ABSTRACT

Characterization of a colorectal cancer migration and invasion-related microRNA miR-338-5p and its target gene PIK3C3


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Background: Colorectal cancer (CRC) has high recurrence and metastasis rate. MicroRNA is an epigenetic factor to regulate cell proliferation, cancer formation and metastasis through regulating tumor suppressor genes or oncogenes. The objective of this study is to identify miRNAs and their target genes related to CRC migration and invasion.

Materials and methods: We detected miR-338-5p expression in 73 CRC specimens by real-time PCR. Cell migration and invasion were analysed by transwell assay. The potential target gene of miR-338-5p is PIK3C3 predicated by TARGET SCAN, micrRNA.ORG, and DIANA LAB target gene prediction software and was confirmed by p-miR-reporter luciferase plasmid assay.

Results: Our study revealed that miR-338-5p was highly expressed in the tumor tissues of recurrent CRC patients (P = 0.0241). We further showed that the expression level of miR-338-5p in the tumor tissues of the metastatic patients was higher than that of non-metastatic patients (p = 0.0447). High miR-338-5p expression increased the migration and invasion of CRC cell SW480 demonstrated by transient transfection of miR-338-5p mimic. Consistently, low miR-338-5p expression decreased the migration and invasion of CRC cell SW480 demonstrated by transient transfection of miR-338-5p inhibitor, indicating that miR-338-5p induced CRC cell migration and invasion. PIK3C3 expression was reversed by transient transfection pCMV-Vps34 plasmid under miR-338-5p over-expression conditions, and migration and invasion ability was inhibited in SW480 cells. Furthermore, PIK3C3 expression was suppressed by sh-Vps34 lenti-virus infection under low miR-338-5p expression conditions, and migration and invasion ability of SW480 cells was increased. It suggests that miR-338-5p induced migration possibly through inhibition of PIK3C3. We also demonstrated that induction of autophagy of SW480 cell by amiodarone (autophagy inducer) induced LC3 puncta formation and LC3 type II expression, and under this condition the migration of SW480 cells was suppressed. We further transiently transfected miR-338-5p mimic into SW480 cells in the presence of amiodarone, LC3 puncta formation and LC3 type II expression were decreased. Furthermore, the migration of SW480 cells was reversed. In conclusion, these data suggests that miR-338-5p induces CRC cell migration and invasion though suppression of autophagy.

Discussion: Our findings reveal that miR-338-5p induces migration and invasion of CRC cells possibly through inhibition of PIK3C3. In summary, miR-338-5p participates in CRC cell migration through suppressing autophagy related PIK3C3 pathway.

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