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_x NPs) to enable magnetic removal of the intraperitoneal MPs [1]. The distribution of the FeO_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].

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