

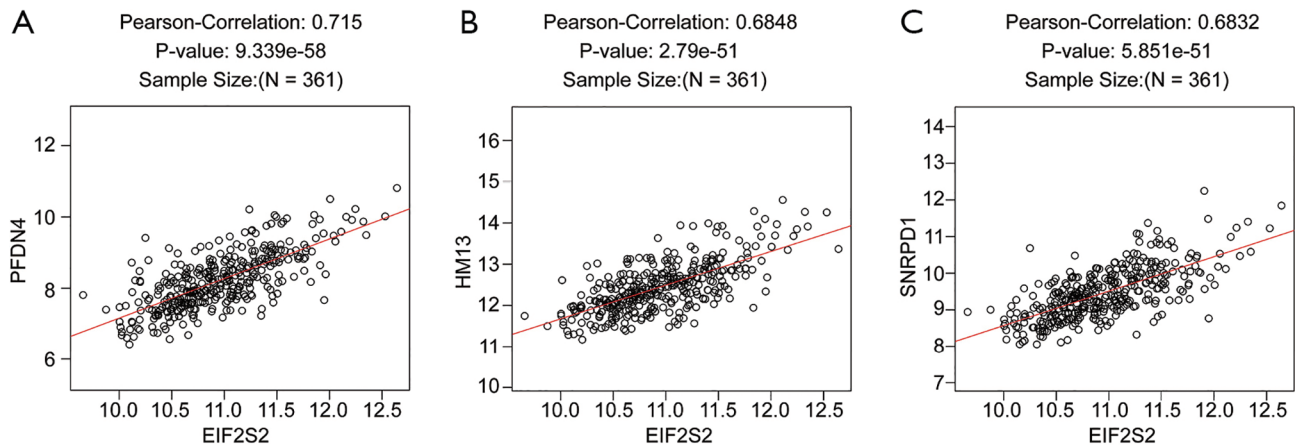
**Table S1** 50 similar genes in LIHC (Gepia2)

| Gene symbol    | Gene ID            | PCC  |
|----------------|--------------------|------|
| <i>UBE2V1</i>  | ENSG00000244687.11 | 0.73 |
| <i>TRMT6</i>   | ENSG00000089195.14 | 0.72 |
| <i>RPN2</i>    | ENSG00000118705.16 | 0.72 |
| <i>CSE1L</i>   | ENSG00000124207.16 | 0.71 |
| <i>PDRG1</i>   | ENSG00000088356.5  | 0.7  |
| <i>SRSF9</i>   | ENSG00000111786.8  | 0.7  |
| <i>MAPRE1</i>  | ENSG00000101367.8  | 0.7  |
| <i>TRPC4AP</i> | ENSG00000100991.11 | 0.7  |
| <i>DDX27</i>   | ENSG00000124228.14 | 0.7  |
| <i>STIP1</i>   | ENSG00000168439.16 | 0.7  |
| <i>RNF34</i>   | ENSG00000170633.16 | 0.69 |
| <i>CCT6A</i>   | ENSG00000146731.10 | 0.69 |
| <i>PIGU</i>    | ENSG00000101464.10 | 0.69 |
| <i>CHMP4B</i>  | ENSG00000101421.3  | 0.69 |
| <i>DENR</i>    | ENSG00000139726.10 | 0.68 |
| <i>SAE1</i>    | ENSG00000142230.11 | 0.68 |
| <i>SRRD</i>    | ENSG00000100104.12 | 0.68 |
| <i>YTHDF1</i>  | ENSG00000149658.17 | 0.68 |
| <i>NXT1</i>    | ENSG00000132661.3  | 0.68 |
| <i>ADSL</i>    | ENSG00000239900.11 | 0.68 |
| <i>TPD52L2</i> | ENSG00000101150.17 | 0.68 |
| <i>MCRS1</i>   | ENSG00000187778.13 | 0.67 |
| <i>YWHAB</i>   | ENSG00000166913.12 | 0.67 |
| <i>CBX3</i>    | ENSG00000122565.18 | 0.67 |
| <i>XRCC6</i>   | ENSG00000196419.12 | 0.67 |
| <i>PHF20</i>   | ENSG00000025293.15 | 0.67 |

**Table S1** (continued)**Table S1** (continued)

| Gene symbol     | Gene ID            | PCC  |
|-----------------|--------------------|------|
| <i>EEF1E1</i>   | ENSG00000124802.11 | 0.67 |
| <i>ATF4</i>     | ENSG00000128272.14 | 0.67 |
| <i>RAN</i>      | ENSG00000132341.11 | 0.67 |
| <i>DNAJC5</i>   | ENSG00000101152.10 | 0.66 |
| <i>LLPH</i>     | ENSG00000139233.6  | 0.66 |
| <i>IARS</i>     | ENSG00000196305.17 | 0.66 |
| <i>EWSR1</i>    | ENSG00000182944.17 | 0.66 |
| <i>DCUN1D5</i>  | ENSG00000137692.11 | 0.66 |
| <i>SNRPB2</i>   | ENSG00000125870.10 | 0.66 |
| <i>DNTTIP1</i>  | ENSG00000101457.12 | 0.66 |
| <i>HNRNPM</i>   | ENSG00000099783.11 | 0.66 |
| <i>UBE2E1</i>   | ENSG00000170142.11 | 0.66 |
| <i>DYNLL1</i>   | ENSG00000088986.10 | 0.66 |
| <i>NAP1L1</i>   | ENSG00000187109.13 | 0.66 |
| <i>CCDC59</i>   | ENSG00000133773.11 | 0.66 |
| <i>POLR3F</i>   | ENSG00000132664.11 | 0.65 |
| <i>EIF2S2P4</i> | ENSG00000128692.8  | 0.65 |
| <i>GLRX3</i>    | ENSG00000108010.11 | 0.65 |
| <i>NCOA5</i>    | ENSG00000124160.11 | 0.65 |
| <i>RPAP3</i>    | ENSG00000005175.9  | 0.65 |
| <i>RALA</i>     | ENSG00000006451.7  | 0.65 |
| <i>XPOT</i>     | ENSG00000184575.11 | 0.65 |
| <i>ARPC2</i>    | ENSG00000163466.15 | 0.65 |
| <i>CCT5</i>     | ENSG00000150753.11 | 0.65 |

LIHC, liver hepatocellular carcinoma; PCC, Pearson correlation coefficient.



**Figure S1** The gene expression correlational analysis between *EIF2S2* and the top three *EIF2S2*-related genes: PFDN4, HM13, and SNRPD1 (LinkedOmics). The scatter plot indicates the Pearson correlations of *EIF2S2* with PFDN4 (A), HM13 (B), and SNRPD1 (C). *EIF2S2*, eukaryotic translation initiation factor 2 subunit beta; PFDN4, prefoldin 4; HM13, histocompatibility minor 13; SNRPD1, small nuclear ribonucleoprotein D1 polypeptide.

**Table S2** Significantly enriched GO annotations (cellular components) of *EIF2S2* in HCC (LinkedOmics)

| Description                    | LeadingEdgeNum | FDR | LeadingEdgeGene  |
|--------------------------------|----------------|-----|--|
| Ribosome                       | 126            | 0   | <i>CHCHD1; DENR; EIF3H; GADD45GIP1; MCTS1; MRPL11; MRPL12; MRPL13; MRPL14; MRPL17; MRPL20; MRPL21; MRPL22; MRPL23; MRPL27; MRPL28; MRPL33; MRPL36; MRPL38; MRPL4; MRPL43; MRPL47; MRPL48; MRPL51; MRPL52; MRPL53; MRPL9; MRPS11; MRPS12; MRPS14; MRPS15; MRPS16; MRPS17; MRPS18A; MRPS2; MRPS21; MRPS23; MRPS24; MRPS25; MRPS26; MRPS30; MRPS34; MRPS5; MRPS7; MTG1; NAA10; NDUFA7; RBM3; RPL10; RPL10A; RPL11; RPL12; RPL13; RPL13A; RPL14; RPL15; RPL17; RPL18; RPL18A; RPL19; RPL21; RPL22; RPL22L1; RPL23; RPL23A; RPL24; RPL26; RPL26L1; RPL27; RPL27A; RPL28; RPL29; RPL30; RPL31; RPL32; RPL34; RPL35; RPL35A; RPL36; RPL36AL; RPL37; RPL37A; RPL38; RPL39; RPL4; RPL41; RPL5; RPL6; RPL7; RPL7A; RPL8; RPLP0; RPLP1; RPLP2; RPS10; RPS11; RPS12; RPS13; RPS14; RPS15; RPS15A; RPS16; RPS17; RPS18; RPS19; RPS2; RPS20; RPS21; RPS23; RPS24; RPS25; RPS27A; RPS29; RPS3; RPS3A; RPS4X; RPS5; RPS6; RPS7; RPS8; RPS9; RPSA; RSL24D1; SURF6; UBA52; ZNF622</i>    |
| Cytosolic part                 | 102            | 0   | <i>BCAS4; BLOC1S3; CASP4; CCT2; CCT3; CCT4; CCT5; CCT6A; CCT7; CCT8; CTU1; DBN1; DTNBP1; ENO1; GET4; GSDMD; MCTS1; NAA10; PIN1; PSMC4; PSMC5; PSMD14; PYCARD; RPL10; RPL10A; RPL11; RPL12; RPL13; RPL13A; RPL14; RPL15; RPL17; RPL18; RPL18A; RPL19; RPL21; RPL22; RPL22L1; RPL23; RPL23A; RPL24; RPL26; RPL26L1; RPL27; RPL27A; RPL28; RPL29; RPL30; RPL31; RPL32; RPL34; RPL35; RPL35A; RPL36; RPL36AL; RPL37; RPL37A; RPL38; RPL39; RPL4; RPL41; RPL5; RPL6; RPL7; RPL7A; RPL8; RPLP0; RPLP1; RPLP2; RPS10; RPS11; RPS12; RPS13; RPS14; RPS15; RPS15A; RPS16; RPS17; RPS18; RPS19; RPS2; RPS20; RPS21; RPS23; RPS24; RPS25; RPS27A; RPS29; RPS3; RPS3A; RPS4X; RPS5; RPS6; RPS7; RPS8; RPS9; RPSA; RSL24D1; SURF6; TCP1; UBA52; ZNF622</i>  |
| Mitochondrial protein complex  | 117            | 0   | <i>ANKZF1; BAX; C12orf65; CHCHD1; CHCHD10; CHCHD6; COX4I1; COX5A; COX5B; COX6A1; COX7A2; COX7A2L; COX7C; CYC1; DAP3; GRPEL2; IMMP1L; MPV17L2; MRPL11; MRPL12; MRPL13; MRPL14; MRPL15; MRPL17; MRPL18; MRPL20; MRPL21; MRPL22; MRPL23; MRPL24; MRPL27; MRPL28; MRPL33; MRPL36; MRPL37; MRPL38; MRPL4; MRPL42; MRPL43; MRPL47; MRPL48; MRPL51; MRPL52; MRPL53; MRPL54; MRPL55; MRPL9; MRPS11; MRPS12; MRPS14; MRPS15; MRPS16; MRPS17; MRPS18A; MRPS18C; MRPS2; MRPS21; MRPS24; MRPS26; MRPS30; MRPS33; MRPS34; MRPS5; MRPS7; MRPS9; MTG1; MTX1; NDUFA1; NDUFA11; NDUFA12; NDUFA13; NDUFA2; NDUFA3; NDUFA4; NDUFA4L2; NDUFA6; NDUFA7; NDUFA8; NDUFA9; NDUFAB1; NDUFB1; NDUFB11; NDUFB2; NDUFB3; NDUFB4; NDUFB5; NDUFB7; NDUFB9; NDUFC2; NDUFS3; NDUFS4; NDUFS5; NDUFS6; NDUFS8; ROMO1; SLC25A6; SUCLG1; SUPV3L1; TIMM10; TIMM13; TIMM17B; TIMM22; TIMM50; TIMM8B; TIMM9; TOMM22; TOMM40; TOMM40L; TOMM5; TOMM6; TOMM7; UQCR10; UQCRB; UQCRRS1; UQCRRH; UQCRRHL; VDAC1</i> |
| Sm-like protein family complex | 32             | 0   | <i>CD2BP2; CLNS1A; EFTUD2; GEMIN6; GEMIN7; LSM10; LSM2; LSM3; LSM4; LSM7; PHF5A; PPIH; PRPF31; PRPF6; RBMX2; SART1; SF3A2; SF3B5; SNRNP40; SNRNP70; SNRPA; SNRPA1; SNRPB; SNRPB2; SNRPC; SNRPD1; SNRPD2; SNRPD3; SNRPE; SNRPF; SNRPG; TXNL4A</i>   |

GO, Gene Ontology; *EIF2S2*, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

**Table S3** Significantly enriched Goannotations (molecular functions) of *EIF2S2* in HCC (LinkedOmics)

| Description                        | LeadingEdgeNum | FDR | LeadingEdgeGene  |
|------------------------------------|----------------|-----|--|
| Structural constituent of ribosome | 111            | 0   | <i>MRPL11; MRPL12; MRPL13; MRPL14; MRPL17; MRPL20; MRPL21; MRPL22; MRPL23; MRPL27; MRPL28; MRPL33; MRPL36; MRPL4; MRPL43; MRPL47; MRPL51; MRPL52; MRPL9; MRPS11; MRPS12; MRPS14; MRPS15; MRPS16; MRPS17; MRPS18A; MRPS2; MRPS21; MRPS23; MRPS24; MRPS25; MRPS30; MRPS34; MRPS5; MRPS7; NDUFA7; RPL10; RPL10A; RPL11; RPL12; RPL13; RPL13A; RPL14; RPL15; RPL17; RPL18; RPL18A; RPL19; RPL21; RPL22; RPL22L1; RPL23; RPL23A; RPL24; RPL26; RPL26L1; RPL27; RPL27A; RPL28; RPL29; RPL30; RPL31; RPL32; RPL34; RPL35; RPL35A; RPL36; RPL36AL; RPL37; RPL37A; RPL38; RPL39; RPL4; RPL41; RPL5; RPL6; RPL7; RPL7A; RPL8; RPLP0; RPLP1; RPLP2; RPS10; RPS11; RPS12; RPS13; RPS14; RPS15; RPS15A; RPS16; RPS17; RPS18; RPS19; RPS2; RPS20; RPS21; RPS23; RPS24; RPS27A; RPS29; RPS3; RPS3A; RPS4X; RPS5; RPS6; RPS7; RPS8; RPS9; RPSA; RSL24D1; UBA52</i> |
| rRNA binding                       | 33             | 0   | <i>EMG1; ERAL1; GTF3A; IMP4; MRPL11; MRPL18; MRPL20; MRPS11; MRPS17; MRPS18A; MRPS7; NOL12; PPAN; RBM3; RPF2; RPL11; RPL12; RPL19; RPL23; RPL23A; RPL37; RPL5; RPL8; RPLP0; RPS11; RPS13; RPS14; RPS18; RPS3; RPS4X; RPS5; RPS9; RRS1</i>  |
| Unfolded protein binding           | 46             | 0   | <i>AAMP; AIP; CALR; CCT2; CCT3; CCT4; CCT5; CCT6A; CCT7; CCT8; CHAF1B; CLN3; DNAJB11; DNAJB13; DNAJB2; GRPEL2; HSP90AA1; HSP90AB1; HSP90B1; HSPA5; HSPA6; HSPA8; HSPD1; HSPE1; HTRA2; MKKS; NAP1L4; NPM1; NUDC; PDRG1; PFDN1; PFDN2; PFDN4; PFDN5; PFDN6; PPIA; PPIAL4C; PPIAL4G; PPIB; PPIE; PPIH; PTGES3; RUVBL2; SERPINH1; TCP1; TTC1</i>   |
| Threonine-type peptidase activity  | 15             | 0   | <i>PSMA1; PSMA2; PSMA3; PSMA4; PSMA5; PSMA6; PSMA7; PSMB1; PSMB10; PSMB2; PSMB3; PSMB4; PSMB5; PSMB6; PSMB7</i>  |

*EIF2S2*, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

**Table S4** Significantly enriched Go annotations (biological processes) of *EIF2S2* in HCC (LinkedOmics)

| Description                                   | LeadingEdgeNum | FDR | LeadingEdgeGene  |
|---|----------------|-----|--|
| Translational initiation                      | 107            | 0   | <i>ATF4; CDC123; COPS5; DENR; EIF1; EIF1AD; EIF2B4; EIF2B5; EIF2S2; EIF2S3; EIF3B; EIF3D; EIF3F; EIF3G; EIF3H; EIF3I; EIF3K; EIF3M; EIF4A1; EIF4E2; EIF4EBP1; EIF5B; EIF6; HSPB1; KHDRBS1; MCTS1; NCBP2; NPM1; PABPC1; POLR2D; POLR2G; PPP1CA; RBM4; RPL10; RPL10A; RPL11; RPL12; RPL13; RPL13A; RPL14; RPL15; RPL17; RPL18; RPL18A; RPL19; RPL21; RPL22; RPL23; RPL23A; RPL24; RPL26; RPL27; RPL27A; RPL28; RPL29; RPL30; RPL31; RPL32; RPL34; RPL35; RPL35A; RPL36; RPL37; RPL37A; RPL38; RPL39; RPL4; RPL41; RPL5; RPL6; RPL7; RPL7A; RPL8; RPLP0; RPLP1; RPLP2; RPS10; RPS11; RPS12; RPS13; RPS14; RPS15; RPS15A; RPS16; RPS17; RPS18; RPS19; RPS2; RPS20; RPS21; RPS23; RPS24; RPS25; RPS27A; RPS29; RPS3; RPS3A; RPS4X; RPS5; RPS6; RPS6KB2; RPS7; RPS8; RPS9; RPSA; UBA52; YTHDF1</i>   |
| Protein localization to endoplasmic reticulum | 80             | 0   | <i>CHMP4B; DDRGK1; KDELR1; RPL10; RPL10A; RPL11; RPL12; RPL13; RPL13A; RPL14; RPL15; RPL17; RPL18; RPL18A; RPL19; RPL21; RPL22; RPL23; RPL23A; RPL24; RPL26; RPL27; RPL27A; RPL28; RPL29; RPL30; RPL31; RPL32; RPL34; RPL35; RPL35A; RPL36; RPL37; RPL37A; RPL38; RPL39; RPL4; RPL41; RPL5; RPL6; RPL7; RPL7A; RPL8; RPLP0; RPLP1; RPLP2; RPS10; RPS11; RPS12; RPS13; RPS14; RPS15; RPS15A; RPS16; RPS17; RPS18; RPS19; RPS2; RPS20; RPS21; RPS23; RPS24; RPS25; RPS27A; RPS29; RPS3; RPS3A; RPS4X; RPS5; RPS6; RPS7; RPS8; RPS9; RPSA; SEC61B; SEC61G; SRP14; SRP19; UBA52; ZFAND2B</i>   |
| Ribonucleoprotein complex biogenesis          | 155            | 0   | <i>AATF; BCCIP; BMS1; BRX1; BYSL; C1QBP; CD2BP2; CLNS1A; CRNKL1; DCAF13; DDX27; DDX49; DDX56; DENR; DHX37; EIF2S3; EIF3B; EIF3D; EIF3F; EIF3G; EIF3H; EIF3I; EIF3K; EIF3M; EIF4A3; EIF6; EMG1; ERI3; EXOSC1; EXOSC3; EXOSC4; EXOSC5; EXOSC7; EXOSC8; FBL; FRG1; GAR1; GEMIN6; GEMIN7; GTF3A; GTPBP4; HSP90AA1; HSP90AB1; IMP4; ISG20; LSM3; LSM4; LYAR; MCTS1; MRPL11; MRPL20; MRPL22; MRPS11; MRPS2; MRPS7; MRTO4; NHP2; NLE1; NOL4; NOL10; NOL12; NOP10; NOP16; NOP2; NOP56; NOP58; NPM1; NPM3; NSA2; NSUN5; PA2G4; PELP1; PES1; PIH1D1; POLR2D; POP4; POP5; PPAN; PRPF19; PRPF31; PRPF6; PTGES3; PWP1; RAN; RBM22; REXO4; RPF2; RPL10; RPL10A; RPL11; RPL12; RPL13A; RPL14; RPL23A; RPL24; RPL26; RPL26L1; RPL27; RPL35; RPL35A; RPL38; RPL5; RPL6; RPL7; RPL7A; RPLP0; RPS10; RPS14; RPS15; RPS16; RPS17; RPS19; RPS2; RPS21; RPS23; RPS24; RPS5; RPS6; RPS7; RPS8; RPS9; RPSA; RRP1; RRP7A; RRP8; RRP9; RRS1; RSL1D1; RSL24D1; RUVBL1; RUVBL2; SART1; SENP3; SF3A2; SNRPB; SNRPC; SNRPD1; SNRPD2; SNRPD3; SNRPE; SNRPF; SNRPG; SURF6; TAF9; TARBP2; TRMT112; TXNL4A; UTP18; UTP6; WDR18; WDR46; WDR74; ZNF593; ZNF622; ZNHIT3</i> |
| rRNA metabolic process                        | 105            | 0   | <i>BMS1; BYSL; DCAF13; DDX27; DDX49; DDX51; DDX56; DEDD2; DHX37; DKC1; EIF4A3; EMG1; ERI3; EXOSC1; EXOSC2; EXOSC3; EXOSC4; EXOSC5; EXOSC7; EXOSC8; FBL; FRG1; FTSJ3; GAR1; GTF3A; GTF3C5; GTF3C6; GTPBP4; H2AFY; H2AFY2; IMP4; ISG20; LAS1L; LYAR; MARS; MPHOSPH6; MRPS11; MRPS9; MRTO4; NAT10; NCL; NHP2; NOB1; NOL4L; NOL10; NOL12; NOP10; NOP2; NOP56; NOP58; NPM3; NSA2; NSUN5; PA2G4; PDCD11; PELO; PELP1; PES1; PIH1D1; POP4; POP5; PWP1; REXO4; RPF1; RPF2; RPL10A; RPL11; RPL14; RPL26; RPL27; RPL35; RPL35A; RPL5; RPL7; RPL7A; RPS14; RPS15; RPS16; RPS17; RPS19; RPS2; RPS21; RPS24; RPS6; RPS7; RPS8; RPS9; RPSA; RRP1; RRP7A; RRP8; RRP9; RRS1; RSL1D1; SART1; SENP3; SMARCB1; TEX10; TRMT112; UTP18; UTP6; WDR18; WDR46; WDR74; ZNHIT3</i>   |

*EIF2S2*, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

**Table S5** Significantly enriched KEGG pathway annotations of EIF2S2 in HCC (LinkedOmics)

| Description               | LeadingEdgeNum | FDR | LeadingEdgeGene  |
|---------------------------|----------------|-----|--|
| Ribosome                  | 103            | 0   | <i>FAU; MRPL11; MRPL12; MRPL13; MRPL14; MRPL17; MRPL20; MRPL21; MRPL22; MRPL23; MRPL27; MRPL28; MRPL33; MRPL36; MRPL4; MRPL9; MRPS11; MRPS12; MRPS14; MRPS15; MRPS16; MRPS17; MRPS18A; MRPS2; MRPS21; MRPS5; MRPS7; RPL10; RPL10A; RPL11; RPL12; RPL13; RPL13A; RPL14; RPL15; RPL17; RPL18; RPL18A; RPL19; RPL21; RPL22; RPL22L1; RPL23; RPL23A; RPL24; RPL26; RPL26L1; RPL27; RPL27A; RPL28; RPL29; RPL30; RPL31; RPL32; RPL34; RPL35; RPL35A; RPL36; RPL36AL; RPL37; RPL37A; RPL38; RPL39; RPL4; RPL41; RPL5; RPL6; RPL7; RPL7A; RPL8; RPLP0; RPLP1; RPLP2; RPS10; RPS11; RPS12; RPS13; RPS14; RPS15; RPS15A; RPS16; RPS17; RPS18; RPS19; RPS2; RPS20; RPS21; RPS23; RPS24; RPS25; RPS27A; RPS29; RPS3; RPS3A; RPS4X; RPS5; RPS6; RPS7; RPS8; RPS9; RPSA; RSL24D1; UBA52</i> |
| Spliceosome               | 52             | 0   | <i>BUD31; CCDC12; CRNKL1; CWC15; EFTUD2; EIF4A3; HNRNPA1; HNRNPA3; HNRNPC; HNRNPM; HSPA6; HSPA8; ISY1; LSM2; LSM3; LSM4; LSM7; MAGOH; MAGOHB; NCBP2; PHF5A; PPIE; PPIH; PPIL1; PQBP1; PRPF19; PRPF31; PRPF6; PUF60; RBM17; RBM22; RBM8A; RP9; SART1; SF3A2; SF3B5; SNRNP40; SNRNP70; SNRPA; SNRPA1; SNRPB; SNRPB2; SNRPC; SNRPD1; SNRPD2; SNRPD3; SNRPE; SNRPF; SNRPG; TXNL4A; U2AF1; U2AF1L4</i>  |
| Proteasome                | 30             | 0   | <i>ADRM1; POMP; PSMA1; PSMA2; PSMA3; PSMA4; PSMA5; PSMA6; PSMA7; PSMB1; PSMB10; PSMB2; PSMB3; PSMB4; PSMB5; PSMB6; PSMB7; PSMC1; PSMC3; PSMC4; PSMC5; PSMD1; PSMD13; PSMD14; PSMD4; PSMD6; PSMD7; PSMD8; PSME2; PSMF1</i>  |
| Oxidative phosphorylation | 58             | 0   | <i>ATP6AP1; ATP6V0B; ATP6V0D2; ATP6V0E1; ATP6V1C1; ATP6V1C2; ATP6V1E1; ATP6V1F; COX17; COX4I1; COX5A; COX5B; COX6A1; COX6B1; COX6C; COX7A2; COX7A2L; COX7B; COX7C; COX8A; CYC1; NDUFA1; NDUFA11; NDUFA12; NDUFA13; NDUFA2; NDUFA3; NDUFA4; NDUFA4L2; NDUFA6; NDUFA7; NDUFA8; NDUFA9; NDUFA11; NDUFB1; NDUFB11; NDUFB2; NDUFB3; NDUFB4; NDUFB5; NDUFB7; NDUFB9; NDUFC1; NDUFC2; NDUFS3; NDUFS4; NDUFS5; NDUFS6; NDUFS8; NDUFV2; PPA1; TCIRG1; UQCR10; UQCR11; UQCRB; UQCRFS1; UQCRH; UQCRHL</i>   |

KEGG, Kyoto Encyclopedia of Genes and Genomes; EIF2S2, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes; FDR, false discovery rate from Benjamini and Hochberg from gene set enrichment analysis (GSEA).

**Table S6** Significantly enriched kinase-target networks of EIF2S2 in HCC (LinkedOmics)

| Geneset        | LeadingEdgeGene   |
|----------------|---|
| Kinase_MAPK1   | <i>ADAM17; AR; ATF2; BCL6; CALD1; CDKN1B; CREBBP; DAPK1; DUSP1; DUSP16; EGFR; EIF4G1; ELK1; EP300; ERG; ESR1; ETS1; FOXO3; GAB1; GAB2; GSK3B; GTF2I; HDAC6; IRS1; JUN; KLF8; LRP6; MAP2K1; MAPK1; MBP; MED1; MYLK; NCOA1; NCOA2; NDEL1; NFKB1; NUP153; ROCK1; ROCK2; RORA; RPS6KA2; RPS6KA5; RXRA; SH2B1; SMAD1; SMAD4; SNAI2; SOS1; SP1; SP3; STIM1; THRB; TOB1; TPPP</i>  |
| Kinase_MAP3K6  | <i>MAPK8</i>  |
| Kinase_DYRK1A  | <i>DYRK1A; FOXO1; LIN52; POLR2A; RCAN1; SF3B1; SPRY2</i>  |
| Kinase_CSNK2A1 | <i>ABCF1; AIP; ANP32A; ANP32B; ARRB2; BCAM; BIRC5; BRMS1; CARD9; CD6; CDC25B; CDC25C; CDC34; CDC37; CDK1; CSNK2B; DDIT3; EEF1D; EIF2S2; EIF3J; EIF4EBP1; EXOSC9; GADD45GIP1; GGA1; GMNN; GPI; H3F3A; HCLS1; HDAC1; HDAC2; HDAC3; HES6; HHEX; HIST1H3C; HIST1H3F; HIST1H3I; HIST1H4C; HMGNI; HNRNPA1; HNRNPC; HOXB7; HSP90AA1; HSP90AB1; IGFBP3; IP6K2; KDM1A; LIG1; MAZ; MCM2; MRTO4; MYB; MYBL2; MYL12B; NCAPG; NCAPH; NCF1; NFKBIB; NPHP1; OTUB1; PACS1; PDCD5; PDIA6; PIN4; PTGES3; RAD1; RAD51; RAD9A; RANGAP1; RGS19; RNF7; RNPS1; RPS6KA4; SET; SLC3A2; SRPK1; SSB; SSRP1; STX1A; TARDBP; TUBB3; TYMS; UBE2R2; XRCC1; XRCC4</i> |
| Kinase_PIM1    | <i>ABCG2; AR; CDKN1B; FOXO3; IRS1; IRS2; MAP3K5; MDM2</i>   |

EIF2S2, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes (GSEA).

**Table S7** Significantly enriched miRNA-target networks of *EIF2S2* in HCC (LinkedOmics)

| Geneset  | LeadingEdgeGene   |
|--|---|
| ATACTGT, MIR-144   | <i>AFF4; APPBP2; ARID1A; ARID2; ARRD3; ATXN1; CALCRL; CLK1; CPEB2; CPEB3; DMD; EPB41; ESRRG; ETS1; FAM126B; FAM76B; FBXL3; FBXW11; FMR1; FNDC3A; FOXO1; GLCCI1; ITS2; KIAA0232; KPNA1; LGR4; MAPK6; MED14; NEDD4; NFE2L2; NR2F2; NR3C1; PALM2; PANK1; PDE7B; PPARA; PPP3R1; PTPN9; PUM1; PURA; QKI; RNF111; SENP7; SIN3A; SLC23A2; SON; SP4; ST6GALNAC3; STAG1; STARD8; SUCLA2; TRIO; UBE4A; UBR3; WDFY3; ZCCHC2; ZDHHC17; ZFX; ZNF800</i>  |
| TAGGTCA, MIR-192, MIR-215                                  | <i>C6orf106; CCNT2; DBT; DDX3X; DDX6; DYRK1A; DYRK3; LARP4; LRRFIP1; MTMR4; NIPBL; NRIP1; RABGAP1; RB1; RICTOR; TMTC3; WDR44</i>  |
| TGTTTAC, MIR-30A-5P, MIR-30C, MIR-30D, MIR-30B, MIR-30E-5P | <i>ABL1; ACAP2; ADRA2B; AFF4; AHNAK; AMOTL2; ANKHD1; ANKRA2; ANKRD17; ARHGEF6; ARID4A; ARID4B; ASB3; ATP2A2; ATXN1; B4GALT6; BAZ2B; BCOR; BRD1; BRWD1; BTBD7; CACNB2; CAMK2D; CCNT2; CCPG1; CDC37L1; CFL2; CLDND1; CPEB2; CPEB4; CPNE8; CRKL; DAG1; DCUN1D3; DET1; DEXI; DHX40; DMD; DNAJC13; DOCK7; EAF1; EBF3; EDEM3; EDNRB; ELL2; ELOVL5; EPB41; EPC2; ERG; ESRRG; EXTL2; FAM13A; FAM160B1; FBXL17; FBXL20; FBXO34; FCHO2; FNDC3A; FRK; FYCO1; GALNT1; GIGYF2; GLCCI1; GOLGA4; GRB10; HECW2; HERC2; HLF; ICK; IKZF2; INSIG2; IRS1; ITGA6; ITGB3; ITS1; JDP2; KCTD3; KHNYN; KIAA0355; KIAA2026; KLF10; KLF9; KLHL20; KLHL24; KPNA3; LARP4; LIN7C; LPP; LRRC8D; LYST; MAGI2; MAML1; MAN1A2; MAP3K5; 44261; MBNL2; MBNL3; MIER3; NAALADL2; NDEL1; NECAP1; NEDD4; NEK4; NFAT5; NFIB; NR4A2; NRIP1; NRP1; OTUD4; PALM2; PCDH17; PCGF5; PER2; PGM1; PHF6; PICALM; PNN; PPARGC1B; PPP1R12A; PPP3R1; PPP4R4; PPTC7; QKI; RAD23B; RALGPS1; RANBP10; RAP2C; RAPGEF4; RAPH1; RASA1; REV1; RHOB; RNF165; SATB2; SCN2A; SCN8A; SCYL3; SEC23A; SGCB; SH3RF1; SIRT1; SLC1A2; SLC38A2; SLC38A7; SLC41A2; SON; SP4; SPEN; SSX2IP; STAG2; STOX2; SYPL1; TAB3; TAOK1; TBC1D15; TIMP3; TMEM47; TNRC6A; TNRC6B; TRPM7; TTBK1; TWF1; UBE3C; UBN1; UNC5C; USP47; WDR44; WDR7; YPEL2; YTHDC1; YTHDF3; ZBTB39; ZBTB41; ZBTB7A; ZCCHC14; ZCCHC2; ZCCHC24; ZDHHC17; ZDHHC21; ZFAND5; ZFX; ZFYVE26; ZNF507; ZNF644</i> |
| TACTTGA, MIR-26A, MIR-26B                                  | <i>ABHD2; ACADSB; ACBD5; AKAP6; ALDH5A1; APC; ARID2; ARPP19; ATF2; ATM; ATP11C; ATPAF1; BAZ2B; BHLHE40; BRWD1; BTBD7; CEP350; CLASP2; CLDND1; CREBZF; DAPK1; DMXL1; EIF3A; EPC2; FAM120A; FBXO11; FNIP1; G3BP2; GRHL3; GSK3B; IGF1; KALRN; KLF10; LARP4; MAN2A1; MED13L; MIB1; MXI1; NAP1L5; NDFIP2; NRIP1; NTN4; OSBPL11; OTUD4; PALMD; PAN3; PCK1; PHF6; PHLDB2; PPP3R1; PSD3; PURA; RANBP10; RAP2C; RLF; RNF6; RPS6KA2; RTF1; SALL1; SH3D19; SLC1A1; SLC38A2; SLC4A4; SMAD1; SMAD4; TAB3; TNRC6A; TNRC6B; TOB1; TRIB2; UBE4B; UBR3; USP25; USP9X; WNK3; YPEL1; YTHDF3; ZCCHC24; ZFHX4; ZFX; ZNF217; ZNF462</i>   |
| GCTTGAA, MIR-498   | <i>ANKRD28; ARRD3; ATPAF1; CCNT2; CELF1; CPNE8; DCAKD; DCBLD2; DICER1; EXOC5; FERMT2; FYTDD1; HBP1; HIPK1; IRF2; ITS1; KLF12; NCOA1; PACSIN2; PALM2; PHF6; PIK3R1; PSD3; PTCH1; RNF11; RNF125; SMC1A; SNRK; SS18L1; TSC22D2; TSC22D3; ZFP36L1; ZNF518A</i>  |

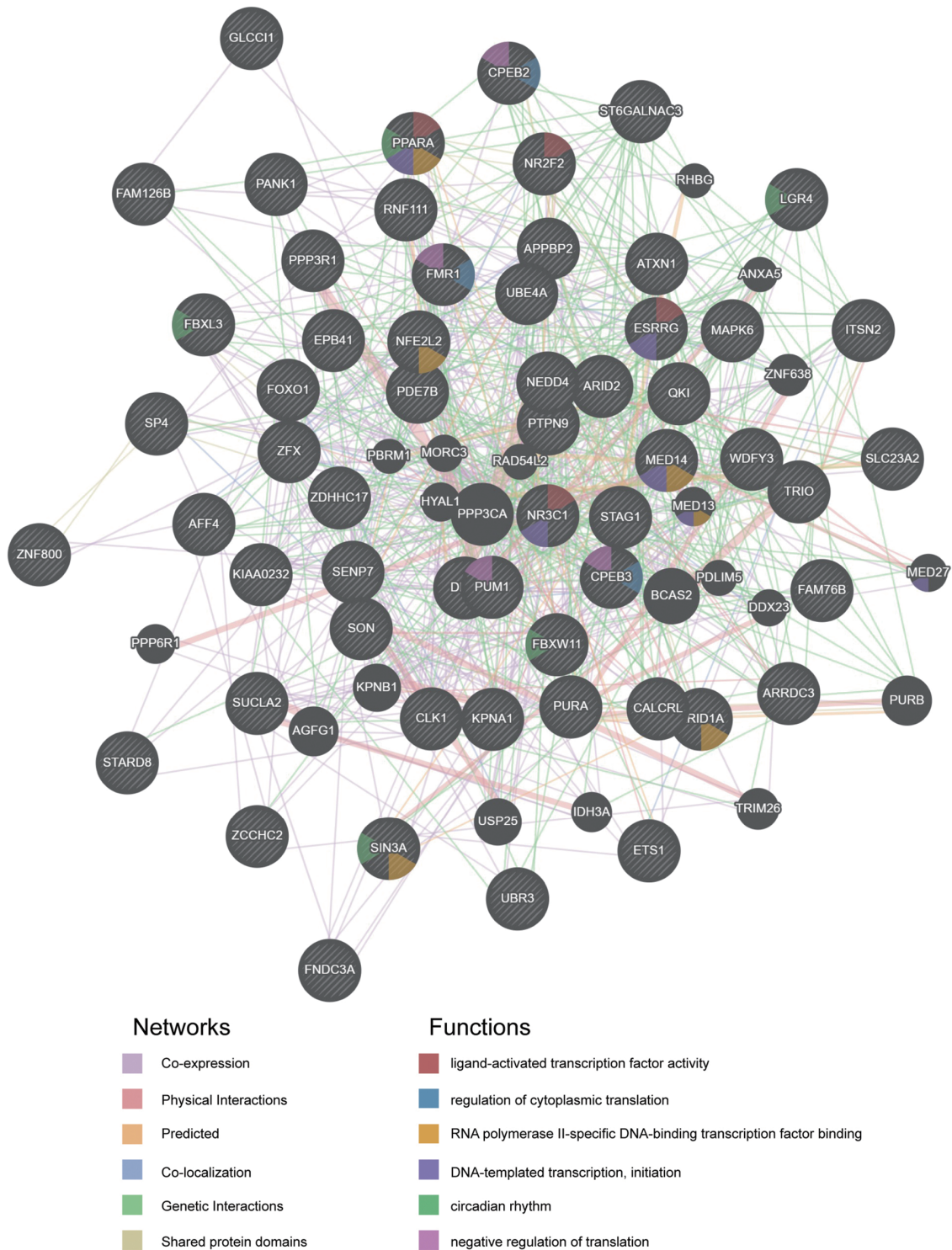
*EIF2S2*, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes (GSEA).

**Table S8** Significantly enriched transcription factor-target networks of *EIF2S2* in HCC (LinkedOmics)

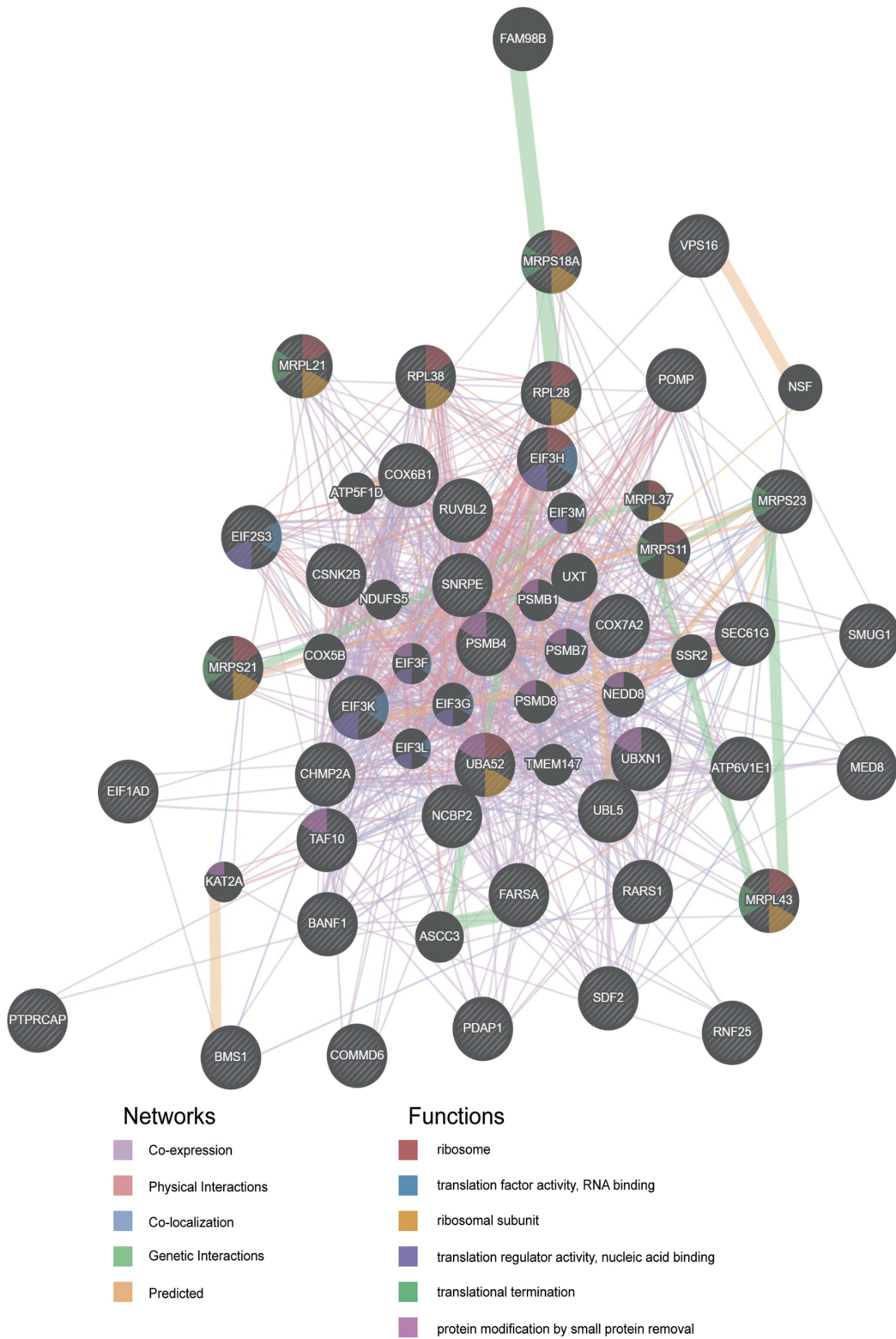
| Geneset              | LeadingEdgeGene   |
|----------------------|---|
| GGAANCGGAANY_UNKNOWN | <i>ATP6V1E1; BANF1; BMS1; CHMP2A; COMMD6; COX6B1; COX7A2; CSNK2B; EIF1AD; EIF2S3; EIF3H; EIF3K; FARSA; MED8; MRPL21; MRPL43; MRPS18A; MRPS21; MRPS23; NCBP2; PDAP1; POMP; PSMB4; PTPRCAP; RARS; RNF25; RPL28; RPL38; RUVBL2; SDF2; SEC61G; SMUG1; SNRPE; TAF10; UBA52; UBL5; UBXN1; VPS16</i>   |
| V\$FREAC2_01         | <i>AKT2; ARID4A; ATXN1; BCAS3; BRIP1; CADM1; CALD1; CELF6; CHD2; CLPX; CREBL2; DUSP1; EHBP1; ERG; EZH1; FRY; HBP1; HIBADH; HIPK1; IGF1; IKZF2; IL6ST; INHBA; KLF12; KLF3; KLHL24; LIN54; LRP5; MAP4K5; MBNL1; MBNL2; NFIB; NFIX; NIPBL; NNT; PCF11; PHLPP1; PIK3C2A; PPM1D; PROX1; PURA; RASGEF1B; RMND5A; RORA; SCRIN3; SERINC3; SIN3A; SMAD1; SNX13; TET2; THRA; TOB1; TPP2; TXNIP; UBE2H; ZADH2; ZFH3; ZFH4; ZNF362; ZNF385B</i>   |
| YNGTTNNNATT_UNKNOWN  | <i>ABLIM1; ACADSB; AMFR; AR; ARL6IP1; ASPA; ATP2A2; CALD1; CAMK1D; CHD2; CHD6; CHMP1B; CHN2; CLMN; CPEB4; CTNND1; DAAM1; DCUN1D1; DIS3L; DMD; DOCK4; DSG1; FAM120A; FMR1; FOXN3; GARNL3; HIPK1; IFIH1; IFT81; IKZF2; IKZF5; ITGA1; JMJD1C; KIF13A; KLF9; MAGI1; MAML3; MIA2; MXI1; NECAP1; NEDD4; NFIB; NFIX; NIPBL; NUMB; PAN2; PGRMC1; PHF6; PIK3R1; POFUT1; PPP2R5E; R3HDM2; RAPH1; RSF1; RUNX1T1; S1PR1; SATB1; SEC24D; SLC2A12; SLC33A1; SLC5A3; SMARCA2; SORBS2; SOX5; SP4; STAG2; STARD13; TAB2; TCF12; THRB; THSD4; TOB1; TSC22D2; WDTC1; ZBTB37; ZFPM2; ZNF148; ZNF638; ZNF641</i> |
| V\$FREAC4_01         | <i>BTBD8; CADM1; CALD1; CAMK1D; CITED2; CTCF; DUSP1; EMP1; ERG; FRY; GFRA1; IGF1; IKZF2; INHBA; KLF12; MAST4; MBNL2; NAALADL2; NEDD4; NNAT; PER2; PHLPP1; PLS3; PUM2; PURA; RUNX1T1; SIN3A; SLC31A1; SNX13; TAF5L; TECTA; TET2; TMOD3; TNMD; UBE2H; UBXN10; USP34; ZADH2; ZBTB37; ZC3H6; ZFX; ZNF385B</i>   |
| V\$FOXO4_02          | <i>ACVR1B; ARFIP1; ARID1B; ARID4A; ATXN1; CADM1; CASC2; CELF6; CFL2; CHD2; CITED2; CLPX; COL8A1; CREBL2; CXXC5; DIXDC1; DOCK4; ELAVL2; ELOVL6; EMP1; ERG; EZH1; FGF12; FOXO1; FRY; GFRA1; HBP1; HMCN1; IKZF2; IKZF4; IL6ST; KLF12; KLHL24; KREMEN1; LRP5; NAP1L5; NEDD4; NFATC3; NFIX; NNAT; NR3C1; NR4A2; NTN1; OTUD7B; PDGFD; PDK4; PHLPP1; PKN2; PTCH1; PURA; RASGEF1B; RSF1; RUNX1T1; SASH1; SATB2; SCRIN3; 44443; SH3GL3; SLC10A7; SLMAP; SMAD1; STAG2; TEK; TEX2; THRA; TNRC6A; TXNIP; UBE2H; UGCG; VSIG2; ZADH2; ZFYVE9; ZNF362; ZNF521; ZNF827</i>                                  |

*EIF2S2*, eukaryotic translation initiation factor 2 subunit beta; HCC, hepatocellular carcinoma; LeadingEdgeNum, the number of leading edge genes (GSEA).





**Figure S2** The protein-protein interaction network of 144 miRNA target networks (GeneMANIA). The network and function analyses showing the gene set enrichment by GeneMANIA. The different edge colors represent the different bioinformatics analysis methods: co-expression, website prediction, pathway, physical interactions, and co-localization. The different node colors indicate the different biological functions of the different gene sets.



**Figure S3** The protein-protein interaction network of transcription factor GGAANCGGAANY\_UNKNOWN target networks (GeneMANIA). The network and function analyses show the gene set enrichment by GeneMANIA. The different edge colors represent the different bioinformatics analysis methods: co-expression, website prediction, pathway, physical interactions, and co-localization. The different node colors indicate the different biological functions of the different gene sets.