**Table S1.** Clinicopathological characteristics and follow-up data of 120 patients with HCC

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | TUG1 expression | | *P* value |
| Low | High |  |
| **Gender** |  |  | 0.258 |
| Male (n=75) | 34 | 41 |  |
| Female (n=45) | 26 | 19 |  |
| **Age (years)** |  |  | 0.273 |
| ≤52 (n=57) | 25 | 32 |  |
| >52 (n=63) | 35 | 28 |  |
| **Tumor size (cm)** |  |  | 0.032 |
| ≤5 (n=39) | 25 | 14 |  |
| >5 (n=81) | 35 | 46 |  |
| **Lung metastasis**  Yes (n=60)  No (n=60) | 22  38 | 38  22 | 0.004 |
| **HBV**\* **infection**  Yes (n=74)  No (n=46) | 31  29 | 43  17 | 0.024 |
| **AJCC stage**  I (n=25)  II (n=46)  III (n=34)  IV (n=15) | 20  20  15  5 | 5  26  19  10 | 0.008 |
| **miR-524-5p**  Low  High | 21  39 | 39  21 | 0.001 |
| **SIX1 mRNA** |  |  | 0.011 |
| Low | 37 | 23 |  |
| High | 23 | 37 |  |

\*HBV, hepatitis B virus.

Differences between groups were determined by the Chi-square test.

**Table S2.** Primes sequences used in this study

|  |  |
| --- | --- |
| Gene | Sequences (5′-3′) |
| TUG1-forward  TUG1-reverse  GAS5-forward  GAS5-reverse  H19-forward  H19-reverse  MALAT1-forward  MALAT1-reverse  MEG3-forward  MEG3-reverse  NEAT1-forward  NEAT1-reverse  XIST-forward  XIST-reverse  SIX1-forward  SIX1-reverse  GAPDH-forward  GAPDH-reverse  miR-524-5p-forward  miR-524-5p-reverse  U6-forward  U6-reverse | CAGCAAATCCATCTGAAC  ACTGGCTTCATTCTCTAC  CACAGGCATTAGACAGAAAGC  TCCTTACCCAAGCAAGTCATC  GCGGGTCTGTTTCTTTACTTCC  CTTTGATGTTGGGCTGATGAGG  TTTCTTCCTGCTCCGGTTC  TTTCAGCTTCCAGGCTCTC  CTGGGTCGGCTGAAGAACTG  AGGGCGGGTCTCTACTCAAG  CCTCCCTTTAACTTATCCATTC  TCCACCATTACCAACAATAC  CTACCGCTTTGGCAGAGAATG  GCCTCCCGATACAACAATCAC  AAGGTGAGTGGTGTATTG  TGCTGTGAAGAGATAGTG  AATCCCATCACCATCTTC  AGGCTGTTGTCATACTTC  GCGCTACAAAGGGAAGCAC  AGTGCAGGGTCCGAGGTATT  CTCGCTTCGGCAGCACA  AACGCTTCACGAATTTGCGT |

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**Figure S1.** **Characterization of CAFs and NFs.** Microscopic observation of primary CAFs and NFs. Scale bar: 100 μm.

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**Figure S2.** **Identification and internalization of exosomes.** (A) TEM images of CAFs/NFs-derived exosomes (CAFs-exo/NFs-exo) (scale bar: 200 nm). (B) Protein levels of exosomal markers CD63, CD9, and TSG101. (C) Confocal microscopic images showing internalization of exosomes by HepG2 cells (scale bar: 50 μm).

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**Figure S3. Effects of CAFs-derived exosomal TUG1 on HepG2 cell metastasis *in vivo*.** Effects of exosomes derived from the CAFs with or without TUG1 shRNA adenovirus infection on (A, B) metastasis (scale bar: 200 μm) (n = 6) and (C) survival duration of mice (n = 15). The data are expressed as the mean + SD (n = 6). \*\*\**P* < 0.001 vs blank. ###*P* < 0.001 vs CAFs-exo.

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**Figure S4. The effects of CAFs-derived exosomes on HepG2 cells are inhibited by TUG1 knockdown.** (A, B) Migration and invasion, (C) glucose uptake, (D) LDH activity, (E) lactate, and (F) ATP content, (G) TUG1 expression, and (H, I) MMP-2, MMP-9, HK2, and LDHA expressions were measured in HepG2 treated with CAFs-exo and transduced with shTUG1 or shNC. The data are expressed as the mean + SD (n = 3). \*\*\**P* < 0.001 compared with shNC.