

FEATURES

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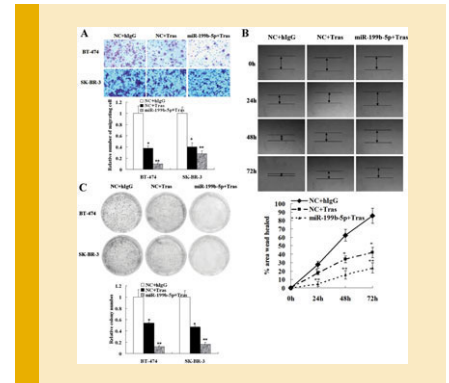
MiR-199b-5p Targets HER2 in Breast Cancer Cells

Chen Fang, Yu Zhao, and Baoyu Guo

1457

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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.



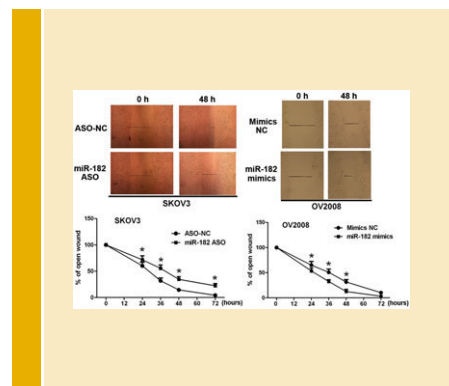
MicroRNA-182 Promotes Cell Growth, Invasion, and Chemoresistance by Targeting Programmed Cell Death 4 (PDCD4) in Human Ovarian Carcinomas

Yu-Quan Wang, Ren-De Guo, Rui-Meng Guo, Wei Sheng, and Li-Rong Yin

1464

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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.



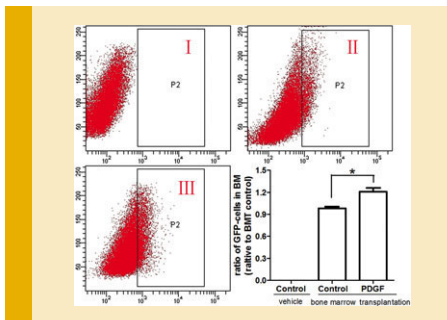
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Platelet-Derived Growth Factor-BB Accelerates Prostate Cancer Growth by Promoting the Proliferation of Mesenchymal Stem Cells

1510

Jiwen Cheng, Huama Ye, Zhiyong Liu, Chuanliang Xu, Zhensheng Zhang, Yan Liu, and Yinghao Sun

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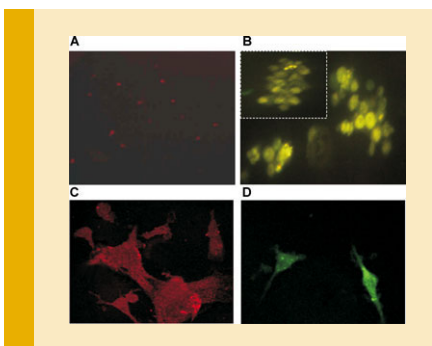
Mesenchymal stem cells (MSCs) favor cancer growth by facilitating immunosuppression status in tumor microenvironment. However, the function and mechanism of MSCs in initiating and developing prostate cancer remains to be fully understood. In this study, it is first found that MSCs promoted prostate cancer (PCa) tumor growth in vivo and cell proliferation in vitro by using PCa cell strain RM-1. Both exogenous and endogenous MSCs could be recruited into the tumor microenvironment by using bone-marrow transplantation model. It is further demonstrated that PDGF-BB produced by RM-1 cell promoted MSCs proliferation in vivo and in vitro, which was abrogated by Si-RNA specific to PDGF-BB. And inflammatory cytokines, such as interferon gamma, tumor necrosis factor alpha, and anti-inflammatory cytokine transformation growth factor alpha, further increased the ability of RM-1 to produce PDGF-BB. Overall, PCa cells produced PDGF-BB favors the proliferation of MSCs, which may elicit immunosuppressive function and enable PCa cells to escape from the immunity surveillance in tumor inflammatory microenvironment.

Overexpression of MicroRNA-122 Enhances In Vitro Hepatic Differentiation of Fetal Liver-Derived Stem/Progenitor Cells

1575

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MicroRNAs (miRNAs) are a versatile class of tiny non-coding RNAs involved in regulation of various biological processes. miRNA-122 (miR-122) is specifically and abundantly expressed in human liver. However, the role of miR-122 in differentiation of fetal liver stem/progenitor cells into hepatocytes remains unclear. In this study, dual positive CD34 β /CD117 β expressing human fetal liver stem/progenitor cells was enriched by magnetic cell sorting and cultured in vitro. The level of miR-122 was found to be increased at specific time intervals. Interestingly, during the differentiation process of hepatocyte-like cells, the increase in expression of miR-122 was positively correlated with expression of hepatocyte-specific genes. The status of differentiation process was improved by transfection of miR-122 into enriched stem/progenitor cells. The expression level of hepatic-specific genes as well as liver-enriched transcription factors (LETfs) was significantly increased by overexpression of miR-122 in fetal liver stem/progenitor cells. Thus, the study delineated the role of hepato-specific miR-122 in differentiation of fetal liver stem/progenitor cells into hepatocyte-like cells which could be used as a therapeutic target molecule to generate abundant hepatocytes.