66

Identification of a microRNA profile in urine with diagnostic and prognostic value for clear cell renal cell carcinoma

Eur Urol Suppl 2019; 18(1);e89

Oto J [1], Solmoirago M.J [1], Pérez-Ardavin J. [2], Sánchez-González J.V [2], Plana E. [3], Hervás D. [4], Fernández-Pardo Á. [1], Yelo M. [1], Vera C.D [2], Martínez-Sarmiento M. [2], España F. [1], Navarro S. [1], Medina P. [1]

[1]Medical Research Institute Hospital La Fe, Dept. of Haemostasis, Thrombosis, Arteriosclerosis and Vascular Biology Research Group, Valencia, Spain, [2]La Fe University and Polytechnic Hospital, Dept. of Urology, Valencia, Spain, [3]La Fe University and Polytechnic Hospital, Dept. of Angiology and Vascular Surgery Service, Valencia, Spain, [4]Medical Research Institute of Hospital La Fe, Biostatistics Unit, Valencia, Spain

Introduction & Objectives: Renal cell carcinoma (RCC) is the most common type of urinary malignancy. Clear cell RCC (ccRCC) is the predominant RCC subtype, accounting for 70–80% of RCC. microRNAs (miRs) are small non-coding RNAs that regulate protein expression. miRs have been proved to regulate cancer progression and represent potential diagnostic and prognostic biomarkers. Our aim was to find a profile of miRs in urine capable of distinguishing between ccRCC patients and controls.

Materials & Methods: Two clinical groups were recruited: 54 RCC patients from whom three urine samples were obtained (t_0= before surgery, t_1=3 months after surgery, t_2=one year after surgery) and 58 healthy volunteers (controls) with an ultrasound scan to rule out urological tumours from whom one urine sample was obtained. The expression level of 179 miRs was studied in urine of 16 selected ccRCC patients (at t_0 and t_1) and 16 controls, age and gender matched, using the Serum/plasma Focus microRNA PCR Panel V4 (Exiqon). An endogenous reference miR was selected as that with the highest stability using RefFinder software. Normalization of miR expression was conducted with the $^{\Delta\Delta}$Ct method, and subsequently results were also normalized with the level of creatinine. Statistical analysis was performed using R (v3.2.3).

Results: The most stable miR was miR-20a-5p and therefore we used it as endogenous reference. We adjusted an Elastic Net logistic regression model for the diagnosis of ccRCC using the miR expression levels in urine of patients at t_0 and controls. This model included 3 miRs: miR-200a-3p, miR-34a-5p and miR-365a-3p. Moreover, with the Wilcoxon test we identified 5 dysregulated miRs comparing the miR expression level of patients at t_0 and controls: miR-200a-3p, let-7d-5p, miR-205-5p, miR-34a-5p and miR-365a-3p. Furthermore, we identified 5 dysregulated miRs comparing patients at t_0 and $t_{1:}$ let-7d-5p, miR-152-3p, miR-30c-5p, miR-362-3p and miR-30e-3p. These last 5 miRs could be involved in the prognosis of ccRCC.

Conclusions: We have obtained a urine profile of 3 miRs with potential diagnostic value for ccRCC. We also identified 5 dysregulated miRs in patients comparing before and after surgery, and other 5 dysregulated miRs comparing patients and controls discovering an easy and non-risk procedure to achieve a closer personalized follow-up in high-risk patients. Our findings could shed light on the molecular mechanism of ccRCC. Validation of our statistical models in a larger cohort of patients is required. ISCIII-FEDER (PI14/00079, PI14/00512, FI14/00269, CPII15/00002, PI17/00495), GVA (PrometeoII/2015/017, ACIF/2017/138), Sociedad Española de Trombosis y Hemostasia.