European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences | 2019; 23: 9840-9847

Long noncoding RNA ZFAS1 promotes hepatocellular carcinoma proliferation by epigenetically repressing miR-193a-3p

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Abstract. – OBJECTIVE: Hepatocellular carcinoma (HCC) is one of the most common malignant tumors. Long noncoding RNAs (lncRNAs) play important roles in many diseases. Therefore, the aim of this study was to investigate the role of lncRNA ZFAS1 in th[illegible] development of HCC and to explore its u[illegible]ing mechanism.

PATIENTS AND METHODS: Real Tim[illegible]antitative Polymerase Chain Reaction (RT-[illegible]R) was utilized to detect ZFAS1 expression i[illegible]sue samples of HCC patients. Subsequen[illegible] Cell Counting Kit-8 (CCK-8) ass[illegible]ny formation assay, and EdU incorp[illegible]ay were performed to detect the f[illegible]ction o[illegible]FAS1 in vitro. Furthermore, me[illegible]nism as[illegible]s were performed to explore t[illegible]racti[illegible] ZFAS1 and miR-193a[illegible]p.

RESULTS: ZFAS[illegible]was sig[illegible]tly highly expressed in H[illegible]issues than[illegible]of adjacent normal tis[illegible]he growth ab[illegible]f HCC cells was mar[illegible]ly [illegible]ed after ZFAS[illegible] was silenced. Howe[illegible]r, the g[illegible]ability of HCC cells was rema[illegible]bly promote[illegible] ZFAS1 overexpressio[illegible]oreover, RT-qP[illegible]sults revealed that m[illegible]93a-3p was significantly down-regulate[illegible] the ov[illegible]expression of ZFAS1. However, mi[illegible]-3p [illegible] significantly up-regulated via the k[illegible] of ZFA[illegible] Further experiments showed [illegible]iR-193[illegible]p was a direct target of [illegible]S1 in H[illegible]

[illegible]CLUSIO[illegible]FAS1 could enhance the pro[illegible]ation of H[illegible]C cells by suppressing miR-193[illegible]p, which might be a potential therapeutic ta[illegible]

[illegible]Words:
[illegible] noncoding RNA, ZFAS1, Hepatocellular carcino[illegible]C), MiR-193a-3p.

Introduction

[illegible]epatocellula[illegible]rcinoma (HCC) is one of the co[illegible]n prima[illegible]iver cancers, which accounts for [illegible]eading cause of cancer-related deaths[1]. HCC is defined as a primary tumori[illegible]esis in the liver. Meanwhile, it mainly occurs [illegible] suffering from chronic liver cirrho[illegible] o[illegible]patitis B or C. Currently, HCC–related mortality is significantly higher in developing countries, especially in China, where hepatitis B virus (HBV) is particularly prevalent among people[2,3]. During the past several years, therapeutic advances have been achieved in HCC prevention and management. However, the prognosis of patients with HCC remains poor. Approximately 600,000 patients die of HCC annually[4], with 5-year overall survival rate lower than 20%[5,6]. Therefore, it is urgent to understand the underlying molecular mechanism of HCC and improve the prognosis of HCC patients.

Long noncoding RNAs (lncRNAs) are known as transcripts longer than 200 nt, with no protein-coding function. Some studies[7] have uncovered the vital role of lncRNAs in the regulation of cellular biological processes. For instance, lncRNA LINC00261 promotes the migration of gastric cancer cells by regulation of epithelial-mesenchymal transition. The knockdown of lncRNA MALAT1 remarkably suppresses cell viability and mobility in renal cell cancer *via* activating the PI3K/Akt signaling pathway[8]. In addition, significantly inhibited cell migration can be observed by the knockdown of lncRNA MALAT1 in esophageal squamous cell carcinoma[9].

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MicroRNAs (miRNAs) are another type of non-coding RNAs with 19–22 nucleotide in length. Previous studies[10] have reported that miRNAs participate in numerous biological progressions in many diseases, including cancers. For example, miR-219-5p suppresses cell growth and migration in malignant melanoma through targeting BCL-2. Overexpression of miRNA-370 promotes the proliferation of human prostate cancer cells through the down-regulation of FOXO1[11]. Furthermore, miRNA-613 functions as a tumor suppressor in the progression of colorectal cancer by targeting FMNL2[12].

LncRNA ZFAS1 plays an important role in tumor biology and development. However, the exact function of lncRNA ZFAS1 in HCC and the potential molecular mechanism have not been fully elucidated.

Patients and Methods

Tissue Samples

A total of 60 cancer tissues and paired ad[illegible] normal tissues were obtained from HCC [illegible] who underwent surgery at Jining No.1 [illegible]le's Hospital. All fresh tissues collected from s[illegible]y were stored immediately at –80°C for use. [illegible] investigation was approved by the Ethics Co[illegible]mittee of Jining No.1 People'[illegible]. Signe[illegible] written informed consents w[illegible] obta[illegible] from all participants before the stu[illegible]

Cell Culture

Human HCC cel[illegible]es (Bel-[illegible]nd HepG2) and normal liver [illegible]thelial cell l[illegible]2) were purchased from [illegible]erican Type C[illegible]re Collection (ATC[illegible] Man[illegible] VA, USA). All cells were cultured in Dulbe[illegible] Modified Eagle's Medium [illegible]MEM; Gibco, R[illegible]lle, MD, USA) consisti[illegible] of 10% fetal bovine s[illegible]rum (FBS; Gibco, R[illegible]ville, M[illegible]D, USA) and penicillin/streptomy[illegible]side[illegible]he cells were maintained in an incuba[illegible]ining 5% [illegible]O_2 at 37°C.

Ce[illegible]ansfecti[illegible]

T[illegible] cDNA oligonucleotides specifically targe[illegible]h-ZFAS1) and lentivirus against [illegible]ynthesized by GenePharma (Shang[illegible] China). Subsequently, they were cloned into a [illegible]-EF1a-EGFP-F2A-Puro vector (Biosettia Inc., [illegible] Diego, CA, USA). After that, sh-ZFAS1 and ZFAS1 lentivirus were transfected into Bel-7402 and HepG2 HCC cells accord[illegible] instructions of Lipofectamine 200[illegible]nvitroge[illegible] Carlsbad, CA, USA), respectively[illegible] h later, Real Time-quantitative Polymera[illegible]ain Reaction (RT-qPCR) was used to verify [illegible]nsfection efficiency.

RNA Extraction an[illegible]T-qPCR

TRIzol reagent [illegible]itrogen[illegible]Carlsbad, CA, USA) was utilized [illegible]pa[illegible] total R[illegible]A in tissues and cel[illegible] Sub[illegible]ly, the [illegible]racted RNA was reve[illegible]ly transcr[illegible]to [illegible]plementary deoxyr[illegible]e nucleic aci[illegible]) through the revers[illegible]iption Kit (Ta[illegible]Ra Biotechnology [illegible]., Ltd[illegible]lian, China). The primer sequences used for [illegible]PCR were as follows: ZFA[illegible]imers forwar[illegible]CTATTGTCCTGC-C[illegible]GAG-3′, reverse: 5′-GTCAGGAGATC-[illegible]AGGTTGTAG-3′; Glyceraldehyde 3-phos[illegible]ate dehydrog[illegible]e (GAPDH) primers forward: [illegible]CAAAATC[illegible]ATGGGGCAATGCTGG-3′ a[illegible]verse 5′[illegible]GATGGCATGGACTGTGGT-CA[illegible] thermal cycle was as follows: pre-dena[illegible]on at 95°C for 1 min, followed by [illegible] cycles at 95°C for 15 s, 60°C for 30 s, and 72°C

Cell Counting Kit-8 (CCK-8) Assay

The proliferation of HCC cells in 96-well plates was monitored every 24 h by the CCK-8 assay (Dojindo Molecular Technologies, Inc., Kumamoto, Japan). The absorbance at 450 nm was detected by a spectrophotometer (Thermo Fisher Scientific, Rockford, IL, USA).

Colony Formation Assay

HCC cells were first seeded into 6-well plates for 10 days. After that, formed colonies were fixed with 10% formaldehyde for 30 min and stained with 0.5% crystal violet for 5 min. Image-Pro Plus 6.0 (Silver Spring, MD, USA) was used for data analysis.

Ethynyl Deoxyuridine (EdU) Incorporation Assay

According to the manufacturer's protocol, the EdU Kit (Roche, Mannheim, Germany) was utilized to monitor the proliferation of transfected cells. Zeiss Axiophot Photomicroscope (Carl Zeiss, Oberkochen, Germany) was performed to capture representative images.

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Luciferase Reporter Gene Assay

The Luciferase reporter gene assay kit (Promega, Madison, WI, USA) was used to detect the luciferase activity of HCC cells. Briefly, the 3′-UTR of ZFAS1 cloned into the pGL3 vector (Promega, Madison, WI, USA) was identified as wild-type (WT) 3′-UTR. QuickChange Site-Directed Mutagenesis kit (Stratagene, La Jolla, CA, USA) was used for site-directed mutagenesis of the miR-193a-3p binding site in ZFAS1 3′-UTR, which was named as mutant (MUT) 3′-UTR. Then, the cells were transfected with WT-3′-UTR or MUT-3′-UTR and miR-ctrl or miR-193a-3p for 48 h, respectively. Finally, the luciferase assay was conducted on the dual Luciferase reporter assay system (Promega, Madison, WI, USA).

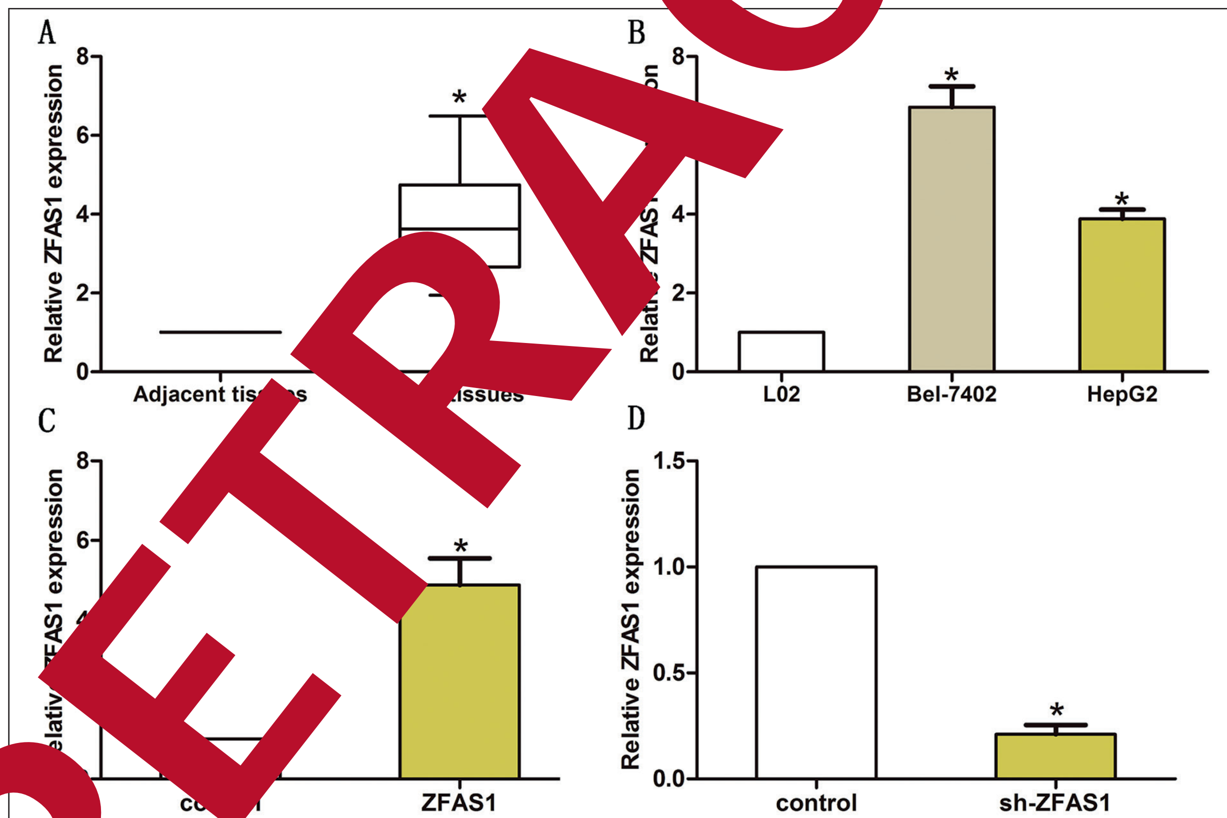
Statistical Analysis

Statistical Product and Service Solutions (SPSS) 20.0 (SPSS, Chicago, IL, USA) was used for all statistical analysis. Independent-sample *t*-test was selected when appropriate. [illegible] considered statistically significant. [illegible]

Results

ZFAS1 Expression Le[illegible] in HCC [illegible] and Cells

First, the ZFAS1 [illegible]pression [illegible] 60 HCC patients' tissues and 2 [illegible]ell[illegible]es was [illegible]tected *via* RT-qPCR. [illegible]sults [illegible] that Z[illegible]1 was significantly [illegible]egulated [illegible]C [illegible]ue samples compar[illegible] that of adja[illegible]mal tissues (Figure 1[illegible]). [illegible]while, ZFAS1 [illegible]pression was significa[illegible]y hig[illegible] HCC cells than in L02 cells (Figure 1B). In [illegible]tudy, the HepG2 and Bel[illegible]ell lines we[illegible]sen for overexpres[illegible] [illegible] knockdown of ZFAS1, respectively. The [illegible]nsfection efficiency was confirmed by RT-qP[illegible] (Figure 1C [illegible] 1D).



Fig[illegible]on level of ZFAS1 was significantly up-regulated in HCC tissues and cell lines. **A,** ZFAS1 expression in[illegible]ntly in HCC tissues compared with adjacent tissues. **B,** Expression level of ZFAS1 relative to GAPDH in [illegible]an HCC cell lines and L02 (normal liver epithelial cell) was determined by RT-qPCR. **C,** ZFAS1 expression in HepG2 H[illegible]lls transfected with ZFAS1 lentivirus and control vector was detected by RT-qPCR. **D,** ZFAS1 expression in Bel-7402 H[illegible] transfected with sh-ZFAS1 and control vector was detected by RT-qPCR. GAPDH was used as an internal control. Data w[illegible] presented as mean ± standard error of the mean. *p<0.05.

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Overexpression of ZFAS1 Promoted Proliferation of HepG2 HCC Cells

The results of the CCK8 assay showed that overexpression of ZFAS1 significantly enhanced the growth ability of HepG2 cells (Figure 2A). The colony formation assay also revealed that the number of formed colonies increased remarkably after ZFAS1 was overexpressed in HepG2 cells (Figure 2B). Moreover, the results of EdU incorporation assay demonstrated that the percentage of EdU positive cell... significantly after overexpression ... ZFAS1 ... HepG2 cells (Figure 2C).

Silence of ZFAS1 Suppresse... Proliferation of Bel-74... HCC ...

The results of the CC...8 assay sho... silence of ZFAS1 si...ficantly inhibite...

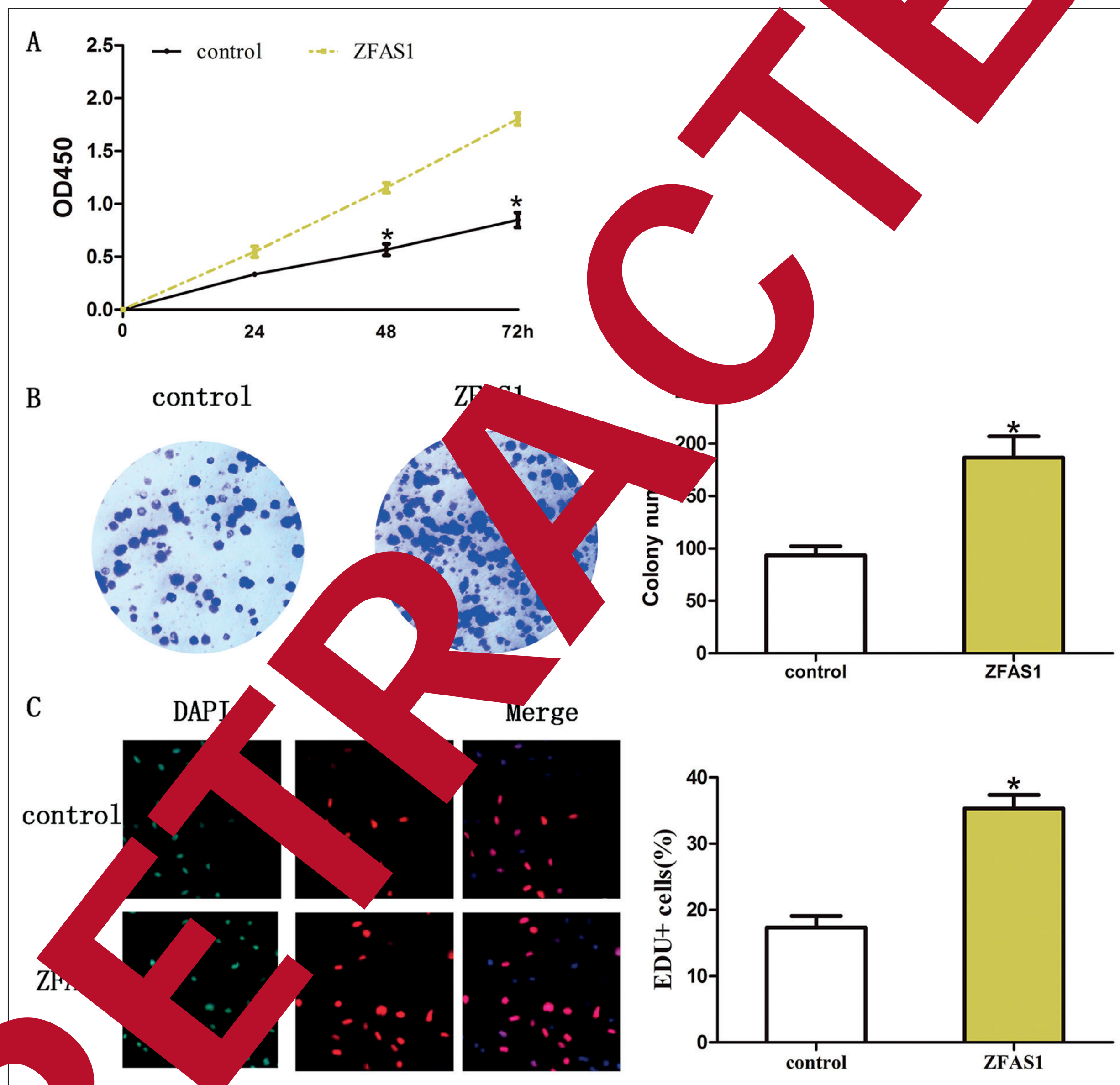

Fig... ession of ZFAS1 promoted HepG2 HCC cell proliferation. **A,** CCK8 assay showed that overexpression of ZF... y enhanced the proliferation in HepG2 HCC cells. **B,** Colony formation assay showed that the number of ...nies increased significantly *via* overexpression of ZFAS1 in HepG2 HCC cells (magnification ×40). **C,** EdU incorporation ...howed that the number of EdU positive cells increased significantly *via* overexpression of ZFAS1 in HepG2 HCC cells (m...tion ×20). The results represented the average of three independent experiments (mean ± standard error of the mean)... <0.05, as compared with control cells.

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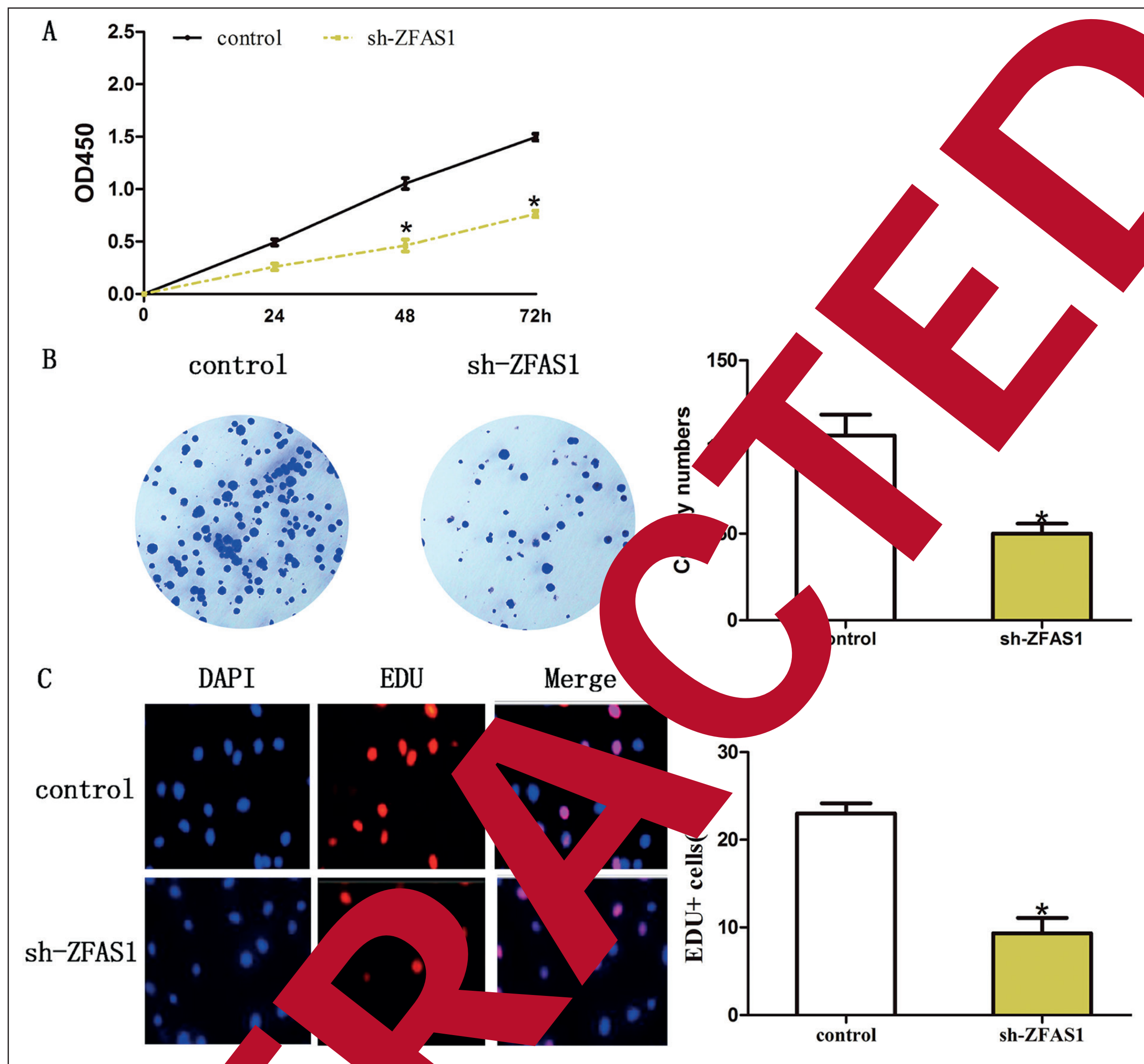


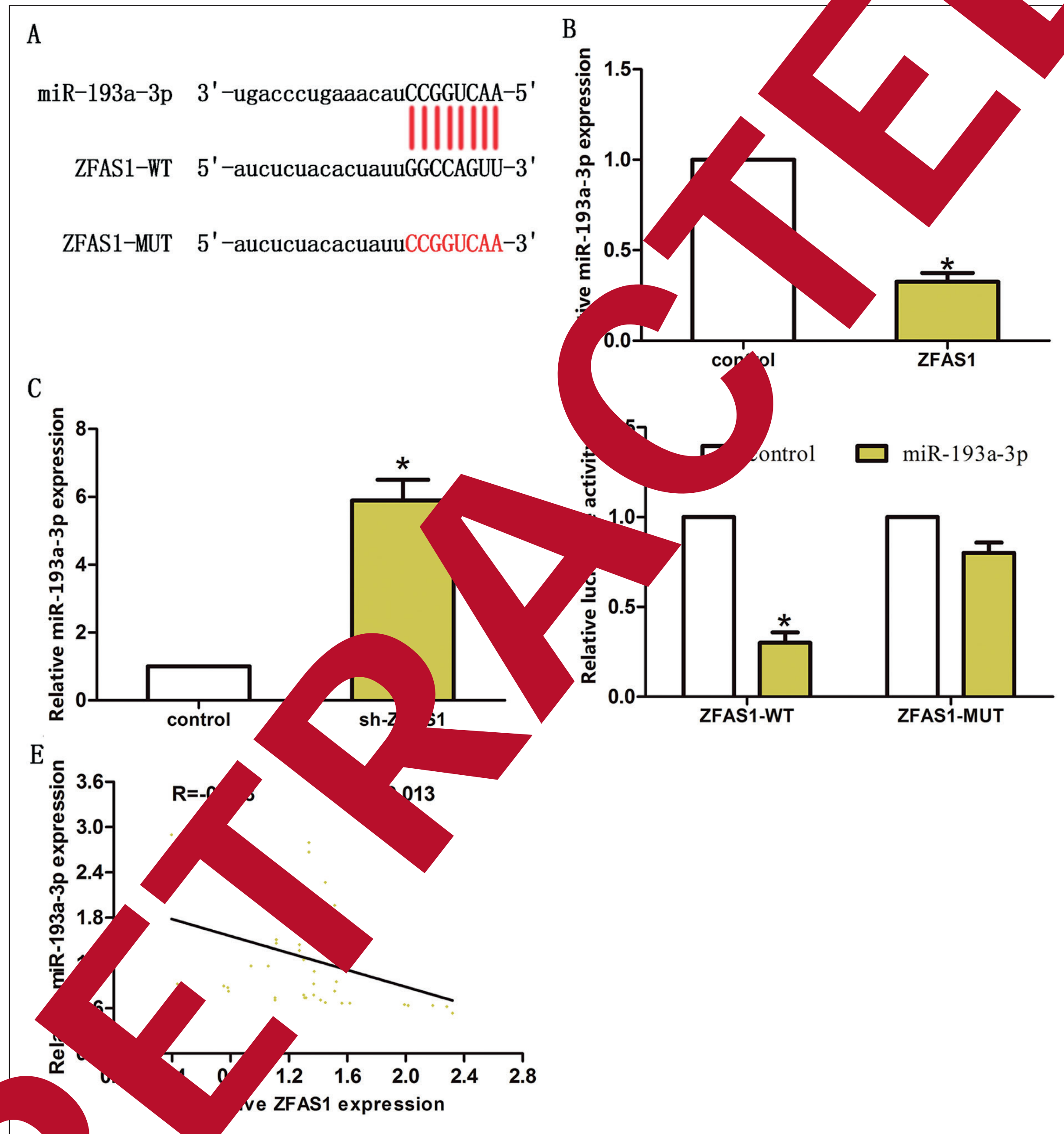
Figure 3. Knockd[illegible]FAS1 inhibited B[illegible] HCC cell proliferation. **A,** CCK8 assay showed that the silence of ZFAS1 significantly repr[illegible] t[illegible]feration of Bel-7[illegible]2 HCC cells. **B,** Colony formation assay showed that the number of colonies decreased remar[illegible]ly *via* s[illegible]f ZFAS1 in Bel-7402 HCC cells (magnification ×40). **C,** EdU incorporation assay showed that the num[illegible]r of EdU positi[illegible] decreased significantly *via* silence of ZFAS1 in Bel-7402 HCC cells (magnification ×40). The r[illegible]s represented the a[illegible] of three independent experiments (mean ± standard error of the mean). $*p<0.05$, as compare[illegible]h control cells.

growth a[illegible] of B[illegible]402 cells (Figure 3A). [illegible]olony [illegible] assay indicated that the nu[illegible] of form[illegible]olonies was remarkably reduc[illegible] after ZFAS1 was silenced in Bel-7402 cel[illegible]3B). Furthermore, the results of [illegible] incorp[illegible]ation assay illustrated that the per[illegible]age of EdU positive cells was remarkably r[illegible] after the silence of ZFAS1 in Bel-7402 cells [illegible]gure 3C).

Interaction Between MiR-193a-3p and ZFAS1 in HCC

DIANA LncBASE Predicted v.2 (http://carolina.imis.athena-innovation.gr/diana_tools/web/index.php?r=lncbasev2%2Findex-predicted) was used to search for miRNAs that contained complementary base with ZFAS1. MiR-193a-3p is a tumor suppressor gene that has been found to suppress cancer cell proliferation. Therefore,

among these miRNAs, we focused on miR-193a-3p which was interacted with ZFAS1 (Figure 4A). Indeed, the RT-qPCR assay showed that the expression of miR-193a-3p was significantly lower in ZFAS1 lentivirus cells than in control cells (Figure 4B). However, the expression of miR-193a-3p was markedly higher in [illegible] cells than in control cells (Figure [illegible]). Luciferase reporter gene assay revealed that co-transfection of ZFAS1-WT and mi[illegible]a-3p largely



Fig[illegible]al repression between ZFAS1 and miR-193a-3p. **A,** Binding sites of miR-193a-3p on ZFAS1. **B,** MiR-[illegible] decreased in ZFAS1 lentivirus group compared with control group. **C,** MiR-193a-3p expression increased [illegible]-ZFAS1 group compared with control group. **D,** Co-transfection of miR-193a-3p and ZFAS1-WT strongly decreased [illegible]se activity, while co-transfection of miR-193a-3p and ZFAS1-MUT did not change luciferase activity. **E,** Linear co[illegible] between the expression level of miR-193a-3p and ZFAS1 in HCC tissues. The results represented the average of three [illegible]pendent experiments Data were presented as the mean ± standard error of the mean. *p<0.05.

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decreased the luciferase activity (Figure 4D). Furthermore, correlation analysis demonstrated that miR-193a-3p expression was negatively correlated with ZFAS1 expression in HCC tissues (Figure 4E).

Discussion

In the past decades, the morbidity and mortality of HCC have been increasing worldwide, especially in developing countries. Hepatocarcinogenesis is a complex process, which is associated with the accumulation of genetic and epigenetic changes during the HCC progression. Currently, lncRNAs have been shown as important regulators of HCC. For example, through the regulation of miR-202-5p, lncRNA NORAD enhances the progression of HCC *via* the modulation of TGF-beta pathway[13]. The down-regulation of lncRNA P7 facilitates the proliferation of HCC cells through the modulation of the STAT1-MAPK signal pathway. Meanwhile, it is associated with unfavorable prognosis of HCC patients[14]. As a sponge of miR-149, lncRNA SNHG8 enhances tumorigenesis and metastasis in HCC[15].

LncRNA ZFAS1 (LncRNA ZNFX1 antisense RNA 1), located on the chromosome 20q[illegible]3, has been found involved in the progression of many diseases. Gao et al[16] have indicated that ZFAS1 participates in the development of [illegible]ogenesis. For instance, ZFAS1 promotes the proliferation of glioma cells through the activation of the Notch signaling pathway. ZFAS1 is [illegible] in gastric cancer and can [illegible] epithelial-mesenchymal transition *in vitro*[17]. ZFAS1 enhances the malignancy of ovarian cancer by regulating Sp1[18]. In this study, we found that ZFAS1 was significantly up-regulated in HCC tissues and cell lines. Besides, the silence of ZFAS1 significantly repressed the proliferation of HCC cells, while the overexpression of ZFAS1 promoted the proliferation of HCC cells. The above results indicated that ZFAS1 promoted the proliferation of HCC and might [illegible] as an oncogene.

Recently, [illegible] et al [illegible] have revealed that lncRNAs interact with microRNAs in many diseases. Meanwhile, microRNAs expression can be activated by lncRNAs. For example, the silence of [illegible] inhibits cell growth and migration in [illegible]blastoma through the inhibition of miR-5095. Knockdown of lncRNA TUG1 depresses the proliferation and invasion of osteosarcoma cells *via* sponging miR-153[20]. Furthermore, lncRNA SPRY4-IT1 functions as an oncogene in bladder cancer through the up-regulation of [illegible] sponging miR-101-3p[21].

Numerous microRNAs have been reported as dysregulated in various types of cancer. Recent studies have suggested that miR-193a-3p functions as a tumor suppressor in multiple malignant tumors. For example, miR-193a-3p serves as a tumor suppressor in lung cancer and inhibits the development of lung cancer *via* targeting KRAS. The proliferation and metastasis of renal cell carcinoma are regulated by miR-193a-3p[illegible]. MiR-193a-3p suppresses the progression of [illegible]ogenesis in colorectal cancer by targeting KRAS[24]. In the present study, the potential interaction between miR-193a-3p and ZFAS1 was predicted through the bioinformatics software. Subsequent experiments showed that miR-193a-3p could directly bind to ZFAS1 through the luciferase reporter gene assay. In addition, miR-193a-3p expression was significantly suppressed by the up-regulation of ZFAS1. However, the downregulated ZFAS1 expression could induce a reverse outcome. Furthermore, the expression of miR-193a-3p was negatively correlated with ZFAS1 in HCC tissues. All these results indicated that ZFAS1 might [illegible] tumorigenesis of HCC through directly targeting miR-193a-3p.

Conclusions

In sum, ZFAS1 was remarkably up-regulated in HCC tissues. Furthermore, it could facilitate cell proliferation in HCC by targeting miR-193a-3p. These findings suggested that ZFAS1 might contribute to therapy for HCC as a prospective target.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87-108.
2) Liu ZH, Zhang YF, Xu ZD. UNC119 promoted cell growth and migration by Wnt/ β-catenin signal and TGF- β /EMT signal pathway in hepatocellular carcinoma. J BUON 2018; 23: 1717-1724.

3) Liu B, Yang XF, Liang XP, Wang L, Shao MM, Han WX, Wu YH. Expressions of MiR-132 in patients with chronic hepatitis B, posthepatitic cirrhosis and hepatitis B virus-related hepatocellular carcinoma. Eur Rev Med Pharmacol Sci 2018; 22: 8431-8437.
4) Maluccio M, Covey A. Recent progress in understanding, diagnosing, and treating hepatocellular carcinoma. CA Cancer J Clin 2012; 62: 394-399.
5) Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin 2018; 68: 7-30.
6) Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang XS, Bannon F, Ahn JV, Johnson CJ, Bonaventure A, Marcos-Gragera R, Stiller C, Azevedo e Silva G, Chen WQ, Ogunbiyi OJ, Rachet B, Soeberg MJ, You H, Matsuda T, Bielska-Lasota M, Storm H, Tucker TC, Coleman MP; CONCORD Working Group. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet 2015; 385: 977-1010.
7) Fan Y, Wang YF, Su HF, Fang N, Zou C, Li WF, Fei ZH. Decreased expression of the long noncoding RNA LINC00261 indicate poor prognosis in gastric cancer and suppress gastric cancer metastasis by affecting the epithelial-mesenchymal transition. J Hematol Oncol 2016; 9: 57.
8) Li Z, Ma Z, Xu X. Long noncoding RNA [illegible] correlates with cell viability and mobility [illegible]rget[illegible]ing miR223p in renal cell carcinoma via t[illegible]3K/Akt pathway. Oncol Rep 2019; 41: 1113-11[illegible]
9) Wang X, Li M, Wang Z, Han S, Tang X, Ge Y, [illegible] L, Zhou C, Yuan Q, Yang M. Silencing of long n[illegible] coding RNA MALAT1 by mi[illegible]d miR-2[illegible] inhibits proliferation, migra[illegible]vasion o[illegible] esophageal squamous c[illegible]arcinom[illegible]lls. J Biol Chem 2015; 290: 39[illegible]935.
10) Long J, Menggen Q, Wu[illegible]i Q[illegible] 5p inhibits the gro[illegible]th a[illegible]sis o[illegible]g-nant melanoma [illegible]rgeting [illegible] Biomed Res Int 2017; 2017: [illegible]2502.
11) Wu Z, Sun [illegible]W, He J, Mao [illegible]regulation of Mic[illegible]NA[illegible]duces proliferation in human prost[illegible]e cance[illegible]y downregulating the transc[illegible]tion factor FO[illegible]LoS One 2012; 7: e458[illegible]
12) Li [illegible]e Z, Li Z, Chen S, Li B. MicroRNA-613 targets [illegible]L2 and s[illegible]ppresses progression of colorectal [illegible]er. Am[illegible]ransl Res 2016; 8: 5475-5484.
13) Y[illegible]B, Peng [illegible]ei CY, Lu JC, Gao C, Shen ZZ, [illegible]F, Hua[illegible]Y, Ke AW, Shi GM, Fan J. The lon[illegible]di[illegible]RNA NORAD enhances the [illegible]F-β pat[illegible] promote hepatocellular car[illegible]oma progr[illegible]ion by targeting miR-202-5p. J [illegible]l Physiol 2019; 234: 12051-12060.
14) [illegible], Wang C, Wang K, Lai C, Yan J, Fan H, Sun [illegible]Wang Z, Zhang P, Yu L, Hong Z, Lei G, Sun B, Gao Y, Xiao Z, Ji X, Wang R, Wu J, Wang X, Zhang S, Yang P. Decreased long inte[illegible] coding RNA P7 predicts unfavora[illegible] and promotes tumor proliferati[illegible]a the modulation of the STAT1-MAPK p[illegible]ay in hepatocellular carcinoma. Oncotar[illegible]18; 9: 36057-36066.
15) Dong J, Teng F, Guo W, [illegible]g J, Di[illegible]Z. LncRNA SNHG8 promot[illegible]he tumorig[illegible]an[illegible] metastasis by spong[illegible]miR-149-5p and [illegible] tumor recurrence [illegible]hepatocellular carci[illegible]a. Cell Physiol Bioc[illegible]2018; 5[illegible]262-2274.
16) Gao K, Ji Z, She K, [illegible] L. Long[illegible]-coding RNA ZF[illegible] is a[illegible]vourable[illegible]gnostic factor and[illegible]motes gli[illegible] pr[illegible]ession by activatio[illegible]he Notch signa[illegible]way. Biomed Pharm[illegible]2017; 87: 555-56[illegible]
17) Zho[illegible] Wan[illegible] H, Tan Q, Qiu S, Chen S, Jing W, Yu M, Liang C[illegible]Tu J. Increased expression of long-noncoding [illegible]FAS1 is associated with [illegible]ial-mesenchyma[illegible]nsition of gastric cancer. Aging (Albany NY) 2016; 8: 2023-2038.
18) Xia B, Hou Y, Chen H, Yang S, Liu T, Lin M, Lou G. Long non-co[illegible] RNA ZFAS1 interacts with miR-150-5p to re[illegible]ate Sp1 expression and ovari[illegible] cancer ce[illegible]alignancy. Oncotarget 2017; 8: [illegible]1954[illegible]
19) Ren[illegible], Xue J, Xi Z, Hu L, Pan SJ, Sun Q. Long noncoding RNA SNHG7 promotes the progres[illegible]ion and growth of glioblastoma via inhibition of [illegible]95. Biochem Biophys Res Commun 2018; 4[illegible]712-718.
20) Wang H, Yu Y, Fan S, Luo L. Knockdown of long noncoding RNA TUG1 inhibits the proliferation and cellular invasion of osteosarcoma cells by sponging miR-153. Oncol Res 2018; 26: 665-673.
21) Liu D, Li Y, Luo G, Xiao X, Tao D, Wu X, Wang M, Huang C, Wang L, Zeng F, Jiang G. LncRNA SPRY4-IT1 sponges miR-101-3p to promote proliferation and metastasis of bladder cancer cells through up-regulating EZH2. Cancer Lett 2017; 388: 281-291.
22) Fan Q, Hu X, Zhang H, Wang S, Zhang H, You C, Zhang CY, Liang H, Chen X, Ba Y. MiR-193a-3p is an important tumour suppressor in lung cancer and directly targets KRAS. Cell Physiol Biochem 2017; 44: 1311-1324.
23) Liu L, Li Y, Liu S, Duan Q, Chen L, Wu T, Qian H, Yang S, Xin D. Downregulation of miR-193a-3p inhibits cell growth and migration in renal cell carcinoma by targeting PTEN. Tumour Biol 2017; 39: 1010428317711951.
24) Mamoori A, Wahab R, Islam F, Lee K, Vider J, Lu CT, Gopalan V, Lam AK. Clinical and biological significance of miR-193a-3p targeted KRAS in colorectal cancer pathogenesis. Hum Pathol 2018; 71: 145-156.

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