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FULL LENGTH ARTICLE

The potential value of CDV3 in the prognosis evaluation in Hepatocellular carcinoma

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Abstract CDV3 is correlated with tumorigenesis and may affect some biological process in cancer. In this study, we explore the role of CDV3 in HCC. According to the TCGA data base, CDV3 is over-expressed in HCC tissues. Up-regulation of CDV3 is correlated with lower over-all survival rate in HCC patients. In HCC samples from our hospital, CDV3 is also enriched in cancer tissues and CDV3 expression associated with HCC pathological T stage. What is more, higher CDV3 expression could forecast poor survival rate in HCC patients. In conclusion, CDV3 is a biomarker of HCC and could be a potential therapeutic target.

Introduction

Hepatocellular carcinoma (HCC), a highly vascularized tumor, is the third leading cause of cancer death worldwide, and the second in China.[1,2] Due to existed therapies are insufficient for the high frequency of tumor recurrence after liver resection, the prognosis of HCC patients remains pessimistic. Therefore it is of great importance to establish the identity of new targets for therapeutic approach to improve the prognosis of HCC patients after surgical resection.

CDV3 (carnitine deficiency-associated gene expressed in ventricle 3), also known as H41, was documented as an unidentified gene in breast cancer in 1999.[3] CDV3 expression correlated to the expression of Her2 and the sensitivity

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of photon-irradiation and simultaneous PTX-treatment in breast cancer.[4] And CDV3 was up-regulated in colorectal adenocarcinoma and gastric cancer.[5–7] However, few is known about the role of CDV3 in HCC.

In our present research, we found that CDV3 was up-regulated in The Cancer Genome Atlas (TCGA) database. And we extensively evaluated the CDV3 expression pattern and confirmed its contribution to patients' survival rate after HCC surgical resection in our department. Results presented in this study suggest that CDV3 is significant overexpressed in HCC tissues, and its over-expression indicates poor prognosis. We propose that CDV3 is a novel powerful predictor for HCC prognosis and a new potential adjuvant treatment target for HCC after surgical resection.

Materials and methods

Study subjects

Samples from 50 patients with HCC receiving liver resection at our hospital (First Affiliated Hospital, Chongqing medical University, Chongqing, China) between 2006 and 2010 were collected in this study. Letter of consent was obtained from all patients, and the experimental protocols were approved by the local ethics committee. Patient charts were reviewed to obtain clinical data about age, gender, tumor size, TNM stage (AJCC), and death or time of last follow-up. Patient survival was calculated from the day of surgery until death, in month.

TCGA dataset and analysis of the differentially expressed mRNAs and the clinical significance

To validated the expression of mRNAs, 51 cases of normal liver tissues and 270 cases of HCC tissues were obtained from TCGA database (https://tcga-data.nci.nih.gov/tcga/). Furthermore, the Kaplan–Meier method was used to estimate the prognostic significance of the mRNAs for OS, and survival curves were compared through the log-rank test. This study met the publication guidelines provided by TCGA.

RT-PCR and immunohistochemistry

The regents used and the detailed procedures of RT-PCR, western blot and IHC were performed as before.[8]

Statistical analysis

The analysis was performed using SPSS version 17.0. The chi-square test or Fisher's exact test was used to evaluate the clinicopathologic parameters. Over-all survival and tumor-free survival rates were calculated with the Kaplan–Meier method, and the statistical difference between survival curves was determined with the log-rank test. Statistical significance was accepted if $p < 0.05$.

Results

Validation of the CDV3 expression and impact of CDV3 expression on survival from the TCGA cohort

We analyzed CDV3 expression and impact of CDV3 expression on survival from the TCGA cohort. By compare 51 cases of normal liver tissues and 270 cases of HCC tissues in TCGA data base, CDV3 expression was significantly increased ($p < 0.001$) in HCC tissues (Fig. 1A). After analyzing 179 patients' survival rate in TCGA, CDV3 was found to be a bad prognostic value (HR = 1.71 and $p = 0.040$) for HCC after surgical resection (Fig. 1B).

CDV3 is up-regulated in HCC tissues

To validate the data of TCGA, we performed RT-PCR and Immunohistochemistry of CDV3 in HCC tissues. The expression of CDV3 in the samples from 50 patients with HCC receiving

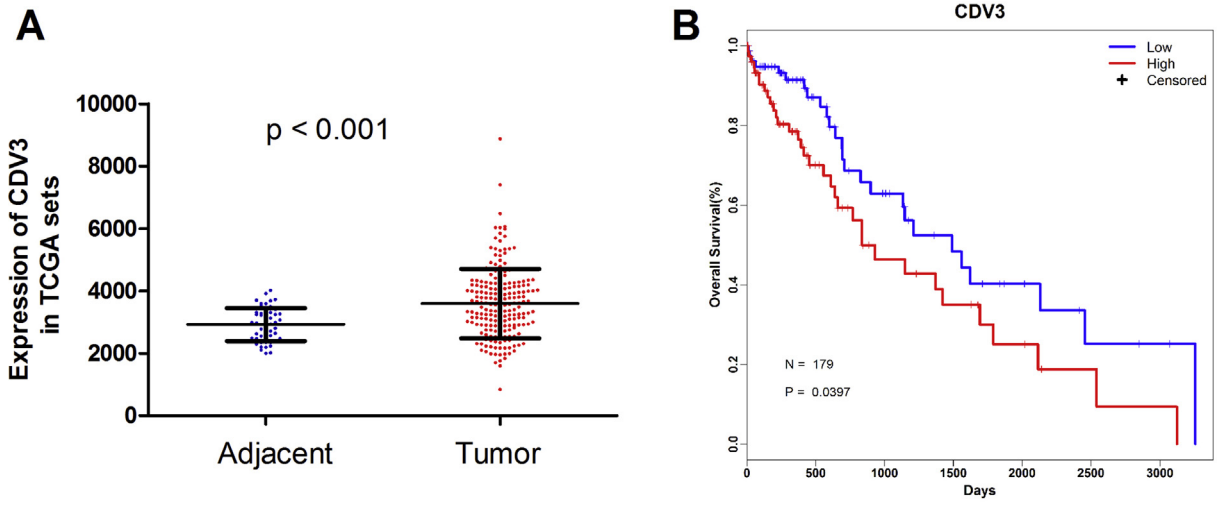

Figure 1 Validation of the CDV3mRNA expression and the impact of CDV3 expression on survival from the TCGA cohort. A. The expression of CDV3 mRNA for 51 cases of normal liver tissues and 270 cases of HCC tissues in TCGA data base. B. Kaplan–Meier survival analysis of overall survival (OS) for CDV3 mRNA.