論 文 要 旨

MicroRNA signature of small cell lung cancer after treatment failure: impact on oncogenic targets by *miR-30a-3p* control

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Abstract

Small cell lung cancer (SCLC) is associated with a high mortality rate and limited treatment efficacy. We created a microRNA (miRNA) expression signature by RNA sequencing using specimens from patients with SCLC who had failed treatment. Forty-nine miRNAs were downregulated in SCLC tissues and were candidate tumor-suppressive miRNAs. In this signature, both guide and passenger strands were downregulated for five miRNAs (*miR-30a*, *miR-34b*, *miR-34c*, *miR-223*, and *miR-4529*). Recent studies have revealed that passenger strands of miRNAs are involved in the molecular pathogenesis of human cancer. Although *miR-30a-5p* (the guide strand) has been shown to be a tumor suppressive miRNA in various types of cancers, *miR-30a-3p* (the passenger strand) function is not well characterized in SCLC cells. We investigated the functional significance of *miR-30a-3p* and oncogenic genes regulated by *miR-30a-3p* in SCCLC cells. Ectopic expression assays showed that *miR-30a-3p* expression inhibited cell proliferation and induced cell cycle arrest and apoptosis in two SCLC cell lines. Furthermore, *in silico* database searches and gene expression assays identified 25 genes as putative targets of *miR-30a-3p* in SCLC cells. Luciferase reporter assays revealed that downstream neighbor of SON (*DONSON*) was directly regulated by *miR-30a-3p* in SCLC cells. *DONSON* knockdown induced cell cycle arrest in SCLC cells, and *DONSON* overexpression was detected in SCLC clinical samples. Analyzing the regulatory networks of tumor suppressive miRNAs may lead to the identification of therapeutic targets in SCLC.