Poster 26: Development of patient derived ovarian cancer organoids with native immune cells
Presenting Author: Leah Wormack, MD, MS, University of California San Francisco

Topic
Ovarian

Objectives
Patient derived organoid models from human tumor specimens offer a novel opportunity to evaluate the individual tumor and develop personalized therapies. The standard submerged organoid model allows for proliferation of tumor cells, but not growth and recapitulation of native immune cells. Air liquid interface (ALI) organoid models offer the ability to culture the native tumor immune microenvironment, further enhancing prediction of patient response to therapies and a personalized approach to treatment. We sought to develop ovarian cancer patient derived organoids using the standard submerged and novel ALI models and utilize these models for therapeutic testing.

Methods
Ovarian tumor specimens were collected intraoperatively. Two methods of organoid culture were performed: submerged and ALI. In the submerged organoid model, the tumor was serially digested to single cells which were then suspended within a collagen matrix. In the ALI model, tumor is minced and suspended with a double layer of collagen matrix and then cultured with interleukin-2 (IL-2) to stimulate proliferation of immune cells. The ALI model was evaluated using immunofluorescence (IF) to identify the immune cells.

Results
We have collected a cohort of 6 ovarian tumors during primary cytoreduction as well as interval cytoreduction in those with significant residual disease. In the submerged method, organoid growth occurred within the first 5 days and was sustained for 14 days. These organoids were able to undergo replicable passaging with consistent cell viability. Organoids from the ALI method developed within 3 days and continued to show sustained growth for up to 35 days. The growth of both tumor and immune cells in the ALI model was assessed using immunofluorescence (IF). IF was performed on ALI organoids 30 days after plating utilizing DAPI nuclear marker, Ki-67 proliferation marker, and CD45 T-cell marker which demonstrated presence of both organized tumor and immune cells (Figure 1).

Conclusions
We demonstrated sustained growth of ovarian cancer organoids which showed retention of native immune cells in an ALI organoid model. The ALI model will enable evaluation of the tumor immune microenvironment and opportunity to develop personalized therapies. Future directions include treatment of organoids with novel therapies to validate the effects on the immune response.

Uploaded File(s)
Abstract Table or Graph
NWNUUGRI-2091836-1-ANY.pdf