Inhibition of cell migration and invasion by miR-29a-3p in a colorectal cancer cell line through suppression of CDC42BPA mRNA expression

ABSTRACT

The objective of this study was to determine the effect of miR-29a-3p inhibitor on the migration and invasion of colorectal cancer cell lines (CRC) and the underlying molecular mechanisms. miR-29a-3p was detected using reverse transcription-quantitative polymerase chain reaction (RT-qPCR) in the CRC cell lines HCT11, CaCo2, HT29, SW480 and SW620. An invasive subpopulation designated SW480-7 was derived from the parental cell line, detected by Transwell and Transwell Matrigel assays. Cytoskeleton Regulators RT2 profiler PCR array and western blot analysis were utilized to identify the alterations in expression of downstream mRNAs. siRNA against CDC42BPA was transfected into SW480-7 and effects on cell migration and invasion were investigated. Data obtained showed that miR-29a-3p was detected in these five CRC cell lines. miR-29a-3p inhibitor had no effect on viability but stimulated cell migration and invasion of SW480-7 cells. In contrast, miR-29a-3p mimic suppressed cell migration and invasion. TargetScan miRBD and DIANA were employed to identify the potential direct target genes of miR-29a-3p in the Cytoskeleton Regulators RT2-Profiler PCR array. Cytoskeleton Regulators RT2-Profiler PCR array data showed that 3 out of the 5 predicted targets genes, CDC42BPA (2.33-fold), BAIAP2 (1.79-fold) and TIAM1 (1.77-fold), in the array were upregulated by miR-29a-3p. A significant increase in expression IQGAP2, PHLDB2, SSH1 mRNAs and downregulation of PAK1 mRNA was also detected with miR-29a-3p inhibition. Increase in CDC42BPA, SSH1 and IQGAP2 mRNA expression correlated with increased protein level in miR-29a-3p transfected SW-480-7 cells. Silencing of CDC42BPA (an enhancer of cell motility) partially abolished miR-29a-3p inhibitor-induced stimulation of cell migration and invasion. miR-29a-3p expression in stage II and III CRC is relatively lower than that of stage I CRC. However, the data need to be interpreted with caution due to the small sample size. In conclusion, inhibition of miR-29a-3p stimulates SW480-7 cell migration and invasion and downstream expression IQGAP2, PHLDB2, SSH1 mRNAs are upregulated whilst PAK1 mRNA is downregulated. Silencing of CDC42BPA expression partially reduces miR29a-3p inhibitor-induced migration and invasion of SW480-7 cells.

Keyword: Cell migration; Invasion; miR-29a-3p; Colorectal cancer cell line; CDC42BPA mRNA expression