**Supplementary Table 1**.

Demographic and clinical characteristics of 19 HCC patients analysed.

| **Variable** | |
|---|---|
| Age, mean ± SEM | 61.2 ± 2.2 |
| Age, range | 46-77 |
| Males, n (%) | 17 (89.5) |
| **Underlying disease**, n (%) | |
| Cirrhosis | 16 (84.2) |
| Hepatitis C virus | 4 (21.1) |
| Alcoholic | 11 (57.9) |
| Diabetes | 2 (10.5) |
| **Tumor stage**, n (%) | |
| BCLCA | 15 (78.9) |
| BCLCB | 3 (15.8) |
| BCLCC | 1 (5.3) |

BCLC, Barcelona Clinic Liver Cancer.

**Supplementary Table 2.** Sequence of oligonucleotide primers used for quantitative PCR.

| **Gene** | **Accesion number** | **Forward primer (5’ – 3’)** | **Reverse primer (5’ – 3’)** |
|---|---|---|---|
| **Human** | | | |
| *hOCT1* total | NM_003057 | TGCAGACAGGTTTGGCCGT | GCCCGAGCCAACAAATTCTGTGAT |
| *hOCT1* Full length | NM_003057 | GATTTTTATCTCACCTGACCTGCACTGGTT | AGGCCCAACACCGCAAACA |
| *hOCT1* Spliced | NM_003057 | GGAAGCGCACCTTCATCCTGAT | CAGGTGCCCGAGGGTTCT |
| *hAUF1* | NM_001003810 | GTAAGAACGAGGAGGATGAAGGGAAAATGT | TTGATCCATGACCTTATCTACACTCTCCGA |
| *hCUGBP* | NM_006560 | CCTCAGAGCAAAGGGTGCTGTT | TCCTGTCTTCCACTGCATTGTTCTTCT |
| *hHUR* | NM_001419 | CGGGATAAAGTAGCAGGACACAGCTT | GGGCGAGCATACGACACCTT |
| *hTTP* | NM_003407 | CTGCCATCTACGAGAGCCTCCT | GCGAAGTGGGTGAGGGTGA |
| *hBRF1* | NM_004926 | GCGTGTGGGACTCCAGACA | TCTTGTTACCCTTGCATAAAACTTCGCTCA |
| *hBRF2* | NM_006887 | CCCGTTATTCGTCGTGGCTCAA | CCAGGGATTTCTCTGTCTTGCACA |
| *hFBP2* | NM_003685 | GTTGGAAGATGGAGATCAACCGGAGA | GTCATTGAAGTCCTTGGGGGAGGAT |
| *hGAPDH* | NM_002046 | TGAGCCCGCAGCCTCC | TACGACCAAATCCGTTGACTCC |
| *hHPRT1* | NM_000194 | GCCCTGGCGTCGTGATTAGT | AGCAAGACGTTCAGTCCTGTCCATAA |
| **Mouse** | | | |
| *mOct1* | NM_009202 | TCGTCACTGAGTTTAACCTGGTGTGT | TTACGGCCAAACCTGTCTGCAA |
| *mGapdh* | NM_008084 | ACACTGAGCAAGAGAGGCCCTA | GGGTGCAGCGAACTTTATTGATGGTATT |
| **Rat** | | | |
| *rOct1* | NM_012697 | CATTGCAGACAGGTTTGGCCGTAA | GCAGGCGAAAGAGCAACATGGAT |
| *rActb* | NM_031144 | TCTGTGTGGATTGGTGGCTCTA | CTGCTTGCTGATCCACATCTG |

**Supplementary Table 3.** Sequence of forward (F) and reverse (R) oligonucleotide primers used for cloning.

| Gene | | Oligonucleotide sequence 5' – 3' |
|---|---|---|
| *hOCT1* | F | CCAAGGTTCCTTAATTAAGCCAAGATGCCCACCGTGGAT |
| | R | GGAACCTTGGTTAATTAAGGTGCCCGAGGGTTCTGA |
| *hOCT3* | F | AATTGGCCACGCGTACCATGCCCTCCTTCGACG |
| | R | AACCTTGGACTAGTAAGGTGAGAGCGGGAAACTGG |
| *sh-OCT1* | F | CGCGTAAGAACGGTGGCGATCATGTACCAGATGGTTCAAGAGACCATCTGGTACATGATCGCCACCGTTCTTTTTTTGGAAAT |
| | R | CGATTTCCAAAAAAAGAACGGTGGCGATCATGTACCAGATGGTCTCTTGAACCATCTGGTACATGATCGCCACCGTTCTTA |
| *sh-Luc2* | F | CGCGTCTGACGCGGAATACTTCGATTCAAGAGATCGAAGTATTCCGCGTCAGTTTTTGGAAATCG |
| | R | CGATTTCCAAAAACTGACGCGGAATACTTCGATCTCTTGAATCGAAGTATTCCGCGTCAGACGCG |
| *hsa-mir-330* | F1 | CGCGTCTTTGGCGATCACTGCCTCTCTGGGCCTGTGTCTTAGGCTCTGCAAGA |
| | R1 | GGTTGATCTTGCAGAGCCTAAGACACAGGCCCAGAGAGGCAGTGATCGCCAAAGA |
| | F2 | TCAACCGAGCAAAGCACACGGCCTGCAGAGAGGCAGCGCTCTGCCCAT |
| | R2 | CGATGGGCAGAGCGCTGCCTCTCTGCAGGCCGTGTGCTTTGCTC |
| *hsa-mir-769* | F1 | CGCGTGCCTTGGTGCTGATTCCTGGGCTCTGACCTGAGACCTCTGGGTTCTGAGCTGTGATGTT |
| | R1 | GAGCAACATCACAGCTCAGAACCCAGAGGTCTCAGGTCAGAGCCCAGGAATCAGCACCAAGGCA |
| | F2 | GCTCTCGAGCTGGGATCTCCGGGGTCTTGGTTCAGGGCCGGGGCCTCTGGGTTCCAAGCTTTTTGGAAAT |
| | R2 | CGATTTCCAAAAAGCTTGGAACCCAGAGGCCCCGGCCCTGAACCAAGACCCCGGAGATCCCAGCTCGA |
| *hsa-mir-141* | F1 | CGCGTCGGCCGGCCCTGGGTCCATCTTCCAGTACAGTGTTGGATGGTCTAAT |
| | R1 | GCTTCACAATTAGACCATCCAACACTGTACTGGAAGATGGACCCAGGGCCGGCCGA |
| | F2 | TGTGAAGCTCCTAACACTGTCTGGTAAAGATGGCTCCCGGGTGGGTTCTTTTTGGAAAT |
| | R2 | CGATTTCCAAAAAGAACCCACCCGGGAGCCATCTTTACCAGACAGTGTTAGGA |
| *hsa-mir-6806* | F1 | CGCGTTGCTCTGTAGGCATGAGGCAGGGCCCAGGTTCCAT |
| | R1 | ATCACATGGAACCTGGGCCCTGCCTCATGCCTACAGAGCAA |
| | F2 | GTGATGCTGAAGCTCTGACATTCCTGCAGTTTTTGGAAAT |
| | R2 | CGATTTCCAAAAACTGCAGGAATGTCAGAGCTTCAGC |
| *hsa-mir-1287* | F1 | CGCGTGTTGTGCTGTCCAGGTGCTGGATCAGTGGTTCGAGTCTGAGCCT |
| | R1 | GGCTTTTAAAGGCTCAGACTCGAACCACTGATCCAGCACCTGGACAGCACAACA |
| | F2 | TTAAAAGCCACTCTAGCCACAGATGCAGTGATTGGAGCCATGACAATTTTTGGAAAT |
| | R2 | CGATTTCCAAAAATTGTCATGGCTCCAATCACTGCATCTGTGGCTAGAGT |
| *hsa-mir-1468* | F1 | CGCGTGGTGGGTGGTTTCTCCGTTTGCCTGTTTCGCTGATGTGCATTC |
| | R1 | AGTTGAATGCACATCAGCGAAACAGGCAAACGGAGAAACCACCCACCA |
| | F2 | AACTCATTCTCAGCAAAATAAGCAAATGGAAAATTCGTCCATCTTTTTGGAAAT |
| | R2 | CGATTTCCAAAAAGATGGACGAATTTTCCATTTGCTTATTTTGCTGAGAATG |

**Supplementary Table 4.** Selected miRNA based on expression-related criteria

| **Expression-related criteria for microRNA selection** | |
|---|---|
| **1** | Predicted miRNA interaction with hOCT1 by at least two of the following on-line tools: miRBase, data integrated portal, DIP analysis, EMBL.EBI, miRDB, miRTar, and microrna. |
| **2** | Clearly expressed in HCC as described in TCGA with a value of >10 RPMMM (reads per million of miRNA mapped) |
| **3** | Relationship between miRNA levels and the expression of hOCT1 in HCC according to TCGA:<br>i) inverse correlations were preferred<br>ii) positive correlations with r≥0.11 were discarded |

**Selected microRNA**

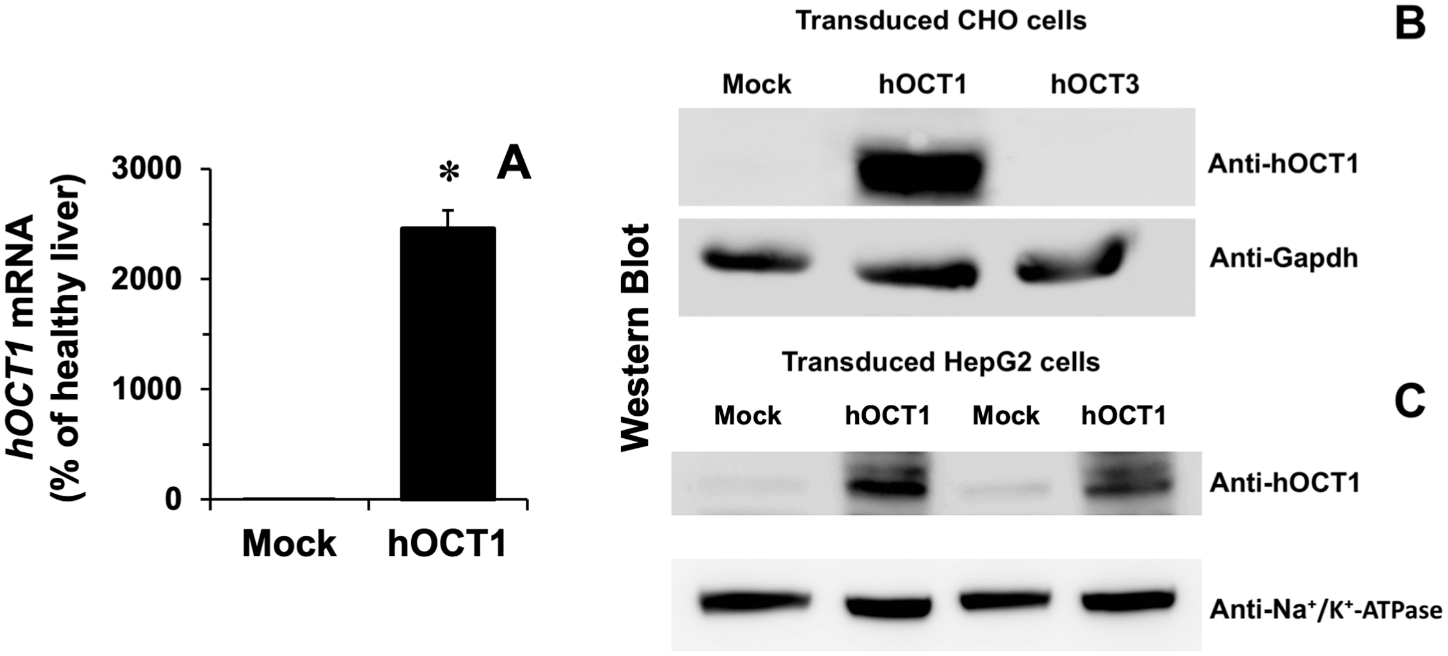
| **microRNA** | **Correlation with *hOCT1* mRNA** | **r** |
|---|---|---|
| hsa-miR-330-3p | inverse | -0.4050 |
| has-miR-1269a | inverse | -0.3500 |
| hsa-miR-769-3p | inverse | -0.2943 |
| hsa-miR-541-3p | inverse | -0.2774 |
| hsa-miR-141-5p | inverse | -0.1718 |
| hsa-miR-598 | inverse | -0.0946 |
| hsa-miR-1468-3p | inverse | -0.0897 |
| hsa-miR-1-2 | inverse | -0.0801 |
| hsa-miR-324-5p | inverse | -0.0618 |
| hsa-let.7d | inverse | -0.0082 |
| hsa-miR-1287-3p | direct | 0.1003 |

**Supplementary Table 5.** Selected miRNA based on structure-related criteria

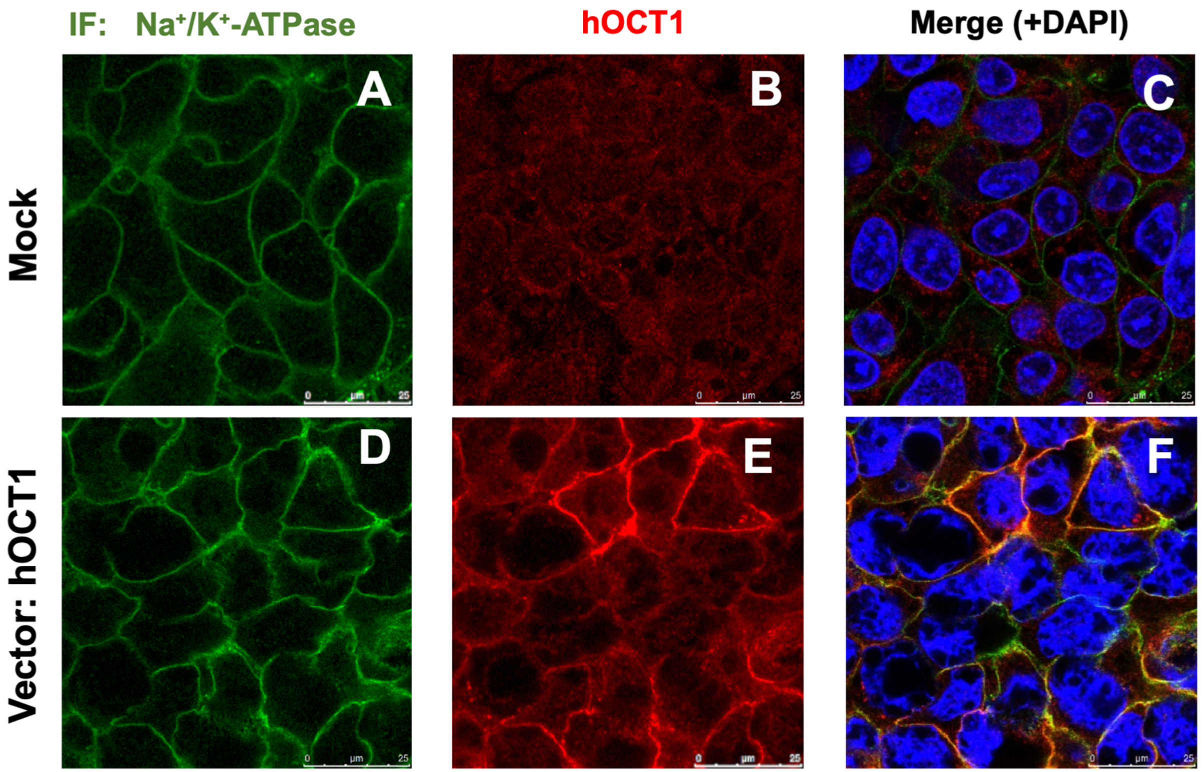
| miRNA selection based on structure-related criteria | | | | | |
|---|---|---|---|---|---|
| **Criteria** | **a** | **b** | **c** | **d** | **Score** |
| hsa-miR-1468-3p | 3 | 3 | 1 | 3 | 10 |
| hsa-miR-330-3p | 2 | 3 | 2 | 2 | 9 |
| hsa-miR-6806-5p | 2 | 3 | 2 | 2 | 9 |
| hsa-miR-1287-3p | 2 | 3 | 1 | 3 | 9 |
| hsa-miR-141-5p | 2 | 3 | 1 | 2 | 8 |
| hsa-miR-769-3p | 2 | 3 | 1 | 2 | 8 |

Micro-RNA from Supplementary Table 3 with the highest score calculated based on structure-related criteria were selected. Based on published evidence on the potential interest of hsa-mir6806-5p, this was also included in the analysis. The weight of each criteria was stablished between 1 and 3. Definition of structure-related criteria was as follows:

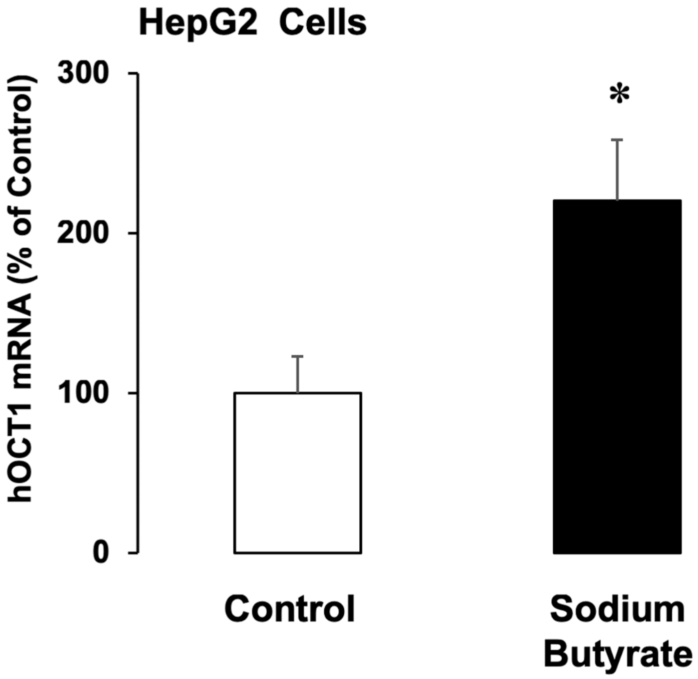
a) Proportional to the number of matching nucleotides
b) Involvement in the binding of microRNA “seed structure”
c) Presence of complementary binding nucleotides near the microRNA binding site
d) Presence of AU nucleotides near the complementary binding site



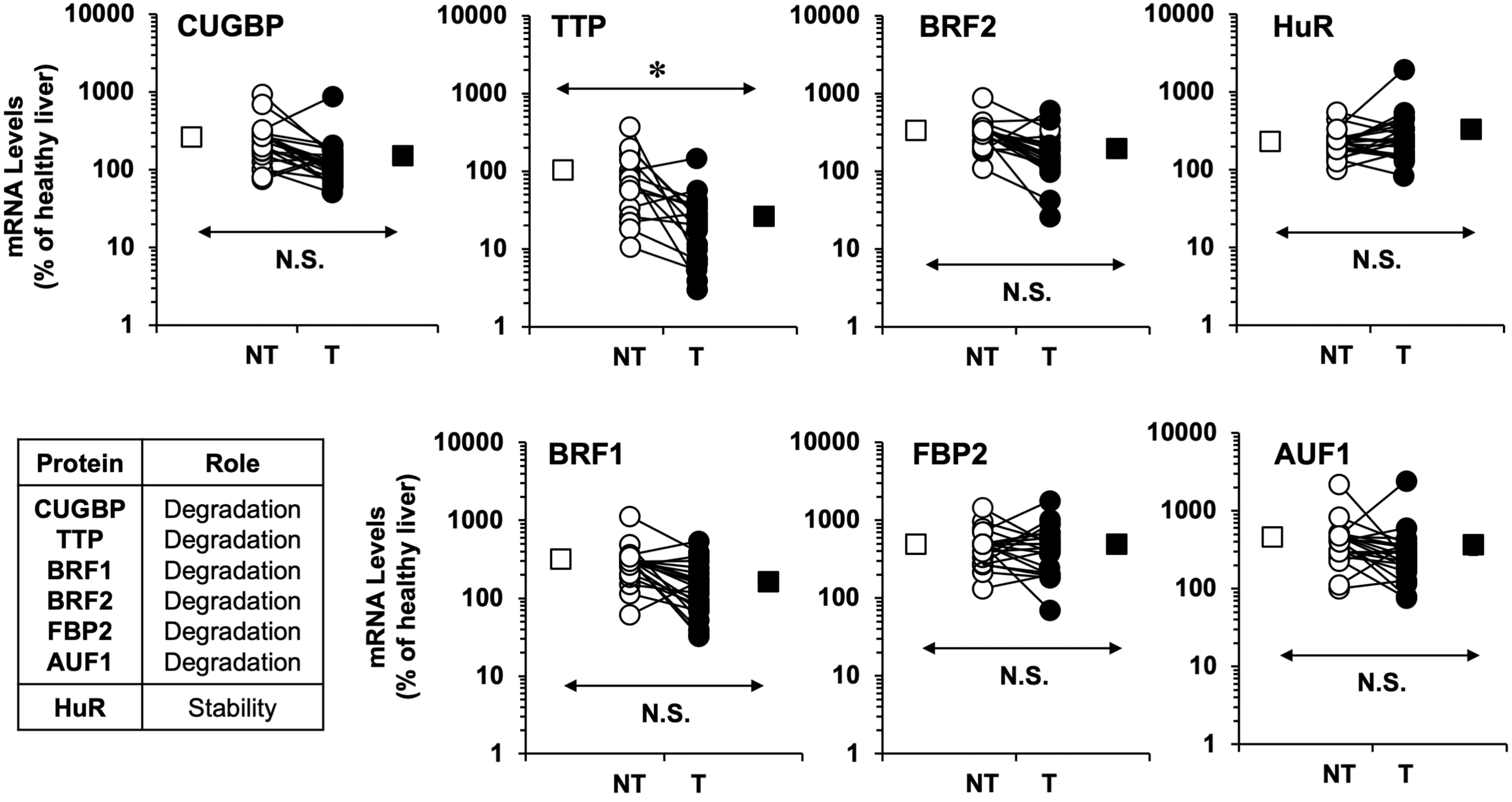
**Supplementary Figure 1.** (A) Relative *hOCT1* mRNA levels in HepG2 cells transduced with lentiviral vectors either empty (Mock) or containing the *hOCT1* coding sequence. Results are mean±SEM (n=5). *, $P<0.05$ on comparing both groups by Student *t*-test. (B) Specificity test of the primary antibody used in immunoblotting against hOCT1. CHO cells were transduced with empty vectors (Mock) or vectors containing hOCT1 or hOCT3 coding sequence. Immunoblot was carried out with cell lysates. Gapdh was used for normalization. (C) Immunoblots (n=5) were then performed in crude preparations of cell membranes obtained from HepG2 cells (Mock and hOCT1). $Na^+/K^+$-ATPase was used as normalizer.



**Supplementary Figure 2.** Immunofluorescence detected by confocal microscopy in HepG2 cells transduced with Mock vectors (A-C) or hOCT1 (D-F) stained with anti-hOCT1 (red) and anti-Na$^+$/K$^+$-ATPase (green) antibodies. Merge images (C and F) show the nuclei stained with DAPI.



**Supplementary Figure 3.** Relative expression (mRNA levels) of hOCT1 in HepG2 cells after incubation without or with 5 mM sodium butyrate for 24 h. Results are mean±SEM (n=5). *, $P<0.05$ on comparing both groups by paired *t*-test.



| Protein | Role |
|---|---|
| CUGBP | Degradation |
| TTP | Degradation |
| BRF1 | Degradation |
| BRF2 | Degradation |
| FBP2 | Degradation |
| AUF1 | Degradation |
| HuR | Stability |

**Supplementary Figure 4.** Relative expression (mRNA levels) in biopsies (n=13) of hepatocellular carcinoma (HCC) of genes involved in favouring mRNA degradation or stability (see table in the inset) as determined by RT-qPCR in the tumour (T) and paired adjacent non-tumour (NT) tissue. Results are shown as individual values (circles) and mean±SEM (squares). *, $P<0.05$ comparing T with NT; N.S., not significant difference.