P63 MicroRNA-30a downregulation: Biomarker in Clear Cell Renal Cell Carcinoma

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Introduction & Objectives: Renal Cell Carcinomas (RCC) are the most lethal urological cancers comprising a heterogeneous group of malignancies. Among these, clear cell renal cell carcinoma (ccRCC) carries worse prognosis when compared to other common histological subtypes. Approximately 25% of ccRCC patients present distant metastasis at the time of diagnosis, and 20-50% of patients diagnosed and surgically treated with curative intent, develop metastatic disease within few years. Thus, it is of great importance to identify diagnostic and prognostic biomarkers that might aid in ccRCC patient's clinical management. MicroRNAs (miRs) have been described as deregulated in different types of malignancies, including ccRCC. Among these, miR-30a was implicated in ccRCC metastatic process and progression. Conversely, it was reported to be downregulated in ccRCC, suggesting a putative tumour-suppressor function. Nonetheless, the exact role of miR-30a in ccRCC is still controversial and needs to be clarified.
Thus, we aimed to investigate the diagnostic and/or prognostic potential of miR-30a deregulation in ccRCC.

Materials & Methods: Two hundred and fifty ccRCC patients diagnosed at IPO-Porto were enrolled, after informed consent. In addition, 28 renal normal tissues (RNT) collected from upper urinary tract urothelial carcinoma patients served as controls. RNA was extracted using Trizol reagent, miRNAs cDNA was synthesized and amplified by RT-qPCR for expression quantification.

Results: MicroRNA-30a, was identified as significantly downregulated ($P<0.05$) in ccRCC in TCGA database and was independently validated in an IPO-Porto's cohort. Indeed, miR-30a showed significantly lower levels ($P<0.0001$) in ccRCC compared with RNT. Moreover, miR-30a downregulation was significantly associated with clinicopathological features, specifically higher pathological stages (I vs IV, $P=0.0244$; II vs IV, $P=0.0373$; III vs IV, $P=0.0384$), metastatic dissemination ($P=0.0482$) and recurrence ($P=0.0057$). The medium follow-up time was 58.48 (range: 29.70-84.21) months. In survival univariable analysis, advanced pathological stage and higher nuclear grade associated with worse disease-free survival (DFS) ($P<0.0001$ and $P=0.0113$) and disease-specific survival (DSS) ($P<0.0001$ and $P=0.0007$). Notably, lower miR-30a expression (75^{th} percentile) levels significantly associated both with shorter time to relapse ($P=0.0051$) and shorter disease-specific survival ($P=0.0486$). Nonetheless, in multivariable analysis, only advanced pathological stage retained independent prognostic value for DFS (III vs IV: $HR=4.185$ $P<0.0001$). This later result might be due the rather limited follow-up time.

Conclusions: The lack of accurate diagnostic and/or prognostic biomarkers for ccRCC constitutes a major challenge in daily management of these patients. Future studies including cohorts of patients with larger follow-up time is required to confirm our findings.