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Frequent methylation and oncogenic role of microRNA-34b/c in small-cell lung cancer

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Frequent methylation and oncogenic role of microRNA-34b/c in small-cell lung cancer
Previous ArticleStrong anti-tumor effect of NVP-AUY922, a novel Hsp90 inhibitor, on non-small cell lung cancer
Next ArticleTetraiodothyroacetic acid and its nanoformulation inhibit thyroid hormone stimulation of non-small cell lung cancer cells in vitro and its growth in xenografts

Abstract

Small-cell lung cancer (SCLC) is an aggressive tumor with a dismal prognosis among primary lung cancers. MicroRNAs (miRNAs) can act as oncogenes or tumor-suppressor genes in human malignancy. The miR-34 family is comprised of tumor-suppressive miRNAs, and its reduced expression by methylation has been reported in various cancers, including non-small cell lung cancer (NSCLC). In this study, we investigated the alteration and tumor-suppressive impact of miR-34s in SCLC. The methylation of miR-34a and miR-34b/c was observed in 4 (36%) and 7 (64%) of 11 SCLC cell lines, respectively. Among the 27 SCLC clinical specimens, miR-34a and miR-34b/c were methylated in 4 (15%) and 18 (67%), respectively. In contrast, 13 (28%) miR-34a methylated cases and 12 (26%) miR-34b/c methylated cases were found in 47 NSCLC primary tumors. The frequency of miR-34b/c methylation was significantly higher in SCLC than in NSCLC ($p < 0.001$). The expressions of miR-34s were reduced in methylated cell lines and tumors and restored after 5-aza-2′-deoxycytidine treatment, indicating that methylation was responsible for the reduced expression of miR-34s. Because the frequency of methylation was higher in miR-34b/c, we focused on miR-34b/c for a functional analysis. We examined the effect of miR-34b/c introduction on cell proliferation, migration and invasion. The transfection of miR-34b/c to two SCLC cell lines (H1048 and SBC5) resulted in the significant inhibition of cell growth, migration, and invasion, compared with control transfectants. Our results indicate that the aberrant methylation of miR-34b/c plays an important role in the pathogenesis of SCLC, implying that miR-34b/c may be a useful therapeutic target for SCLC.

Keywords

- Methylation
- MicroRNA
- MicroRNA-34b/c
- Small cell lung cancer
- Non-small cell lung cancer
- p53

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