論 文 要 旨

Tumour-suppressive *microRNA-144-5p* directly targets *CCNE1/2* as potential prognostic markers in bladder cancer

松下　良介

Background:

Analysis of a microRNA (miRNA) expression signature of bladder cancer (BC) by deep-sequencing revealed that clustered miRNAs *microRNA* (*miR*)*-451a*, *miR-144-3p*, and *miR-144-5p* were significantly downregulated in BC tissues. We hypothesised that these miRNAs function as tumour suppressors in BC. The aim of this study was to investigate the functional roles of these miRNAs and their modulation of cancer networks in BC cells.

Methods:

The functional studies of BC cells were performed using transfection of mature miRNAs. Genome-wide gene expression analysis, in silico analyses, and dual-luciferase reporter assays were applied to identify miRNA targets. The association between *miR-144-5p* levels and expression of the target genes was determined, and overall patient survival as a function of target gene expression was estimated by the Kaplan-Meier method.

Results:

Gain-of-function studies showed that *miR-144-5p* significantly inhibited cell proliferation by BC cells. Four cell cycle-related genes (*CCNE1*, *CCNE2*, *CDC25A*, and *PKMYT1*) were identified as direct targets of *miR-144-5p*. The patients with high *CCNE1* or *CCNE2* expression had lower overall survival probabilities than those with low expression (P=0.025 and P=0.032).

Conclusion:

miR-144-5p functions as tumour suppressor in BC cells. *CCNE1* and *CCNE2* were directly regulated by *miR-144-5p* and might be good prognostic markers for survival of BC patients.