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Contribution of miR-145-5p/Ago2 complex to the regulation of epithelial-mesenchymal transition

Claudia Tito[1], Teresa Bellissimo[1], Silvia Masciarelli[1], Federica Ganci[2], Veronica Sorrentino[3], Natale Porta[3], Mirko Cirenza[3], Giuseppe Cavallaro[5], Antonella Calogero[4], Giulia Fontemaggi[2], Vincenzo Petrozza[3,4], Giovanni Blandino[2] and Francesco Fazi[1]

[1] Department of Anatomical, Histological, Forensic & Orthopedic Sciences, Section of Histology & Medical Embryology, Sapienza University of Rome, Italy;
[2] Oncogenomic and Epigenetic Unit, "Regina Elena" National Cancer Institute, Rome, Italy;
[3] Pathology Unit, ICOT, Latina, Italy;
[4] Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy;
[5] Department of Surgery P. Valdoni, Sapienza University of Rome, Italy;

The epithelial-mesenchymal transition (EMT) is essential for cell fate determination during development but it is involved in pathological processes like cancer as well, being one of the first steps in the mechanisms leading to metastasis. miR-145-5p is one of the most widely recognized tumor-suppressor miRNAs, able to regulate cell migration and EMT through the contribution of the RISC complex in which Argonaute (Ago) proteins are required for target recognition and gene silencing [1]. Ago2 is an important member of the Ago family and its overexpression correlates with a transformed phenotype in breast cancer cells [2]. With the aim to unravel miR-145-5p/Ago2 contribution to the suppression of cancer progression in epithelial tumors, here we show that: i) miR-145-5p and Ago2 are down-regulated in breast tumor vs normal tissues; ii) the restored expression of miR-145-5p in breast cancer cell lines results in the reduction of tumor phenotype; iii) Ago2 expression is positively and specifically regulated by miR-145-5p; iv) miR-145-5p-dependent Ago2 induction is necessary for the inhibition of cell migration; v) when Ago2 is depleted, the formation of an alternative miR-145-5p/Ago1 active complex redirects miR-145-5p tumor suppressor function and correlates with a more invasive phenotype in breast cancer cells. These results open to the identification of miR-145-5p/Ago2-dependent molecular networks involved in the maintenance and progression of cancer phenotype.

References

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Keywords
EMT, miR145-5p, Ago2 protein