Suppression of miRNA-708 by polycomb group promotes metastases by calcium-induced cell migration.

Department of Cardiothoracic Surgery, Weill Cornell Medical College of Cornell University, New York, NY 10065, USA.

Abstract
The progression of cancer to metastatic disease is a major cause of death. We identified miR-708 being transcriptionally repressed by polycomb repressor complex 2-induced H3K27 trimethylation in metastatic breast cancer. miR-708 targets the endoplasmic reticulum protein neuronatin to decrease intracellular calcium level, resulting in reduction of activation of ERK and FAK, decreased cell migration, and impaired metastases. Ectopic expression of neuronatin refractory to suppression by miR-708 rescued cell migration and metastasis defects. In patients with breast cancer, miR-708 expression was decreased in lymph node and distal metastases, suggesting a metastasis-suppressive role. Our findings uncover a mechanistic role for miR-708 in metastasis and provide a rationale for developing miR-708 as a therapeutic agent against metastatic breast cancer.

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PMID: 23328481 [PubMed - indexed for MEDLINE]