EMT Related microRNA-200 Family as the Tumor Suppressive microRNA in Renal Cell Carcinoma

Introduction and Objective: Renal cell carcinoma (RCC) is the most common neoplasm of the adult kidney, and clear cell RCC represents the most common renal cancer histology. However surgical treatment is provided for localized disease, relapse or metastasis of the patient is caused in a considerable ratio. At present, metastatic RCC is difficult to treat and the process of metastasis is not well understood. Therefore, it is crucial to find molecular mechanisms based on recent genome analysis in RCC oncogenesis and metastasis. Based on the microRNA (miRNA) expression signature of RCC revealed that *miR-200* family significantly reduced in RCC cells. The *miR-200* family (*miR-200b*, *miR-200a* and *miR-429* are encoded by single polycistronic transcript on chromosome 1p36.33 and *miR-200c* and *miR-141* are cluster on chromosome 12 p13.31) of miRNA plays a major role to epithelial to mesenchymal transition (EMT) by targeting transcription repressors, zinc-finger E-box binding homeobox (ZEB1) and ZEB2. In this study, we investigated the functional significance of *miR-200* family and identified the novel cancer pathways in RCC.
Materials and Method: Cell proliferation and invasion assay was performed by restoration of mature *miR-200* family (*miR-200a*, *miR-200b*, *miR-200c*, *miR-429* and *miR-141*) in RCC cell lines. Genome-wide gene expression analysis was performed to identify the molecular networks of *miR-200* family by microarray analysis.
Results: The mRNA expression levels of *ZEB1* and *ZEB2* were significantly decreased by *miR-200* family (*miR-200a*, *miR-200b*, *miR-200c*, *miR-429* and *miR-141*) transfectantion in RCC cells. Restoration of each miRNAs significantly inhibited cell proliferation in RCC cells. Interestingly, the morphological changes were recognized by *miR-200* family transfection in RCC cell lines. Gene expression analysis showed more than ten candidate genes were searched for *miR-200* family targets and these genes were up-regulated in RCC clinical specimens.
Conclusion: Our data suggest that *miR-200* family function as tumor suppressors in RCC. EMT-related tumor suppressive *miR-200* family mediates novel molecular targets provide new insights into the potential mechanisms of RCC oncogenesis and metastasis.