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MicroRNA miR-143 suppresses cervical cancer cell migration

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Introduction

Cervical cancer is a common and lethal cancer in women. MicroRNAs (miRNAs) are small noncoding RNAs approximately 22 nucleotides in length that repress target mRNAs by binding to their 3'-untranslated regions (3'-UTR). miRNAs are important regulators of a broad range of biological processes including cellular differentiation, proliferation and apoptosis. Down regulation of the microRNA miR-143 is reported in most microRNA profiling studies on cervical cancer including a study we conducted. However, the biological significance of this suppression of miR-143 level is unclear.

Objectives

To investigate the effect of miR-143 on cervical cancer cell migration and invasion.

Methodology

Cervical cancer cell lines HeLa (HPV18 positive), SiHa (HPV16 positive), and C33A (HPV negative) were transfected with expression constructs of miR-143 and control small RNA. Transfected cells were assayed for migration and invasion ability in transwell assay and scratch wound healing assay. Genes dysregulated by miR-143 overexpression were identified by pathway focused qPCR array.

Result

HeLa and SiHa overexpressing miR-143 exhibited reduced ability to migrate and invade in transwell assay. HeLa and SiHa transfected with miR-143 also migrated slower in scratch wound healing assay. However, miR-143 transfected C33A migrate at a similar rate as control transfected cell, suggesting the migration suppression effect of miR-143 is HPV dependent. To shed light on the mechanism of migration suppression, expression levels of 84 cell mobility related genes were compared in HeLa cells transfected with control and miR-143 using a pathway focused qPCR array. Six genes downregulated more than 2-fold were identified, with the gene Rac1 guanine nucleotide exchange factor ARHGEF7 being the most highly downregulated gene by miR-143. Downregulation of β-pix, the protein product of ARHGEF7, upon miR-143 overexpression could be demonstrated by western blotting. Our results showed that miR-143 play important HPV dependent roles in cervical cancer cell motility.