論 文 要 旨

Regulation of *KIF2A* by Antitumor *miR-451a* Inhibits Cancer Cell Aggressiveness Features in Lung Squamous Cell Carcinoma

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Abstract

In the human genome, *miR-451a* is encoded close to *miR-144* on chromosome region 17q11.2. Our previous study showed that both strands of pre-*miR-144* acted as antitumor miRNAs and were involved in lung squamous cell carcinoma (LUSQ) pathogenesis. Here, we aimed to investigate the functional significance of *miR-451a* and to identify its targeting of oncogenic genes in LUSQ cells. Downregulation of *miR-451a* was confirmed in LUSQ clinical specimens, and low expression of *miR-451a* was significantly associated with poor prognosis of LUSQ patients (overall survival: $p = 0.035$, disease-free survival: $p = 0.029$). Additionally, we showed that ectopic expression of *miR-451a* significantly blocked cancer cell aggressiveness. In total, 15 putative oncogenic genes were shown to be regulated by *miR-451a* in LUSQ cells. Among these targets, high kinesin family member 2A (*KIF2A*) expression was significantly associated with poor prognosis (overall survival: $p = 0.043$, disease-free survival: $p = 0.028$). Multivariate analysis showed that *KIF2A* expression was an independent prognostic factor in patients with LUSQ (hazard ratio = 1.493, $p = 0.034$). Aberrant *KIF2A* expression promoted the malignant transformation of this disease. Analytic strategies based on antitumor miRNAs and their target oncogenes are effective tools for identification of novel molecular pathogenesis of LUSQ.