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Important differences between exosome biosignatures from prostate cancer patient plasma samples and prostate cancer cell lines

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Background

Exosomes are endosome-derived vesicles secreted by many cell types, including tumor cells. The vesicles are formed intracellularly by invagination followed by fusion with the multivesicular body (MVB). The MVB ultimately merges with the plasma membrane, leading to exocytosis of the exosomes, which consequently have a similar membrane protein composition as their cell of origin; this provides the exosomes with unique biosignatures. Furthermore, these circulating exosomes participate in cellular communication by transporting mRNAs, microRNAs, and proteins to target cells where they can elicit biological responses. This study compared the biosignatures identified from prostate cancer (PCa) cell line-derived exosomes to those found in exosomes isolated from the plasma of PCa patient samples.

Methods

To develop an exosome-specific protein and RNA signature for PCa, we studied RNA and surface membrane protein profiles with FACS of exosomes derived from four prostate cancer cell lines, VCaP, 22Rv1, LNCaP and DU145. The exosome biosignatures identified from the cell lines were then measured in plasma exosomes isolated from PCa patients.

Results

We found that each of the four cell lines had different exosome-specific mRNA expression levels and exosome surface protein contentThe mRNA exosome biosignatures identified in the four cell lines were not found in the exosomes from plasma samples of patients with PCa. Using a combination of antibodies for B7H3, PSMA and CD63 we identified by flow cytometry a protein signature from all prostate cancer cell line exosome populations that defined a specific subpopulation of exosomes containing all 3 proteins on their surface. Interestingly, this same exosome subpopulation was not found in exosomes derived from patients with prostate cancer. Additionally, exosome-specific mRNA expression of two mRNA transcripts often found to be overexpressed in PCa, STEAP1 and SPINK1, was consistently identified in exosomes derived from prostate cancer cell lines VCaP and 22Rv1, but were only found in the plasma derived exosomes from one out of eight patients with PCa.

Conclusions

Our results show that prostate cancer cell lines are not appropriate models for the development of exosome-specific disease profiles in prostate cancer; this will be investigated in additional cell lines. We find that patient samples are essential to identify disease-specific exosome biosignatures. These findings support the development of a versatile diagnostic platform based on exosome-specific biosignatures found in the plasma of patient samples for prostate and other cancers.

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