FEATURES

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MiR-199b-5p Targets HER2 in Breast Cancer Cells

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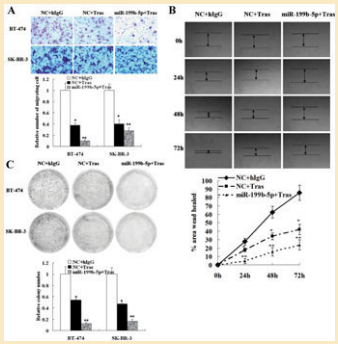
HER2 (ErbB2) has been reported to be overexpressed in 20–30% of breast cancer and confers poor survival because of high proliferation and metastasis rates. MicroRNAs are small noncoding RNAs that are responsible for the post-transcriptional regulation of target genes. It was found miR-199b-5p inhibited HER2 expression by direct targeting its 3'-untranslated region (3'UTR) in breast cancer cells. In addition, miR-199b-5p inhibited HER2 downstream signaling by ERK1/2 and AKT pathways in breast cancer cells. Besides, transwell migration, wound healing, and clonogenicity were obviously inhibited by overexpression of miR-199b-5p in HER2-positive breast cancer cells. It was also found that miR-199b-5p could enhance the suppression of trastuzumab on cell migration and clonogenicity. These results suggest that miR-199b-5p may have the potential to be a novel important alternative therapeutic target for HER2-positive breast cancer.



MicroRNA-182 Promotes Cell Growth, Invasion, and Chemoresistance by Targeting Programmed Cell Death 4 (PDCD4) in Human Ovarian Carcinomas

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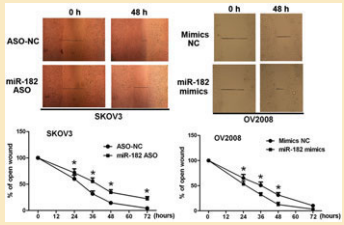
As an important tumor suppressor, programmed cell death 4 (PDCD4) influences transcription and translation of multiple genes, and modulates different signal transduction pathways. However, the upstream regulation of this gene is largely unknown. This study found that microRNA-182 (miRNA-182, miR-182) was upregulated, whereas PDCD4 was downregulated in ovarian cancer tissues and cell lines. Blocking or increase of miR-182 in ovarian cancer cell lines led to an opposite alteration of endogenous PDCD4 protein level. Using fluorescent reporter assay, the direct and negative regulation of PDCD4 by miR-182 was confirmed, which was dependent on the predicted miR-182 binding site within PDCD4 30 untranslated region (30 UTR). MTT and colony formation assays suggested that miR-182 blockage suppressed, whereas miR-182 mimics enhanced viability and colony formation of ovarian cancer cells. These effects may partly be attributed to the cell cycle promotion activity of miR-182. miR-182 also contributed to migration and invasion activities of ovarian cancer cells. Furthermore, miR-182 reduced the chemosensitivity of ovarian cancer cells to CDDP and Taxol, possibly by its anti-apoptosis activity. Importantly, all the alterations of the above cellular phenotypes by blocking or enhancing of miR-182 could be alleviated by subsequent suppression or ectopic expression of its target PDCD4, respectively. The conclusion is that in ovarian cancer cells, miR-182 acts as an oncogenic miRNA by directly and negatively regulating PDCD4.



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