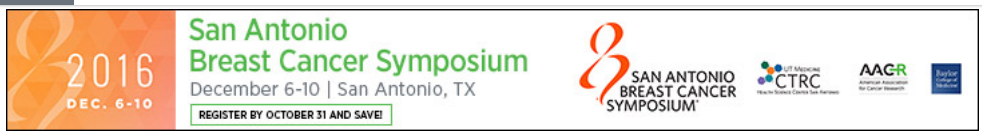

Cancer Research

Research Article

miR-214 and miR-148b targeting inhibits dissemination of melanoma and breast cance

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Article Figures & Data Info & Metrics PDF

Abstract

miR-214 and miR-148b have been proposed to antagonize the effects of each other in enabling or blocking metastasis, respectively. In this study, we provide evidence deepening their role and interrelationship in the process of metastatic dissemination. Depleting miR-214 or elevating miR-148b blocked the dissemination of melanoma or breast cancer cells, an effect that could be accentuated by dual alteration. Mechanistic investigations indicated that dual alteration suppressed passage of malignant cells through the blood vessel endothelium by reducing expression of the cell adhesion molecules ITGA5 and ALCAM. Notably, transendothelial migration in vitro and extravasation in vivo impaired by singly alterating miR-214 or miR-148b could be overriden by overexpression of ITGA5 or ALCAM in the same tumor cells. In clinical specimens of primary breast cancer or metastatic melanoma, we found a positive correlation between miR-214 and ITGA5 or ALCAM along with an inverse correlation of miR-214 and miR-148b in the same specimens. Our findings define an antagonistic relationship of miR-214 and miR-148b in determining the dissemination of cancer cells via tumor-endothelial cell interactions, with possible implications for microRNA-mediated therapeutic interventions aimed at blocking cancer extravasation.

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