

The sensitizer role of miR-375 and c-Myc biomarkers in rectal cancer

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The incorporation of chemoradiation prior to resection of the tumour has revolutionized the management of locally advanced rectal cancer. However, a large proportion of these patients are resistant to preoperative treatment schedule. It is critical to discover new strategies to increase chemoradiation effect for therapeutic purposes, as well as to identify molecular mechanisms resulting in therapeutic response, thus improving clinical practice by identification of patients who would response to treatment. We recently reported that c-Myc gene expression correlates negatively with this resistance in patients with cancer rectal; patients with higher levels of c-Myc mRNA showed significantly better response. Although c-Myc plays a key role in gene expression, the post transcriptional regulation by microRNAs (miRNA) of this transcription factor itself still poorly understood. Next, we carried out integrated analysis of miRNA and mRNA expression profiling in 45 pre-treatment rectal tumours. Further, expression of miRNAs and c-Myc, and their relationship with clinicopathological factors and patient survival was analysed. As a result, we found that 12 miRNAs were differentially expressed between responder and non-responder rectal cancer patients. Functional classification revealed an association between differentially expressed miRNAs and c-Myc. Subsequent quantitative real-time PCR results showed that both, miR-148 and miRNA-375 levels were significantly lower in responder compared to non-responder patients. Notably, the higher level of miRNA-375 was significantly positively correlated with c-Myc. These results suggest that miRNA-375 and its targeted c-Myc play an important role as predictive biomarker of response to neoadjuvant treatment in patients with locally advanced rectal cancer, but still not suitable for prognosis.

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