Poster 31: In vitro low passage patient-derived cells demonstrate lack of faithfulness to original sample

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Topic: Translational Research

Objectives

Patient derived (PD) cells have greater faithfulness to original tissue than immortalized cell lines and are preferred as a model for cancer research. However, growth in vitro may induce changes in the PD cells. This project aimed to characterize changes induced in PD cells by in vitro culture.

Methods

Gynecologic cancer samples were collected through an IRB-approved institutional biobank and cultured in vitro. Stemness, epithelial, and mesenchymal factors, as well as let7i expression were analyzed with quantitative real time polymerase chain reaction (RT-qPCR) and flow cytometry in the original samples. The samples were then processed and cultured in vitro. Prior to 10th passage, flow cytometry and qPCR analyses were repeated, and normalized to the original sample. Descriptive statistics and t-tests were used to identify the changes induced by in vitro culture, with $p \leq 0.05$ as statistically significant.

Results

Original sample histology included high grade serous ovarian carcinoma (HGSOC) and uterine and ovarian carcinosarcoma (CS). We noted heterogeneity of miRNA, mRNA, and protein expressions on original samples. All cultured samples demonstrated changes in miRNA and mRNA levels from their original samples (Figure 1). Three different samples had significant decreases in levels of LIN28A, OCT4, and Occludin after growth in vitro. Further analysis of a HGSOC (PD23) at early passage (EP, passages 2, 3, and 4) compared with later passage (LP, passage 7) showed significant differences between EP and the original sample in OCT4 ($p=0.0042$) and Occludin ($p=0.0042$), differences which were no longer significant in LP. There were no significant differences between EP and LP.

Conclusions

In vitro, PD cells quickly lose expression of stemness-associated genes. These may reflect selection and amplification of cells best adapted to growth outside the tumor microenvironment. Further research is needed to evaluate if three-dimensional growth or other conditions can better mimic the original tissue.

Abstract Table or Graph

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