

Elevated expression of eukaryotic translation initiation factor 3H is associated with proliferation, invasion and tumorigenicity in human hepatocellular carcinoma

SUPPLEMENTARY TABLES

Supplementary Table S1: Sequences of primers and siRNA used

| Genes | | Sequence |
|--------------|-------------------|----------------------|
| EIF3H | Sense primer | GTGCTTTTGGGTCTGGTTGT |
| | Anti-sense primer | AGCCACGTGAAGATGATCA |
| GAPDH | Sense primer | GCACCGTCAAGGCTGAGAAC |
| | Anti-sense primer | TGGTGAAGACGCCAGTGGA |
| EIF3H-siRNAs | SiRNA-1 | GCAAGTGCAGATAGATGGC |
| | SiRNA-2 | GTGCAGATAGATGGCCTTG |
| | SiRNA-3 | GAAGAAGGACAAGGAACTG |

Supplementary Table S2: Univariate analysis of clinical outcomes of 215 HCC patients

| Variable | RFS (%)* | P value | OS (%)* | P value |
|---------------------------------------|----------------|---------|----------------|---------|
| Age: >53/<53 | 51.8/49.2 | 0.721 | 77.8/69.9 | 0.268 |
| Gender: male/female | 46.4/68.4 | 0.021 | 70.6/82.7 | 0.221 |
| HBs antigen: +/- | 51.5/45.6 | 0.325 | 76.9/66.6 | 0.109 |
| Liver cirrhosis: +/- | 52.1/49.6 | 0.732 | 72.5/77.8 | 0.589 |
| Serum albumin (g/L): >40/≤40 | 51.5/48.6 | 0.627 | 71.0/75.2 | 0.616 |
| Serum bilirubin (μmol/L): >17/≤17 | 53.7/45.7 | 0.063 | 70.1/75.0 | 0.320 |
| HBe antigen: +/- | 34.0/66.0 | 0.000 | 59.2/89.1 | 0.000 |
| Tumor size (cm): >5/≤5 | 53.5/43.6 | 0.236 | 76.0/62.1 | 0.065 |
| Number of tumor: Solitary/Multiple | 61.2/44.5 | 0.015 | 82.5/69.5 | 0.024 |
| Edmondson Grade: I+II/III | 25.4/59.9 | 0.000 | 49.7/83.5 | 0.000 |
| Micro-vascular Invasion: +/- | 16.3/54.8 | 0.000 | 49.6/76.0 | 0.024 |
| Satellite | 30.3/61.5 | 0.000 | 62.9/81.7 | 0.002 |
| Encapsulation: complete/- | 41.5/59.7 | 0.005 | 65.5/83.9 | 0.001 |
| TNM stage: I/II/III | 64.5/52.3/17.4 | 0.000 | 85.8/57.0/46.3 | 0.000 |
| BCLC stage: A/B/C | 57.6/35.1/16.4 | 0.000 | 78.5/61.0/50.1 | 0.001 |
| ALT (U/L): >40/≤40 | 48.5/52.6 | 0.539 | 71.0/74.9 | 0.644 |
| AFP (μg/L): >20/≤20 | 42.1/68.7 | 0.001 | 70.2/83.9 | 0.023 |
| EIF3H | 61.5/40.2 | 0.000 | 79.9/66.0 | 0.005 |

RFS: Recurrence-Free Survival; OS: Overall Survival; *the time follow-up ended is used to calculate the Recurrence-Free Survival and Overall survival; p value by Long-rank test less than 0.05 was considered statistical significant.

Supplementary Table S3: Multivariate analysis for factors related to HCC RFS

| Variable | Univariate | | | Multivariate | | |
|-----------------------------------------|------------|---------------|---------|--------------|-------------|---------|
| | HR | 95% CI | P value | HR | 95% CI | P value |
| Age(year) >53/ ≤53 | 1.002 | 0.991-1.012 | 0.737 | | | |
| Gender: male/femal | 1.214 | 1.048-2.635 | 0.018 | 1.199 | 0.808-1.781 | 0.397 |
| HBsAg: positive/negative | 1.339 | 0.941-1.905 | 0.138 | | | |
| HBeAg: positive/negative | 1.196 | 0.906-1.580 | 0.186 | | | |
| Liver cirrhosis: +/- | 1.263 | 0.956-1.670 | 0.098 | | | |
| Antiviral therapy | 1.290 | 0.932-1.784 | 0.122 | | | |
| TBL(μmol/L): >17 / ≤17 | 0.989 | 0.961-1.019 | 0.476 | | | |
| ALB (g/dL):>40 / ≤40 | 0.982 | 0.942-1.023 | 0.386 | | | |
| ALT (U/L): >40 / ≤40 | 1.001 | 0.997-1.006 | 0.477 | | | |
| TNM stage: I/ II/ III | 1.612 | 1.296-3.148 | 0.006 | 1.012 | 0.986-1.023 | 0.446 |
| Number of tumor: Solitary / Multiple | 1.056 | 0.934-1.136 | 0.423 | | | |
| BCLC stage: A/B/C | 1.764 | 1.372-3.721 | 0.004 | 0.946 | 0.649-1.381 | 0.780 |
| Edmondson-Steiner grade: I + II/III | 1.573 | 1.282-3.521 | 0.015 | 1.088 | 0.827-1.430 | 0.548 |
| Tumour encapsulation:No/ Complete | 1.832 | 1.346-2.567 | 0.031 | 1.122 | 0.843-1.493 | 0.435 |
| Micro- vascularinvasion(+/-) | 1.593 | 1.392-2.764 | 0.012 | 1.290 | 0.932-1.784 | 0.122 |
| Macro- vascularinvasion(+/-) | 1.843 | 1.251-2.682 | 0.037 | 1.339 | 0.941-1.905 | 0.138 |
| EIF3H | 1.411 | 1.064-1.871 | 0.017 | 1.979 | 1.297-2.996 | <0.001 |
| AFP(≤20ug/L vs >20ug) | 1.634 | 1.120-2.385 | 0.011 | 1.841 | 1.062-3.167 | 0.0260 |
| Tumor size (≤5 cm vs>5 cm) | 1.957 | 1.444-2.654 | <0.001 | 2.539 | 1.520-4.256 | <0.001 |
| Satellite (presence vs absence) | 2.2820 | 1.7111-3.0435 | <0.001 | 2.358 | 1.460-3.702 | 0.0020 |

HCC: Hepatocellular carcinoma; HR: Hazard ratio; CI: Confidence interval; TBL: Total bilirubin; ALB: Albumin; ALT: Alanine aminotransferase; PT: Prothrombin time; PLT: Blood platelet; AFP: Alpha-fetoprotein.

Supplementary Table S4: Multivariate analysis for factors related with HCC OS

| Variable | Univariate | | | Multivariate | | |
|------------------------------------------|------------|-------------|---------|--------------|-------------|---------|
| | HR | 95%CI | P value | HR | 95%CI | P value |
| Age(year) >53/ ≤53 | 1.023 | 0.891-1.412 | 0.268 | | | |
| Gender: male/femal | 1.241 | 1.108-1.842 | 0.021 | 1.024 | 0.732-1.204 | 0.371 |
| HBsAg: positive/negative | 1.134 | 0.654-1.487 | 0.109 | | | |
| HBeAg: positive/negative | 1.785 | 0.896-4.382 | 0.081 | | | |
| Liver cirrhosis: +/- | 1.084 | 0.695-1.423 | 0.589 | | | |
| Antiviral therapy | 1.082 | 0.341-1.396 | 0.267 | | | |
| TBL(μmol/L): >17/ ≤17 | 0.765 | 0.201-1.138 | 0.320 | | | |
| ALB (g/dL):>40/ ≤40 | 0.934 | 0.672-1.104 | 0.784 | | | |
| ALT (U/L): >40/ ≤40 | 1.003 | 0.984-1.014 | 0.841 | | | |
| TNM stage: I/II/III | 2.434 | 1.783-3.627 | 0.001 | 1.145 | 0.863-1.616 | 0.061 |
| Number of tumor: Solitary/ Multiple | 1.172 | 0.734-2.354 | 0.074 | | | |
| BCLC stage: A/B/C | 2.821 | 1.452-3.783 | 0.001 | 1.106 | 0.721-1.854 | 0.104 |
| Edmondson-Steiner grade: I + II / III | 2.153 | 1.637-4.526 | 0.001 | 1.004 | 0.632-1.657 | 0.568 |
| Tumour encapsulation:No/ Complete | 2.145 | 1.738-3.728 | 0.001 | 1.013 | 0.832-1.751 | 0.168 |
| Micro-vascularinvasion(+/-) | 1.379 | 1.168-2.872 | 0.024 | 1.109 | 0.768-1.892 | 0.117 |
| Macro-vascularinvasion(+/-) | 1.572 | 1.265-2.783 | 0.036 | 1.125 | 0.547-2.691 | 0.276 |
| EIF3H | 1.527 | 1.237-2.351 | 0.005 | 1.927 | 1.775-2.582 | 0.002 |
| AFP(≤20ug/Lvs >20ug/L) | 1.568 | 1.254-2.249 | 0.023 | 1.035 | 0.836-1.762 | 0.126 |
| Tumor size (≤5 cm vs>5 cm) | 1.752 | 1.267-2.893 | 0.035 | 2.134 | 1.628-3.458 | 0.001 |
| Satellite (presence vs absence) | 1.882 | 1.543-2.762 | 0.012 | 1.258 | 0.837-1.453 | 0.076 |

HCC: Hepatocellular carcinoma; HR: Hazard ratio; CI: Confidence interval; TBL: Total bilirubin; ALB: Albumin; ALT: Alanine aminotransferase; PT: Prothrombin time; PLT: Blood platelet; AFP: Alpha-fetoprotein.

Supplementary Table S5: Clinicopathological characteristic of HCC patients included

| Variable | Cohort 1 ♦ | Cohort 2 ▲ | Cohort 3 ● |
|----------------------------------------|------------|------------|------------|
| All cases | 40 | 215 | 65 |
| Age(year): >53/<53 | 16/24 | 85/130 | 20/45 |
| Gender: male/female | 31/9 | 180/35 | 49/16 |
| HBs antigen: +/- | 37/3 | 195/20 | 55/10 |
| Liver cirrhosis: +/- | 29/11 | 141/74 | 44/21 |
| Serum albumin (g/L): >40/≤40 | 31/9 | 157/58 | 40/25 |
| Serum bilirubin (μmol/L): >17/≤17 | 10/30 | 57/158 | 15/50 |
| HBe antigen: +/- | 16/24 | 70/145 | 16/39 |
| Tumor size (cm): >5/≤5 | 14/26 | 75/140 | 27/38 |
| Number of tumor: Solitary/ Multiple | 32/8 | 171/44 | 55/10 |
| Edmondson Grade: I+II/III | 7/33 | 68/147 | 25/40 |
| Micro-vascular Invasion: +/- | 11/29 | 65/150 | 20/45 |
| Macro-vascular Invasion: +/- | 4/36 | 19/196 | 8/57 |
| Pathological Satellite: +/- | 15/25 | 88/127 | 28/37 |
| Encapsulation: complete/- | 25/15 | 120/95 | 36/29 |
| ALT (U/L): >40/≤40 | 18/22 | 98/117 | 35/30 |
| AFP (μg/L): >20/≤20 | 35/5 | 159/56 | 40/25 |

Patients of group ▲ were independent from patients of group ♦, and patients of group ● were selected from group ▲ with well-preserved serum.