MICRORNA-200 EXPRESSION IN LUNG CANCER

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**Abstract:** MicroRNA-200 family (miR-200a, -200b, -200c, -429, and -141) is an important regulator of epithelial-to-mesenchymal transition (EMT). In lung cancer and other cancers, EMT is the underlying step of metastasis. MiR-200 regulate epithelial identity via inhibiting transcriptional factors ZEB1 and ZEB2, which regulate the expression of E-cadherin and other genes controlling cell polarity. In the present study, we hypothesize that restoring miR-200a, -200b, -200c in H1299 non-small cell lung cancer cells decreases the expression of EMT/migration/invasion genes and restores the expression of E-cadherin. Cell lines H1299, BEAS-2B, small airway epithelial cells (SAEC) were cultured according to the supplier’s recommendations (ATCC). Human miRIDIAN shMIMIC lentiviral miRNA for hsa-miR-200a, -200b, -200c, and control scrambled microRNA (Open Biosystems) were used for infection of H1299 cells. After stable transfection, mRNA and cell lysate were analyzed for gene expression (qPCR) and protein level (Western blot). Quantification of miR-200 expression in human lung cancer stage I biospecimens indicated a very low level of miR-200b, -200c, and miR-429, respectively a 0.3-, 0.5-, and 0.5-fold decrease vs normal tissue. Restoring miR-200a in NSCLC H1299 cells down-regulated EMT genes vimentin, and CD44, and migration/invasion genes DLC1, and ATRX. Activators of EMT, ZEB1 and ZEB2, were induced by re-expressing miR-200. These results indicate that loss of miR-200b, -200c, or -429 mediate the expression of EMT marker genes and restoring miR-200 level induces the expression of epithelial marker, E-cadherin. Translational, these data also suggest development of novel lung cancer treatment therapies which should take into consideration miR-200.

**Keywords:** Metastatic lung cancer, microRNA-200, VE-cadherin, EMCT, H1299 cells,

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