DOWN-REGULATION OF MicroRNA-298 ASSOCIATED WITH DOXORUBICIN CHEMORESISTANCE OF HUMAN BREAST CANCER

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Background: Multidrug resistance is a major impediment to the success of cancer chemotherapy. We found that the increased expression of P-glycoprotein is associated with Doxorubicin resistance in metastatic breast cancer cells (Bao. L et. American Journal of Pathology Vol. 178. No.2 February 2011). However, the mechanism by which P-glycoprotein expression is regulated in chemoresistant breast cancer cells is unclear. Recent studies indicate that microRNAs act as modulators of gene expression in cancer and cancer therapy. But its role in chemoresistance still unclear. The goal of our study is to study the role of microRNAs involved in P-glycoprotein expression. Aim: To investigate how microRNA-298 alters the p-glycoprotein expression and overcome the Doxorubicin resistance of human breast cancer.


Results: We developed Doxorubicin resistant (MDA-MB-231-R) and sensitive cells (MDA-MB-231-S) from human breast cancer cell line (MDA-MB-231). High level P-glycoprotein expression in MDA-MB-231-R was confirmed by Western Blot. In microarray assay, MicroRNA-298 expression is down-regulated in MDA-MB-231-R and confirmed by Northern blot. MicroRNA-298 mimic inhibited luciferase activity from the construct with the MDR1 3'-UTR in a dose-dependent manner by Luciferase reporter Assay. Repression of p-glycoprotein expression by microRNA-298 mimic transfection in the cells increased nucleus translocation of Doxorubicin and sensitivity of MDA-MB-231-R cells to Doxorubicin by MTT Assay.

Conclusion: We have shown that expression of MicroRNA-298 is negatively correlated with MDR1 expression in MDA-MB-231 human breast cancer cells. Furthermore, the elevated level of micro-298 by transfection of micrRNA mimic not only downregulates expression of p-glycoprotein and also partially overcome Doxorubicin chemoresistance in MDA-MB-231-R cells.