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

Claudia Tito1, Teresa Bellissimo1, Silvia Masciarelli1, Federica Ganci2, Veronica Sorrentino3, Natale Porta3, Mirko Cirenza3, Giuseppe Cavallaro5, Antonella Calogero4, Giulia Fontemaggi2, Vincenzo Petrozza3,4, Giovanni Blandino2 and Francesco Fazi1

1Department of Anatomical, Histological, Forensic & Orthopedic Sciences, Section of Histology & Medical Embryology, Sapienza University of Rome, Italy; 2Oncogenomic and Epigenetic Unit, “Regina Elena” National Cancer Institute, Rome, Italy; 3Pathology Unit, ICOT, Latina, Italy; 4Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy; 5Department 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 Argo-naut (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

Keywords
EMT, miR145-5p, Ago2 protein