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Título	The association of a single-nucleotide variant in the microRNA-146a with advanced colorectal cancer prognosis
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Resumo	The aim of this study was to evaluate the association of single-nucleotide variant n.60G>C (rs2910164) of microRNA (miR)-146a, related to suppressing of BRCA1/2 DNA repair protein, with the risk and survival of colorectal cancer patients, as well as miR-146a and BRCA1/2 levels and miR binding efficiency. The genotypes were identified in 125 colorectal cancer patients and 276 controls using TaqMan polymerase chain reaction assay. The miR-146a and BRCA1/2 levels were assessed by quantitative-polymerase chain reaction protocols. Primary precursor of miR-146a containing G (wild-type) and C (variant) allele were cloned into pcDNA.3.3 vector and co-transfected in HT-29 colorectal cancer cell line. Luciferase reporter assay was performed to assess miR-146a binding to BRCA2 3'-untranslated region in HT-29. The differences between groups were calculated using chi-square or Fisher's exact test, logistic regression, and Mann-Whitney test. The prognostic impact of single-nucleotide variant genotypes on overall survival was evaluated by Kaplan-Meier estimate and Cox regression. The GC or CC genotypes prevalence was similar in patients and controls (50.4% vs 50.7%, p = 0.74). However, patients with tumors in advanced stage with miR-146a GG genotype had 2.41 more chance of dying than GC or CC genotypes. In addition, tumor tissues of patients with GG genotype presented higher miR-146a (p = 0.02) and lower BRCA1 (p = 0.01) and BRCA2 (p < 0.0001) levels when compared to those with GC or CC genotypes. In fact, pcDNA.3.3-miR-146a-G presented increased binding capacity to the 3'-untranslated region of BRCA2 (p = 0.001) compared to pcDNA.3.3-miR-146a-C. In addition, the G allele altered the binding affinity between miR-146a and its BRCA2 3'-untranslated region target (p < 0.001),

	thus enhancing suppression of BRCA2 expression. Our results suggest that single-nucleotide variant rs2910164 does not influence the colorectal cancer risk in Brazilian patients; however, the GG genotype could act as a factor of worse prognosis in patients with advanced disease due to suppression of BRCA1/2 modulated by miR-146a.
Fomento	