|  |  |  |
| --- | --- | --- |
| A) |  | *Up-regulated genes in both HCV liver tissues and PBMCs \*\*(47)* |
|   | GENE BANK NUMBER | symbol  | HCV+ liver tissues  | HCV+ PBMCs |   |
|   |   |   | FOLD CHANGE |   FOLD CHANGE |  |
|   |   |  P53 PATHWAYS (2) |
|   | NM\_053056 | CCND1 | 4,9 | 3,75 | Cyclin D1 |
|   | NM\_005225 | E2F1 | 7,81 | 5,8 | E2F transcription factor 1 |
|   |   |  WNT BETA CATENIN (7) |
|   | NM\_003394 | WNT10B  | 22,96 | 21,9 | Wingless-type MMTV integration site family, member 10B |
|   | NM\_003392 | WNT5A  | 8,09 | 5,421 | Wingless-type MMTV integration site family, member 5A |
|   | NM\_032642 | WNT5B  | 4,6 | 8,57 | Wingless-type MMTV integration site family, member 5B |
|   | NM\_030756 | TCF7L2  | 16,61 | 20,51 | Transcription factor 7-like 2 (T-cell specific, HMG-box)  |
|   | NM\_002335 | LRP5  | 3,15 | 6,37 | Low density lipoprotein receptor-related protein 5  |
|   | NM\_012242 | DKK1  | 12,8 | 13,42 | Dickkopf homolog 1 (Xenopus laevis)  |
|   | NM\_003015 | SFRP5 | 6,69 | 5,04 | Secreted frizzled-related protein 5 |
|   |   |  FIBROSIS (2) |
|   |   NM\_004465 | FGF10 | 13,2 | 12,44 |   Fibroblast growth factor 10 |
|   |   NM\_002006 | FGF2 | 8,6471 | 6,3 |   Fibroblast growth factor 2 |
|   |   |  INSULIN PATHWAYS (4) |
|   | NM\_005524 | HES1 | 4,28 | 5,85 | Hairy and enhancer of split 1, (NOTCH SIGNALS) |
|   | NM\_000208 | INSR | 6,98 | 7,38 | Insulin receptor  |
|   | NM\_003749 | IRS1 | 3,99 | 3,9 | Insulin receptor substrate 2 |
|   | NM\_001042 | GLUT4  | 15,28 | 12,61 | Glut 4 |
|   |   | PPAR'S AND ENERGY METABOLISM (4) |
|   | NM\_006238 | PPARD | 2,46 | 2,6 | PPARdelta  |
|   | NM\_013261 | PPARGC1A | 32,24 | 26,92 | pgc1alpha |
|   | NM\_000116 | TAZ | 67,23 | 35,54 | Tafazzin  |
|   | NM\_133263 | PPARGC1B | 8,07 | 4,49 | Pgc1beta  |
|   |   | NUCLEAR RECEPTOR AND METABOLISM (10) |
|   | NM\_001093 | ACACB | 2,96 | 3,42 | Acetyl-CoA carboxylase beta |
|   | NM\_001442 | FABP4 | 2,57 | 3,2 | Fatty acid binding protein 4, adipocyte  |
|   | NM\_004104 | FASN | 2,93 | 5,77 | Fatty acid synthase  |
|   | NM\_005693 | NR1H3  | 5,21 | 12,17 | Liver X receptor alpha (LXR) |
|   | NM\_004176 | SREBF1 | 8,44 | 6,69 | Sterol regulatory element binding transcription factor 1 |
|   | NM\_021969 | NR0B2 | 4,77 | 4,97 | Nuclear receptor subfamily 0, group B, member 2 |
|   | NM\_033131 | SIRT3 | 2,5135 | 2,05 |  Sirtuin 3 |
|   | NM\_014079 | KLF15 | 4,18 | 5,73 |  Kruppel like factor 15 |
|   | NM\_016531 | KLF3 | 3,65 | 6,03 |  Kruppel like factor 3 |
|   | NM\_000376 | SHH | 28,2218 | 13,97 |  Sonic Hedgehog |
|   |   |  INFLAMMATION and TGF BETA PATHWAYS (11) |
|   | NM\_199454 | PRDM16 | 4,65 | 13,78 | PR domain containing 16 |
|   | NM\_130851 | BMP4 | 25,07 | 23,47 | Bone morphogenetic protein 4 |
|   | NM\_001200 | BMP2 | 3,97 | 6,79 | Bone morphogenetic protein 2 |
|   | NM\_130851 | BMP7 | 6,52 | 4,51 | Bone morphogenetic protein 7 |
|   | NM\_001928 | CFD | 5,53 | 5,75 | Adipsin |
|   | NM\_000474 | TWIST 1 | 24,07 | 28,83 |  Twist 1 |
|   | NM\_020415 | RETN | 32,51 | 30,19 | Resistin  |
|   | NM\_001018082 | ADIG | 22,78 | 29,42 | Adipogenin  |
|   | NM\_004797 | ADIPOQ | 3,12 | 2,55 | Adiponectin, C1Q and collagen domain containing |
|   | NM\_000230 | LEP | 7,17 | 6,38 | Leptin  |
|   | NM\_000237 | LPL | 4,5 | 9,64 | Lipoprotein lipase  |
|   |   |   |   |   |   |  |
|   |   | SIGNAL TRASDUCTION and REGULATION (7) |
|   | NM\_000793 | DIO2 | 14,2 | 16,82 | Deiodinase, iodothyronine, type II |
|   | NM\_003836 | DLK1 | 3,88 | 9,27 | Delta-like 1 homolog (Drosophila) |
|   | NM\_004364 | CREB1 | 7,4597 | 36,86 |  CAMP responsive element binding 1 |
|   | NM\_005357 | GATA2 | 2,7537 | 2,05 |  GATA 2 bindinf protein |
|   | NM\_005251 | FOXC2 | 3,71 | 2,53 | Forkhead box C2 (MFH-1, mesenchyme forkhead 1) |
|   | NM\_000399 | EGR2 | 17,45 | 10,06 | Early growth response 2 |
|   | NM\_004364 | CEBPA | 5,3 | 4,2 | CCAAT/enhancer binding protein (C/EBP), alpha |
|   |   |  |  |  |  |
| B) |  | *Down-regulated genes in both HCV+ liver tissues and PBMCs (6)* |
|   | GENE BANK NUMBER | symbol | HCV+ liver tissues | HCV+ PBMCs |
|   |   |  | FOLD CHANGE | FOLD CHANGE |
|   |   |  |  |  |  |
|   | NM\_004089 | TSC22D3 | 0 | 0 | TSC22 domain family, member 3 |
|   | NM\_033131 | WNT3A | 0,0003 | 0,0001 | Wingless-type MMTV integration site family, member 3A |
|   | NM\_021833 | UCP1 | 0,001 | 0,0016 | Uncoupling protein 1 (mitochondrial, proton carrier) |
|   | NM\_000376 | VDR | 0 | 0 | Vitamin D (1,25- dihydroxyvitamin D3) receptor |
|   | NM\_005430 | WNT1 | 0 | 0 | Wingless-type MMTV integration site family, member 1 |
|   | NM\_003502 | AXIN1 | 0,3908 | 0,3196 | axin1 |
| C) | *No-modulated genes in both HCV+ liver tissues and PBMCs (8)* |  |
|   | GENE BANK NUMBER | symbol  |   | HCV+ liver tissues | HCV+ PBMCs |   |
|   |   |  |  | FOLD CHANGE |   FOLD CHANGE |   |
|   | NM\_005572 |  | LMNA | 1,0935 | 0,9968 | Lamin A/C |
|   | NM\_004235 |  | KLF4 | 0,9119 | 0,7112 | Kruppel-like factor 4 (gut) |
|   | NM\_000389 |  | CDKN1A | 0,9962 | 0,9064 | Cyclin-dependent kinase inhibitor 1A (p21, Cip1) |
|   | NM\_005011 |  | NRF1 | 0,8016 | 0,6815 | Nuclear respiratory factor 1 |
|   | NM\_012238 |  | SIRT1 | 1,4083 | 1,458 | Sirtuin 1 |
|   | NM\_012237 |  | SIRT2 | 0,6538 | 0,9242 | Sirtuin 2 |
|   | NM\_005417 |  | SRC | 1, 284 | 0,8933 | V-src sarcoma viral oncogene |
|   | NM\_001315 |  | MAPK14 | 0,9025 | 0,8518 | Mitogen-activated protein kinase 14 |
| D) | *Analysis of modulated genes in only HCV liver tissues or PBMCs (23)* |   |
|   | GENE BANK NUMBER | Symbol |  | HCV+ liver tissues | HCV+ PBMCs |   |
|   |   |  |  |  FOLD CHANGE | FOLD CHANGE |   |
|   | NM\_000024 |   | ADRB2 | 0,00 | nm | Adrenergic, beta-2-, receptor, surface |
|   | NM\_000029 |   | AGT | 159,07 | nm | Angiotensinogen (serpin peptidase inhibitor, clade A |
|   | NM\_001147 |   | ANGPT2 | Nm | 2,76 | Angiopoietin 2 |
|   | NM\_000075 |   | CDK4 | 4,50 | nm | Cyclin-dependent kinase 4 |
|   | NM\_004064 |   | CDKN1B | 0,39 | nm | Cyclin-dependent kinase inhibitor 1B (p27, Kip1) |
|   | NM\_005194 |   | CEBPB | 2,03 | nm | CCAAT/enhancer binding protein (C/EBP), beta |
|   | NM\_005195 |   | CEBPD | Nm | 3,39 | CCAAT/enhancer binding protein (C/EBP), delta |
|   | NM\_004083 |   | DDIT3 | 2,13 | 0,44 | DNA-damage-inducible transcript 3 |
|   | NM\_000800 |   | FGF1 | 2,72 | nm | Fibroblast growth factor 1 (acidic) |
|   | NM\_002015 |   | FOXO1 | Nm | 2,26 | Forkhead box O1 |
|   | NM\_002051 |   | GATA3 | 0,41 | 2,24 | GATA binding protein 3 |
|   | NM\_003749 |   | IRS2 | Nm | 4 | Insulin receptor substrate 2 |
|   | NM\_002228 |   | JUN | Nm | 4,88 | Jun proto-oncogene |
|   | NM\_016270 |   | KLF2 | 0,05 | nm | Kruppel-like factor 2 (lung) |
|   | NM\_005357 |   | LIPE | Nm | 6,04 | Lipase, hormone-sensitive |
|   | NM\_005036 |   | PPARA | 16,49 | nm | Peroxisome proliferator-activated receptor alpha |
|   | NM\_015869 |   | PPARG | 6,03 | nm | Peroxisome proliferator-activated receptor gamma |
|   | HS\_446678 |   | NCOA2 | 4,07 | nm | Nuclear receptor coactivator 2 |
|   | HS\_137510 |   | NCOR2 | 2,59 | nm | Nuclear receptor corepressor 2 |
|   | NM\_000321 |   | RB1 | 16,52 | nm | Retinoblastoma 1 |
|   | NM\_175636 |   | RUNX1T1 | 2,75 | nm | Runt-related transcription factor 1 (cyclin D-related) |
|   | NM\_002957 |   | RXRA | 30,05 | nm | Retinoid X receptor, alpha |
|   | NM\_003012 |   | SFRP1 | 8,82 | nm | Secreted frizzled-related protein 1 |

FOOTNOTES The results are the fold change respect to HDs; \*\* the up-regulated genes were divided in respect their functions