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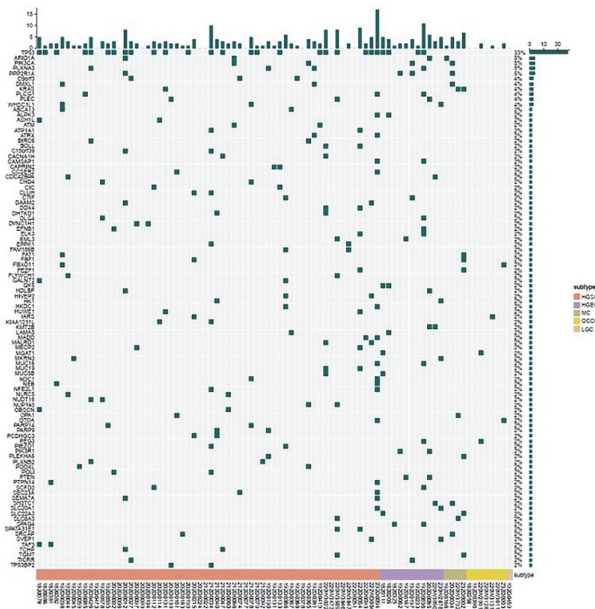
THE NEOANTIGENS LANDSCAPE ASSOCIATED WITH HISTOLOGICAL SUBTYPES IN EPITHELIAL OVARIAN CANCER

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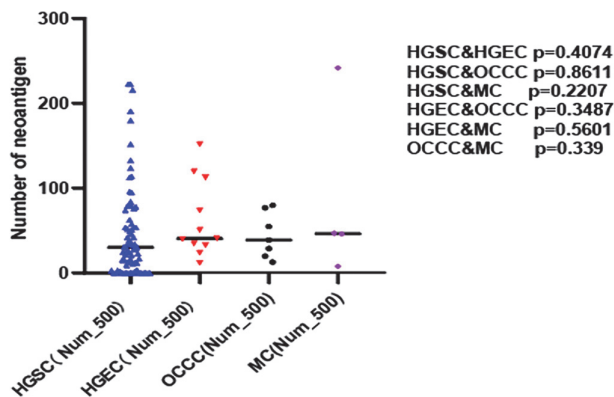
10.1136/ijgc-2023-IGCS.313

Introduction Neoantigens play a critical role in cancer immunotherapy. Epithelial ovarian cancer (EOC) is a strong heterogeneity tumor, often an immune desert, but immunotherapy is extremely important for intent to cure of cancer. We investigated neoantigen landscape of EOC, tried to select patients who are appropriate to immunotherapy.

Methods 97 patients with EOC from May 2015 to April 2023 were included. Neoantigens were predicted by whole-exome sequencing (WES) and RNA-seq. Mutated peptides with a binding affinity of $IC_{50} < 500$ nM were regarded as candidate neoantigens. Patient's clinical information were collected and statistical calculations were performed.



Abstract EP239/#122 Figure 1



Abstract EP239/#122 Figure 2

Results Of the 97 patients (74 High-grade serous carcinoma (HGSC), 11 Endometrioid carcinoma (EC), 4 Mucinous tumor (MC), 7 Clear cell carcinoma (CCC), and 1 poorly differentiated carcinoma), the detection rate of neoantigens was 85.6%. The number of neoantigens in HGSC, EC, MC, and CCC was 0–223 (30.5), 12–152 (41), 8–242 (39) and 13–80 (46.5), respectively (range, SD). CCC, EC and MC had more neoantigens than HGSC, although the difference was not significant. Among predicted neoantigens, the TP53 gene accounted for the largest proportion at 33%, followed by ARID1A, PIK3CA, PLXNA3 and PPP2R1A genes.

Conclusion/Implications In this study, CCC, EC and MC carried more neoantigens, suggesting that they may benefit more from immunotherapy, however, we should expand the sample size to explore whether the difference is significant. Based on this study findings, future clinical trials of immunotherapy for EOC should consider enrolling more patients with CCC, EC, and MC subtypes, instead of focusing mostly on HGSC patients as in previous trials.

EP240/#613

INHERITED LANDSCAPE AND A SPECIFIC RAD51D MUTATION OF CHINESE OVARIAN CANCER PATIENTS

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10.1136/ijgc-2023-IGCS.314

Introduction Gene mutations in ovarian cancer demonstrate ethnic differences, and data among Chinese is still insufficient. Here, we elucidated the inherited landscape of Chinese ovarian cancer patients, and further investigated the functional implication of a Chinese-specific enriched RAD51D mutation.

Methods Between 2015 and 2018, 373 consecutive ovarian cancer patients were prospectively enrolled. Mutations of BRCA1/2, other HRR genes and MMR genes were analyzed by next-generation sequencing. A specific pathogenic RAD51D mutation was identified, and its functional implications were investigated by CCK-8 and Colony formation, transwell migration and drug sensitivity assays.

Results Overall, 31.1% (116/373) of patients harbored at least one pathogenic or likely pathogenic germline variant. BRCA1 and BRCA2 accounted for 16.09% and 5.36% respectively, with one patient harboring both mutations. Besides, 32 (8.58%) patients carried other HRR gene mutations, while 3 (0.8%) patients had MMR gene mutations. RAD51D mutation ranked third (8/373, 2.1%) and the rate was much higher compared with other population. Remarkably, all eight patients had a K91fs variant, and presented with satisfactory platinum response and favorable prognoses. This variant conferred enhanced sensitivity to PARP inhibitors in ovarian cancer cells. However, effects on platinum sensitivity were inconsistent among different cell lines. Only under the background of TP53 mutation, RAD51D K91fs mutation could increase the sensitivity to cisplatin.

Conclusion/Implications Our study revealed the inherited landscape of ovarian cancer, and identified a specific enriched RAD51D mutation of Chinese ovarian cancer patients. It can serve as an important reference for ovarian cancer management and provide a potential treatment target.