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Design of a human omentum tissue model to investigate ovarian cancer cell adhesion and invasion

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Ovarian cancer is one of the most common causes of cancer-associated female deaths. Since most patients show an asymptomatic early-stage disease, this cancer is typically diagnosed when already metastasized. Ovarian cancer cells disseminate intraperitoneally as single cells or multicellular spheroids and preferentially colonize the greater omentum, a visceral fold in the abdominal cavity. Disease progression is commonly accompanied by ascites formation, an excessive accumulation of peritoneal fluid within the abdominal cavity containing cytokines, growth factors, and extracellular matrix molecules.
Here, the development of a full-thickness human omentum model using bioprinting technology is presented, which allows the study of ovarian cancer spreading and provides a platform to test new therapeutic strategies.
As a first step, bioprinting parameters were optimized to obtain reproducible printing results to perform the subsequent experiments. Then, the effect of artificial and patient-derived ascites on the morphology and functionality of the mesothelial cell line MeT-5A and the adhesion of the ovarian cancer cell line SKOV-3 was investigated. This study revealed that MeT-5A cells show reduced biological responsiveness to the presence of ascites when compared to primary peritoneal mesothelial cells. Thereafter, a reproducible multi-cellular omentum tissue model was developed, which mimics the local structural heterogeneities of the omentum *in vivo*. Both, ovarian cancer cell adhesion and metastatic outgrowth were investigated. As a last project, the design of vessel-like constructs allowing the perfusion of tissue models is described. Stable and leakproof polytetrafluoroethylene tubes were fabricated, which supported endothelial barrier formation. This approach provides a platform to evaluate new therapeutic strategies under perfusion.
In summary, this thesis describes the development of a human omentum tissue model and investigates its applicability in studying ovarian cancer cell spreading. A perfusion system is introduced to further use this tissue model as a platform to test new therapeutic strategies.

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