MicroRNA-215 functions as a tumor suppressor and directly targets ZEB2 in human pancreatic cancer

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ABSTRACT. It has been shown that microRNA-215 (miR-215) is dysregulated in several human malignancies, and this correlates with tumor progression. However, its expression and function in pancreatic cancer is still unclear. The aim of this study was to explore the effects of miR-215 on pancreatic cancer formation and progression. Using quantitative RT-PCR, we detected miR-215 expression in pancreatic cancer cell lines and primary tumor tissues. The association of miR-215 expression with clinicopathological factors and prognosis was also analyzed. We then observed the effects of miR-215 on the biological behavior of pancreatic cancer cells. Lastly, the potential regulatory function of miR-215 on ZEB2 expression was investigated. miR-215 expression levels were significantly downregulated in pancreatic cancer samples and cell lines. Decreased miR-215 expression was significantly associated with large tumor size, advanced TNM stage, lymph node metastasis, vessel invasion, and lower overall survival. Multivariate regression analysis corroborated that downregulation of miR-215 was an independent unfavorable prognostic factor. Overexpression of miR-215 inhibited pancreatic cancer cell

proliferation, invasion, and migration; promoted cell apoptosis *in vitro*; and suppressed tumorigenicity *in vivo*. Further, ZEB2 was confirmed as a direct target of miR-215 by using a luciferase reporter assay. These findings indicate that miR-215 may act as a tumor suppressor in pancreatic cancer cells, and could serve as a novel therapeutic target for miR-based therapy.

Key words: Pancreatic cancer; MicroRNA-215; Proliferation; Prognosis; Cancer invasion

