Background

Epithelial ovarian cancer (EOC) affects nearly 22,000 women annually and is the leading cause of death from gynecologic cancer in the United States. Five-year cure rates are <40% and approximately 14,000 will die each year. Large-scale efforts are currently underway to use molecular profiling via next generation sequencing (NGS) technology to guide treatment in cancer patients with poor prognosis, but limited application of NGS in ovarian cancer has been reported. In this report, we previously described Ex Vivo 3D Drug Response Profiling (EV3D™ DRP) was used to identify response differences between newly diagnosed and relapsed ovarian cancer patients and correlated with NGS of primary ovarian tissue.

Methods

1. Tumor Acquisition and Processing

- Patient consented for IRB approved prospective biology study
- Subject demographics
  - Newly diagnosed: 61%
  - Relapse: 39%
  - Serous cell carcinoma: 72%
  - Clear cell carcinoma: 14%
  - High grade: 56%

2. EV3D Assay

- EV3D DRP platform
  - Mixed cell types
  - ECM free
  - 3D Spheroid
  - 2.5k cells/well
  - 8 drugs, 7 day turnaround

- EV3D NGS directed DRP platform
  - Mixed cell types
  - 3D Microtumor
  - Perfusion culture
  - Drugs defined by NGS
  - 14-19 days in culture

3. Data Analysis

- NGS
  - TP53 (C242S) 1%
  - EV (p53) 10%
  - K562 (%)
  - 3D IC50 (µM)

- Correlation
  - Pearson correlation coefficient
  - EV3D IC50 (µM) 0.95
  - 2D IC50 (µM) 0.98

Figure 1: NGS identified mutations correlate with EV3D DRP. (A) Patient tumors collected by KIYATEC closely mimic global mutation rates (Ross, 2013). (B) Response to LY 294002 correlated with the presence of a PI3K mutation in EV3D DRP better than in 2D cell culture. (C) KIY OV 028 was identified as having an EGFR and p53 mutation. When treated with drugs, it showed a positive response to both Erlotinib and Afatinib along with no response to Trametinib. (D) KIY OV 026 was identified by NGS as having a number of mutations including MET, NFI, TSC2, and p53. It responded to both LY294002 and Crizotinib.

Figure 2: EV3D DRP response to carboplatin correlates with relapse. When matched EV3D and 2D samples are both treated with carboplatin under the same conditions, a significantly different response is detected when comparing the response of newly diagnosed patients and relapse patients in EV3D tested samples. This significantly different response is not detected in 2D however. This indicates that EV3D may be better able to detecting resistance phenotype than 2D.

Figure 3: EV3D DRP to Carboplatin correlates with CA-125. Newly diagnosed patient samples were received following 3 cycles of neoadjuvant carboplatin/paclitaxel. Following EV3D DRP, KIY OV 033 showed response to Carboplatin that correlated with CA-125 measured post-treatment while KIY OV 034 had a lower response to Carboplatin, correlating with a lack of CA-125 reduction following neoadjuvant therapy.

Conclusions

- We have successfully isolated cells and performed EV3D DRP on 66% of patient samples
- We can readily identify mutations within the patient samples and our rates mimic those of the general population
- EV3D DRP results for targeted therapies correlates with the presence of known mutations rapidly identified in a CLIA laboratory
- EV3D DRP may predict clinical response to neoadjuvant carboplatin therapy