AACR Abstract

Plasma exosomes are a robust biosignature for prostate cancer

Christine Kuslich, Traci Pawlowski, Jeff Kimbrough, Ta Deng, Teresa Tinder, Joon Kim and David Spetzler

We have developed a novel, versatile, mulitplexed exosome-based diagnostic platform that can identify highly specific and sensitive disease biosignatures. This platform has been used to identify a plasma-based exosome biosignature for prostate cancer (PCa) that is superior to current tests, which rely on increased levels of either PSA in the blood or elevated levels of the PCA3 transcript in the urine. Unfortunately, PSA levels can also be elevated due to confounding conditions like benign prostate hyperplasia (BPH) and prostatitis. PCA3, while appearing to be prostate cancer specific, only offers moderate benefit over the performance of PSA, and requires a digital rectal exam to obtain a suitable specimen for analysis. The screening and diagnosis of PCa would be significantly improved by identifying biomarkers that are both highly specific and sensitive as well as easily surveyed from the blood or urine. Exosomes are endosome-derived vesicles between 40-100 nm in diameter that are secreted by many cell types including the epithelial cells of the prostate. In blood exosomes appear to participate in cellular communication by transporting mRNAs, microRNAs and proteins from their cell of origin to target cells where they can elicit biological responses. The quantity and protein topography of exosomes shed from cancer cells varies considerably compared to those shed from normal cells. Thus, the concentration of plasma exosomes with molecular markers indicative of the disease state can be used as a robust and informative blood-based biosignature for PCa and other diseases.

In this study we report the results of a novel multiplexed diagnostic platform for quantifying and profiling exosomes in plasma that was used to develop an exosome-derived biosignature composed of 7 different surface membrane protein biomarkers. These biomarkers include proteins specific to: exosomes generally (CD9, CD81, and CD63), exosomes from prostate epithelial cells (PSMA, and PCSA), and tumor-associated exosomes (EpCam and B7H3). We used this exosome-specific PCa biosignature to profile 29 PCa patients and 31 age-matched men from the general population.

This blood-based exosome assay correctly identified PCa patients with a sensitivity of 83% and specificity of 90%, AUC = 0.881. Additionally, the assay clearly distinguished between PCa and BPH patients. When we included patients with BPH (n=15) the sensitivity was 83% and the specificity of the test remained significant at 85%, AUC = 0.844. Further analysis revealed that 2 of the exosome-associated markers (PCSA and B7H3) showed significant differences between stage II and stage III disease using a Kolmogorov-Smirnov test ($p = 0.009, 0.0271$).

This initial study demonstrates the ability of an exosome-derived biosignature patient profile to distinguish PCa from both normal and BPH and may ultimately allow PCa progression and therapeutic monitoring to be analyzed through a simple blood test.

CARIS™
LIFE SCIENCES