論 文 要 旨

Regulation of *TPD52* by antitumor *microRNA-218* suppresses cancer cell migration and invasion in lung squamous cell carcinoma

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Abstract

The development of targeted molecular therapies has greatly benefited patients with lung adenocarcinomas. In contrast, these treatments have had little benefit in the management of lung squamous cell carcinoma (lung SCC). Therefore, new treatment options based on current genomic approaches are needed for lung SCC. Aberrant microRNA (miRNA) expression has been shown to promote lung cancer development and aggressiveness. Downregulation of *microRNA-218* (*miR-218*) was frequently observed in our miRNA expression signatures of cancers, and previous studies have shown an antitumor function of *miR-218* in several types of cancers. However, the impact of *miR-218* on lung SCC is still ambiguous. The present study investigated the antitumor roles of *miR-218* in lung SCC to identify the target genes regulated by this miRNA. Ectopic expression of *miR-218* greatly inhibited cancer cell migration and invasion in the lung SCC cell lines EBC-1 and SK-MES-1. Through a combination of in silico analysis and gene expression data searching, tumor protein D52 (*TPD52*) was selected as a putative target of *miR-218* regulation. Moreover, direct binding of *miR-218* to the 3'-UTR of *TPD52* was observed by dual luciferase reporter assay. Overexpression of TPD52 was observed in lung SCC clinical specimens, and knockdown of *TPD52* significantly suppressed cancer cell migration and invasion in lung SCC cell lines. Furthermore, the downstream pathways mediated by *TPD52* involved critical regulators of genomic stability and mitotic checkpoint genes. Taken together, our data showed that downregulation of *miR-218* enhances overexpression of *TPD52* in lung SCC cells, promoting cancer cell aggressiveness. Identification of tumor-suppressive miRNA-mediated RNA networks of lung SCC will provide new insights into the potential mechanisms of the molecular pathogenesis of the disease.