#135 - Exome sequencing analysis of primary and recurrent ovarian carcinomas

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**Background & Purpose**

Ovarian carcinomas (OCs) are highly sensitive to platinum-based therapy, however most of OCs eventually relapse. This study aimed to compare genomic profiles in primary vs. recurrent OCs.

**Patients & Methods**

Primary, recurrent and normal tissue triplets obtained from 15 patients were subjected to exome sequencing. The comparison included 1) spectrum of driver mutations [Tamiboro et al., 2018; PMID: 29582815], 2) tumor mutation burden (TMB), 3) HRD score [Telli et al., 2016; PMID: 26957504], 4) mutational signatures [Degasperi et al., 2020; PMID: 32118208].

**References**


**Results**

All other mutation present in primary tumors remained in the genome through the treatment course. One or several new other somatic mutations emerged in 6/15 (40%) recurrent lesions. These alterations involved RS1 and ELAC2 (n = 1), TNC (n = 1), TRIO and KRKBX (n = 1), PAX5 and CDH10 (n = 1), SOX9 (n = 1), ABCB4 and EEF1A1 (n = 1) genes. Recurrent tumors demonstrated small but statistically significant increase of TMB as compared to primary lesions (4.7 vs. 3.0 per megabase, p = 0.01). HRD demonstrated high degree of similarity within primary/recurrent tumor pairs. PLATINUM mutation signature was characteristic for platinum-sensitive relapses, but not for platinum-resistant recurrences or chemotherapy tumors (p = 0.02).

**Figure 1.** Copy number alterations in primary [Pr] and recurrent [Rec] ovarian carcinomas

**Figure 2.** Mutational signatures in paired ovarian carcinoma samples

**Conclusions**

HRD score remains stable through the treatment history. PLATINUM mutation signature reflects not only the mere fact of prior exposure to platinum-based therapy, but also the efficacy of this therapeutic regimen.

**Abbreviations:**

HRD - homologous recombination deficiency, MMRR - mismatch repair, OC - ovarian carcinomas, Pr - primary tumor, Rec - recurrent tumor, TMB - tumor mutation burden, WT - wild-type

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