

Analysis of miR-195 and miR-497 expression, regulation and role in breast cancer

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Purpose: To investigate expression, regulation, potential role and targets of miR-195 and miR-497 in breast cancer.

Experimental design: The expression patterns of miR-195 and miR-497 were initially examined in breast cancer tissues and cell lines by Deep sequencing; Northern blotting and quantitative real-time PCR. Combined bisulfite restriction analysis and bisulfite sequencing were carried out to study the DNA methylation status of miR-195 and miR-497 genes. Breast cancer cells stably expressing miR-195 and miR-497 were established to study their role and targets. Finally, normal, fibroadenoma and breast cancer tissues were employed to analyze the correlation between miR-195/497 levels and malignant stages of breast tumor samples.

Results: MiR-195 and miR-497 were significantly down-regulated in breast cancer. The methylation state of CpG islands upstream of the miR-195/497 gene was found to be responsible for the down-regulation of both miRNAs. Forced expression of miR-195 or miR-497 suppressed breast cancer cell proliferation and invasion. Raf-1 was identified as a novel direct target of miR-195 and miR-497. miR-195/497 expression levels in clinical specimens were found to be correlated inversely with malignancy of breast cancer.

Conclusion: Our data imply that both miR-195 and miR-497 play important inhibitory roles in breast cancer malignancy and may be the potential therapeutic and diagnostic targets.