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LETTER TO THE EDITOR Open Access

Differential distribution and enrichment of non-coding RNAs in exosomes from normal and Cancer-associated fibroblasts in colorectal cancer

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Abstract

Exosome production from cancer-associated fibroblasts seems to be an important driver of tumor progression. We report the first in-depth biotype characterization of ncRNAs, analyzed by Next Generation Sequencing and Bioinformatics, expressed in established primary human normal and cancer-associated fibroblasts (CAFs) from cancer and normal mucosa tissues from 9 colorectal cancer patients, and/or packaged in their derived exosomes. Differential representation and enrichment analyses based on these ncRNAs revealed a significant number of differences between the ncRNA content of exosomes and the expression patterns of the normal and cancer-associated fibroblast cells. ncRNA regulatory elements are specifically packaged in CAF-derived exosomes, supporting a specific cross-talk between CAFs and colon cancer cells and/or other stromal cells, mediated by exosomes. These sncRNAs are potential biomarkers present in cancer-associated fibroblast-derived exosomes, which should thereby contribute to developing new non-invasive diagnostic, prognostic and predictive methods for clinical applications in management of cancer patients.

Keywords: Colon Cancer, Liquid biopsy, Tumor microenvironment, Exosomes, Non-coding RNAs, Next generation sequencing

Tumor progression is deeply influenced by the local microenvironment. Fibroblasts usually named as cancer-associated fibroblasts (CAFs), are one of the most abundant and active cell types of the tumor microenvironment (TME). CAFs seem to regulate many aspects of tumorogenesis involving interactions between the malignant cells and other cells of the TME [1].

Exosomes, released by cells are important mediators of intercellular communication. In the tumor context, exosomes released by cancer cells transmit signals to cancer cells and also to stromal cells generating an active TME which promotes tumor progression [2]. Exosomes are also released by both cancer cells and stromal cells not only into the cancer microenvironment, but also into circulation [2]. Significant amounts of miRNAs packaged into exosomes were detected in many types of liquid biopsy samples [2], and certain types of circulating miRNAs strongly correlates with progression of different cancer types [3], however, few information about others ncRNAs contained in exosomes is unknown.

In the past decade large-scale analyses have focused on the comprehensive identification of non-coding RNAs (ncRNAs) and of new ones such us the long ncRNAs (lncRNAs). lncRNAs are poorly conserved and regulate gene expression by diverse

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