87P  Mir-506-3p synergistically represses breast cancer progression through altering cell cycle regulators

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Background: Mounting evidence demonstrated the potential of miR-506-3p to be employed in the diagnosis and treatment of a wide range of human malignancies due to its differential expression pattern and distinct biological roles. Despite the pivotal tumor suppressor role miR-506-3p plays in breast cancer (BC), it is frequently downregulated. Moreover, its role in governing cell cycle progression was not extensively studied in BC. Myc, E2F and Rb proteins are key players in cell cycle regulation. In BC, the CDK-RB-E2F axis is extensively deregulated by several genetic mutations. Additionally, the potent proto-oncogene Myc is highly expressed in BC. Thus, we aimed at uncovering the role miR-506-3p plays in cell cycle regulation in BC.

Methods: pMyc-TA-Luc, pE2F-TA-Luc and pRb-TA-Luc vectors have response elements or enhancer elements of cMyc, Rb, and E2F cell cycle regulatory proteins, respectively. MDA-MB-231 cells were transfected with the aforementioned cell cycle vectors as well as an empty pLuc vector containing an unspecific binding site (used as a control) (Clontech, Germany). After 24 hrs, cells were co-transfected with miR-506-3p. Some cells were exposed to the transfection reagent only (mock cells). Relative luciferase activity was measured after 48 hrs by Steady-Glo® Luciferase Reporter Assay. Unspecific (baseline) luminescence detected for empty pTAL-Luc vector was subtracted from all values. Functional characterization of miR-506-3p was performed in MDA-MB-231 triple-negative breast cancer (BC) cells and MCF-7 HR+ cells to investigate its impact on several hallmarks of cancer using MTT and wound-healing assays.

Results: Ectopic expression of miR-506-3p led to a significant decrease in cMyc and E2F proteins with a concomitant increase in Rb protein compared to mock cells. Since miR-506-3p has seldomly been investigated in BC, the performed functional analysis of miRNA-506-3p revealed a significant decrease in the cellular viability and migration capacity of both MDA-MB-231TNBC cells and in MCF-7 HR+ BC cells.

Conclusions: This study highlights a novel underlying mechanism of miR-506-3p as a tumor suppressor in BC through inhibiting cell cycle progression. This suggests its potential use in personalized BC therapy.

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