論 文 要 旨

Involvement of Dual Strands of *miR-143* (*miR-143-5p* and *miR-143-3p*) and Their Target Oncogenes in the Molecular Pathogenesis of Lung Adenocarcinoma

氏　　名　　眞田　宏樹

Abstract

Our analyses of tumor-suppressive microRNAs (miRNAs) and their target oncogenes have identified novel molecular networks in lung adenocarcinoma (LUAD). Moreover, our recent studies revealed that some passenger strands of miRNAs are contributed to cancer cell malignant transformation. Downregulation of both strands of the *miR-143* duplex was observed in LUAD clinical specimens. Ectopic expression of these miRNAs suppressed malignant phenotypes in cancer cells suggesting that these miRNAs have tumor-suppressive activities in LUAD cells. Here, we evaluated *miR-143-5p* molecular networks in LUAD using genome-wide gene expression and miRNA database analyses. Twenty-two genes were identified as potential *miR-143-5p*-controlled genes in LUAD cells. Interestingly, the expression of 11 genes (*MCM4*, *RAD51*, *FAM111B*, *CLGN*, *KRT80*, *GPC1*, *MTL5*, *NETO2*, *FANCA*, *MTFR1*, and *TTLL12*) was prognostic factors for the patients with LUAD. Furthermore, knockdown assays using siRNAs showed that downregulation of *MCM4* suppress cell growth, migration and invasion in LUAD cells. Aberrant expression of MCM4 was confirmed in the clinical specimens of LUAD. Thus, we showed that *miR-143-5p* and its target genes were involved in the molecular pathogenesis of LUAD. Identification of tumor-suppressive miRNAs and their target oncogenes may be an effective strategy for elucidation of the molecular oncogenic networks of this disease.