論 文 要 旨

Dual tumor-suppressors *miR-139-5p* and *miR-139-3p* targeting *matrix metalloprotease 11* in bladder cancer.

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Our recent study of the microRNA (miRNA) expression signature of bladder cancer (BC) by deep-sequencing revealed that two miRNA, *microRNA-139-5p*/*microRNA-139-3p* were significantly downregulated in BC tissues. The aim of this study was to investigate the functional roles of these miRNA and their modulation of cancer networks in BC cells. Functional assays of BC cells were performed using transfection of mature miRNA or small interfering RNA (siRNA). Genome-wide gene expression analysis, *in silico* analysis and dual-luciferase reporter assays were applied to identify miRNA targets. The associations between the expression of miRNA and its targets and overall survival were estimated by the Kaplan-Meier method. Gain-of-function studies showed that *miR-139-5p* and *miR-139-3p* significantly inhibited cell migration and invasion by BC cells. The matrix metalloprotease 11 gene (*MMP11*) was identified as a direct target of *miR-139-5p* and *miR-139-3p*. Kaplan-Meier survival curves showed that higher expression of *MMP11* predicted shorter survival of BC patients ($P = 0.029$). Downregulated *miR-139-5p* or *miR-139-3p* enhanced BC cell migration and invasion in BC cells. *MMP11* was directly regulated by these miRNA and might be a good prognostic marker for survival of BC patients.