AACR Abstract

Identification and characterization of exosome subpopulations to provide the foundation for a novel exosome-based cancer diagnostic platform

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Background

Exosomes are endosome-derived vesicles between 40-100 nm in diameter that are secreted by most cell types and can be distinguished from other types of microvesicles released from the cell by a characteristic protein composition. Furthermore, it is known that exosomes transport mRNAs, microRNAs (miR) and proteins, all of which can be used to identify the cell from which they are derived and can be exploited for noninvasive molecular profiling. Differential expression of exosomal miRs between cancer and normal patient samples has been described previously. In this study we identified various exosome subpopulations by their particular surface protein topography. Subsequently, we characterized plasma-derived exosomal RNA content of each subpopulation for their specific association with a cancer phenotype. We have exploited the protein topography and RNA content of exosomes found in plasma from patients with cancer, benign prostatic hyperplasia (BPH), and unaffected individuals in order to characterize and identify the exosome subpopulations that are indicative of a given disease state. We intend to use the various biosignatures of these exosome subpopulations to develop a diagnostic platform to aid in the screening and diagnosis of various cancers.

Methods

Using flow cytometry (FACS) and cell sorting techniques, we separated plasma-derived exosomes into protein-specific subpopulations by using membrane-specific protein biomarkers (e.g. EpCam).

Results

We consistently found that exosomes from PCa patients had the highest percentage of exosomes labeled with EpCam, PSMA and CD-9 compared to exosomes from normal, BPH and CRC patients. Additionally, for each subpopulation of exosomes separated by FACS, we used quantitative expression profiling of miRs to identify expression signatures specific to cancer patients. We found that the RNA content of various subpopulations of exosomes, defined by their membrane protein biosignature, was unique. In an exosome subpopulation where proteins CD-9 and CD-81 are on the surface, miR 141 is significantly overexpressed in exosomes from prostate cancer patient plasma compared to exosomes derived from normal plasma. Interestingly, miR 9 was significantly overexpressed in exosomes from BPH plasma in EpCam and PSMA exosomes but not in exosomes of the same subpopulation isolated from normal and PCa plasma, supporting the idea that exosome biosignatures can be used to distinguish between BPH and PCa. Additionally, miR 491 was overexpressed in EpCam expressing exosomes derived from colon cancer plasma compared to normal and PCa.

Conclusion

These findings highlight the potential of exosome biosignature profiles for use as a diagnostic marker of disease and provide the foundation for a novel exosome-based diagnostic platform that can be used through a non-invasive blood test.

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