Applications of laser ablation-inductively coupled plasma-mass spectrometry imaging in experimental peritoneal metastatic cancer research regarding tissue engineered biomaterials

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Peritoneal metastasis occurs when primary tumors metastasize to the peritoneal cavity as a result of an extensive communication between cancer-associated fibroblasts (CAFs), mesothelial cells and disseminated cancer cells. Extracellular matrix (ECM) proteins are secreted by the CAFs and form receptive micro-environments for peritoneal implantation of cancer cells. Typically, peritoneal metastases originate from ovarian and colorectal cancer [1]. Since the reintroduction of intraperitoneal chemotherapy combined with a priori surgical cytoreduction, there is a trend towards long-term survival as five-year survival rates of 50% were published [2]. Nevertheless, peritoneal metastasis is still life-threatening and requires adequate preventive and therapeutic strategies [1]. The development of new and more patient-relevant preclinical models can enhance the therapeutic progress. The LECR group tissue-engineered a new implantable heterocellular 3D hybrid hydrogel-polylactic acid scaffold model that biomimicks the tumor micro-environment of peritoneal metastases. This scaffold model could serve as a platform technology for in vitro and in vivo drug penetration and efficacy studies [2]. Hereby, LA-ICP-MS imaging can be deployed as a micro-analytical technique to determine the (sub-)cellular quantitative distribution of platinum group metal-based anticancer compounds, e.g., cisplatin [3], in the tumor micro-environment of the scaffold model.

The role of CAFs can be exploited to design biomimetic traps, in the form of gelatin microparticles (MPs) with a CAF-derived ECM-surface, in order to mislead cancer cells and to prevent peritoneal implantation, resulting into delayed peritoneal metastasis and prolonged survival. For in vivo experiments, the MPs were loaded with iron oxide nanoparticles (FeO\textsubscript{x} NPs) to enable magnetic removal of the intraperitoneal MPs [1]. The distribution of the FeO\textsubscript{x} NPs within thin sections of paraffin-embedded Ca-rich MPs can be mapped via LA-ICP-MS/MS imaging, relying on the use of chemical resolution and of mass-shift approaches to avoid the strong spectral overlap affecting the signals of the most abundant Ca and Fe isotopes. This approach is based on pressurizing the collision/reaction cell (CRC) of a tandem ICP-MS instrument with a reactive gas, allowing one to selectively convert the analyte ion(s) into reaction product ion(s) that can be measured free from spectral interference at another mass-to-charge ratio [4].


