Proteomic Characterization of Renal Cell Carcinoma Using MALDI-MS Imaging

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Renal cell tumors represent a group of histologically and molecularly heterogeneous diseases. Besides the three major subtypes (clear cell renal cell carcinoma (ccRCC), papillary renal cell carcinoma (pRCC), and chromophobe renal cell carcinoma (chRCC)), many more malignant and benign subtypes exist. Mass Spectrometry Imaging (MSI) goes far beyond microscopy, as it enables the assessment of spatial molecular arrangements directly from the tissue. Samples from 92 patients were included in two tissue microarrays (TMAs): 28 ccRCC, 20 chRCC, 18 pRCC, and 19 oncocytomas. The TMAs were subjected to on-tissue trypic digestion followed by matrix application (α-cyano-4-hydroxycinnamic acid). Samples were analyzed utilizing a Bruker rapiX MALDI-TOF mass spectrometer. Data analysis was performed by using the SCiLs Lab and FlexImaging 5.0 software (Bruker), and statistical analysis were performed on the statistical software environment R. The same tissue sections were then stained with hematoxylin and eosin for histological evaluation. The measured mass spectrometry data was utilized for training machine learning (ML) models following the formal clinical diagnosis. The models performed with accuracies of 98% and above, high sensitivity and specificity. External validation of the ML models was carried on whole-mount tissue sections, resulting in correct classification of the tumor regions. Feature extraction of the top 10 features per tumor subtype was compared pairwise. The resulting features (Table 1) were consistently associated with a particular pathology. Proteins such as, keratin type 2, cytoskeletal 7 (CK7), vimentin, and collagens showed a higher correlation with specific tumor types. This pilot study showcases the applications of MSI as a supplementary approach to be added to the pathologist’s toolbox, as it can be integrated with the ongoing efforts to advance digital pathology for diagnostic assistance. Additionally, it provides further insights on biomarkers for additional confirmation using the traditional histopathological methods and can disclose potential treatment targets.

m/z Neoplasia 805.4 RO 862.4 chRCC 959.5 RO 1104.5 pRCC 1117.3 chRCC 1169.6 chRCC 1289.6 RO 1406.6 pRCC 1428.7 ccRCC 1493.7 chRCC Table 1: Outcome from feature selection per tumor type.

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