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MEETING ABSTRACT

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Colorectal cancer cell line-derived extracellular vesicles induce changes in mesenchymal stem cell phenotype and secretory properties

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Background: Solid tumours show accumulation of stromal fibroblasts that influence disease progression. The origin of cancer-associated fibroblasts (CAFs) is still unclear, with mesenchymal stem cells (MSCs) being considered as one of the possible contributors [1]. MSCs are multipotent cells positive for CD73, CD90 and CD105, and, besides their normal physiological roles, MSCs are also present in tumour microenvironment (TME) where they show tumour-promoting effects [2,3]. Extracellular vesicles (EVs) are membrane-bound vesicles containing different biomolecules including mRNA, miRNA, siRNA and other RNA fragments, and cancer cell-secreted vesicles are able to modulate stromal cell properties [4]. In colorectal cancer (CRC), the EV concentration in TME correlates to the invasive potential of cancer cells [5].

Objectives: The purpose of the study was to analyse CRC cell line-derived EV uptake and co-localisation in skin MSCs and to assess their effect on MSC properties.

Methods: EVs were isolated from SW480 and SW620 cell culture supernatants using size-exclusion chromatography and sepharose gel filtration. MSCs were incubated with SYTO RNA Select-labelled EVs alone or in the presence of uptake inhibitors covering different pathways. Next, MSCs were analysed for EV uptake and subcellular localisation using flow cytometry and fluorescence microscopy. MSCs were also analysed for alterations in cell phenotype, CAF gene expression and cytokine secretion using flow cytometry, qPCR and ELISA methods.

Results: CRC cell line-derived EVs enter sMSCs where they co-localise with cell nuclei and endoplasmic reticulum. The EV uptake is most effectively blocked with the dynamin-2 inhibitor dynasore. Exposure to cancer cell EVs results in down-regulated CD90 expression, increased VEGF and IL-8 secretion, altered FAP expression, upregulated chemokine gene expression as well as increased TERT expression in MSCs.

Conclusions: Alterations in MSC properties following exposure to EVs are associated with MSC shift towards cancer-associated fibroblast phenotype.

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Keywords: mesenchymal stem cells – extracellular vesicles – stromal cells – tumour microenvironment

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