signaling. Our integrated multi-omics analysis unexpectedly revealed an exposome-related mutational signature to be associated with EEEC leading to EEEC specific CTNNB1 and SIGLEC10 hotspot mutations and downstream protein pathway disturbance. Interestingly, in EEECs $SIGLEC10^{Q144K}$ mutation resulted in aberrant Siglec-10 protein expression and promoted progestin resistance by interacting with ERα. We identified and validated four (EEF1E1, ILVBL, SRPK1 and NUDT5) biomarkers of progestin resistance.

Conclusion/Implications Our study provides a unique high-quality proteogenomic resource of EEECs, and explicates the distinct clinical and molecular characteristics of EEECs, encompass-ing obesity, genetic susceptibility, and environmental exposure, that are concomitant with pathogenesis and progestin resistance. Furthermore, we identified biomarkers for progestin response in EEEC fertility-sparing treatment. These attributes can be utilized to promote primary prevention and early detection of EEECs.

PR026/#185 PROTEOGENOMICS DECIPHER DISTINCT METASTASIS PATTERNS AND BIOMARKERS OF ENDOMETRIAL CARCINOMA

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Introduction Endometrial carcinoma is a common gynecologic malignancy, and lymph node metastasis greatly affects patient outcomes. Proteogenomics analysis has emerged as a powerful tool for identifying molecular mechanisms involved in cancer progression and metastasis, offering potential for biomarkers discovery and personalized treatment strategies.

Methods In this study, we utilized WES, proteomics, and multiplex immunohistochemistry to investigate the metastasis patterns of different molecular subtypes in a cohort of 96 EC patients with lymph-node metastasis and 126 without metastasis. Our aim was to elucidate the molecular characteristics that distinguish between these two groups and identify potential biomarkers for metastasis.

Results Proteogenomics analysis identified two distinct metastasis patterns of EC associated with TME. One pattern is characterized by an immune-cold phenotype, which is predominantly observed in patients with the MSI subtype. These patients often exhibit JAK1 mutations, defects in immunoproteasome components and HLA complexes, leading to deficiencies in antigen presentation pathways, resulting in immune evasion. The other is characterized by an immune-hot phenotype, mainly distributed in the CNL and few MSI subtype, with significant infiltration of macrophages and upregulation of integrin pathways, promoting tumor cells to undergo mesenchymal transition. Additionally, we explored and validated three consensus biomarkers shared across diffrerent molecular subtypes for predicting lymph-node metastasis.

Conclusion/Implications Our research provides an unprecedented large-scale multi-omics resource of lymphatic metastasis EC, offering novel insights and new biomarkers for effectively stratifying high-risk patients for lymphatic metastasis. We have deciphered two distinct metastasis patterns in EC, which can be exploited for the development of personalized screening and targeting strategies.

PR027/#815 CLINICAL IMPACT OF ULTRASTAGING OF SENTINEL LYMPH NODE MAPPING WITH INDOCYANINE GREEN INJECTION IN PATIENTS WITH ENDOMETRIAL CANCER

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Introduction This retrospective study aimed to confirm the clinical impact of ultrastaging of sentinel lymph node (SLN) mapping with Indocyanine green (ICG) injection in patients with endometrial cancer (EC).

Methods This retrospective study obtained data from the electronic medical records of Severance Hospital. The subjects included patients with EC who have undergone surgical staging with SLN mapping using ICG injection between June 2014 to December 2017 at Severance Hospital. The SLN paraffin blocks were sliced into two or three layers at an interval of 200 μm between the layers by 3 μm thickness. The immunohistochemistry was performed with anti-cytokeratin antibodies AE1/AE3.

Results A total of 138 patients included (no metastasis (NM), n=124, 89.9%; macro-metastasis (MAC), n=2, 1.4%; micro-metastasis (MM), n=11, 8.0%; isolated tumor cells (ITC), n=1, 0.7%). A total of 1006 paraffin blocks were examined (NM, n=984, 97.8%; MAC, n=2, 0.2%; MM, n=13, 1.3%; ITC, n=7, 0.7%). The 5-year disease-free survival significantly differed according to the results of ultrastaging (NM, 94.9%; MAC and MM, 69.2%; p<0.001). The 5-year overall survival was no significant difference in the status of ultrastaging (NM, 97.4%; MAC and MM, 100%; p=0.579). Analyzing the Cox proportional hazards model, the prognostic factor of recurrence was ultrastaging (Hazard Ratio 5.70, [95% Confidence Interval 1.50–21.68], p=0.011). The ultrastaging had no prognostic impact on the overall survival.

Conclusion/Implications The ultrastaging detected more MAC, MM, and ITC of SLN and was a prognostic factor of recurrence in patients with EC. Further study is needed for the clinical impact of ultrastaging for adjuvant therapy of EC.

PR028/#496 THE EFFICACY OF METFORMIN IN MEGESTROL ACETATE-BASED FERTILITY-SPARING TREATMENT FOR PATIENTS WITH ENDOMETRIAL ATYPICAL HYPERPLASIA AND ENDOMETRIAL CANCER: LONG-TERM OUTCOMES OF A RANDOMISED CONTROLLED TRIAL

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Introduction To assess the long-term efficacy of metformin in megestrol acetate(MA)-based fertility-sparing treatment for patients with endometrial atypical hyperplasia (EAH) and endometrioid endometrial cancer (EEC).

Methods Patients with EAH or EEC were firstly stratified, then randomised to receive MA (160 mg orally, daily) or MA

(160 mg orally, daily) plus metformin (500 mg orally, three times a day).

Results The complete remission rate, disease-free survival (DFS) rate and pregnancy rate had no significant difference between two treatment groups. However, the DFS rate was higher in the metformin plus MA group than in the MA-only group in non-obese (body mass index<28 kg/m^2) patients with EAH (hazard ratio [HR] = 2.677, 95% confidence interval [CI] = 1.066–6.727; Log Rank P = 0.029), while had a lower tendency in obese patients with EAH (HR = 0.224, 95% CI = 0.045–1.223; Log Rank P = 0.062). According to cox proportional hazards regression analysis, undergoing assisted reproductive treatment (HR = 2.358, 95% CI = 1.069–5.204; Log Rank P = 0.034) was identified as an independent risk factor for recurrence, whereas younger patients were found to have a higher probability to achieve pregnancy (HR = 0.568, 95% CI = 0.332–0.973; Log Rank P = 0.039).

Conclusion/Implications Currently, there is no sufficient evidence to support that the utilization of metformin plus MA can significantly improve the prognosis of patients with EAH or EEC compared to MA monotherapy. However, obese patients with endometrial lesions may benefit from the addition of metformin.

PR029/#227 ROBOT-ASSISTED VERSUS CONVENTIONAL LAPAROSCOPIC SURGERY FOR ENDOMETRIAL CANCER: LONG-TERM COMPARISON OF OUTCOMES

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Introduction There is a lack of multi-institutional large-volume and long-term follow-up data on comparisons between robot-assisted surgery and conventional laparoscopic surgery. This study compared the surgical and long-term survival outcomes between patients who underwent robot-assisted or conventional laparoscopic surgery for endometrial cancer.

Methods We retrospectively reviewed the data of patients from five large academic institutions who underwent either robot-assisted or conventional laparoscopic surgery for the treatment of endometrial cancer between 2012 and 2017, ensuring at least 5 years of potential follow-up. Intra- and postoperative outcomes, long-term disease-free survival, and overall survival were compared.

Results The study cohort included 1,003 unselected patients: 551 and 452 patients received conventional laparoscopic and robot-assisted surgery, respectively. The median follow-up duration was 57 months. Postoperative complications were significantly less likely to occur in the robot-assisted surgery group than in the laparoscopic surgery group (7.74% vs. 13.79%, P = 0.002). There were no significant differences in survival: 5-year disease-free survival was 91.2% versus 90.0% (P = 0.628) and overall survival was 97.9% versus 96.8% (P = 0.285) in the robot-assisted and laparoscopic surgery cohorts, respectively. Cox proportional hazard regression models demonstrated that the mode of surgery was not associated with disease-free survival (hazard ratio, 0.897; confidence interval, 0.563–1.429) or overall survival (hazard ratio, 0.791; confidence interval, 0.330–1.895) after adjusting for confounding factors.

Conclusion/Implications Robot-assisted surgery for endometrial cancer is associated with similar long-term survival outcomes but fewer postoperative complications as compared to conventional laparoscopic surgery.

PR030/#559 PAX2 IS REGULATED BY ESTROGEN/PROGESTERONE THROUGH PROMOTER METHYLATION IN ENDOMETRIOID ADENOCARCINOMA AND TAKE THE IMPORTANT ROLE IN CARCINOGENESIS VIA THE AKT/MTOR SIGNALING PATHWAY

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Introduction PAX2 (Paired box 2) and PTEN inactivation were reportedly as important biomarkers for endometrioid intraepithelial neoplasia (EIN) and Endometrioid endometrial carcinoma (EEC). However, though PTEN was extensively studied, the role of PAX2 in EEC carcinogenesis still remains unclear.

Methods Public databases and clinical paired paraffin-embedded tissues were used to analyze PAX2 expression in EEC. Cell function tests and mouse xenograft models were utilized to study the biological functions of PAX2. Pyrosequencing and demethylating drug 5-Aza-dc were used to verify promoter methylation in clinical tissues and cell lines, respectively. The mechanism underlying the regulatory effect of estrogen (E2) and progesterone (P4) on PAX2 expression was investigated by receptor block assay and double luciferase reporter assay.

Results PAX2 expression was significantly down-regulated in EIN and EEC tissues, its overexpression inhibited EEC cell malignant behaviors in vivo and in vitro and inhibited the AKT/mTOR signaling pathway. PAX2 inactivation in EEC was related to promoter methylation, and its expression was regulated by E2 and P4 through their receptors via promoter methylation.

Conclusion/Implications Our findings elucidated the expression and function of PAX2 in EEC and firstly provided hitherto undocumented evidence of the underlying molecular mechanisms. PAX2 expression is suppressed by estrogen prompting its methylation through estrogen receptor. Furthermore, PAX2 regulates the AKT/mTOR signaling pathway to influence EEC progression.

PR031/#378 A PREDICTIVE MODEL FOR LYMPH NODE METASTASIS USING A TUMOR LOCATION IN PRESUMED EARLY-STAGE ENDOMETRIOID ENDOMETRIAL CANCER PATIENTS

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