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EXPTEL: A Novel Non-Destructive Method for Mining Soluble Tumor Biomarkers

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Introduction: Secreted cancer proteins are important modulators of tumor growth and progression. This protein group has always been considered a major source of potential biomarkers. Unfortunately identification of novel and clinically useful secreted tumor-specific proteins is difficult since their concentration in serum or urine is very low. Alternatively to this, mining tissue proximal fluid has emerged as a powerful approach to identify potential candidate biomarkers. However, current methods rely on ex vivo culture that takes considerable time and exposes tissue biopsies to uncontrolled degradation through endogenous proteases.

Aim: Aim of the project is the discovery of new soluble biomarkers for early detection, diagnosis or prognosis of human cancer disease.

Methods: In the present work we have developed a novel and efficient method for the collection and analysis of tumor secretome. The approach, which we termed Expel, extracts soluble tumor biomarkers within few minutes and without altering the tissue morphology. For this purpose a small tissue biopsy is incubated in a slightly hypertonic extraction buffer while subjected to alternating pressure. Upon extraction the tissue is fixed in formalin and can be used for histological analysis. The soluble extract is further prepared for proteomic analysis using bottom-up mass spectrometry approach.

Results: In a proof of concept study we have extracted and analysed soluble biomarkers from human colorectal carcinoma liver metastases as well as primary colorectal tumors. In an extensive tissue validation study we confirm that Expel procedure does not alter tissue morphology or subsequent molecular pathology tests. The comparison of proteins identified in tumor lesions with those found in adjacent normal tissues revealed a group of differentially expressed soluble proteins. Their potential usefulness as diagnostic or predictive markers is currently being explored

Conclusions: The Expel protocol provides clinicians with a new tool enabling them to non-destructively discover new biomarkers and preserve precious tissues (like colon polyps) for pathology evaluation

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Metabolomic, Proteomic and Preclinical Imaging of Patient Derived Tumor Xenografts for Improving Treatment of Liver Metastases Patients

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Introduction: Successful translational research relies on animal tumor models that can veritably recapitulate the human situation. Most is done today using mouse xenografts, which are based on cultured cancer cells. However, these cell lines have considerably diverged from their original tumors, critically losing the genetic and proteomic diversity typically found in tumors. This drawback is at the origin of the recent surge of interest in patient-derived tumor explants (PDX), which consists in grafting human tumor directly in immunocompromised mice.

Aim: Although the PDX model is promising, little is known on how well are the functional proteomic and metabolomic aspects conserved from the original patient to the model. Our study aims to broaden this knowledge. A further question concerns the clinical utility of this model and to what extent can functional data obtained on PDX help improve treatment for cancer patients.

Methods: In the current study we have successfully established PDX from 4 individual colorectal carcinoma and 4 liver metastases patients. We have used advanced pre-clinical imaging based on PET/CT (18FDG) and 9T MRI to functionally monitor tumor behavior in mice and compare this information to data obtained in the patient. All xenografts were evaluated using PERCIST criteria and compared to the original patient data. We further employ matrix-assisted laser desorption/ionization (MALDI) imaging technique to show for the first time a comparative metabolomic profile of the patient tumor and several generations of PDX.

Results: Owing to a validated set of histological markers we confirm that the PDX models have conserved histological features with the original tumor. With the preclinical imaging and the MALDI imaging technique we were able to determine the metabolic signature of the cancer cells and the stroma respectively, and we could assess the impact of generation-dependent evolution of the PDX.

Conclusions: Our study contributes to a better understanding of the behavior of the tumor and its evolution in a model that can be useful for biomarker discovery, outcome prediction or treatment design.

Radiology, Pathology and Nuclear Medicine

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Does intraoperative pancreatoscopy affect surgical management of intraductal papillary mucinous tumor of the pancreas ?

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Introduction: Because of the potential malignant growth of intraductal papillary mucinous tumor of the pancreas (IPMTP), precise diagnosis of malignant lesions is essential for complete surgical resection.