癌預後因子之準確度分析

Accuracy of Magnetic Resonance Image Predicts Pathologic Prognostic Factors of Endometrial Endometrioid Cancer

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論文發表方式：
口頭報告

論文歸類：
婦癌

Background: We aimed to identify the correlations and accuracy of preoperative magnetic resonance imaging (MRI) and postoperative pathologic characteristics of endometrial endometrioid carcinoma (EEC).

Patients and methods: We recruited 540 EEC women who underwent staging surgery at a single medical institute. The preoperative (MRI), clinical and 6 pathological parameters including myometrial invasion, cervical invasion, adnexal involvement, extrauterine metastasis, and pelvic and/or para-aortic nodal metastasis were recorded and analyzed. The correlations and accuracy between preoperative MRI findings and these parameters were calculated.

Results: The percentages of same match between preoperative MRI-assessed clinical stages and postoperative surgical stages were 84.8 % (286/337) in FIGO stage IA, 53.1% (42/79) in FIGO stage IB, 35.4% (11/31) in stage II, 5.0% (1/20) in FIGO stage IIIA, 33.3% (1/3) in FIGO stage IIIB, 27.8% (10/36) in FIGO stage IIIC1, 58.8% (10/17) in FIGO stage IIIC2, and 82.3% (14/17) in FIGO stage IVB.

The accuracy (consistency) between radiologists and pathologists were 80.0% in deep myometrial invasion, 91.1% in cervical invasion, 91.5% in adnexal involvement, 91.5% in extrauterine metastases, and 87.6% and 90.9% in pelvic and para-aortic nodal metastases.

Conclusions: Preoperative MRI contributes could be an excellent tool to predict the pathologic parameters of endometrial endometrioid carcinoma, even adnexal, extrauterine and lymph node metastases.

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在子宮頸刮片中使用甲基化和突變標記用於子宮內膜和子宮頸病變檢測

Methylation and mutation markers in cervical scrapings for endometrial and cervical lesions detection

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論文發表方式：
口頭報告

論文歸類：
婦癌

Objective: Endometrial and cervical cancers are common gynecologic diseases. Based on the success of cytological Pap smear screening, cervical scrapings are a good source of DNA for molecular testing. In addition to genetic lesions, DNA methylation is a promising biomarker. We assessed the usefulness of combining genetic and epigenetic biomarkers from cervical scrapings to detect endometrial and cervical lesions.

Materials and Methods: We performed a retrospective case-control study of 115 consecutive cervical scrapings from patients with abnormal uterine bleeding who underwent surgery for diagnostic evaluation. Our study cohort enrolled endometrial cancer (n = 46), normal endometrium (n = 12), benign uterine lesions (n = 20), endometrial hyperplasia (n = 18), cervical intraepithelial lesion (CIN 2)/CIN 3 (n = 10) and in situ/invasive cervical squamous cell carcinoma (n = 9). Quantitative methylation-specific PCR and mass spectrometry were used for DNA methylation and genetic mutation analysis. Logistic regression was used to evaluate the clinical performance of these candidate biomarkers.

Results: Panels of hypermethylated BHLHE22/CDO1/HAND2 (87.0% sensitivity and 86.0% specificity) and BHLHE22/CDO1/TBX5 (89.1% sensitivity and 80.0% specificity) showed significant differences and could distinguish benign from malignant endometrial lesions. Cervical lesions do not affect the methylation states of these four genes (BHLHE22, CDO1, TBX5, and HAND2). Unexpectedly, PTEN and TP53 mutations were commonly found in cervical scrapings of the normal endometrium (25% and 33.3%, respectively) and in cases with benign uterine lesions (10% and 50%, respectively). Combinations of any one mutation of PTEN and TP53 mutations had a sensitivity of 91.3%, but a specificity of only 42.0% for endometrial cancer detection. Finally, PTEN and TP53 mutations were found in 13% and 9% of cervical squamous cell carcinoma, respectively.

Conclusions: Adding PTEN/TP53 mutation testing to BHLHE22/CDO1-based methylation testing did not improve the detection of endometrial cancer. Cervical lesions showed low methylated BHLHE22, CDO1, TBX5, and HAND2 genes.

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2702

循環腫瘤細胞作為卵巢癌新的生物標記
Circulating tumor cells in ovarian cancer as a novel biomarker

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論文發表方式：
口頭報告

論文歸類：
婦癌

Background: Epithelial ovarian cancer (EOC) is the third leading cause of mortality among female malignancies in Taiwan. Over half of the patients are stage III-IV at initial diagnosis. The majority of patients will go to remission soon even after aggressive treatment. CA-125 is currently used as a biomarker for EOC with low sensitivity and specificity.

Circulating tumor cells (CTCs) have been introduced as a biomarker for multiple types of cancers, including EOC. Here, we report the validation results by two cancer cell lines and the preliminary results on EOC patients using Cell RevealTM system which is a silicon-based microfluidic platform for circulating rare cells (CRCs) detection.

Materials and Methods: The CTC platform is composed of two systems: an automatic CTC enrichment and capturing system using nanostructured microfluidic chip as well as an automatic cell identification and location system. CTCs were captured with anti-EpCAM antibodies. Spiking tests of two cell lines were used for the evaluation of capture efficiency. In this study, CTCs were defined with EpCAM+/APN/CD45-/DAPI+. In the trial on EOC, women without ovarian tumor were recruited as the control group and women with ovarian tumor were included in the test group.

Results: The capture rates for the spiking tests are high. For the EOC study, no CTC was detected in women without ovarian tumor or with benign ovarian tumor. Most women with ovarian cancer had detectable CTCs.

Conclusions: The present proof-of-concept study demonstrates that a high positive detective value of CTCs in EOC patients. Therefore, CTCs detection may provide useful information for the management of EOC patients as a real-time and non-invasive biomarker.

Conflicts of interest
All authors declare no conflict of interests.

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OC7

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2739

晚期上皮性卵巢癌在初次減積手術後不同化學治療方式的患者癒後 - 單一醫學中心 10 年經驗

Outcome of Different Adjuvant Chenotherapies In Advanced Stage Epithelial Ovarian Cancer After Primary Debulking Surgery - A Single Institute, 10 years Experience

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論文發表方式：
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論文歸類：
婦癌

Ovarian cancer (OC) is the 8th most common cancer of women in 2018 in Taiwan, and epithelial OC is the most common histological type. Due to its unclear pathogenesis, non-specific symptoms and non-useful screening methods, about 70% cases are found to be advanced disease while primary intervention. High recurrence rate within 2 year after primary management and low 5-year survival rate are the characteristics of advanced OC.

Primary debulking surgery plus post-operative platinum-base chemotherapy are the milestone to treat advanced OC. In the choice of adjuvant chemotherapy, many results from Gynecologic Oncology Group (GOG) trials in the United States played the critical role to improve the progressing free survival (PFS) after primary debulking surgery since 1996. Paclitaxel plus cisplatin is better than cyclophosphamide plus cisplatin in 1996. Paclitaxel plus carboplatin has equal PFS as paclitaxel plus carboplatin in GOG-158 in 2003. Intraperitoneal chemotherapy with paclitaxel and cisplatin in optimal debulked OC patients has promising PFS in GOG-175 in 2007. Dose dense paclitaxel plus 3-week carboplatin dramatically improved PFS in Japan's GOG trial (JGOG-3092). Adding bevacizumab in traditional paclitaxel-carboplatin chemotherapy has better PFS in GOG-218 & ICON-7 since 2014. However, which setting of chemotherapy has most favorable PFS cannot be known due to cross-trials comparison is not feasible.

We would like to conduct a retrospective, chart review trial for advanced epithelial OC patients in a single institute between 2008 to 2017, in order to summarize the adjuvant therapies ever used in our hospital and to calculate PFS, overall survival and survivor conditions. In addition, surgical factors (optimal or sub-optimal) will also be obtained for logistic regression comparison in our study. Currently 788 cases were enrolled into our trial, after delicate chart-review and statistics calculation, the final result will be reported in then annual meeting of Taiwanese Associtation of OB/GYN in February, 2021. Finally, multi-center trial like Taiwan GOG trial will be prepared and proposed for case expansion and more reliable outcome of such dazzling therapies.

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探討早期子宮頸癌患者接受生育保留性手術後之預後及懷孕成果

Outcome and subsequent pregnancy after fertility preserving surgery of early stage cervical cancer

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論文發表方式：
口頭報告

論文歸類：
婦癌

OBJECTIVE:
To investigate the outcome and subsequent pregnancy in young patients of early stage cervical cancer (CxCa) after conservative surgery.

METHODS:
We retrospectively reviewed medical records of patients with stage IA1-IB1 CxCa undergoing conservative surgeries at one medical institute from March, 2004 to November, 2017.

RESULTS:
Thirty-two patients were recruited and analyzed, including 17 patients with stage IA1 CxCa and 15 patients with stage IB1 CxCa. The median follow-up duration was 4.1 years. The median age was 32 years old, and more than half (53.1%) of the patients had yet got pregnant. All of the 17 stage IA1 patients received conization (either by cold knife or loop electrosurgical excision procedure). In 15 patients with IB1 CxCa, five received conization with or without bilateral pelvic lymph node dissection (BPLND), three received abdominal radical trachelectomy (RT) plus BPLND and 7 received transvaginal RT plus BPLND.

Two stage IA1 patients with positive section margin involved by carcinoma or HSIL suffered from disease recurrence 2 years and 3 years after surgery. One stage IB1 patient with positive section margin and lymphovascular space invasion suffered from disease recurrence 5 months after surgery.

Among the 17 stage IAI patients, 8 (47.1%) got pregnant during follow-up, and 6 got live births. One of them had normal spontaneous delivery twice. Among the 15 stage IBI patients, 3 (20%) patients, including one received abdominal radical trachelectomy, got pregnant and live births during follow-up.

CONCLUSIONS:
Fertility preserving surgeries, including conization and radical trachelectomy can be an alternative procedure other than hysterectomy in selected young patients of early stage cervical cancer with fertility needs.

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2874

具淋巴結轉移的卵巢癌患者復發形式的分析

The patterns of failure following treatment of epithelial ovarian cancer with lymph node metastasis

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口頭報告

論文歸類：
婦癌

Objective:
The aim of this study was to investigate the patterns of failure following treatment of patients with epithelial ovarian cancer (EOC) who had retroperitoneal lymph node metastasis at the time of diagnosis.

Materials and Methods:
This is a retrospective cohort study conducted at MacKay Memorial Hospital. We collected the data of patients with histologically proved EOC with retroperitoneal lymph node metastasis who completed primary cytoreductive surgery followed by platinum-based adjuvant chemotherapy at our institution from 2015 through 2019. Patients diagnosed with first recurrence of EOC were enrolled in this study. Patients received neoadjuvant chemotherapy, with persistent or progressive disease on completion of the initial treatment were excluded. The recurrence patterns were studied using clinically indicated image scans, categorizing them into retroperitoneal nodal recurrences, intraperitoneal recurrences, and distant metastatic disease.

Results:
Among 435 patients diagnosed with EOC during this study period, 173 (39.8%) were at advanced stage. Seventy-six patients had retroperitoneal lymph node involvement at the time of diagnosis. After surgical treatment and adjuvant chemotherapy, there were 8 patients with initial lymph node metastasis developed recurrent disease. Of the patients who had recurrence, four relapsed in the pelvic/para-aortic lymph nodes, three developed intraperitoneal recurrent disease, and one had distant metastasis.

Discussion:
The results of our study revealed that among EOC cases who received surgical treatment and adjuvant chemotherapy, initial retroperitoneal lymph node involvement might not be a significant risk factor for recurrence. In our study group, there was a trend that recurrent disease developed in the retroperitoneal lymph nodes, which might be a result of persistent disease due to the inaccessibility of this space to both chemotherapy and surgical approach. Further study to obtain large-scale data for confirmation of this finding should be conducted to evaluate the benefit of specialized treatment program or targeted surveillance in this group of patient.

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OC10

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2784

低分化漿液性卵巢癌臨床預後因子之探討-兩家醫學中心之研究

Clinical factors associated with prognosis in low grade serous carcinoma of ovary: a two-center study

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論文發表方式：
口頭報告

論文歸類：
婦癌

Abstract

Objective: This study was designed to evaluate clinical factors affecting survivals in low grade serous ovarian carcinoma

Methods: The patients who were diagnosed with low grade (grade 1) serous ovarian cancerbetween 2000 and 2018 from Samsung Medical Center, Seoul, Korea and National Taiwan University, Taipei, Taiwan were eligible for the study. Patient's baseline medical records including optimality of surgery, the number of cycles of adjuvant chemotherapy and time interval from surgery to initial chemotherapy (Time to Chemotherapy, TTC) were assessed. Patients who had neoadjuvant chemotherapy was excluded. A Cox proportional hazard regression analysis was used to evaluate the independent effect of each clinical factors on progression free survival (PFS) and overall survival (OS).

Results: We found 84 patients with low grade serous ovarian cancer from two centers. The mean age at diagnosis was 49 years old. FIGO stage III (44, 52.4%) was most common followed by stage I (30, 35.7%). The median intervals of TTC was 12 days (range, 9-18 days).Based on the FIGO stage, the preoperative CA 125 was significantly elevated and progression free survival was markedly decreased in advanced disease compared with early disease($p = 0.019$ and $p = 0.002$, respectively). For stage I, patients with IC showed poor survivals as opposed to IA and IB regardless of number of cycles of adjuvant chemotherapy. For advanced disease, no gross residual disease after primary cytoreductive surgery showed modest gain in progression free and overall survivals as compared with residuals equal to or more than 1 cm ($p = 0.125$, $p = 0.239$, respectively). In multivariate analysis for progression free and overall survivals, age, preoperative CA-125, TTC, the level of residual disease, and the number of cycles of adjuvant chemotherapy were not associated with
prognosis.

Conclusion: Our study found that known prognostic factors in high grade serous carcinoma of ovary did not show any impact on survivals in low grade disease except for FIGO stage. Further studies should be needed to understand clinical behavior of this unique disease in epithelial ovarian carcinoma.

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OC11

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3389

分子巴氏塗片通過 DNA 甲基化檢測卵巢癌

Molecular Pap smear for detection of ovarian cancer by DNA methylation

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論文發表方式：
口頭報告

論文歸類：
婦癌

Objective: Ovarian cancer (OC) is the most lethal gynecological cancer, worldwide, largely due to its vague and nonspecific early-stage symptoms, resulting in most tumors being found at advanced stages. Moreover, due to its relative rarity, there are currently no satisfactory methods for OC screening, which remains a controversial and cost-prohibitive issue. Here, we demonstrate that Papanicolaou test (Pap test) cervical scrapings, instead of blood, can reveal genetic/epigenetic information for OC detection, using specific and sensitive DNA methylation biomarkers.

Materials and Methods: We analyzed the methylomes of tissues (50 OC tissues versus 6 normal ovarian epithelia) and cervical scrapings (50 OC patients versus 6 normal controls), and integrated public methylomic datasets, including 79 OC tissues and 6 normal tubal epithelia. Differentially methylated genes were further classified by unsupervised hierarchical clustering, and each candidate biomarker gene was verified in both OC tissues and cervical scrapings by either quantitative methylation-specific polymerase chain reaction (qMSP) or bisulfite pyrosequencing. A risk-score by logistic regression was generated for clinical application.

Results: One hundred and fifty-one genes were classified into four clusters, and nine candidate hypermethylated genes from these four clusters were selected. From this, we found an OC-associated panel comprising AMPD3, NRN1, and TBX15, reaching a sensitivity of 81.0%, specificity of 89.5%, and OC detection accuracy of 0.91 (95% CI, 0.82–1), in the testing set, and a detection accuracy of 0.88 (95% CI, 0.87 to 0.88), by logistic regression, with ten-fold cross-validation and 200 replications. Patients with risk scores > 0.514 conferred a disease odds ratio of 24.4 (95% CI, 8.4 to 71.2), compared to those without the disease.

Conclusions: Ovarian cancer detection from cervical scrapings is feasible, using particularly promising epigenetic biomarkers such as AMPD3/NRN1/TBX15. Further validation is warranted.

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OC12

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子宮頸抹片中的內膜癌甲基化基因指數之研發與應用

Research and Development of Endometrial cancer-specific methylation Score in Pap Smear

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論文發表方式：
口頭報告

論文歸類：
婦癌

Objective: Endometrial cancer (EC) is a common gynecological cancer whose incidence is increasing annually in Taiwan and worldwide. A feasible biomarker is urgent to identify for detecting EC patients. The cervical scrapings is a potential material and sampled by a non-invasive procedural for molecular testing. DNA methylation has demonstrated as a promising cancer biomarker. Our previous study has discovered some novel genes for EC detection. However, hypermethylation of some genes can be detected in uterine myoma. This study intended to identify EC-specific hypermethylated genes in cervical scrapings using a methylomic approach.

Materials and Methods: We generated methylomics profiles of the endometrial tissues and cervical scrapings from 17 of myoma and 10 of EC patients using a Methylation 450K BeadChip. The methylomics profiles of tissues including 308 of EC from TCGA used to identify the differential methylated genes. Unsupervised hierarchical clustering of methylation profiles used to reduce candidate genes. We verified in pools DNA from EC tissues and cervical scrapings, and validated in 168 of cervical scrapings of a training and testing sets using qMSP. Both sets comprised specimens from endometrioid-type EC (n=28), uterine myoma (n=28), and healthy controls (n=28) patients, respectively. A logistic regression was used to generate an EC-score to evaluate the performance of each methylation signal and gene combinations.

Results: We selected 45 methylated genes, which could be clustered into 7 subgroups. Ten genes demonstrated consistent hypermethylation in tissues and cervical scrapings. Three genes, BHLHE22, CDO1, and Gene-T had the best performance. The sensitivities of individual genes were 81.4–89.3% and specificities were 55.4–91.0% in training and testing sets. An EC-score calculated by combining methylation levels of BHLHE22/CDO1/Gene-T can reach 92.9% of sensitivity, 91.1% of specificity, and 0.96 of accuracy (95% CI, 0.90–0.99). The methylation panel was also applied to cervical scrapings of endometrial hyperplasia, atypical endometrial hyperplasia, and type-II ECs patients to show 70%, 75% and 100% of detection rate, respectively.

Conclusions: This present study further improved the performance of endometrial cancer detection using cervical scrapings. An EC-score generated by BHLHE22/CDO1/Gene-T is promising to change the clinical practice of women with abnormal bleeding.

稿件編號： OC13 臨時收件編號： 3314	**免疫檢查點抑制劑 pembrolizumab 治療復發子宮頸癌的成效-林口長庚醫院經驗** **Pembrolizumab for recurrent cervical cancer - pilot experience in a tertiary center of Taiwan** 董秀容[1] 張廷彰[1] 賴瓊慧[1] 長庚醫療財團法人林口長庚紀念醫院
論文發表方式： 口頭報告 論文歸類： 婦癌	Introduction: Recurrent cervical cancer remains a clinical challenge. Patients who had treatment failure of primary CCRT usually received several line of chemotherapy and finally died from cervical cancer with short progression-free time. In the era of immune-check point inhibitor, pembrolizumab demonstrated durable antitumor activity and manageable safety in patients with advanced cervical cancer as KEYNOTE-158. We aim to share our experience of pembrolizumab in recurrent cervical cancer. Methods: We retrospectively reviewed clinical records of 12 cervical cancer patients who received pembrolizumab in 2016-2018 at Chang Gung Memorial Hospital, Linko branch, a medical center in Taoyuan, Taiwan. Patients with histology confirmed recurrent cervical cancer that was not feasible for surgical treatment received pembrolizumab with salvage radiotherapy and/or chemotherapy. Pembrolizumab was applied as 2mg/kg every three weeks during salvage therapy. Patients were followed until November 11, 2019. The response to treatment after salvage therapy was evaluated using RECIST 1.1. Pembrolizumab was continued for 3-8 cycles after salvage to evaluate response. Results: Twelve patients included 4 with the histologic diagnosis of squamous cell carcinoma, 4 with adenocarcinoma, 3 with adenosquamous, and one small cell carcinoma. Eight of the 12 patients were in FIGO or AJCC pathological stage III-IVB, one with stage II adenosquamous carcinoma and three with pathological IB adenocarcinoma. Median time to first recurrence was 35.2 months (range 7-115.0). Six patients had CCRT using platinum-based chemotherapy as their primary therapy. Six patients received radical hysterectomy and followed by adjuvant chemoradiation. All patients received the pembrolizumab therapy at recurrence. They received multiple cycles of chemotherapy before pembrolizumab. Then pembrolizumab was applied with or without chemoradiatherapy. Ten of 12 patients received pembrolizumab with radiotherapy. Six patients showed complete response, 1 partial response and 5 disease progression after treatment. The median overall survival from primary diagnosis was 64.1 months (range from 26.3 to 183.0 months). The median progression free survival with pembrolizumab was 17.1 months (range 5.2-36.0). Conclusion: Our experience showed encouraged outcome by adding pembrolizumab to salvage therapy for recurrent cervical cancer. In combining chemoradiation therapy, we can achieve higher response rate.

台灣婦產科醫學會 109 年度年會暨擴大學術研討會

論 文 摘 要

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Olaparib 使用在復發性卵巢癌真實世界經驗分享

A Retrospective Study of Olaparib in Patients with Recurrent Ovarian Cancer

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論文歸類：
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婦癌

OBJECTIVES:

Olaparib, a poly-adenosine diphosphate ribose polymerase (PARP) inhibitors is approved as maintenance in patients with platinum-sensitive recurrent ovarian cancer and salvage therapy after chemotherapy treatment failure. The current study is aimed to investigate the real world data.

MATERIAL AND METHODS:

In this retrospective study, patients of recurrent ovarian cancer treated with Olaparib are collected and analyzed in Chang Gung Memorial Hospital in Taiwan. Primary objectives are the effectiveness including progression-free survival, overall response rate and safety of Olaparib.

RESULTS:

From July 2018 through November 2019, a total of 32 patients were analyzed. Around 60% of patients received BRCA testing. 66% have BRCA1 mutation and 33% have BRCA2. Mean duration of the use of Olaparib is around 14 weeks and mean dose is 513 mg/day. A fairly good response and clinical benefit rate were found on patients receiving Olaparib with achieving either a complete, partial response or staying in stable disease status. Adverse effects were minimal and the most frequent toxicity was anemia.

CONCLUSIONS:

In the current study, Olaparib provide good clinical benefit with only limited toxicity. More data are required to demonstrate its effectiveness in the real world setting.

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PD-L1 的阻斷通過調節樹突狀細胞成熟來增強癌症免疫治療。

Blockade of PD-L1 Enhances Cancer Immunotherapy by Regulating Dendritic Cell Maturation

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論文歸類：
婦癌

Background: Immunosuppression induced by tumors attenuates the anti-tumor effects of cancer immunotherapy. Immuno-inhibitory checkpoint, PD-L1, regulated by tumor cells and antigen-presenting cells (APCs) dampened the activation ofT cells from PD-1/PD-L1 axis. PD-L1 expressed APCs rather than tumor cells played an essential role of anti-tumor effects of anti-PD-L1 monotherapy in preclinical tumor models. To further investigate how PD-L1 interfered the antigen-specific anti-tumor efficacy and immune responses modulated by PD-L1 expressed APCs, we evaluated the anti-tumor effects and possible mechanisms of an antigen-specific protein vaccine combined with PD-L1 blockade.

Methods: Using the HPV16 E6/E7+ syngeneic mouse tumor model, we investigated whether anti-PD-L1antibody increases the antigen-specific immune response and anti-tumor effects induced by the E7-specific PEK protein vaccine, as well as the possible mechanisms regarding activation of APCs.

Results: Anti-PD-L1 antibody combined with the PEK protein vaccine generated more potent E7-specific immunity (including the number and cytotoxic activity of E7-specific cytotoxic CD8+ T lymphocytes) and anti-tumor effects than protein vaccine alone. Anti-PD-L1 antibody could enhance the maturation of dendritic cells in tumor-draining lymph nodes and tumors in tumor-bearing mice treated with combinatorial therapy.

Conclusions: PD-L1 blockade overturns the immunosuppressive status of the tumor microenvironment and then enhances the antigen-specific immunity and anti-tumor effects generated by an antigen-specific protein vaccine through modulating APCs. Antigen-specific immunotherapy combined with APCs targeting modality by PD-L1 blockade have high translational potential in cancer therapy.

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3359

卵巢亮細胞癌臨床病理型態與預後之相關性：單一醫學中心之分析

The impact of clinicopathologic characteristic on prognostic relevance of ovarian clear cell carcinoma: analysis from one tertiary hospital

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論文歸類：
婦癌

Objective: The current study was designed to explore the association between different clinicopathological characteristics as well as immunochemistry (IHC) staining and disease prognosis in patients with ovarian clear cell carcinoma(OCCC).

Materials and Methods: We retrospective collected clnicopathological data as well as different IHC staining in surgical specimen from 89 cases diagnosed as ovarian clear cell carcinoma between Jan., 2008 to Dec., 2016 in Kaohsiung Chang Gung Memorial Hospital. The correlation between clinical pathological characteristics, expression level of protein by ICH including P53, P16, ER(estrogen receptor) and PR(progesterone receptor) as well as the presence of concurrent endometriosis and clinical outcome were analyzed.

Results:

Among 89 cases with OCCC, 51 cases(57.3%) in stage I, 13 cases(14.6%) in stage II, 20 cases(22.5%) in stage III, and 5 cases(5.6%) in stage IV were identified. The average age of all-staged patients was 50 years old. The overall survival rate(OS) and progression free survival rate(PFS) was highest in stage I with 90% and 84% and gradually decreased by stages(P

Protein expression in tumor tissue of P53, P16, ER(estrogen receptor), PR(progesterone receptor), HNF-1 beta and Napsin A were assessed in 47 cases (52.8%) by IHC staining. There is no significant difference of OS and PFS in patients with different expression level of P53, P16 and ER, while patients with PR less than 10% expression had significant better OS (92.9% vs. 50%, p=0.01, and PFS (82.1% vs. 33.3%, p=0.007) than those with more than 10% expression.

We found partients with concurrent endometriosis at the same side of tumor had better OS (94.7% vs. 66.2%, P=0.018)and PFS (94.7% vs. 53.8%, P=0.002) when compared with cases without endometriosis or having endometrioisis at contralateral side of tumor. In addition, we also disclosed that cases with CA-125 higher than 50 U/ml before treatment, when compared with subject with lower than 50 U/ml , would have worsen survival (OS 66.0% vs. 86.4%, p=0.02, PFS 52.8% vs. 86.4%, p=0.008).

Conclusions: In our analysis, patients with lower than 10% of PR expression in cancer cells, concurrent endometriosis at the same side of tumor and pre-treatment CA-125 lower than 50 U/ml would have better disease survival in OCCC. Larger prospective trials in the future are needed to explore the roles of these parameters.