Universität Basel

Research Project

The underestimated role of the human omentum in metastatic spread

Third-party funded project

Project title The underestimated role of the human omentum in metastatic spread
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High-grade serous ovarian (SOC), peritoneal (SPC) and tubal cancers (STC) are diagnosed in 75% of cases at advanced stage disease in women, when 5 year survival is only 20%. All three cancers have the same histological appearance and are diagnosed and treated the same way. However, knowledge is increasing that whilst all three arise via p53 mutations, they origin from different sites and have different genetic drivers. Whilst STC/SOC is defined by having the biggest tumor volume in the tubes/ovaries and only metastatic disease in the omentum, SPC presents with massive omental tumor-load with no invasion into the ovaries or tubes. Until now, there are no published data to support a different origin for SPC because it seems to be specifically located in the omentum. However, unpublished work from us has shown a revolutionary result: on genetic, proteomic and glycomic level, STC/SOC are distinct to SPC and should therefore be diagnosed and especially treated individually. Correct classification of these cancers, identifying the place of origin and their distinct development would change the paradigm that they are all the same disease which is relevant for the treatment regime and possible survival of women.Since SPC develops specifically in the omentum, we aim to (a) reveal the human omental structure in situ and (b) to design, based on the in-situ information, a relevant 3D human model mimicking the development of SPC.Like the omentum, the fallopian tubes and ovaries are covered by mesothelial cells with submesothelial vascular and lymphatic networks where resident macrophages mature; a robust 3D in vivo-like model, which allows the assessment of cancer cell mesothelial clearance and invasion as well as stem cell population studies has not been designed before and is highly innovative. We will use native tissue and for the first-time tissue-engineered omentum including 3D cell printing technology. Molecular analyses will be performed by deconstructing and reconstructing both omental models, systematically exposing the structures to normal tubal epithelial and serous tubal cancer cells. Hereby, we aim to understand the mechanism of invasion and thus develop new therapeutic targets. Together, these results have the potential to invalidate medical textbooks and shift the paradigm of diagnosis and treatment of high grade serous adenocarcinomas of apparently tubal, ovarian and peritoneal origin.

Keywords omentum; serous peritoneal cancer; metastasis; serous ovarian cancer; stem cells; 3D printing; tissue engineering; scaffolds
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