EP318/#571 CIRCULATING TUMOR DNA-BASED MOLECULAR RESIDUAL DISEASE DETECTION FOR THE MONITORING OF HIGH-GRADE SEROUS OVARIAN CANCER

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Introduction Standard treatment for epithelial ovarian cancer involves surgery and platinum-based chemotherapy, but recurrence or disease progression still occurs in over 70% of patients. CtDNA-based MRD testing may be a potential biomarker for disease surveillance.

Methods Primary ovarian cancer with stage II-IV of HGOC patients was recruited in this study. Tumor sample was collected for whole exome sequencing (300x). Proprietary algorithm was used to select 30–40 single nucleotide variants for each patient. Blood was collected and MRD was detected by multiplex PCR-based sequencing (OriMIRACLE S^{TM}, 100,000x) using the customized panel (NCT05027828).

Results As of the summary submission, we have completed WES sequencing for 20 patients, of which 11 carry HRR pathway mutations. Among the 13 patients who underwent pre- and post-operative ctDNA monitoring, 11 were ctDNA positive before surgery. We found a significant decrease in ctDNA variant allele frequency (VAF) before and after surgery (before: median VAF 0.95%, after: median VAF 0.04%, p=0.0054). Additionally, Pearson correlation analysis showed a positive correlation between pre-treatment ctDNA VAF and CA125 levels (R=0.685, p=0.017). The median VAF of ctDNA in stage IV patients was higher than that in stage I-III patients (2.14% vs. 0.56%, p=0.69). All the 13 patients were negative for MRD after completion of chemotherapy. Follow-up is ongoing.

Conclusion/Implications MRD testing is feasible for monitoring epithelial ovarian cancer patients, with over 80% of HGSOC patients being MRD-positive at baseline. The MRD status was generally consistent with the clinical status of the patients. The performance of MRD in predicting recurrence of HGSOC is still under investigation.

EP319/#1479 OVULATION RELEASES FIBRONECTIN TO PROMOTE PERITONEAL SEEDING OF PRECANCEROUS AND CANCEROUS HIGH-GRADE SEROUS CARCINOMA CELLS ORIGINATING FROM THE FALLOPIAN TUBE EPITHELIUM THROUGH INTEGRIN B1 SIGNALING

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Introduction Previously, we have discovered ovulatory follicular fluid (FF) carries transforming signals to promote full-course carcinogenesis of fallopian tube epithelium (FTE), the origin of ovarian high-grade serous carcinoma[https://pubmed.ncbi.nlm.nih.gov/33530497/]. This study investigated FF-fibronectin(FN) in peritoneal seeding of transforming FTE cells.

Methods Partially and fully transformed FTE cells were treated with FF, paired peritoneal fluid (PF), or recombinant FN. Transformation phenotypes were evaluated in FTE cells with/without ITGB1 knock-down. Peritoneal seeding was evaluated by IVIS after i.p. xenograft together with FF in NSG mice.

Results Cell migration-promoting activity was observed after treating with >100-KDa FF or FN protein which was three times higher in FF than in the paired PF. Compared to the full-transformation activity of FF, FN specifically promoted cell proliferation, migration, or invasion. ITGB1- KD caused lower cell proliferation, peritoneal attachment, and AIG. It also reduced the migration-and proliferation-promoting effects of FF and FN. Compared to FF treatment which generally increased p-FAK, p-SRC, p-ERK, and p-AKT, FN treatment increased p-FAK and p-SRC. Looking into the changes in FF- and FN-treated cells, ITGB1-KD resulted in a decrease of p-ERK, p-SRC, or p-FAK and an increase of p-AKT. In the mouse i.p. xenograft tumorigenesis model, depletion of FN from FF showed in a marked reduction of intraperitoneal seedings at week 7, and ITGB1-KD resulted in a decrease at day 12.

Conclusion/Implications The results disclose proliferation-, migration- and invasion-promoting activities of FN abundantly present in ovulatory FF, which promotes peritoneal seedings of transformed FTE cells. Integrin β1 primarily mediates this activity.

EP321/#854 LNCRNA PART1 AUGMENTS PARPI SENSITIVITY IN OVARIAN CANCER

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Introduction The inhibitor of PARP (PARPi) is one of the most concerned drugs recently. Since both PARPi and platinum act through DNA damage, we intend to find targets for overcoming PARPi resistance through the differences of gene expression between platinum-resistant and platinum-sensitive ovarian patients in TCGA.

Methods We divided ovarian cancer patients in TCGA into platinum-sensitive and platinum-resistant groups and conducted differential gene analysis on them. MTT assay was used to draw the drug concentration tolerance curve of ovarian cancer cells. The effect of PART1 on cell growth was detected by EdU and CCK8 assays. Western blot was used to detect the effect of PART1 on DNA damage repair pathway. The effect of PART1 on PARPi sensitivity in vivo was verified by subcutaneous tumor formation in nude mice . RNA-seq was conducted to analyse the changes of gene and pathways.

Results LncRNA PART1 was significantly down-regulated in platinum-resistant patients in TCGA. CCK8 assays indicated knockdown of PART1 could confer resistance of cisplatin and olaparib on ovarian cancer cells. Cell