Cancer-associated fibroblasts secreted exosomal miR-146a promotes bladder cancer stem-like features

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Introduction

Urinary bladder cancer (UBC) patients at muscle invasive stage have poor clinical outcome, due to high propensity for progression. Chemoresistance and subsequent recurrence of cancers are driven by a subpopulation of cancer stem-like cells (CSCs). Cancer-associated fibroblasts (CAFs), one of the principal constituents of the tumor stroma, play an important role in tumor development. Exosomal microRNAs (miRNAs) are emerging mediators of cancer-host crosstalk with other cells around. However, it is unclear whether CAFs from UBC promote cancer progression through exosomal miRNAs.

Methods

CAFs and normal fibroblasts (NFs) were isolated from human bladder cancer specimens and adjacent normal tissues. CAFs and NFs were subcutaneously co-injected with bladder cancer cell lines (T24 and 5637) into male athymic nude mice. Exosomes isolated from conditional media of NFs and CAFs were used for in vitro study and miRNA microarray analysis. Sphere formation assay and ALDH enzyme activity were used for representation of CSCs features. Human UBC samples were enrolled to analyze their potential clinical relevance.

Results

CAFs and normal fibroblasts (NFs) were isolated from human bladder cancer specimens and adjacent normal tissues. CAFs and NFs were subcutaneously co-injected with bladder cancer cell lines (T24 and 5637) into male athymic nude mice. Exosomes isolated from conditional media of NFs and CAFs were used for in vitro study and miRNA microarray analysis. Sphere formation assay and ALDH enzyme activity were used for representation of CSCs features. Human UBC samples were enrolled to analyze their potential clinical relevance.

Conclusions

Cancer-associated fibroblasts secreted exosomal miR-146a promotes bladder cancer stem-like features in vitro and in vivo. Exosomal miR-146a is associated with clinical bladder cancer recurrence.