論 文 要 旨

Downregulation of matrix metalloproteinase 14 by the antitumor miRNA, *miR-150-5p*, inhibits the aggressiveness of lung squamous cell carcinoma cells

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Abstract.

In the present study, in order to elucidate the aggressive nature of lung squamous cell carcinoma (LUSQ), we investigated the oncogenic RNA networks regulated by antitumor microRNAs (miRNAs or miRs) in LUSQ cells. The analysis of our original miRNA expression signatures of human cancers revealed that *microRNA-150-5p* (*miR-150-5p*) was downregulated in various types of cancer, indicating that *miR-150-5p* acts as an antitumor miRNA by targeting several oncogenic genes. Thus, the aims of this study were to investigate the antitumor roles of *miR-150-5p* in LUSQ cells and to identify oncogenes regulated by *miR-150-5p* that are involved in the aggressive behavior of LUSQ. The downregulation of *miR-150-5p* was validated in clinical samples of LUSQ and cell lines (SK-MES-1 and EBC-1). The ectopic overexpression of *miR-150-5p* significantly suppressed cancer cell aggressiveness. Comprehensive gene expression analyses revealed that *miR-150-5p* regulated 9 genes in the LUSQ cells. Among these, matrix metalloproteinase 14 (*MMP14*) was found to be a direct target of *miR-150-5p*, as shown by luciferase reporter assay. The knockdown of *MMP14* using siRNA against MMP14 (si-*MMP14*) significantly inhibited cancer cell migration and invasion. The overexpression of MMP14 was detected in clinical specimens of LUSQ by immunohistochemistry. On the whole, these findings suggest that the downregulation of *miR-150-5p* and the overexpression of *MMP14* may be deeply involved in the pathogenesis of LUSQ.