Abstract #249

DISTINCT VAGINAL MICROBIOME OVARIAN CANCER PATIENTS – A POSSIBLE SCREENING AND PROGNOSTIC BIOMARKER?


Introduction/Background Microbiome plays an important role in development of cancer and response to chemotherapy. Vaginal microbiome constitutes a new study field. We aim to examine the significance of vaginal microbiome in epithelial ovarian cancer.

Methodology A prospective cohort study was conducted for evaluating the vaginal microbiome in newly diagnosed epithelial ovarian cancer (NEOC) patients, post-chemotherapy (PC) patients and healthy women. Samples were collected using a swab. DNA was extracted and amplified by PCR using universal primers of the prokaryotic 16S ribosome. Next-generation sequencing and taxonomical classification was then performed.

Results Vaginal swab samples were collected from 21 NEOC patients, 27 PC and 22 controls. The microbiome analysis revealed statistically significant findings. Clostridiales bacterium S5 A14a and Anaerovoracaceae family were found to be abundant in patient who had previous malignancies (p<0.01) Clostridiales bacterium S5 A14a was also abundant in patient who had no pregnancies in the past (p<0.001). Clostridia UCG 014 family was found prominent in patient who died of disease (p<0.01).

Conclusion We demonstrated a significant difference in vaginal microbiome in EOC patients who had a history of other malignancies. Interestingly, the Clostridiales species that are prominent are studied as a risk factor for developing tumors in PTEN carrier and Anaerovoracaceae was linked to esophageal cancer. We also demonstrated Clostridia UCG 014 abundance in patients that died of disease, a finding that was previously shown in mice studies and in patients with lung cancer. This may suggest a group of patients that can benefit from microbiome mapping as a screening tool and as a marker for poor prognosis.

Expanding research in this field may lead to early diagnosis, disease prevention, and targeted therapy in patients with EOC.

Abstract #256

EXOSOMAL MIR-148A-3P SERVES AS TUMOR SUPPRESSOR FOR OVARIAN CANCER

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Introduction/Background Ovarian cancer (OVCA) develop resistance to cisplatin during treatment. Exosome is associated with chemoresistance in various cancers, whereas such a role in OVCA is not yet clear.

Methodology The exosomes were extracted by ultracentrifugation. High-Throughput sequencing was used to measure miRNA levels in exosomes isolated by A2780 and cisplatin-resistant A2780-DDP. Integrated with public databases, exosomal miRNAs associated with cisplatin-resistance, prognosis were identified using computational studies, including 113 machine learning-based integrative procedures and other comprehensive algorithms. The crucial miR-148a-3p was selected for further investigation based on comprehensive bioinformatics approaches. Gain- or loss-functional assays were performed to define the function of miR-148a-3p, including Quantitative real-time PCR, Western Blot, CCK8, colony formation, transwell, wound healing, flow cytometry, and dual-luciferase reporter assays. The plasma exosomes and surgical tissues were collected to detect the expression level.

Results The exosomes were characterized by measuring protein markers, performing nanoparticle tracking analyses and transmission electron microscopy. 126 differentially expressed and 12 prognostic exosomal miRNAs were observed. The prognostic exosomal miRNAs-related cluster and signature were established and validated, indicating their clinical and biological significance. Comprehensive bioinformatics approaches demonstrated crucial role of miR-148a-3p in prognosis and cisplatin-resistance. Low expression of miR-148a-3p was observed in cell and tissues, especially cisplatin-resistant samples. Nevertheless, miR-148a-3p was overexpressed in plasma exosome and cisplatin-resistant cell exosomes. We confirmed the findings in both publicly available expression profiling (a series of datasets) and the samples we collected. We found that miR-148a-3p suppressed proliferation, migration, invasion, cisplatin-resistance, and induced apoptosis, indicating the role of tumor suppressor for miR-148a-3p. Ulteriorly, the inhibition of exosome release induced miR-148a-3p intracellular accumulation, the opposite was observed in the stimulative of exosome.

Conclusion Our data elucidated an unappreciated mechanism of miR-148a-3p in tumor suppressing and cisplatin resistance for OVCA. We uncovered that exosome exclusion of miR-