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Oncologists Congress 2020: Extracellular Vesicles as means of interconnection within the tumor microenvironment - Ilaria Giusti, University of L'Aquila, Italy

Ilaria Giusti
University of L'Aquila, Italy

Background: Cancer derived extracellular vesicles (EVs) are involved in many cancer related processes: angiogenesis, invasion and motility induction, immune surveillance evasion, apoptosis escape, drug resistance promotion. Recent findings revealed their role in modulating the stromal cells' behavior, especially fibroblasts. Tumor associated fibroblasts, indeed, have been proven to actively participate in tumor progression; they can be "educated" by tumor cells, acquiring an activated state that identify them as Cancer Associated Fibroblasts (CAFs). CAFs are able, in turn, to support cancer progression enhancing the biological activities of cancer cells, supporting angiogenesis, immunosuppression and chemoresistance.
Extracellular vesicles (EVs) are small-membrane vesicles secreted by most cells types with the role to provide intercellular communication both locally and systemically. The transfer of their content between cells, which includes nucleic acids, proteins and lipids, confers the means for these interactions and induces significant cellular behaviour changes in the receiving cell. EVs are implicated in the regulation of numerous physiological and pathological processes, including development and neurological and cardiovascular diseases. Importantly, it has been shown that EV signalling is essential in almost all the steps necessary for the progress of carcinomas, from primary tumours to metastasis. In this review, we will focus on the latest findings for EV biology in relation to cancer progression and the tumour microenvironment.

Previous studies demonstrated that the human ovarian cancer cell line CABA I release many EVs heterogeneous in size in a time-dependent mode; a nearly pure population of small EVs (sEVs) and a mixed population of small and large EVs (mEVs) which are assumed to correspond to exosomes and microvesicles+exosomes, respectively.
Experimental data: sEVs and mEVs were able to induce normal human dermal fibroblasts (NHDF) to acquire a CAF-like morphology and to express CAFs' specific markers. Moreover, they differently effected the biologic activity of activated fibroblasts in terms of proliferation, motility and invasiveness.
When observed by Scanning Electron Microscopy, the surface of EVs-activated NHDF revealed a diffuse release of EVs, a very sporadic phenomenon in untreated cells, leading to hypothesize that activation leads to a modulation of NHDF secretome. Indeed, EVs-activated fibroblasts' secretome affected the biological activities of bystander cells (including fibroblasts, endothelial and tumor cells) in terms of invasiveness, motility and tube formation.
Conclusion: Ovarian cancer cells can modulate fibroblasts' behavior through the release of EVs, activating them to a CAFs-like state. The different subpopulations of sEVs and mEVs show a different ability to stimulate this process suggesting a different cargo composition. EVs- activated fibroblasts, in turn, affect bystander cells' behavior to be more advantageous for cancer progression.

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