Abstract

Background: Colorectal cancer (CRC) manifests after the accumulation of genetic and epigenetic alterations. Recently, microRNAs (miRNAs) have been shown to play a critical role in tumor progression in various cancers, and their expression is currently considered to be an important diagnostic/predictive/prognostic biomarker. We aimed to evaluate the potential of miRNAs as prognostic biomarkers for advanced CRC.

Patients and Methods: To evaluate the potential of miRNAs as prognostic biomarkers for advanced CRC, miRNA arrays were performed on CRC specimens derived from tumors with various molecular statuses (e.g., *KRAS*/*BRAF*/microsatellite instability [MSI]) and their paired normal mucosal specimens. Next, we confirmed the reproducibility of the results obtained from the miRNA array by accessing The Cancer Genome Atlas (TCGA) data portal and evaluating 67 patents with stage IV CRC from a cohort of 597 CRC patients.

Results: The miRNA array revealed that *miR-31-5p* (*miR-31*) was specifically upregulated in CRCs with the *BRAF* V600E mutation, which is associated with a poorer prognosis, especially among individuals with the non-MSI phenotype. We confirmed the association between this *BRAF* mutation and miR-31 expression levels using the TCGA data portal. Of the 67 patients with stage IV CRC, 15 (22%) and 4 (6%) showed *KRAS* and *BRAF* V600E mutations, respectively. All 67 tumors showed a non-MSI phenotype. Since the median of *miR-31* expression was 3.45 (range: 0.003778–6330.531), we set the cut-off value to 4.0, and all tumors were categorized into two groups (high or low *miR-31* expression). The high *miR-31* expression group (n=33) was significantly related to poor mortality (univariate hazard ratio = 2.12, 95% confidence interval: 0.23–0.95, $P = 0.03$) and had a worse median survival time (MST; 20.1 months) than did the low *miR-31* expression group [n=34] (MST 38.3 months; $P = 0.03$), indicating that *miR-31* is a promising prognostic biomarker for advanced CRC.

Conclusion: We believe that performing a functional analysis of *miR-31* expression may lead to the development of new medicines for the treatment of genetic subtypes of CRC.

Keywords

colorectal cancer, miRNA, miR-31, *BRAF*, prognostic biomarker