Prof. Gerolama Condorelli

Department of Molecular Medicine and Medical Biotechnology , Federico II University of Naples, Italy

*email: gecondor@unina.it, www.docenti.unina.it/gerolama.condorelli*

## Abstract

Despite many novel therapeutic approaches, breast cancer remains one of the leading causes of cancer mortality among women. Recent findings indicate that cancer-associated fibroblasts (CAFs), the major components of the tumor microenvironment, play a crucial role in breast cancer progression, but how they promote tumorigenesis is poorly understood. Increasing evidence indicates that exosomes, membrane vesicles sized 30-100 nm in diameter, may vehicolate their cargo, including microRNAs (miRs), thus affecting the biological behaviour of recipient cells.

Therefore, one alternative mechanism of the promotion of breast cancer progression by CAFs may be through cancer-associated fibroblast-secreted exosomes, which would deliver oncogenic miRs to breast cancer cells.

In order to investigate the potential role of miRs in stroma-tumor communication, we profiled miR expression in exosomes from cancer-associated fibroblasts compared to normal fibroblasts. We found that in CAF exosomes the levels of miR-21, miR-378e, and miR-143 were increased as compared to normal fibroblast exosomes. By immunofluorescence experiments, we demonstrated that PKH26-labeled-exosomes could be transferred from fibroblasts to T47D breast cancer cells. Furthermore, we elucidated that cy3-labeled-miRs (cy3-miR-21, cy3-miR-143, cy3-miR-378e) were shuttled into T47D cells via CAF exosomes. Moreover, for the first time, we provided evidence of the role of CAF exosomes and their miR contents in the induction of the stemness phenotype in different breast cancer cells, BT549, MDA-MB-231 and T47D. We also studied miRs effects on tamoxifen resistance. We conclude that CAFs strongly promote the development of an aggressive phenotype of breast cancer cells through exosome-mediated delivery of these oncogenic miRs.