AACR Abstract

Plasma exosome-based biosignatures: A novel method for early diagnosis of colorectal cancer

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

Background

We have developed an exosome-based diagnostic platform that can identify highly specific biosignatures in exosomes derived from the blood of patients with colorectal cancer (CRC). While colonoscopy is the gold standard to screen and identify colon cancer it is estimated half of patients who are recommended for colonoscopy are not compliant. Often the lack of compliance is because many perceive a colonoscopy as an uncomfortable and invasive procedure. An ideal first step toward increasing participation in preventive strategies would be the development of a less invasive diagnostic test that could identify those patients that have a blood-based biosignature indicative of the need for biopsy by colonoscopy. Ideally this strategy would result in cancers being identified earlier and prevent disease-free individuals from undergoing an unnecessary invasive procedure. Current blood-based tests rely on increased levels of either carcinoembryonic antigen (CEA) or carbohydrate antigenic determinant (CA 19-9). Unfortunately, CEA and CA 19-9 are neither organ-specific nor tumor-specific. In an attempt to provide a better blood-based biosignature for CRC we have developed a novel exosome-based diagnostic platform that is able to identify patients with CRC using an exosome-specific biosignature derived from plasma. Exosomes are endosome-derived vesicles between 40-100 nm in diameter that are secreted by most cell types, including tumor cells. In this study, we demonstrate that a novel exosome-based assay can diagnose CRC from surface membrane protein biosignatures on exosomes derived from peripheral blood of patients with CRC.

Methods

We isolated exosomes from plasma of patients both with and without CRC. Exosome surface proteins (CD9, CD81, CD63, EpCam, EGFR, and STEAP) were used in a multiplex assay to capture and detect exosomes. The quantity of exosomes with significant concentrations of these surface proteins lead to the development of an exosome-specific biosignature that differentiated CRC samples from normal.

Results

Exosomes present in blood plasma of patients provide a unique signature by which CRC can be diagnosed as early as histological grade 1. The biosignature is composed of 7 different exosomal surface membrane protein markers, which include both exosome and cancer-specific proteins. Measurement of the exosomal biosignature in plasma differentiated patients with CRC (n=20) diagnosed by biopsy from individuals from the general population (n= 20) with a sensitivity of 85% and specificity of 85%. The CRC samples analyzed were comprised of AJCC/UICC stage I (n=10), IIA (n=6), and IIIB (n=4).

Conclusion

We have shown for the first time that biosignatures identified in exosomes derived from the blood of patients with CRC provide the foundation on which to develop a highly sensitive and specific test that could help physicians screen, diagnose and treat patients with CRC.

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