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