論 文 要 旨

Regulation of *LOXL2* and *SERPINH1* by antitumor *microRNA-29a* in lung cancer with idiopathic pulmonary fibrosis.

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Abstract

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease that is refractory to treatment and carries a high mortality rate. IPF is frequently associated with lung cancer. Identification of molecular targets involved in both diseases may elucidate novel molecular mechanisms contributing to their pathology. Recent studies of microRNA (miRNA) expression signatures showed that microRNA-29a (miR-29a) was downregulated in IPF and lung cancer. The aim of this study was to investigate the functional significance of miR-29a in lung cancer cells (A549 and EBC-1) and lung fibroblasts (MRC-5) and to identify molecular targets modulated by miR-29a in these cells. We confirmed the downregulation of miR-29a in clinical specimens of IPF and lung cancer. Restoration of miR-29a suppressed cancer cell aggressiveness and fibroblast migration. A combination of gene expression data and in silico analysis showed that a total of 24 genes were putative targets of miR-29a. Among them, lysyl oxidase-like 2 (LOXL2) and serpin peptidase inhibitor clade H, member 1 (SERPINH1) were direct targets of miR-29a by luciferase reporter assays. The functions of LOXL2 and SERPINH1 contribute significantly to collagen biosynthesis. Overexpression of LOXL2 and SERPINH1 was observed in clinical specimens of lung cancer and fibrotic lesions. Downregulation of miR-29a caused overexpression of LOXL2 and SERPINH1 in lung cancer and IPF, suggesting that these genes are involved in the pathogenesis of these two diseases.