

EXTRACELLULAR VESICLES IN THE TREATMENT OF CANCERS

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Background and Aims. The cancer microenvironment plays a central role in cancer development, growth and homeostasis. This paradigm suggests that cancer fibroblasts support cancers, probably in response to stimuli received from the cancer cells. We aimed at investigating if extracellular vesicles (EVs) can shuttle microRNA (miR) species between cancer associated fibroblasts and cancer cells.

Methods. We extracted EVs according to published protocols. EVs were studied for their miR content by qRT-PCR. EVs were transfected with select miR species and utilized *in vitro* as well as *in vivo* in a rat model of cholangiocarcinoma.

Results. miR-195 is downregulated in cholangiocarcinoma cells, as well as in adjoining fibroblasts. Furthermore, we report that EVs shuttle miR-195 from fibroblasts to cancer cells. Lastly, we show that fibroblast-derived EVs, loaded with miR-195, can be administered in a rat model of cholangiocarcinoma, concentrate within the tumor, decrease the size of cancers, and improve survival of treated rats.

Conclusions. EVs play a salient role in trafficking miR species between cancer cells and cancer associated fibroblasts in human CCA. Understanding of these mechanisms may allow devising of novel therapeutics.