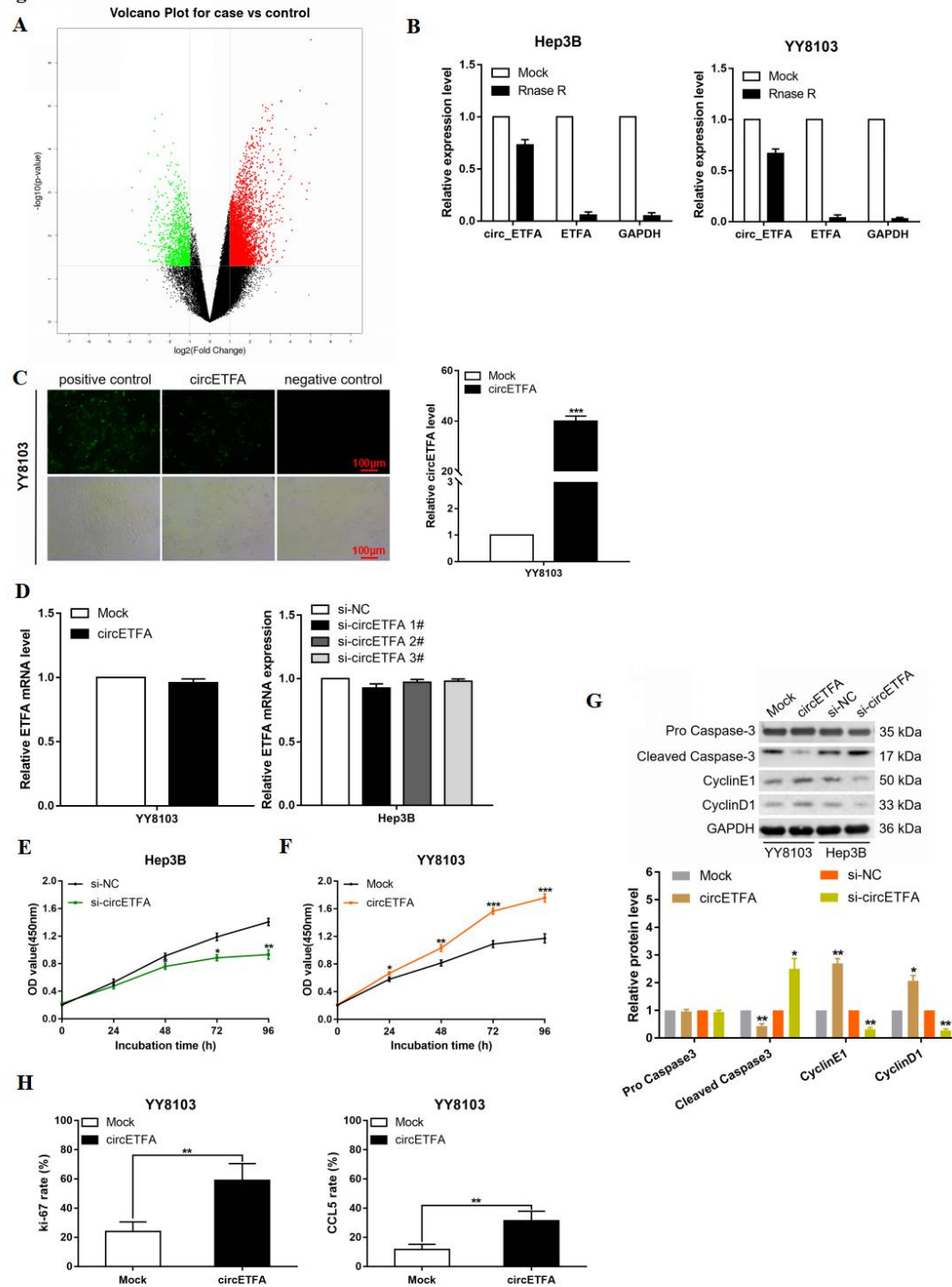


## Supplemental Material

**Figure S1**



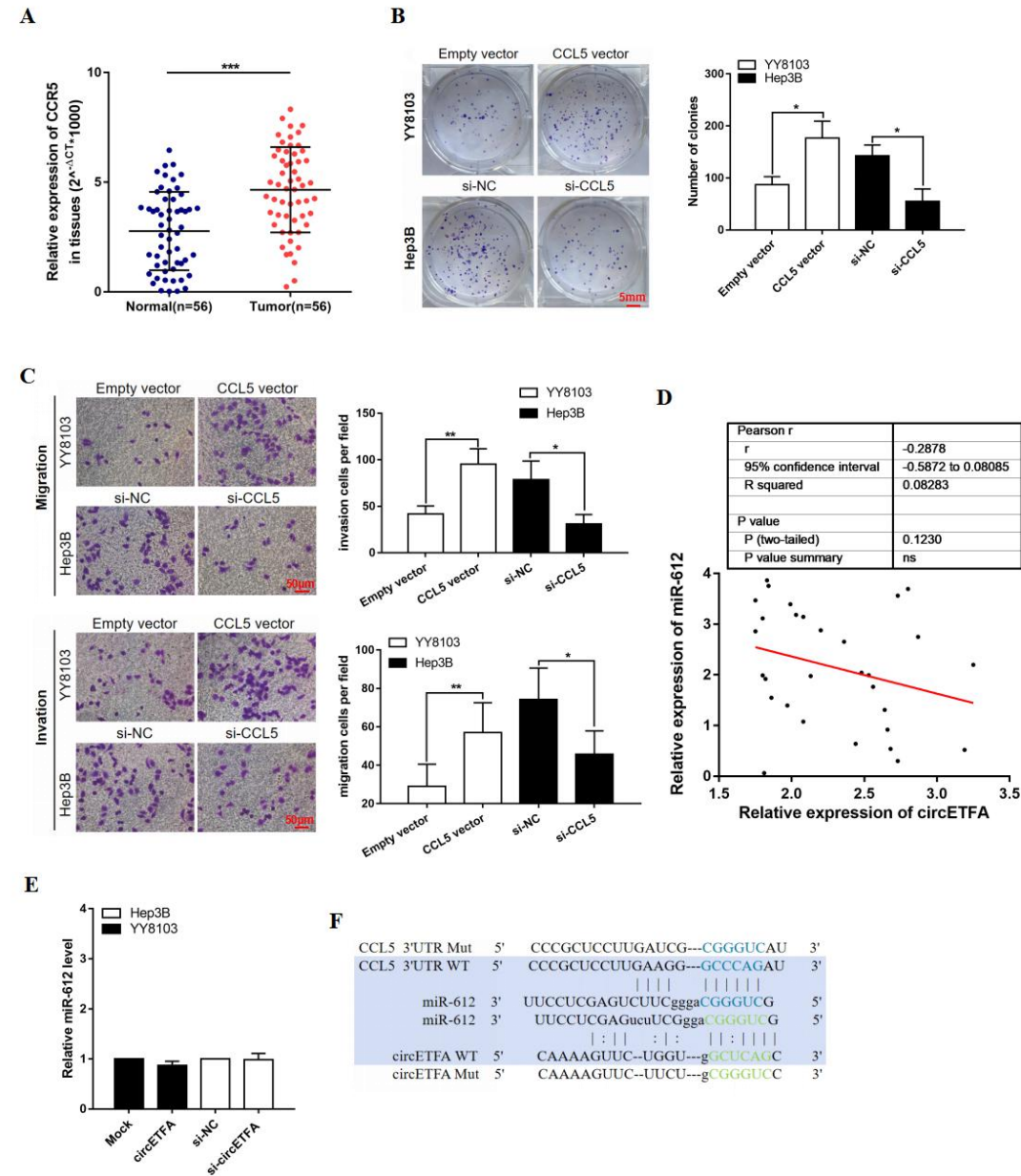
**Figure S1. Identification and characterization of circETFA.**

(A) The volcano plot showed that the circRNAs were significantly upregulated and downregulated. (B) RNase R tolerance tests excluded trans-splicing and genome rearrangements. (C) The lentivirus infection system was used to establish a YY8103

cell line stably overexpressing circETFA. (D) Overexpression or knockdown of circETFA had no effect on linear mRNA expression. (E-F) CCK-8 detection on cell proliferation after overexpression or knockdown of circETFA. (G) Western blot analysis of apoptosis- and cell-cycle-related proteins in YY8103 and Hep3B that knocking down or overexpressing circETFA. (H) The positivity rates of Ki-67 and CCL5 in the immunohistochemistry of subcutaneous tumor formation. Data are shown as the mean  $\pm$  SD. \* $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$

CircRNA, circular RNA; CCL5, C-C motif chemokine ligand 5; CCK-8, Cell Counting Kit-8

**Figure S2**



**Figure S2. Effect of CCL5 on proliferation and invasion in vitro.**

(A) CCR5 expression in HCC tissues. (B) Clone formation experiments showed that CCL5 promoted proliferation. (C) Transwell experiments showed that CCL5 promoted invasion and migration. (D) Correlation between circETFA and miR-612 in HCC tissues. (E) The expression of hsa-mir-612 was detected in HCC cells overexpressing or knocking down circETFA. (F) Wild-type and mutant

circETFA/CCL5 fragments of the 3'-UTR luciferase reporter gene were constructed.

Data are shown as the mean  $\pm$  SD. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$

CCL5, C-C motif chemokine ligand 5; HCC, hepatocellular carcinoma; UTR, untranslated region

Figure S3

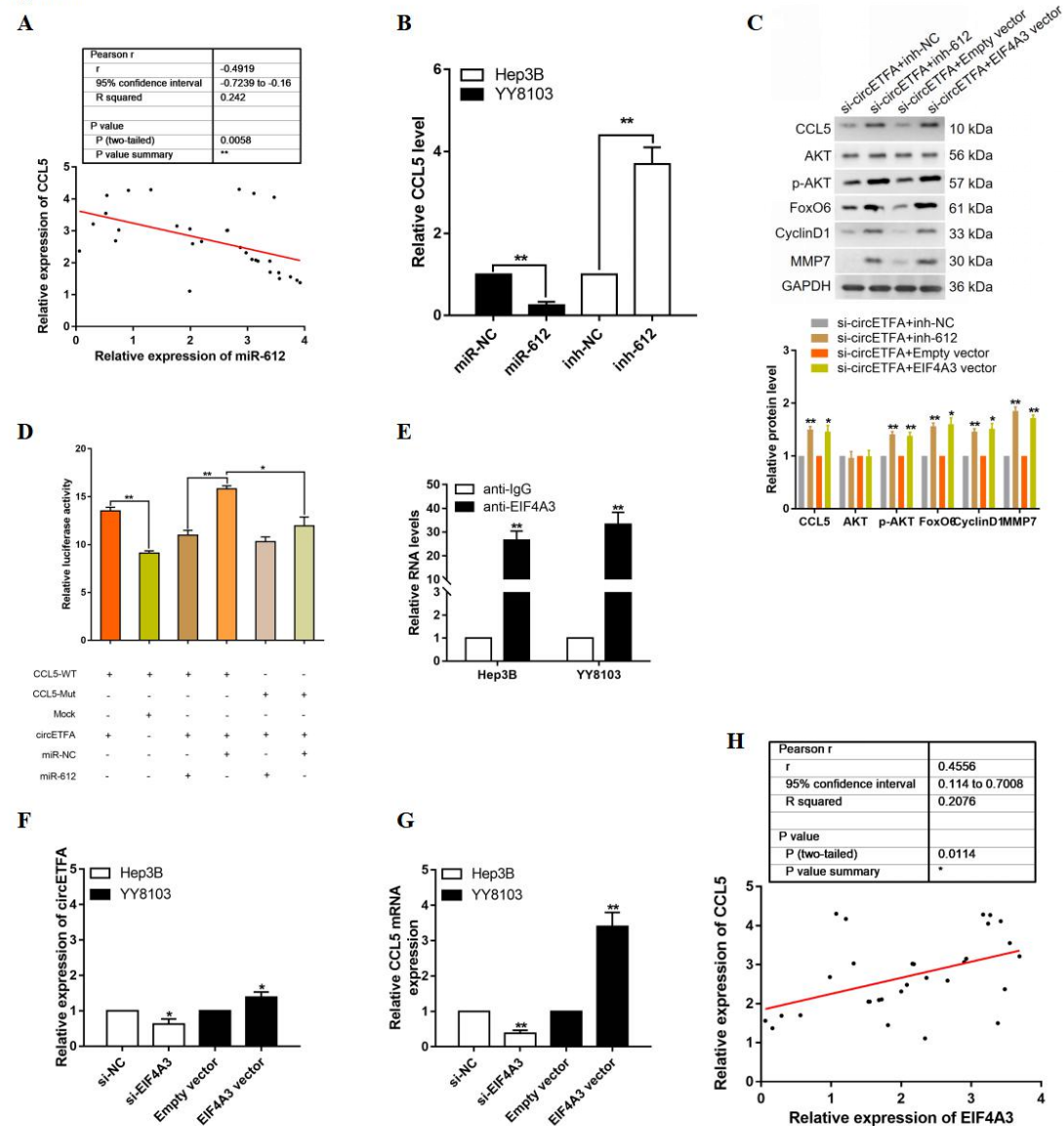


Figure S3. Correlation between circETFA and key molecules in HCC.

(A) The correlation between miR-612 and CCL5 in HCC tissues. (B) CCL5 expression in HCC cell treated with miR-612 mimics or inhibitors. (C)

Co-transfection partially rescued the expression of CCL5. (D) Luciferase reporter gene experiment among circETFA, miR-612, and CCL5. (E) RIP experiments for EIF4A3 were performed and co-predicted RNA was detected by qRT-PCR. The fold enrichment of circETFA in the Hep3B and YY8103 cells was matched using IgG as a control. (F-G) The effect of EIF4A3 on the expression of circETFA and CCL5. (H) Correlation between EIF4A3 and CCL5 in HCC organization. The data are shown as mean  $\pm$  SD. \* $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$

HCC, hepatocellular carcinoma; CCL5, C-C motif chemokine ligand 5; EIF4A3, eukaryotic initiation factor 4A3; qRT-PCR, quantitative reverse transcription-polymerase chain reaction

**Supplementary Table S1 (Excel)**

**Supplementary Table S2 (Excel)**

**Supplementary Table S3 (Excel)**

**Supplementary Table S4**

|                                                                |                                                                      |
|----------------------------------------------------------------|----------------------------------------------------------------------|
| CircRNA ID                                                     | hsa_circ_0036412                                                     |
| Genomic Length                                                 | 3119 bp                                                              |
| Best Transcript                                                | NM_000126 Primers                                                    |
| Samples                                                        | Ag04450, Bj, Gm12878, H1hesc, Helas3, Hepg2, Huvec, K562, Mcf7, Nhek |
| GenomicSeq                                                     | hsa_circ_0036412                                                     |
| RNA-binding protein sites matching to circRNAs                 |                                                                      |
| RNA-binding protein sites matching flanking regions of circRNA |                                                                      |
| RNA-binding Protein                                            | # Tags                                                               |
| AGO2                                                           | 2                                                                    |
| C22ORF28                                                       | 1                                                                    |
| DGCR8                                                          | 1                                                                    |
| EIF4A3                                                         | 5                                                                    |
| FMRP                                                           | 2                                                                    |
| FUS                                                            | 1                                                                    |
| FXR2                                                           | 1                                                                    |

|         |   |
|---------|---|
| HuR     | 3 |
| IGF2BP1 | 1 |
| IGF2BP2 | 1 |
| IGF2BP3 | 1 |
| PTB     | 1 |
| TDP43   | 1 |
| ZC3H7B  | 2 |

**Supplementary Table S5**

| <b>Primers</b>        |                           |
|-----------------------|---------------------------|
| hsa_circ_0036412 F    | ACTTCCAGGCCTCATTGCTAC     |
| hsa_circ_0036412 R    | CGTGTGGCTGCAGTAATGGT      |
| hsa_circ_0036411 F    | AGCATGATGTGTACAAAGGCCTAC  |
| hsa_circ_0036411 R    | CTTTTGCTATGCCTGCTACTTTACA |
| hsa_circ_0036409 F    | ACACATCTGTGCTGGAGCATCT    |
| hsa_circ_0036409 R    | TGCTTCTGAGTTGCCAAAATCAA   |
| hsa_circ_0003620 F    | TCGGAAAGGCCTCATTGCTAC     |
| hsa_circ_0003620 R    | TAAGCAGGACACTTCACCTCCA    |
| hsa_circ_0028071 F    | TTCTATGACCCTGACACCAGCA    |
| hsa_circ_0028071 R    | GGCTTCCCCTGTTCCACATT      |
| hsa_circ_0000437 F    | AGATTGCCAGAAAAATATGCAGGA  |
| hsa_circ_0000437 R    | AAAGGCAGCAACACCCCATT      |
| hsa_circ_0097182 F    | ATGCCCAAGAGGGGACTTGA      |
| hsa_circ_0097182 R    | CTGCCATACCATGACCGTGC      |
| hsa_circ_0028067 F    | GGTTACATGCCCAAGAGGGG      |
| hsa_circ_0028067 R    | AGCTGACTACCAGGGCCATA      |
| hsa_circ_0006852 F    | GGGATGGGTACATGCCCAA       |
| hsa_circ_0006852 R    | GCCACGATGCCGACTCTCTT      |
| hsa_circ_0008092 F    | TCAACACATTCAGCAGCAAGG     |
| hsa_circ_0008092 R    | TCCTTCTCCTGGCAATCTCACA    |
| ETFA F                | AGCTGAGCATGCAAATGATTCC    |
| ETFA R                | GCCACCTTGTCACATTTGGT      |
| GAPDH F               | GGGAGCCAAAAGGGTCAT        |
| GAPDH R               | GAGTCCTTCCACGATACCAA      |
| CCL5 F                | CTGCTTTGCCTACATTGCCC      |
| CCL5 R                | TCGGGTGACAAAGACGACTG      |
| EIF4A3 F              | AGGATATGGGGATTCTGCTCTC    |
| EIF4A3 R              | GTGAAATGACCCAAGACTACACA   |
| U6 F                  | CTCGCTTCGGCAGCACA         |
| U6 R                  | AACGCTTCACGAATTTGCGT      |
| <b>siRNA sequence</b> |                           |

|                             |                             |
|-----------------------------|-----------------------------|
| si-circETFA 1#              | GGCCTACTTCCAGGCCTCA         |
| si-circETFA 2#              | CCTACTTCCAGGCCTCATT         |
| si-circETFA 3#              | TCCCTGCCCTTTGACAGTG         |
| si-EIF4A3                   | GGTCTGTCACTCATGGGTT         |
| si-CCL5                     | GCAGAGGATCAAGACAGCA         |
| <b>FISH probe</b>           |                             |
| circETFA probe-1            | ATGAGGCC+TGGAAG+TAGGCCT     |
| circETFA probe-2            | AATGAGGCC+TGGAAG+TAGGCC     |
| circETFA probe-3            | TAGCAA+TGAGGCC+TGGAAGTA     |
| <b>Pulldown probe</b>       |                             |
| circETFA probe-1            | ATGAGGCC+TGGAAG+TAGGCCT     |
| circETFA probe-2            | AATGAGGCC+TGGAAG+TAGGCC     |
| circETFA probe-3            | TAGCAA+TGAGGCC+TGGAAGTA     |
| hsa-miR-612                 | AAGGAGC+TCAGAAGCCC+TGCCCAGC |
| <b>Mimics and inhibitor</b> |                             |
| hsa-miR-612 mimics F        | GCUGGGCAGGGCUUCUGAGCUCCUU   |
| hsa-miR-612 mimics R        | AAGGAGCUCAGAAGCCCUGCCCAGC   |
| hsa-miR-612 inhibitor R     | AAGGAGCUCAGAAGCCCUGCCCAGC   |