P23 Organ-specific uptake of cancer-associated extracellular vesicles

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Linxweiler J., Kolbinger A., Saar M., Stöckle M., Junker K.

Saarland University, Department of Urology, Homburg Saar, Germany

Introduction & Objectives: Cancer cells secrete extracellular vesicles (EVs) to establish a tumor growth and invasion promoting local microenvironment and to prepare distant organ systems for metastatic seeding (so-called premetastatic niches). Furthermore, cancer-associated EVs may play a role in the often observed organotropism, i.e. the phenomenon that many cancer entities tend to metastasize preferably into specific organ-systems. In this project, we aimed to examine in a mouse model if the uptake of circulating cancer-cell secreted EVs by different organ systems differs depending on the cancer entity (prostate cancer, renal cell carcinoma, bladder cancer).

Materials & Methods: EVs from the conditioned medium of three tumor cell lines and respective non-malignant cell lines (kidney: 786-O, Hek293; bladder: T24, HCV29; prostate: VCaP, BPH1) were isolated by ultracentrifugation, fluorescence labelled (PKH26), washed and quantified. Subsequently, the labelled EVs were intravenously injected into 4 mice per cell line and the mice were sacrificed 12 or 24 hours later (n=2 for each time point). Various organs were retrieved during autopsy (brain, lungs, liver, kidneys, spleen, prostate, bladder, skeletal muscle, adrenals). Cryosections from these organs were examined for the presence of fluorescence-labelled EVs by laser-scanning microscopy.

Results: EVs from all three tumor entities were taken up in the brain (786-O>T24>VCaP), the liver (786-O=VCaP>>T24), the lung (786-O>T24=VCaP) and the spleen (786-O=T24>VCaP). In contrast, no EVs were detectable in the kidneys, the adrenals, the prostate, skeletal muscle and the urinary bladder. Aside from the brain (12h>24h) there was no difference in the quantity of EV signals after 12 and 24h. The results from benign cell lines, the exact quantification of EV signals and the elucidation of subcellular structures/cell types in which EVs were present after 12 or 24h (blood vessels, plasma membrane, lysosomes, fibroblasts, macrophages, epithelial cells) is still pending, but will be available at the time of presentation at ESUR2019.

Conclusions: Cancer-associated EVs were taken up in our mouse model not entirely organ-specific but in different amounts depending on tumor entity. Our observations hints to an organotropism in EV uptake, which might play a role in the organotropism observed during the metastatic spread of urological tumors. However, this will have to be proven functionally in further experiments using parallel or sequential injection of mice with cancer cells and cancer-associated EVs from different origins.