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Research Paper

Circular RNA CircHIPK3 Promotes Gemcitabine Sensitivity in Bladder Cancer

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Abstract

Purpose: Recent studies showed circular RNA (circRNA) played important regulatory roles in tumors, including genesis of chemotherapy resistance. In this study, the role of circHIPK3 on chemotherapy resistance of bladder cancer (BC) will be clarified.

Methods: Real-time quantitative PCR was applied to examine the circHIPK3 expression. The gemcitabine sensitivity and cell proliferation viability were analyzed by Cell Counting Kit-8 assay. Double-stained flow cytometry was used to detect the cell apoptosis.

Results: In BC tissues and cell lines, the circHIPK3 expression was down-regulated. Its expression had a negative correlation with pathological grade, lymph node metastasis and gemcitabine insensitivity of BC patients. CircHIPK3 was a independent prognostic biomarker for BC patients. The expression of circHIPK3 in T24/gem and J82/gem cell lines (resistant to gemcitabine) was down-regulated significantly. The over-expression of circHIPK3 decreased IC50 of gemcitabine and promoted gemcitabine's cytotoxicity in T24/gem and J82/gem cells.

Conclusions: The circHIPK3 is low-expressed in BC and is an independent prognostic biomarker for BC patients. The low-expression of circHIPK3 is associated with the insensitivity to gemcitabine of BC patients, over-expression of circHIPK3 promotes gemcitabine sensitivity in BC.

Key words: bladder cancer; circular RNA; circHIPK3; chemotherapy; gemcitabine

Introduction

Bladder cancer (BC) is one of the ten most common tumors in the whole body and the most common malignant tumors in urinary system [1]. In the West, the incidence of BC is second only to prostate cancer in urogenital tumors, while it occupies the first place in China [1-3]. Bladder urothelial carcinoma is the most common pathological type of BC, accounting for more than 90% of the total number of BC patients.

Chemotherapy is one of the most effective means to treat BC at present, which reduced significantly the risk of recurrence and metastasis, and improve evidently the prognosis of BC patients [4]. Nevertheless, the resistance of cancer cells to chemotherapy drugs often leads to chemotherapy failure.

Recently, circular RNA (circRNA) is a hotspot in the field of life science research, it is a special kind of non-coding RNA molecule. Because the closed ring structure is not affected by RNA exonuclease, circRNAs are more stable and difficult to degrade. CircRNA molecules are rich in microRNA binding sites and act as competitive endogenous RNA (ceRNA) to play the role of microRNA sponge in cells [5,6]. By interacting with tumor-associated microRNAs, circRNAs play important regulatory roles in tumorigenesis [7-10].