Abstracts

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**ESTABLISHMENT OF PERITONEAL DECM SCAFFOLDS FOR 3D CULTURE OF OVARIAN CANCER ORGANOIDS**

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**Introduction/Background** Recently, ovarian cancer organoids have been developed, showing promising advantages compared to traditional 2D cell culture and mouse models. Organoids are 3D cell cultures and conventionally cancer cells are embedded in a gel composed of extracellular matrix (ECM) proteins. These gels do not fully mimic the native ECM of a human tumour. Natural ECM scaffolds can be generated by decellularization of different tissues (dECM). The aim of this study is to generate and characterize peritoneal extracellular matrix (PerMa) scaffold and compare to already established small intestinal submucosal scaffold (SIS). The PerMa scaffold will be used in the establishment of an ovarian cancer organoid platform.

**Methodology** A protocol for decellularization of porcine and human peritoneum was developed. The permeability of the scaffolds was assessed with diffusion assay. Multiphoton microscopy and rheological analyses were done to assess the collagen structure and biophysical properties of the scaffolds. Cell cultures of ovarian cancer cell lines and primary patient cells were set up.

**Results** The decellularization was validated with histology and DNA quantification. Cell cultures were successfully established with ovarian cancer and fibroblast cell lines and primary patient cells. Growth characteristics differed significantly on PerMa and SIS. We went on to investigate whether there are structural or biophysical differences that might explain this. We found no differences in the permeability to low (4 kDa) or high (40 kDa) molecular weight molecules between SIS and PerMa, but multiphoton microscopy revealed different organization of collagen fibres. Further, rheological analyses showed differences in elasticity (storage modulus, G') and viscosity (loss modulus, G'x).

**Conclusion** We have established and characterized a 3D model of ovarian cancer that better represents the tumour microenvironment. In the future we will use this model system to establish patient-derived ovarian cancer organoids with potential application for tumour biology research and personalized medicine.

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**TROP-2 EXPRESSION AND THE TUMOR IMMUNE-MICROENVIRONMENT IN CERVICAL CANCER**

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**Introduction/Background** Trophoblast Cell Surface Antigen 2 (TROP-2) is a transmembrane glycoprotein that is overexpressed in various cancers. Moreover, TROP-2 has immunologic relevance, as a target for tumor reactive T-cells. We performed a pilot study of 123 cervical cancers to test whether TROP-2 expression may be associated with tumor immune-microenvironment.

**Methodology** We performed immunohistochemical analysis of whole tumor sections from patients with cervical cancer who underwent primary surgery between 2000 and 2020 at our institution. TROP-2 expression was evaluated using anti-TROP-2 monoclonal antibody clone MAB650. Immune biomarkers including PD-L1 (22C3), CD3 (PS1), and CD8 (4B11) were also evaluated. TROP-2 and PD-L1 positive was defined as H-score ≥10 and combined positive score (CPS) ≥1, respectively. Each whole tumor section was evaluated for intratumoral tumor-infiltrating lymphocytes (TILs) by using a 40× objective lens, and 5 independent areas with the most abundant TILs were selected. The association between TROP-2 expression and immune biomarkers was analyzed.

**Results** The cohort consisted of squamous cell carcinoma (SCC) (54.5%) and non-SCC (45.5%). In IHC samples, TROP-2 positive was identified in 84.6% and more commonly expressed in SCC (SCC vs. non-SCC; 97.0% vs. 69.6%, p<0.001). Spearman’s correlation analysis showed significant and positive correlations between TROP-2 H-score and immune markers (CD3+TILs, r=0.295, p<0.001; CD8+TILs, r=0.267, p=0.001; PD-L1 CPS, r=0.178, p=0.025). None of the other clinicopathological features were associated with T cell infiltration in the study sample. The percentage of TROP-2-positive patients in the PD-L1-positive or CD3-High group was 89.2% and 93.9%, respectively. After a median follow-up of 67.8 months, TROP-2 expression showed no correlation with DFS and OS (log rank test, p=0.478 and 0.071).