A NEW microRNA-BASED DIAGNOSTIC TEST FOR CLASSIFICATION OF KIDNEY TUMORS

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Background: Renal cancers account for more then 3% of adult malignancies and cause more than 13,000 deaths per year in the US alone. The four most common types of kidney tumors include the malignant renal cell carcinomas clear cell, papillary and chromophobe as well as the benign oncocytoma. These histological subtypes vary in their clinical courses and their prognosis, and different clinical strategies have been developed for their management. In some of the kidney tumor cases it is difficult for the pathologist to distinguish between tumor types on the basis of morphology and immunohistochemistry (IHC). In this work we present the development and validation of a microRNA-based test for classifying primary kidney tumors.

Methods: Over 180 Formalin Fixed Paraffin Embedded (FFPE) samples of primary kidney tumors were collected and reviewed by pathologists from different institutes according to morphology and available IHC labeling data. High-quality total RNA, including the well-preserved microRNA fraction, was extracted from the FFPE samples using a proprietary protocol. Expression levels of hundreds microRNAs were profiled using a custom microarray platform. Technical validation of the array results was performed using qRT-PCR. An assay which classifies the kidney tumors was developed based on the expression of differential microRNAs in these four tumor types. A validation set 201 independent samples was classified using the assay and analyzed blindly.

Results: A set of 24 differential microRNAs was identified that allows accurate classification of kidney tumors. A diagnostic assay based on the microarray technology was developed and clinical validation performed using an independent, blinded sample set. The test was able to produce results for 92% of the validation set of 201 samples with accuracy of 95%

Conclusions: Expression levels of certain microRNAs are highly specific to subtypes of renal cell tumors. These findings were the basis for the development and validation of a standardized diagnostic assay for the classification of renal cell tumors in FFPE samples from resections or biopsies. The validation results showed 95% accuracy and demonstrated again the diagnostic power of microRNAs.

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