

Supplementary information to:

Original article:

**PROTEOMIC ANALYSIS OF HEPATIC EFFECTS OF OKADAIC ACID
IN HEPARG HUMAN LIVER CELLS**

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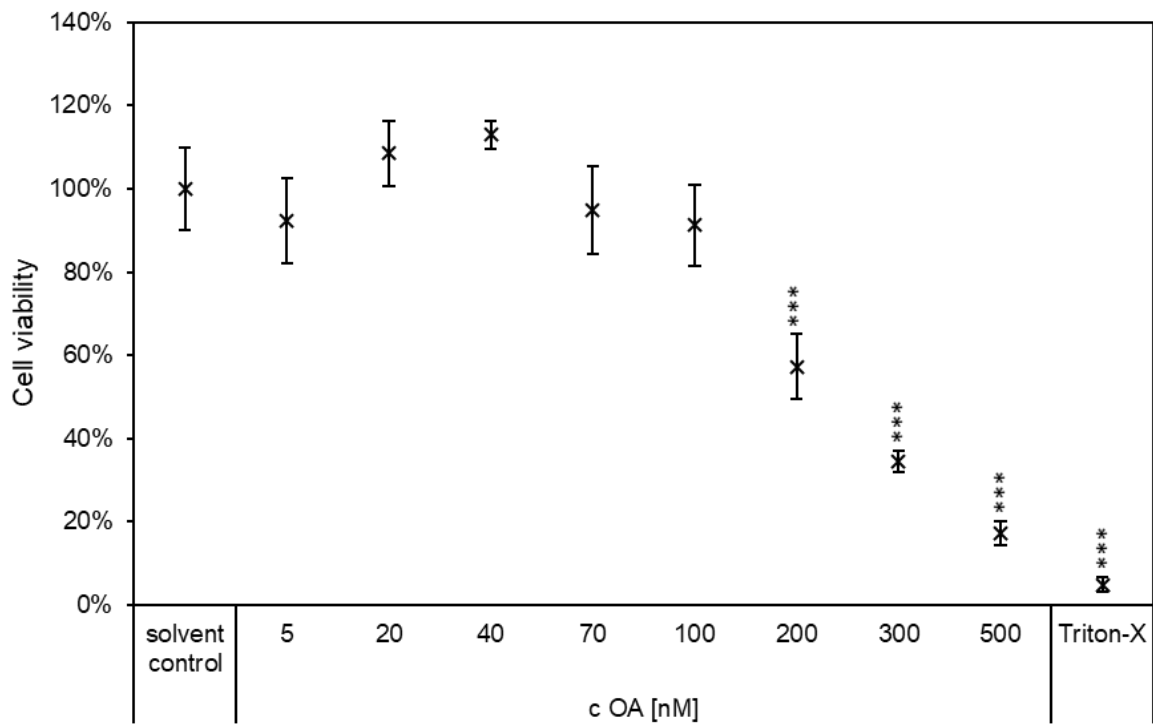
Supplementary Table 1: List of all regulated proteins in both treatment groups. Proteins were isolated from HepaRG cells incubated with 33 or 100 nM OA for 24 h. Proteins were then separated using 2D gel electrophoresis and deregulated proteins were identified using MALDI-MS. Deregulation of individual proteins by OA in mouse intestine (Wang et al., 2012) and in mouse liver (Wang et al., 2021) is presented in the row "comparison with published data": 1, mouse ortholog of detected protein deregulated in Wang et al., 2012; (1), similar protein isoform deregulated in Wang et al., 2012; 2, mouse ortholog of detected protein deregulated in Wang et al., 2021; (2), similar protein isoform deregulated in Wang et al., 2021.

Protein symbol	UniProt Accession number	Protein name	OA 33 nM		OA 100 nM		Comparison with published data
			Fold change (log ₂)	p-value	Fold change (log ₂)	p-value	
ABHD14B	Q96IU4	Protein ABHD14B			-0.657	2.84E-06	
ACAT1	P24752	Acetyl-CoA acetyltransferase 1	0.623	6.58E-03			
ACO2	Q99798	Aconitase 2			-0.606	7.38E-03	
ACO2	Q99798	Aconitase 2			-1.371	5.35E-03	
ACOT1	Q86TX2	Acyl-coenzyme A thioesterase 1	-0.507	5.95E-03			
ACY1	Q03154	Aminoacylase 1			-0.543	1.08E-03	1
ACY1	Q03154	Aminoacylase 1			-0.556	1.12E-04	1
AHSA1	O95433	Activator of 90 kDa heat shock protein ATPase homolog 1	1.088	2.06E-03	0.992	1.39E-04	
AK2	P54819	Adenylate kinase 2			-0.939	4.14E-03	
AKR1A1	P14550	Aldo-keto reductase family 1 member A1			-0.632	7.31E-03	
ALDH1L1	O75891	Aldehyde dehydrogenase 1 family member L1			1.145	7.66E-03	1
ALDH2	P05091	Aldehyde dehydrogenase 2			-0.740	8.33E-03	(1)
ALDOC	P09972	Fructose-bisphosphate aldolase C			1.147	2.29E-03	
ANXA1	P04083	Annexin A1			0.907	1.98E-05	(2)
ANXA1	P04083	Annexin A1			1.191	8.23E-05	(2)
ANXA8	P13928	Annexin A8			-0.680	4.14E-03	(2)
APOE	P02649	Apolipoprotein E			0.898	2.75E-04	
ARFIP1	P53367	Arfaptin-1			-0.538	7.99E-03	
ARG1	P05089	Arginase 1	-1.011	1.48E-06			(1)
BAG2	O95816	BAG family molecular chaperone regulator 2			0.515	9.58E-03	
CAVIN1	Q6NZI2	Caveolae associated protein 1			-0.732	2.75E-04	
CCT5	P48643	T-complex protein 1 subunit epsilon	0.601	1.56E-03	0.837	6.56E-03	(1)
CES1	P23141	Liver carboxylesterase 1	-0.841	8.65E-03			(2)
CMPK1	P30085	UMP-CMP kinase			-0.517	8.33E-03	
CPOX	P36551	Oxygen-dependent coproporphyrinogen-III oxidase			-0.714	4.29E-03	
CRYL1	Q9Y2S2	Lambda-crystallin homolog	-0.639	2.96E-03			
CTSB	P07858	Cathepsin B			-0.930	1.04E-03	
CTSD	P07339	Cathepsin D			-0.698	8.13E-03	
CTSD	P07339	Cathepsin D			-0.703	9.65E-03	
DARS1	P14868	Aspartate--tRNA ligase			-0.860	2.71E-03	

DNPH1	O43598	2'-Deoxynucleoside 5'-phosphate N-hydrolase 1			-0.660	7.40E-04	
DPYSL2	Q16555	Dihydropyrimidinase-related protein 2			-1.026	4.96E-05	
DYNC1I2	Q13409	Dynein cytoplasmic 1 intermediate chain 2			-0.658	6.99E-03	
ECHDC3	Q96DC8	Enoyl-CoA hydratase domain containing protein 3			-0.545	3.94E-04	
ECHS1	P30084	Enoyl-CoA hydratase			-0.645	2.10E-04	
EEF1D	P29692	Elongation factor 1-delta	0.574	2.32E-03	0.674	2.74E-04	(1)
EEF2	P13639	Elongation factor 2			1.266	3.71E-04	1
EEF2	P13639	Elongation factor 2			0.583	5.46E-04	1
EIF1AX	P47813	Eukaryotic translation initiation factor 1A, X-chromosomal	0.529	4.00E-03			(1)
EIF4A3	P38919	Eukaryotic initiation factor 4A-III			0.830	1.13E-03	(1)
EIF4H	Q15056	Eukaryotic translation initiation factor 4H			1.728	6.18E-03	(1)
ENO1	P06733	Alpha-enolase	1.069	1.52E-03			
ERLIN2	O94905	Erlin-2			0.840	7.01E-03	
ETFA	P13804	Electron transfer flavo-protein subunit alpha			-0.675	9.49E-03	
EZR	P15311	Ezrin	0.569	1.43E-04	1.056	3.57E-04	
EZR	P15311	Ezrin	0.654	6.57E-03	0.675	9.79E-03	
EZR	P15311	Ezrin	0.746	3.71E-04	1.094	2.84E-06	
EZR	P15311	Ezrin			1.090	3.11E-05	
FAH	P16930	Fumarylacetoacetase			-0.592	2.80E-03	
FAHD1	Q6P587	Acylpyruvase FAHD1	-0.647	3.33E-03			
FGA	P02671	Fibrinogen alpha chain			0.828	4.10E-03	
FGB	P02675	Fibrinogen beta chain			1.278	2.97E-03	
FGG	P02679	Fibrinogen gamma chain	-0.563		-0.619	1.66E-03	
GAA	P10253	Lysosomal alpha-glucosidase			-0.640	1.38E-03	
GARS1	P41250	Glycine--tRNA ligase			0.845	1.13E-03	
GATD3	P0DPI2	Glutamine amidotransferase-like class 1 domain-containing protein 3			-0.557	3.74E-04	
GLUL	P15104	Glutamine synthetase	-1.054	1.48E-06	-1.462	2.65E-05	
GNMT	Q14749	Glycine N-methyltransferase	-0.907	4.84E-03			
GRB2	P62993	Growth factor receptor bound protein 2			0.884	3.77E-03	
GSTA1	P08263	Glutathione S-transferase A1	-1.109	2.83E-03			
HEBP1	Q9NRV9	Heme binding protein 1			-0.511	9.64E-05	
HEXA	P06865	Beta-hexosaminidase subunit alpha			-0.568	1.86E-03	
HIBCH	Q6NVY1	3-Hydroxyisobutyryl-CoA hydrolase	-1.043	5.99E-03			
HIBCH	Q6NVY1	3-Hydroxyisobutyryl-CoA hydrolase	-0.522	3.60E-04			
HNRNPF	P52597	Heterogeneous nuclear ribonucleoprotein F	-0.728	6.79E-04	-0.756	4.90E-03	1

HNRNPK	P31943	Heterogeneous nuclear ribonucleoprotein K	-0.877	7.40E-07	-1.523	7.40E-07	(1)
HNRNPK	P31943	Heterogeneous nuclear ribonucleoprotein K	-0.554	4.51E-03	-0.800	2.55E-04	(1)
HP	P00738	Haptoglobin	-1.544	2.96E-06	-1.539	1.98E-05	
HSP90B1	P14625	Heat shock protein 90 beta family member 1	-0.844	4.37E-03	-1.539	1.98E-05	1, (2)
HSPA1A	P0DMV8	Heat shock 70 kDa protein 1A	1.108	9.76E-03	0.650	9.61E-06	(1), (2)
HSPA4	P34932	Heat shock 70 kDa protein 4			-0.796	2.18E-03	(1), (2)
HSPA8	P11142	Heat shock cognate 71 kDa protein			-0.833	2.76E-03	(1), (2)
HSPB1	P04792	Heat shock protein beta-1			-0.662	1.78E-05	(1), (2)
IDH1	O75874	Isocitrate dehydrogenase (NADP) 1	-1.972	6.50E-04	-0.950	8.33E-03	
IMMT	Q16891	MICOS complex subunit MIC60			-1.079	6.43E-03	
KRT8	P05787	Keratin 8			1.072	7.14E-03	1, (2)
KRT18	P05783	Keratin 18			0.738	5.56E-03	(1), (2)
LAP3	P28838	Cytosol aminopeptidase			0.669	2.32E-03	
LMNB2	Q03252	Lamin B2	-0.621	8.41E-03			
MAPRE1	Q15691	Microtubule associated protein RP/EB family member 1			0.628	1.18E-03	
MAT1A	Q00266	Methionine adenosyltransferase 1A			-1.100	5.48E-03	2
MCCC2	Q9HCC0	Methylcrotonoyl-CoA carboxylase beta chain			0.600	4.96E-04	
NANS	Q9NR45	Sialic acid synthase	0.778	8.27E-03			
PCNA	P12004	Proliferating cell nuclear antigen	1.354	9.99E-04	1.531	7.66E-03	
PCNA	P12004	Proliferating cell nuclear antigen	1.259	6.80E-06	1.174	3.09E-06	
PDHA1	P08559	Pyruvate dehydrogenase E1 subunit alpha 1	-0.939	7.97E-04			
PDHB	P11177	Pyruvate dehydrogenase E1 subunit beta			-0.575	1.28E-04	
PDIA6	Q15084	Protein disulfide-isomerase A6			1.280	7.97E-03	1, 2
PGM1	P36871	Phosphoglucomutase 1	-0,948	8.30E-03	-1.054	9.69E-03	1
PNP	P00491	Purine nucleoside phosphorylase			0.851	5.76E-03	1
PNPT1	Q8TCS8	Polyribonucleotide nucleotidyltransferase 1			0.959	3.00E-03	
PPIA	P62937	Peptidyl-prolyl cis-trans isomerase A			-0.594	7.49E-03	
PRDX4	Q13162	Peroxiredoxin 4			-1.014	1.98E-05	(1), (2)
PRDX6	P30041	Peroxiredoxin 6	-0.601	1.28E-04	-0.655	1.37E-03	(1), (2)
PRDX6	P30041	Peroxiredoxin 6	0.866	7.48E-04	1.872	2.84E-06	(1), (2)
RAN	P62826	GTP-binding nuclear protein RAN	-0.502	5.64E-03			
RBM8A	Q9Y5S9	RNA-binding protein 8A			-0.861	1.74E-03	
RCN1	Q15293	Reticulocalbin 1	0.867	1.02E-03	0.895	2.30E-04	
SELENBP1	Q13228	Methanethiol oxidase	-0.607	5.24E-03			
SEPTIN2	Q15019	Septin 2	-1.145	1.49E-03	-0.651	5.08E-03	
SERPINA1	P01009	Serpin A1	1.093	8.25E-03			
SERPINB9	P50453	Serpin B9			0.845	1.42E-04	

SFN	P31947	14-3-3 protein sigma	1.108	9.76E-03			
SLC9A3R1	O14745	SLC9A3 Regulator 1	0.903	3.26E-03	1.284	1.23E-03	
SLC9A3R1	O14745	SLC9A3 Regulator 1			0.559	1.28E-04	
SND1	Q7KZF4	Staphylococcal nuclease domain-containing protein 1	-0.693	7.32E-03	1.012	2.29E-03	
SRI	P30626	Sorcin			-0.686	2.84E-06	
TALDO1	P37837	Transaldolase 1			-0.810	5.30E-04	
TBCB	Q99426	Tubulin folding cofactor B			0.691	3.58E-03	
TCP1	P17987	T-complex protein 1 subunit alpha	-0.592	5.48E-04			(1)
TKFC	Q3LXA3	Triokinase/FMN cyclase	-1.103	9.99E-04			
TPT1	P13693	Translationally controlled tumor protein	0.505	5.53E-04	0.503	1.40E-03	
TST	Q16762	Thiosulfate sulfurtransferase			-0.585	1.29E-03	
TUFM	P49411	Tu translation elongation factor, mitochondrial			-1.381	1.41E-04	
TUFM	P49411	Tu translation elongation factor, mitochondrial			-0.531	2.93E-03	
UBQLN1	Q9UMX0	Ubiquilin 1			0.867	7.91E-03	
UROD	P06132	Uroporphyrinogen decarboxylase			-0.664	6.99E-03	
ZYX	Q15942	Zyxin	1.044	1.49E-03	1.752	5.67E-05	
ZYX	Q15942	Zyxin			1.336	2.72E-04	



Supplementary Figure 1: MTT-assay of selected OA concentrations on HepaRG cells. Cells were seeded in 96-well plates and grown for 14 days, after which they were differentiated for another 14 days. They were incubated for 24 h with different OA concentrations. The absorption at 570 nm was measured and directly compared to the viability. Each sample was then compared to an untreated control. Based on the MTT assay, 100 nM and 33 nM OA were picked as non-toxic concentrations. Statistical analysis was performed using t-test (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$).