Integrated genomics analysis of gene and miRNA expression profiles in clear cell renal carcinoma cell lines

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Clear cell renal cell carcinoma (ccRCC) is the most common and malignant tumor in the adult kidney, representing 75-80% of renal primary malignancies. Inactivation of the von Hippel-Lindau (*VHL*) tumor suppressor gene, by mutation, deletion and promoter methylation, occurs in most sporadic ccRCCs and in all inherited cases. Recent evidences showed that microRNAs (miRNAs) are often dysregulated in many tumors, including ccRCC.

We used Caki-1, Caki-2 and A498 cell lines as *in vitro* model of ccRCC pathology, and HK-2 (normal proximal tubular epithelial cell line) as reference sample. We characterized the *VHL* status by direct sequencing and the HIF status by western blot. Affymetrix microarray technology was applied to assess miRNA (onto GeneChip® miRNA Array) and gene expression profiles (onto GeneChip® Human Gene 1.0 ST Array).

Analysis of common differentially expressed miRNAs (DEMs) in RCC cell lines outlined specific miRNAs to be involved in ccRCC and in cancer (e.g. miR-145, miR-29a, miR-342-3p, miR-205, miR-183, miR-197, miR-132, miR-146a and miR-34a). Functional enrichment analysis of common differentially expressed genes (DEGs) highlighted some genes involved in leucocyte transendothelial migration, focal adhesion and p53 signalling pathways (e.g. ATM, FER, CDC27 and GRB10). Additionally, we conducted an integrated analysis to combine gene and miRNA expression profiles and to reconstruct miRNA-gene post-transcriptional regulatory networks involved in RCC pathology. We also compared our expression data with RCC datasets publicly available from NCBI GEO microarray repository. We selected potentially interesting miRNAs and target genes for further validation (by qPCR). This integrated analysis approach may help to unravel the molecular complexity characterizing ccRCC biology, and it will facilitate the elucidation of regulatory circuits important for tumorigenesis and the biological processes under relevant post-transcriptional regulation in ccRCC.