

## 論 文 要 旨

**Tumor-suppressive *microRNA-29* family inhibits  
cancer cell migration and invasion directly targeting *LOXL2*  
in lung squamous cell carcinoma**

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**Abstract.** Lung cancer remains the most frequent cause of cancer-related death in developed countries. A recent molecular-targeted strategy has contributed to improvement of the remarkable effect of adenocarcinoma of the lung. However, such treatment has not been developed for squamous cell carcinoma (SCC) of the disease. Our recent studies of microRNA (miRNA) expression signatures of human cancers showed that the *microRNA-29* family (*miR-29a*, *miR-29b* and *miR-29c*) significantly reduced cancer tissues compared to normal tissues. These findings suggest that *miR-29s* act as tumor-suppressors by targeting several oncogenic genes. The aim of the study was to investigate the functional significance of *miR-29s* in lung SCC and to identify *miR-29s* modulating molecular targets in lung SCC cells. Restoration of all mature members of the *miR-29s* inhibited cancer cell migration and invasion. Gene expression data combined in silico analysis and luciferase reporter assays demonstrated that the *lysyl oxidase-like 2 (LOXL2)* gene was a direct regulator of tumor-suppressive *miR-29s*. Moreover, overexpressed *LOXL2* was confirmed in lung SCC clinical specimens, and silencing of *LOXL2* inhibited cancer cell migration and invasion in lung SCC cell lines. Our present data suggested that loss of tumor-suppressive *miR-29s* enhanced cancer cell invasion in lung SCC through direct regulation of oncogenic *LOXL2*. Elucidation of the novel lung SCC molecular pathways and targets regulated by tumor-suppressive *miR-29s* will provide new insights into the potential mechanisms of oncogenesis and metastasis of the disease.