Poster 30: In vitro characterization of patient-derived samples demonstrates the heterogeneity of high grade serous ovarian cancer

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Topic: Translational Research

Objectives

High grade serous ovarian cancer (HGSOC) is characterized by frequent recurrences and development of chemoresistance. Prior studies in our lab have identified significant heterogeneity among HGSOC patient-derived (PD) cells. This project aimed to further delineate the heterogeneity of PD HGSOC cells and evaluate the relationship between in vitro characteristics and clinical outcomes.

Methods

HGSOC tissue samples were collected through an IRB-approved institutional biobank and cultured in vitro. De-identified clinical information, including homologous recombination (HR) status, cancer treatment, and survival, was abstracted from the medical record. Chemosensitivity was characterized by colorimetric assay to determine half maximal inhibitory concentration (IC50). Epithelial and mesenchymal (EMT) factors, stemness genes, and Let7i expression were evaluated via flow cytometry and quantitative real time polymerase chain reaction (RT-qPCR). Associations were identified by bioinformatics analyses (Principal Component Analyses (PCA)), evaluating clinical characteristics, qPCR and IC50 results, as well as t-tests with significance set at $p \leq 0.05$.

Results

We identified 14 HGSOC PD cells from 13 unique patients for characterization (Table 1). Ten were from primary samples (5 received neoadjuvant therapy). Six patients had HR deficient tumors. Two patients received poly ADP ribose polymerase inhibitors (PARPi) therapy prior to specimen collection, and 6 received it after. Variability was noted among the PD cells in IC50s, as well as in levels of EMT, stemness, and Let7i. On PCA, primary and recurrent samples appeared distinct. Recurrent samples had significantly higher olaparib IC50s than primary samples (99.2uM vs 11.0uM, $p=0.007$), and higher levels of Let7i, relative to normal cells (1.14 vs 0.233, $p=0.029$). Analysis of significant factors as well as trends among characteristics is ongoing. There was no grouping by HR status, overall survival, or subsequent platinum sensitivity.

Conclusions

We identified heterogeneity between PD samples on multiple in vitro characteristics, including those related to EMT and stemness. PCA indicated that primary and recurrent samples appear distinct, with significant differences in PARPi sensitivity and Let-7i level. Further research is needed to understand these associations.

Abstract Table or Graph

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