

GENE PRODUCT	UNALTERED HEPATOCYTES		HEPATOCARCINOGENESIS				
	insulin effect on mRNA	Information	Rat PNL	Rat HCA Array	Human CL/DNL/HCA	Rat HCC Array	Human HCC
ACACA Acetyl-coenzyme A carboxylase α	↑	FOXO1-regulated in liver. Insulin enhances promotor activity. Insulin-induced via SREBP-1c.	↔	1,5	HCA: ↑ Rebouissou S et al (2007) JBC, doi:org/10.1074/jbc.M610725200	1,75	↑ Nelson ME et al (2017) Nature Comm, doi: 10.1038/ncomms14689 Calvisi DF et al (2011) Gastroenterol doi.org/10.1053/j.gastro.2010.12. 006 Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
ACACB	↓	Downregulated by insulin in liver.		0,81		0,58	
ACLY ATP citrate lyase/ synthase	↑	Insulin-induced in liver via SREBP-1c. mTORC1-induced. FOXO1-regulated in liver.	↔	1,12	HCA: ↑ Rebouissou S et al (2007) JBC, doi:org/10.1074/jbc.M610725200	1,43	↑ Yahagi N et al (2005) Eur J Cancer, doi: org/10.1016/j.ejca.2004.12.037; Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Calvisi DF et al (2011) Gastroenterol doi.org/10.1053 /j.gastro.2010.12.006; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
ACSL5	↑	SREBP-1c-induced in liver. FOXO1-regulated in liver.		1,25		1,49	
ALDOA Aldolase A	↑	Insulin-induced via HIF1 α . mTORC1-induced.	+	1,91	CL: ↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138	1,74	↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138 Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Khan MW et al (2015) Cell Death Discov, doi: 10.1038/ cddiscovery.2015.16; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
ALDOB Aldolase B	↑	FOXO1-regulated in liver.).		0,92		0,96	↓ Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
APOA5	↓	Downregulated by insulin in liver.		0,38		0,2	
ASNS Asparagine synthetase	↑	Insulin-induced via ATF4. Insulin-induced via c/EBP β .	+	3,84	CL: ↑ Zhang B et al (2013) Br J Cancer, doi:10.1038/bjc.2013.293 (2013)	5,23	↑ Zhang B et al (2013) Br J Cancer, doi:10.1038/bjc.2013.293 (2013); Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
CD36 Thrombo-spondin receptor)	↑	Insulin-induced in steatosis model.	+	1,59		1,44	↑ Nath A et al (2015) Sci Rep, doi: 10.1038/srep14752
CPT1A Carnitine palmitoyl- transferase I	↓	Insulin-mediated downregulation via SREBP-1c.	-	0,57		0,6	↑ Kurokawa T et al (2011) World J Surg Oncol, doi:10.1186/1477- 7819-9-167
DDR1 Discoidin domain rec. tyrosine kinase 1	↑S	DDR1 enhances insulin-mediated signaling.	+	3,26		2,07	↑ Shen Q. et al (2010) Mol Cancer doi:10.1186/1476-4598-9-227
EGLN3 / PHD3 α -ketogluta-rate- depend. hydroxylase 3 / Prolylhy droxy- lase 3	↔ S	PHD3 depletion leads to impaired insulin signalling in hepatocytes	+	2,52		2,98	↑ Jiang L et al (2018) Oncology letters, doi:10.3892/ol.2017.7302
ELOVL6 Elongation of long-chain fatty acids family member 6	↑	FOXO1-regulated in liver SREBP-1/1c-regulated	+	3,09		3,38	Advanced HCC ↑ Su YC et al (2018) Sc Rep, doi:10.1038/s41598-018-24633-3
ENO1 Enolase	↑	FOXO1-regulated in liver	unch ange d	1,31		1,51	↑ Lee NCW et al (2018) Front Cell Develop Biol, doi: 10.3389 / fcell. 2018.00138 Zhu W et al (2018) Cancer Man & Res, doi:10.2147/CMAR.S182183 Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Nwosu ZC et al (2017) Cell Mol

							Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
ENPP1 Ectonucleotide pyro-phosphatase / phospho- diesterase 1	↓S	Insulin reduces expression in hepatocytes	unchanged	1,21		1,69	↓ Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023
FASN Fatty acid synthetase	↑	FOXO1-regulated in liver mTORC1-induced Insulin-upregulated in fetal sheep liver SREBP-1c-induced Regulated via nuclear insulin-receptor Insulin-induced via SCD1-activated Wnt/β-catenin signaling	unchanged	1,67	HCA: ↑ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	1,7	↑ Yahagi N et al (2005) Eur J Cancer, doi: org/10.1016/j.ejca.2004.12.037; Calvisi DF et al (2011) Gastroenterol, doi: org/10.1053/j.gastro.2010.12.006; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
FBP1 Fructose-1,6- biphosphatase-1	↓	FOXO1-regulated	-	0,74	HCA: ↓ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	0,47	↓ Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Yang J et al (2017) Carcinogen, doi:10.1093/carcin/bgw109; Khan MW et al (2015) Cell Death Discov, doi: 10.1038/ cddiscovery.2015.16; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
G6PC Glucose-6- phosphatase	↓	FOXO1-regulated in liver Downregulated by insulin in liver	-	0,35	HCA: ↓ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	0,43	↓ Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023-; Khan MW et al (2015) Cell Death Discov, doi: 10.1038/ cddiscovery.2015.16; Wang B et al (2012) Hepatology, doi.org/10.1002/hep.25632; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
G6PD Glucose-6- phosphate dehydrogenase	↑	mTOR-induced mTORC1-induced	+	4,66	CL: ↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138	2,61	↑ Lee NCW et al (2018) Fr Cell Dev Biol,doi:10.3389/fcell.2018.00138; Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
GAPDH Glyceraldehyde- 3-phosphate dehydrogenase	↑	FOXO1-regulated in liver IBP/IRE-mediated induction	unchanged	1,24		1,21	↑ Gong Y et al (1996) Hepatol, doi: 10.1002/hep.510230413; Lee NCW et al (2018) Fr Cell Dev Biol,doi:10.3389/fcell.2018.00138 Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Khan MW et al (2015) Cell Death Discov, doi: 10.1038/ cddiscovery.2015.16
GPAM Glycerol-3- phosphate acyltransferase 1	↑	Insulin enhances transcription via SREBP-1c		1,2		1,45	
GPI Glucose-6- phosphate isomerase	↑	FOXO1-regulated in liver mTORC1-induced	unchanged	1,1	HCA: ↑ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	1,95	↑ Lee NCW et al (2018) Fr Cell Dev Biol,doi:10.3389/fcell.2018.00138; Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023
HK1 Hexokinase 1	↑	mTORC1-induced	+	2,04		1,55	
HK2 Hexokinase 2	↑	mTORC1-induced Akt-regulated		1,3	CL: ↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138 DeWaal D et al (2018) Nat Commun, doi.org/10.1038/ s41467-017-02733-4. DL: ↑ Guzman G et al (2015), Dig Dis Sci, doi.org/10.1007%2Fs10620- 014-3364-3 DeWaal D et al (2018) Nat Commun, doi.org/10.1038/ s41467-017-02733-4; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004	1,1	↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138 Guzman G et al (2015), Dig Dis Sci, doi.org/10.1007%2Fs10620- 014-3364-3 DeWaal D et al (2018) Nat Commun, doi.org/10.1038/ s41467-017-02733-4; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004

HK4/GCK Hexokinase 4 / Glucokinase	↑	FOXO1-regulated in liver Insulin-dependent transcription in liver Upregulated by insulin in liver	unchanged	1,02	HCA: ↑ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	1,21	↓ Lee et al (2018) Front Cell Dev Biol, doi:10.3389/fcell.2018.00138; Mathupala SP et al (2006) Oncogene, doi:10.1038/sj.onc.1209603; Perrin-Cocon L et al (2021) Nature Comm, doi.org/10.1038/s42003-021-01749-3
HMGCR 3-Hydroxy-3-methylglutaryl-Coenzyme A reductase / HMG-CoA Reductase	↑	Upregulated by insulin in liver SREBP-2 regulated	+	1,8		2,53	↑ Calvisi DF et al (2011) Gastroenterol doi.org/10.1053/j.gastro.2010.12.006
HMGCS1 Hydroxymethylglutaryl-CoA synthase (cytosolic)	↑	Upregulated by insulin in liver	-	0,62		0,59	
HPD 4-hydroxy-phenylpyruvate dioxygenase	↓	FOXO1-regulated in liver		0,66		0,7	
INSIG1 Insulin-induced gene 1	↓S	Downregulated by insulin in liver	-	0,51		0,57	↓ Fritz VH et al (2019) Z Gastroenterologie, doi:10.1055/s-0038-1677210
INSIG2 Insulin-induced gene 2	↓S	Downregulated by insulin in liver	unchanged	0,61		0,94	
INSR Insulin receptor	(↓)S	FOXO-mediated downregulation in liver	unchanged	0,72		0,92	
IRS2 Insulin receptor substrate 2	↓S	FOXO1-regulated in liver PI3K/Akt-mediated downregulation in liver cells	-	0,61		0,83	↑ Boissan M et al (2005) Am J Pathol, doi:10.1016/S0002-9440(10)62058-5
LDHB Lactate dehydrogenase B	↑	mTORC1-induced Insulin-induced in fetal liver	-	2,06	CL: ↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138	2,43	↓ (protein) Chen R et al (2015) Medicine, doi:10.1097/MD.0000000000001583
LPL Lipoprotein-lipase	↓	FOXO1-regulated in liver		0,64		0,51	
ME1 Malic enzyme	↑	FOXO1-regulated in liver		2,34	HCA: ↑ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	2,45	↑ Calvisi DF et al (2011) Gastroenterol doi.org/10.1053/j.gastro.2010.12.006; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
MFSD2 Major facilitator superfamily domain-containing protein 2	↓	Downregulated by insulin in liver	-	0,38		0,18	↓ Xing S et al (2019) Aging, doi:10.18632/aging.102333
PCK1 Phosphoenolpyruvate-carboxykinase (cytosolic)	↓	FOXO1-regulated in liver Downregulated by insulin in liver/hepatocytes Regulated via nuclear insulin-receptor	-	0,41	HCA: ↓ Rebouissou S et al (2007) JBC, doi.org/10.1074/jbc.M610725200	0,08	↓ Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023; Khan MW et al (2015) Cell Death Discov, doi: 10.1038/cddiscovery.2015.16 Wang B et al (2012) Hepatology, doi.org/10.1002/hep.25632 Liu M X et al (2018) Oncogene, doi:10.1038/s41388-017-0070-6
PDK2 Pyruvate dehydrogenase kinase 2	↓	Downregulated via PI3K/Akt and Foxo.	unchanged	0,78		0,78	↓ Liu ZL et al (2020) Cancer Cell Int, doi.org/10.21203/rs.2.24570/v1
PDK4 Pyruvate dehydrogenase kinase 4	↓	FOXO-regulated	-	0,75		1,25	↓ Yang C et al (2019) J Cancer, doi:10.7150/jca.27226; Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004
PFKL Phosphofructokinase L	↑	mTORC1-induced Insulin-upregulated in murine liver Insulin-upregulated in fetal sheep liver	unchanged	0,81	CL: ↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138	1,15	↔ Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023 ↑ Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138

PGK1 Phosphoglycerat kinase 1	/	mTORC1-induced	unchanged	1,19		1,03	<p>↑</p> <p>Xie H et al (2017) Int J Mol Sci, doi:10.3390/ijms18081630</p> <p>Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138</p>
PHGDH Phosphoglycerate dehydrogenase	↑	FOXO1-regulated in liver Insulin-induced via ATF4 in fibroblasts	+	4,25		5,74	<p>↓</p> <p>Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004</p>
PKLR Pyruvate kinase (liver and RBC)	↑	Insulin-induced in liver FOXO1-regulated in liver	-	1,04	HCA: ↓ Rebouissou S et al (2007) JBC, doi:org/10.1074/jbc.M610725200	2,21	<p>+</p> <p>Lee, S. et al. Network analyses identify liver-specific targets for treating liver diseases. Molecular systems biology 13, 938, doi:10.15252/msb.20177703 (2017).</p> <p>↑</p> <p>Skawran B et al (2008) Mod Pathol, doi.org/10.1038/modpathol.3800998</p>
PKM2				1,35	<p>CL: ↑</p> <p>Lee NCW et al (2018) Front Cell Develop Biol, doi:10.3389/fcell.2018.00138</p> <p>HCA: ↑</p> <p>Rebouissou S et al (2007) JBC, doi:org/10.1074/jbc.M610725200</p>	1,1	<p>↑</p> <p>Lee NCW et al (2018) Fr Cell Dev Biol, doi:10.3389/fcell.2018.0013</p> <p>Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023</p> <p>Chen Z et al (2015) Oncotarget, doi: 10.18632/oncotarget.2991.</p>
RPIA Ribose-5-phosphate isomerase A	↑	FOXO1-regulated in liver mTORC1-induced	unchanged	1,28		1,24	<p>↑</p> <p>Ciou SC et al (2015) Int J Cancer, doi:10.1002/ijc.29361.</p>
SCD1 Stearoyl-CoA desaturase (Δ-9-desaturase)	↑S	FOXO1-regulated in liver mTORC1-induced Akt/PI3K/mTOR-induced in liver Insulin-upregulated SCD1 activates Wnt/β-catenin signaling	+	2,25	HCA: ↑ Rebouissou S et al (2007) JBC, doi:org/10.1074/jbc.M610725200	3,27	<p>↑</p> <p>Yahagi N et al (2005) Eur J Cancer, doi: org/10.1016/j.ejca.2004.12.037</p> <p>Calvisi DF et al (2011) Gastroenterol doi.org/10.1053/j.gastro.2010.12.006</p> <p>Ma MKF et al (2017) J Hepatol, doi:10.1016/j.jhep.2017.06.015</p>
SERPINB1A	↓	Foxo1 –regulated in liver.	+	1,82		0,95	<p>↓ (protein level)</p> <p>Cui X et al (2014) J Mol Histol, doi:10.1007/s10735-013-9529-0</p>
SERPINA12 Serine peptidase inhibitor / clade A	↑	Insulin-induced in murine liver	unchanged	0,98		0,98	
SLC25a22 Mitochondrial glutamate carrier	↓	Downregulated by insulin in liver	-	0,68		0,79	
SLC2A2 / GLUT2 Glucose-transporter type 2	↓	Downregulated by insulin in hepatocytes	unchanged	0,76	CL: ↑ Daskalow et al (2009) Histochem Cell Biol, doi: 10.1007/s00418-009-0590-4	0,83	<p>↓</p> <p>Zhang X et al (2019) Cancers, doi:10.3390/cancers11122023;</p> <p>Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004</p>
SLC2A4/GLUT4 Glucosetransporter type 4	↓	FOXO1-regulated in liver	-	0,82		1,04	
SREBF1/ SREBP1 Sterol regulatory element binding transcription factor 1	↑S	Insulin-induced SREBP-1c rat liver FOXO1-regulated in liver FOXO1-regulated SREBP-1c in rodent liver	-	0,92	HCA: ↑ Rebouissou S et al (2007) JBC, doi:org/10.1074/jbc.M610725200	0,9	<p>↑</p> <p>Calvisi DF et al (2011) Gastroenterol doi.org/10.1053/j.gastro.2010.12.006</p> <p>Li C et al (2014) J Mol Sci, doi:10.3390/ijms15057124</p>
TALDO1	↑	mTORC1-induced		2,36	HCA: ↑ Skawran B et al (2008) Mod Pathol, doi.org/10.1038/modpathol.3800998	1,79	
TKT Transketo-lase	↑	FOXO1-regulated in liver	+	2,7		2,56	<p>↑</p> <p>Qin Z et al (2019) J Exp & Clin Cancer Res, doi:10.1186/s13046-019-1131-1;</p> <p>Nwosu ZC et al (2017) Cell Mol Gastro&Hepatol, doi:10.1016/j.jcmgh.2017.05.004</p>