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Liquid biopsy in clear cell Renal Cell Carcinoma: urinary miR-210-3p as emerging specific biomarker

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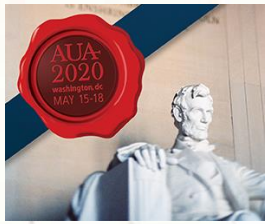
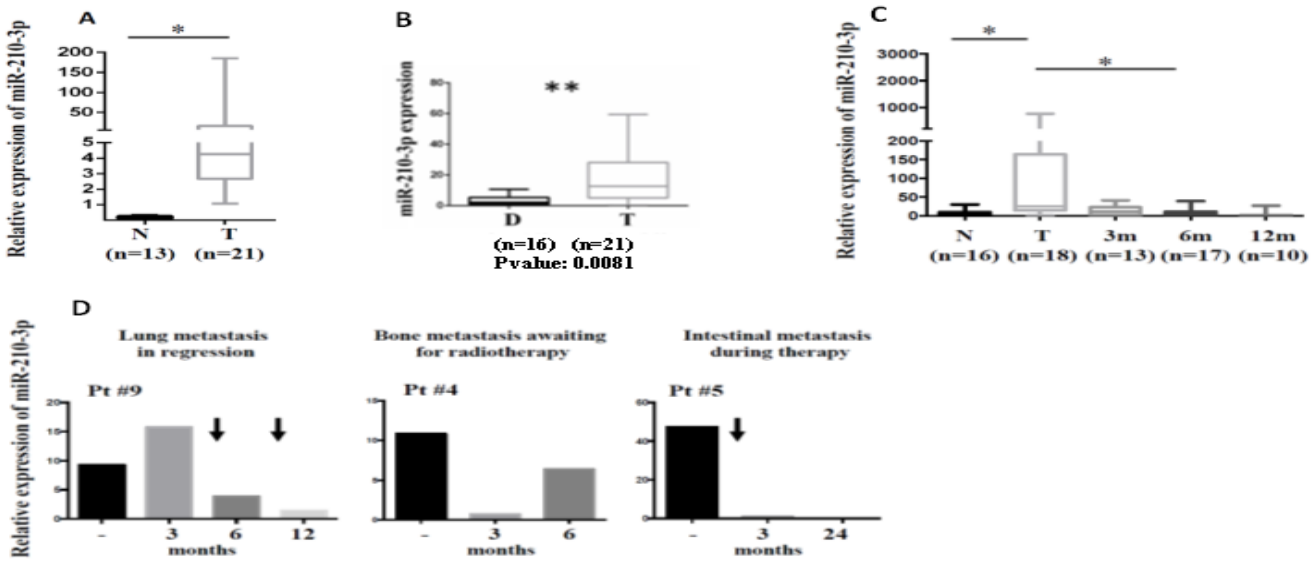


Background

The most common subtype of renal cell carcinoma (RCC) is clear cell RCC (ccRCC) that accounts for 70-80% of all renal malignancies. To date, no useful markers are available in clinical practice for early diagnosis and for optimal patient stratification. MicroRNAs, a class of small non-coding RNA, are emerging as promising molecules in the management of urological tumors suggesting the possibility of using them as non-invasive biomarkers. The aim of this study is to evaluate whether miR-210-3p may be an accurate non invasive diagnostic and prognostic biomarker for ccRCC patients.

Material and methods

This study includes a cohort of 21 ccRCC cases underwent radical or partial nephrectomy. We analyzed by RTpPCR miR-210-3p levels in neoplastic and healthy tissues and in urine specimens collected at surgery and during follow-up visits (from 3 to 24 months) of all ccRCC cases, of which 18 disease-free patients and a small subgroup presenting metastatic progression. Urine samples were also collected from 16 healthy donors with similar demographic features. The specimens were frozen within 30 minutes from collection and stored at -80°C until RNA extraction and microRNA expression analysis.



Evaluation of miRNA levels in tissues and urine specimens from ccRCC patients by RT-qPCR
(A) Box-plot showing the modulation of miR-210-3p in a cohort of 21 matched fresh frozen tissues from ccRCC patients (T) and adjacent normal tissue (N) samples.
(B) Box-plot showing the modulation of miR-210-3p in urine of 21 ccRCC patients (T) and 16 healthy donors (D).
(C) Box plot showing the expression level of miR-210-3p in urine of 18 patients at the time of surgery (T) and during follow-up (3, 6, 12, 24 months from surgery) that show a Disease Free Survival.
(D) Box plot showing the expression level of miR-210-3p in urine collected from 3 metastatic patients at the time of surgery and during follow-up. The arrows specify the time of therapy.

Results

miR-210-3p was upregulated in ccRCC frozen tissues compared to matched normal counterparts. Next, we evidenced that miR-210-3p resulted significantly up-regulated in urine specimens collected from ccRCC patients at the time of surgery, compared to healthy samples. Of note, miR- 210-3p levels resulted significantly reduced in urine samples from disease-free patients during follow-up, compared to the baseline levels (time of surgery). In a small subgroup of patients presenting metastases, the urine levels of miR-210-3p increased and, interestingly, again decreased when responding to medical treatments.

Conclusions

This pilot study highlights the relevance of secreted miR-210-3p as powerful non invasive diagnostic and prognostic biomarker for ccRCC patients, with potential clinical applications from diagnosis to treatment in clinical setting.