

Journal: PEERJ

Manuscript number: 70322

Title: Cell division cycle associated 2 (CDCA2) upregulation promotes the progression of hepatocellular carcinoma in a p53-dependant mannar

BASIC REPORTING

This study aims to determine the role of cell division cycle associated 2 (CDCA2) in hepatocellular carcinoma (HCC) and its underlying molecular mechanism. The background is sufficient. The English need some revision. The figures, tables and images are of high quality. It is self-contained with relevant results regarding the hypothesis.

EXPERIMENTAL DESIGN

The expression of CDCA2 in HCC was studied in 40 pairs of frozen and 48 pairs of paraffin-embedded HCC samples and paracancerous normal samples by qRT-PCR and immunohistochemistry, respectively, and using TCGA datasets. The cellular function of CDCA2 was studied in vitro in the HepG2, Huh7 and SK-Hep1 HCC cell lines.

VALIDITY OF THE FINDINGS

This study revealed elevated expression of CDCA2 in HCC, possibly because of p53 dysregulation, which was associated with worse prognosis of patients. They confirmed the oncogenic role of CDCA2 in HCC *in vitro* and revealed some of the underlying molecular mechanisms. This study indicated the potential value of CDCA2 as a future target for the treatment of HCC.

MAJOR

The scientific method is rigorous, the objectives are clear, it is well explained and justified, the experimental procedures are modern and sound, the experimental design is appropriate, replicates were included, they selected appropriate controls, and the results are interesting. The figures and images are of high quality, and they do not seem to be manipulated.

MINOR

1. The title must be corrected to: “Cell division cycle associated 2 (CDCA2) upregulation promotes the progression of hepatocellular carcinoma in a p53-**dependent manner**”
2. In Abstract. Instead of: “...had been demonstrated in several cancer types, however its involvement...” I suggest: “...have been demonstrated in several cancer types, however their involvement...”
3. In Abstract. Instead of: “...and using TCGA datasets.” I suggest: “...and using the Cancer Genome Atlas (TCGA) database.
4. In Introduction, line 72: “We report...”
5. In RNA extraction and real time PCR (qRT-PCR), line 103: “The mRNA expression levels of the target genes were compared by $2^{-\Delta\Delta Ct}$ ” I did not find this result in the Figures or Tables.
6. In line 235: I did not grasp the difference between Figure 1I with Figure 2G. Both seem related to measures of knockdown efficiency.
7. In Discussion, ¿What does OSCC stand for?

8. In Discussion, line 383: omit “were”

9. In Discussion, line 396: “CDCA2 might have a synergetic effect with mut-p53 in 397 inducing EMT and cell migration.” I do not see from what result(s) it is inferred a synergistic effect. Beside mut-p53 was reported for endocrine carcinomas. ¿Can it be extrapolated to hepatocellular carcinoma?