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MEETING ABSTRACT

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The impact of cancer extracellular vesicles on mesenchymal stem cell phenotype

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Mesenchymal stem/stromal cells (MSCs) are versatile adult stem cells with multilineage differentiation potential that reside in adult organ stroma. MSCs are adherent cells with a spindle-like morphology, which express CD29, CD44, CD73, CD90, and CD105 cell surface markers and lack expression of hematopoietic markers CD45 and HLA-DR [1]. Importantly, MSCs are active producers of paracrine factors that may play an important role in the modulation of inflammatory conditions. Tumor microenvironment (TME) could be regarded as a site of chronic inflammation, and currently the MSC role in the TME is under debate. A considerable evidence demonstrates that MSCs may polarize into two subsets: a tumor-suppressing type of MSCs and tumor-supporting type, ***e.g.*** carcinoma-associated fibroblasts (CAF) [2].

Extracellular vesicles (EVs) secreted by malignant cells are communication tools between cells in TME. Cancer cell-derived EVs may contribute to the cancer metastasis by modulating the MSC functions in the TME [3].

In the present study, we have examined the uptake of primary colorectal cancer (CRC) SW480 and metastatic CRC SW620 cell line-derived EVs in the MSCs and the effect of tumor EV on MSC phenotype and paracrine functions.

CRC EVs were labelled with RNA-specific SytoRNA select dye and uptake was examined by confocal microscopy. Cell surface marker expression was analyzed by flow cytometry, CAF differentiation was assessed by quantitative PCR analysis, secretory factors were assessed by ELISA and Luminex assays.

Our results show that CRC EVs are taken up in MSCs and co-localized with endoplasmatic reticulum in the cell cytoplasm. EVs had no effect on MSC cell surface marker expression whereas the expression of TERT, FAP and α-SMA markers was increased indicating a shift towards CAF phenotype. Additionally, the expression of several inflammatory chemokines and cytokines (***e.g.*** IL-8, VEGF) was induced after MSC exposure to CRC EVs.

We conclude that CRC EVs may serve as a tool to modulate MSC phenotype and paracrine functions within TME.

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Keywords: mesenchymal stem cells – cancer – extracellular vesicles

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