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Are Circulating miRNAs Predictive of Response to Therapy?

Lava Krishna Kannappa, Mohammed Sufian Khalid, Baljit Singh, David Guttery
University Hospitals Leicester, UK
correspondence to Lavakrishna@yahoo.com

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Introduction:
Colorectal cancer (CRC) is the third commonest cancer with nearly 1.4 million new cases identified throughout the world in 2012. There is a pressing need for new non-invasive blood based test to improve early detection and monitoring of CRC. MiRNAs are small non-coding RNAs involved in fundamental cell processes such as proliferation, survival and death. Studies have identified miRNAs in plasma of cancer patients in a stable form. This study aimed to evaluate whether circulating microRNAs are predictive of response to therapy.

Methods:
44 patients with CRC were selected from our institution's CRC surveillance programme. All selected patients at follow-up had no evidence of tumour recurrence on clinical, radiological and endoscopic assessment. Blood samples were obtained pre-treatment and at a median follow-up of 36 months. A total of 32 pairs of blood samples were matched pre- and post-treatment. Plasma RNA was extracted and target miRNAs were identified on pooled case TaqMan Low Density miRNA array (TDLA) cards and quantitative RT-PCR.

Results:
Of the nine microRNAs tested, only miR-134 (P = 0.03), miR-135b (P = 0.03) and miR-431 (P = 0.031) were statistically different in post-treatment samples using a Wilcoxon signed rank test. Comparison of each miRNA with clinicopathological features using multiple linear regression tests showed miR-135b pre-treatment and miR-431 post-treatment levels to be significantly associated with both node status (positive/negative) and number of nodes involved. Pre-treatment miR-132, miR-134, miR-21, miR-27b and miR-184 were also significantly associated with node status. Further, miR-134 post-treatment was significantly associated with gender and miR-203 pre-treatment was significantly associated with all Duke's stages. However, multiple-linear regression of all miRNAs and clinicopathological features revealed only miR-135b levels pre-treatment to be significant in the overall model (P = 0.043).

Conclusion:
MicroRNA levels of miR-134, miR-135b and miR-431 showed a potential response to therapy with higher levels pre-treatment and lower after treatment. miR-135b pre-treatment levels correlated significantly to lymph node status and number. However, larger cohorts of patients are needed to validate these findings.