molecules

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*Supplementary Material*

# A Proteomics Study on the Mechanism of Nutmeg-induced Hepatotoxicity

**Wei Xia [1,†], Zhipeng Cao [1,†], Xiaoyu Zhang [1] and Lina Gao [1,*]**

[1] School of Forensic Medicine, China Medical University, Shenyang 110122, P. R. China; lessenziale123@outlook.com (W.X.); zpcao@cmu.edu.cn (Z.C.); AjaxZhang123@126.com (X.Z.)
† The authors contributed equally to this work.
* Correspondence: lngao@cmu.edu.cn

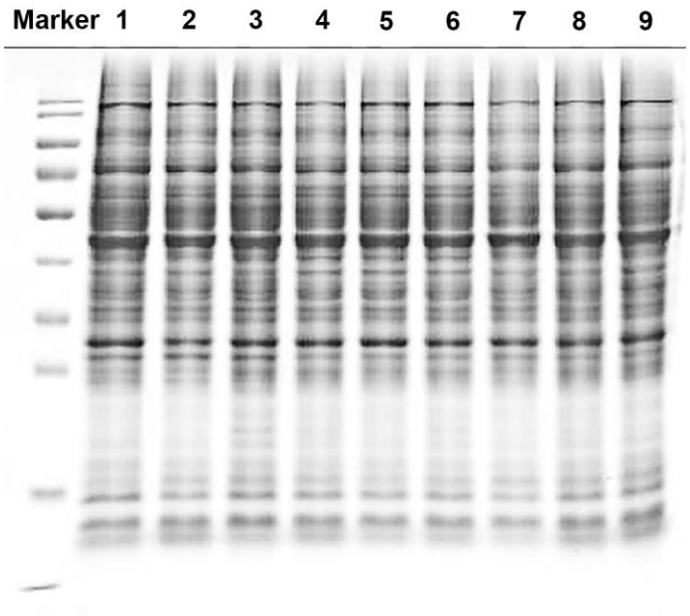


**Figure S1.**

**Table S1.** Peptide fraction separation liquid chromatography elution gradient table.

| Time (min) | Flow rate (mL/min) | Mobile phase A (%) | Mobile phase B (%) |
|---|---|---|---|
| 0 | 1 | 97 | 3 |
| 10 | 1 | 95 | 5 |
| 30 | 1 | 80 | 20 |
| 48 | 1 | 60 | 40 |
| 50 | 1 | 50 | 50 |
| 53 | 1 | 30 | 70 |
| 54 | 1 | 0 | 100 |

**Table 2.** Liquid chromatography elution gradient table.

| Time (min) | Flow rate (nL/min) | Mobile phase A (%) | Mobile phase B (%) |
|---|---|---|---|
| 0 | 600 | 94 | 6 |
| 2 | 600 | 83 | 17 |
| 82 | 600 | 60 | 40 |
| 84 | 600 | 50 | 50 |
| 85 | 600 | 45 | 55 |
| 90 | 600 | 0 | 100 |

**Table S3.** The analysis parameter of Proteome Discoverer 2.2.

| Item | Value |
|---|---|
| Type of Quantification | Reporter Quantification (TMT) |
| Enzyme | Trypsin |
| Max.Missed Cleavage Sites | 2 |
| Precursor Mass Tolerance | 10 ppm |
| Fragment Mass Tolerance | 0.02 Da |
| Dynamic Modification | Oxidation/+15.995 Da (M) and TMT /+229.163 Da (K,Y) |
| N-Terminal Modification | Acetyl/+42.011 Da (N-Terminal) and TMT /+229.163 Da (N-Terminal) |
| Static Modification | Carbamidomethyl/+57.021 Da (C) |

**Table S4.** The DEPs between the low-dose group and the control group.

| Protein | Gene | Fold Change | P value | Trend |
|---|---|---|---|---|
| mRNA | H2-K1 | 0.380 | 0.010 | down |
| Glutamine synthetase | | 0.426 | 0.022 | down |
| Annexin | Anxa6 | 0.447 | 0.032 | down |
| mRNA | H2-D1 | 0.467 | 0.002 | down |
| Ribokinase | Rbks | 0.487 | 0.000 | down |
| Gamma-interferon-inducible lysosomal thiol reductase | Ifi30 | 0.496 | 0.009 | down |
| Coiled-coil-helix-coiled-coil-helix domain-containing 10 | Chchd10 | 0.529 | 0.036 | down |
| T-cell immunoglobulin and mucin domain-containing protein 4 | Timd4 | 0.554 | 0.026 | down |
| Cytochrome c oxidase assembly factor 4 homolog, mitochondrial | COA4 | 0.581 | 0.008 | down |
| Uncharacterized protein | | 0.586 | 0.010 | down |
| Glycine N-acyltransferase-like protein | Gm4952 | 0.590 | 0.029 | down |
| Isoc2a protein | Isoc2a | 0.597 | 0.010 | down |
| Aspartylglucosaminidase | Aga | 0.603 | 0.005 | down |
| Vitamin K epoxide reductase complex subunit 1 | Vkorc1 | 0.606 | 0.008 | down |
| Uncharacterized protein | Igfbp7 | 0.608 | 0.002 | down |
| Mitochondrial intermembrane space import and assembly protein 40 | Chchd4 | 0.630 | 0.003 | down |
| Tetraspanin-9 | Tspan9 | 0.638 | 0.002 | down |
| E3 ubiquitin-protein ligase PPP1R11 | Ppp1r11 | 0.645 | 0.006 | down |
| TP53-regulated inhibitor of apoptosis 1 | Triap1 | 0.646 | 0.031 | down |
| COX assembly mitochondrial protein (Fragment) | Cmc1 | 0.649 | 0.016 | down |
| Dynein light chain Tctex-type 3 | Dynlt3 | 0.650 | 0.004 | down |
| Coagulation factor IX | F9 | 0.661 | 0.007 | down |
| Solute carrier family 25 member 46 | Slc25a46 | 0.661 | 0.036 | down |
| SCAN domain containing 3 | Zbed5 | 0.662 | 0.019 | down |
| Cationic amino acid transporter 2 | Slc7a2 | 0.663 | 0.009 | down |
| Protein phosphatase 1 regulatory subunit 3G | Ppp1r3g | 0.670 | 0.033 | down |
| BRISC and BRCA1-A complex member 2 | Babam2 | 0.672 | 0.010 | down |
| Leptin receptor gene-related protein | Leprot | 0.676 | 0.012 | down |
| Microtubule-associated protein | Mapt | 0.677 | 0.032 | down |
| MHC H-2K antigen | H2-K1 | 0.678 | 0.001 | down |
| Macrophage migration inhibitory factor | Mif | 0.680 | 0.006 | down |
| ADP-ribosylation factor-related protein 1 | Arfrp1 | 0.685 | 0.009 | down |
| Alpha- and gamma-adaptin-binding protein p34 | Aagab | 0.686 | 0.016 | down |
| Alpha-ketoglutarate-dependent dioxygenase FTO | Fto | 0.690 | 0.010 | down |
| Selenoprotein W | Selenow | 0.698 | 0.023 | down |
| Glucose-6-phosphate isomerase | Gpi1 | 0.704 | 0.006 | down |
| Queuine tRNA-ribosyltransferase accessory subunit 2 | Qtrt2 | 0.709 | 0.035 | down |
| Protein S100-A11 | S100a11 | 0.713 | 0.026 | down |
| Lysosomal alpha-glucosidase | Gaa | 0.718 | 0.008 | down |
| Disintegrin and metalloproteinase domain-containing protein 17 | Adam17 | 0.725 | 0.007 | down |
| Tubulointerstitial nephritis antigen-like | Tinagl1 | 0.726 | 0.012 | down |
| CARD domain-containing protein | Card19 | 0.727 | 0.046 | down |
| Thymosin beta-4 | Tmsb4x | 0.727 | 0.020 | down |
| Serum albumin | Alb | 0.727 | 0.000 | down |
| Eukaryotic translation initiation factor 4E type 3 | Eif4e3 | 0.731 | 0.018 | down |
| Casp7 protein | Casp7 | 0.732 | 0.009 | down |
| NADH-ubiquinone oxidoreductase chain 3 | ND3 | 0.733 | 0.044 | down |
| Formin-binding protein 1 | Fnbp1 | 0.734 | 0.002 | down |
| DNA mismatch repair protein | Msh2 | 0.735 | 0.048 | down |
| Protein kinase C | Prkcz | 0.735 | 0.030 | down |

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|---|---|---|---|---|
| KH homology domain-containing protein 4 | Khdc4 | 0.738 | 0.009 | down |
| 3-5 exoribonuclease 1 | Eri1 | 0.739 | 0.024 | down |
| Beta-arrestin-1 | Arrb1 | 0.739 | 0.008 | down |
| Transmembrane 7 superfamily member 3 | Tm7sf3 | 0.741 | 0.047 | down |
| [Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial | Pdk2 | 0.742 | 0.029 | down |
| Ribosomal_L14e domain-containing protein | Rpl14 | 0.743 | 0.002 | down |
| MHC class II antigen D (Fragment) | H2-D1 | 0.745 | 0.021 | down |
| Sodium- and chloride-dependent GABA transporter 2 | Slc6a13 | 0.745 | 0.019 | down |
| Transmembrane protein 11, mitochondrial | Tmem11 | 0.746 | 0.040 | down |
| Eukaryotic translation initiation factor 6 | Eif6 | 0.747 | 0.023 | down |
| Tetraspanin-31 | Tspan31 | 0.747 | 0.016 | down |
| NHP2-like protein 1 | Snu13 | 0.750 | 0.029 | down |
| Neuroplastin | Nptn | 0.751 | 0.030 | down |
| Malignant T-cell-amplified sequence 1 | Mcts1 | 0.752 | 0.024 | down |
| N(G),N(G)-dimethylarginine dimethylaminohydrolase 1 | Ddah1 | 0.753 | 0.013 | down |
| Cytochrome c oxidase assembly factor 6 homolog | Coa6 | 0.756 | 0.015 | down |
| Rho guanine nucleotide exchange factor (GEF) 26 | Arhgef26 | 0.756 | 0.020 | down |
| Dynein light chain 2, cytoplasmic | Dynll2 | 0.763 | 0.010 | down |
| Glutathione peroxidase 3 | Gpx3 | 0.764 | 0.019 | down |
| Mannose-P-dolichol utilization defect 1 | Mpdu1 | 0.767 | 0.004 | down |
| Signal recognition particle 9 kDa protein | Srp9 | 0.768 | 0.042 | down |
| Integrator complex subunit 10 | Ints10 | 0.769 | 0.036 | down |
| Homeodomain-only protein | Hopx | 0.769 | 0.029 | down |
| Cleavage stimulation factor subunit 2 tau variant | Cstf2t | 0.770 | 0.026 | down |
| F-box only protein 21 | Fbxo21 | 0.772 | 0.026 | down |
| DENN domain-containing protein 10 | Dennd10 | 0.773 | 0.040 | down |
| E3 ubiquitin ligase Rnf157 | Rnf157 | 0.774 | 0.039 | down |
| Tetraspanin-4 | Tspan4 | 0.776 | 0.044 | down |
| WD repeat-containing protein 41 | Wdr41 | 0.776 | 0.032 | down |
| F-box/LRR-repeat protein 20 | Fbxl20 | 0.776 | 0.009 | down |
| Glutathione reductase, mitochondrial | Gsr | 0.777 | 0.015 | down |
| Centrosomal protein of 170 kDa | Cep170 | 0.778 | 0.028 | down |
| Mitochondrial import inner membrane translocase subunit Tim8 A | Timm8a1 | 0.784 | 0.022 | down |
| Glutathione S-transferase Mu 7 | Gstm7 | 0.785 | 0.031 | down |
| RNA-binding motif, single-stranded-interacting protein 3 | Rbms3 | 0.785 | 0.005 | down |
| F-box only protein 6 | Fbxo6 | 0.785 | 0.020 | down |
| Protein canopy homolog 3 | Cnpy3 | 0.786 | 0.026 | down |
| Uncharacterized protein | Selenoo | 0.787 | 0.020 | down |
| Glutathione peroxidase 1 | Gpx1 | 0.787 | 0.042 | down |
| ADP-ribosyl cyclase/cyclic ADP-ribose hydrolase 1 | Cd38 | 0.787 | 0.008 | down |
| Mutant fibrillin-1 | Fbn1 | 0.787 | 0.005 | down |
| Transcriptional repressor protein YY1 | Yy1 | 0.787 | 0.036 | down |
| Ubiquinol-cytochrome-c reductase complex assembly factor 2 | Uqcc2 | 0.790 | 0.029 | down |
| Mitochondrial import inner membrane translocase subunit Tim8 B | Timm8b | 0.790 | 0.020 | down |
| Pleckstrin homology domain-containing family O member 2 | Plekho2 | 0.794 | 0.031 | down |
| BolA-like protein 2 | Bola2 | 0.794 | 0.003 | down |
| Delta-aminolevulinic acid dehydratase | Alad | 0.797 | 0.044 | down |
| Phospholipid-transporting ATPase (Fragment) | Atp11b | 0.798 | 0.033 | down |
| Polypyrimidine tract-binding protein 3 | Ptbp3 | 0.799 | 0.010 | down |
| Biotinidase | Btd | 0.800 | 0.004 | down |
| Glutamine synthetase | Glul | 0.801 | 0.007 | down |
| Ubiquitin carboxyl-terminal hydrolase MINDY-1 | Mindy1 | 0.804 | 0.020 | down |

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|---|---|---|---|---|
| Cell adhesion molecule 1 | Cadm1 | 0.804 | 0.004 | down |
| Methyl-CpG-binding protein 2 | Mecp2 | 0.804 | 0.030 | down |
| Dolichyldiphosphatase 1 | Dolpp1 | 0.805 | 0.027 | down |
| Mycophenolic acid acyl-glucuronide esterase, mitochondrial | Abhd10 | 0.806 | 0.012 | down |
| Transmembrane protease serine 6 | Tmprss6 | 0.809 | 0.036 | down |
| Protein tyrosine phosphatase type IVA 2 | Ptp4a2 | 0.810 | 0.014 | down |
| ATP synthase subunit epsilon, mitochondrial | Atp5f1e | 0.811 | 0.017 | down |
| Insulin-like growth factor-binding protein 4 | Igfbp4 | 0.812 | 0.002 | down |
| Synaptophysin-like protein 1 | Sypl1 | 0.812 | 0.015 | down |
| Uncharacterized protein | Srsf9 | 0.813 | 0.025 | down |
| Protein C10 | Grcc10 | 0.814 | 0.043 | down |
| Pre-mRNA-splicing factor 38B | Prpf38b | 0.816 | 0.010 | down |
| Protein BUD31 homolog | Bud31 | 0.816 | 0.006 | down |
| Galectin-related protein | Lgalsl | 0.818 | 0.038 | down |
| Ring finger and CHY zinc finger domain containing 1 | Rchy1 | 0.818 | 0.040 | down |
| Phenazine biosynthesis-like domain-containing protein 2 | Pbld2 | 0.819 | 0.036 | down |
| Serine dehydratase-like | Sdsl | 0.820 | 0.047 | down |
| COMM domain-containing protein 9 | Commd9 | 0.821 | 0.016 | down |
| RNA-binding protein 42 | Rbm42 | 0.821 | 0.031 | down |
| Uncharacterized protein | Prkar1a | 0.823 | 0.014 | down |
| THO complex subunit 3 | Thoc3 | 0.824 | 0.015 | down |
| TGc domain-containing protein | F13a1 | 0.825 | 0.048 | down |
| Calmodulin-regulated spectrin-associated protein 3 | Camsap3 | 0.826 | 0.024 | down |
| RNA-binding protein 3 | Rbm3 | 0.827 | 0.030 | down |
| Guanidinoacetate N-methyltransferase | Gamt | 0.828 | 0.033 | down |
| Protein phosphatase 1 regulatory subunit 37 | Ppp1r37 | 0.828 | 0.013 | down |
| Cytochrome b-c1 complex subunit 6, mitochondrial | Uqcrh | 0.829 | 0.011 | down |
| Peptidyl-prolyl cis-trans isomerase G | Ppig | 0.830 | 0.003 | down |
| CCAAT/enhancer-binding protein zeta | Cebpz | 0.830 | 0.036 | down |
| RNA polymerase-associated protein CTR9 homolog | Ctr9 | 0.831 | 0.050 | down |
| Folliculin-interacting protein 1 | Fnip1 | 0.831 | 0.038 | down |
| Phosphofurin acidic cluster sorting protein 2 | Pacs2 | 0.832 | 0.033 | down |
| Anaphase promoting complex subunit 1 | Anapc1 | 0.833 | 0.041 | down |
| Integrin alpha-3 | Itga3 | 1.200 | 0.040 | up |
| Transmembrane anterior posterior transformation protein 1 | Tapt1 | 1.202 | 0.006 | up |
| 60S ribosomal protein L22-like 1 | Rpl22l1 | 1.203 | 0.047 | up |
| MAP kinase-interacting serine/threonine-protein kinase 1 | Mknk1 | 1.204 | 0.002 | up |
| E3 ubiquitin-protein ligase synoviolin | Syvn1 | 1.206 | 0.029 | up |
| UDP-glucuronic acid decarboxylase 1 | Uxs1 | 1.208 | 0.004 | up |
| Fat storage-inducing transmembrane protein 2 | Fitm2 | 1.209 | 0.003 | up |
| Aquaporin-9 | Aqp9 | 1.209 | 0.036 | up |
| Insulin-like growth factor 2 mRNA-binding protein 3 | Igf2bp3 | 1.210 | 0.047 | up |
| Oxysterol-binding protein | Osbpl2 | 1.211 | 0.025 | up |
| Trafficking protein particle complex subunit 2-like protein | Trappc2l | 1.211 | 0.006 | up |
| Mitochondrial import inner membrane translocase subunit TIM17 | Timm17a | 1.214 | 0.033 | up |
| Required for excision 1-B domain-containing protein | Rex1bd | 1.214 | 0.006 | up |
| Vinexin | Sorbs3 | 1.215 | 0.009 | up |
| Succinyl-CoA:3-ketoacid-coenzyme A transferase | Oxct1 | 1.217 | 0.049 | up |
| DnaJ homolog subfamily C member 22 | Dnajc22 | 1.217 | 0.013 | up |
| Cytochrome P450 2C70 | Cyp2c70 | 1.218 | 0.006 | up |
| Valine--tRNA ligase, mitochondrial | Vars2 | 1.218 | 0.050 | up |
| Uncharacterized protein | Abtb2 | 1.220 | 0.003 | up |
| Cytochrome P450 4V2 | Cyp4v2 | 1.220 | 0.032 | up |

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|---|---|---|---|---|
| Tetraspanin-8 | Tspan8 | 1.221 | 0.025 | up |
| Small cell adhesion glycoprotein | Smagp | 1.221 | 0.006 | up |
| Lipoprotein lipase | Lpl | 1.221 | 0.020 | up |
| UDP-glucuronosyltransferase | Ugt2b1 | 1.223 | 0.005 | up |
| Importin N-terminal domain-containing protein | Ipo13 | 1.225 | 0.032 | up |
| Phosphatidylinositol 4-kinase type 2-beta | Pi4k2b | 1.225 | 0.016 | up |
| GTPase Era, mitochondrial | Eral1 | 1.225 | 0.007 | up |
| Rab22B | Rab31 | 1.226 | 0.042 | up |
| Uncharacterized protein | Uros | 1.226 | 0.006 | up |
| Vacuolar protein sorting-associated protein 51 homolog | Vps51 | 1.227 | 0.006 | up |
| Peptidyl-prolyl cis-trans isomerase FKBP11 | Fkbp11 | 1.227 | 0.011 | up |
| Syntaxin-16 | Stx16 | 1.227 | 0.046 | up |
| S-adenosyl-L-methionine-dependent tRNA 4-demethylwyosine synthase TYW1 | Tyw1 | 1.231 | 0.028 | up |
| Chloride channel protein 2 | Clcn2 | 1.231 | 0.023 | up |
| Heterogeneous nuclear ribonucleoproteins C1/C2 (Fragment) | Hnrnpc | 1.233 | 0.005 | up |
| Uncharacterized protein | Ddx56 | 1.234 | 0.007 | up |
| E3 ubiquitin-protein ligase RNF139 | Rnf139 | 1.235 | 0.020 | up |
| Protein dopey-2 | Dop1b | 1.236 | 0.043 | up |
| Ubiquitin-associated domain-containing protein 2 | Ubac2 | 1.237 | 0.012 | up |
| Structural maintenance of chromosomes flexible hinge domain-containing protein 1 | Smchd1 | 1.242 | 0.031 | up |
| Splicing factor 3b, subunit 3 | Sf3b3 | 1.243 | 0.010 | up |
| HEAT repeat-containing protein 5A | Heatr5a | 1.243 | 0.005 | up |
| MIF4G domain-containing protein | Mif4gd | 1.244 | 0.033 | up |
| Calcium signal-modulating cyclophilin ligand | Camlg | 1.246 | 0.008 | up |
| Replication protein A 32 kDa subunit | Rpa2 | 1.248 | 0.009 | up |
| Leucyl-cystinyl aminopeptidase | Lnpep | 1.249 | 0.003 | up |
| COMM domain-containing protein 10 | Commd10 | 1.249 | 0.026 | up |
| PAM2 domain-containing protein | Paip2 | 1.251 | 0.037 | up |
| Diacylglycerol kinase theta | Dgkq | 1.254 | 0.009 | up |
| Trafficking protein particle complex subunit 10 | Trappc10 | 1.256 | 0.024 | up |
| Rho-related GTP-binding protein RhoC | Rhoc | 1.261 | 0.019 | up |
| Probable ATP-dependent RNA helicase DDX52 | Ddx52 | 1.262 | 0.020 | up |
| Aryl hydrocarbon receptor | Ahr | 1.264 | 0.050 | up |
| Uncharacterized protein | Calu | 1.266 | 0.001 | up |
| TRMT1-like protein | Trmt1l | 1.267 | 0.048 | up |
| Exopolyphosphatase PRUNE1 | Prune1 | 1.267 | 0.039 | up |
| Uncharacterized protein | Ppid | 1.268 | 0.013 | up |
| Ras association domain-containing protein 8 | Rassf8 | 1.270 | 0.020 | up |
| Leucine carboxyl methyltransferase 1 | Lcmt1 | 1.276 | 0.012 | up |
| Receptor expression-enhancing protein | Reep4 | 1.277 | 0.010 | up |
| Spata5 protein | Spata5 | 1.279 | 0.041 | up |
| Proteasome assembly chaperone 4 | Psmg4 | 1.280 | 0.008 | up |
| Carbonyl reductase [NADPH] 3 | Cbr3 | 1.280 | 0.015 | up |
| Acylamino-acid-releasing enzyme (Fragment) | Apeh | 1.281 | 0.002 | up |
| 39S ribosomal protein L42, mitochondrial | Mrpl42 | 1.287 | 0.009 | up |
| Lysoplasmalogenase | Tmem86b | 1.288 | 0.031 | up |
| Estradiol 17-beta-dehydrogenase 2 | Hsd17b2 | 1.290 | 0.036 | up |
| Leucine-rich repeat-containing protein 3 | Lrrc3 | 1.294 | 0.030 | up |
| Complex I assembly factor TMEM126B, mitochondrial | Tmem126b | 1.298 | 0.006 | up |
| Uncharacterized protein | Mrpl40 | 1.299 | 0.014 | up |
| Vacuolar protein sorting-associated protein 37C | Vps37c | 1.299 | 0.000 | up |

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|---|---|---|---|---|
| mRNA-decapping enzyme 1A | Dcp1a | 1.300 | 0.016 | up |
| Periodic tryptophan protein 2 homolog | Pwp2 | 1.300 | 0.032 | up |
| Son of sevenless homolog 1 | Sos1 | 1.303 | 0.020 | up |
| ATP synthase F(0) complex subunit C2, mitochondrial | Atp5mc2 | 1.304 | 0.017 | up |
| Serine protease inhibitor A3K | Serpina3k | 1.307 | 0.010 | up |
| 3-oxo-5-alpha-steroid 4-dehydrogenase | Srd5a1 | 1.315 | 0.010 | up |
| Dynamin-1-like protein | Dnm1l | 1.323 | 0.025 | up |
| NEDD8-activating enzyme E1 regulatory subunit | Nae1 | 1.326 | 0.017 | up |
| Ankyrin repeat domain-containing protein 40 | Ankrd40 | 1.338 | 0.018 | up |
| Alpha-1-acid glycoprotein 1 | Orm1 | 1.342 | 0.007 | up |
| Diacylglycerol kinase | Dgkd | 1.349 | 0.023 | up |
| Beta-galactosidase | | 1.354 | 0.032 | up |
| Cytochrome P450 1A2 | Cyp1a2 | 1.355 | 0.006 | up |
| RNA-binding protein PNO1 | Pno1 | 1.363 | 0.014 | up |
| Monofunctional C1-tetrahydrofolate synthase, mitochondrial | Mthfd1l | 1.367 | 0.044 | up |
| Torsin-1B | Tor1b | 1.379 | 0.009 | up |
| RIKEN cDNA 2210010C04 gene | 2210010C04Rik | 1.380 | 0.019 | up |
| Uncharacterized protein | Amfr | 1.382 | 0.038 | up |
| NADH-ubiquinone oxidoreductase chain 2 | ND2 | 1.383 | 0.035 | up |
| RNA helicase aquarius | Aqr | 1.393 | 0.005 | up |
| Cytochrome P450 2B10 | Cyp2b10 | 1.408 | 0.005 | up |
| HEAT repeat-containing protein 6 | Heatr6 | 1.416 | 0.009 | up |
| Major urinary protein 2 | Mup2 | 1.455 | 0.012 | up |
| WASH complex subunit 3 | Washc3 | 1.462 | 0.011 | up |
| p21-activated protein kinase-interacting protein 1 | Pak1ip1 | 1.521 | 0.002 | up |
| Alpha-globin | Hbat1 | 1.522 | 0.013 | up |
| Mediator of RNA polymerase II transcription subunit 20 | Med20 | 1.617 | 0.018 | up |
| Uncharacterized protein | Cyp7b1 | 1.723 | 0.034 | up |
| Vacuolar protein sorting-associated protein 8 homolog | Vps8 | 2.025 | 0.030 | up |
| Podocalyxin | Podxl | 2.359 | 0.009 | up |

**Table S5.** The DEPs between the high-dose group and the control group.

| Protein | Gene | Fold Change | P value | Trend |
|---|---|---|---|---|
| Histone H1.4 | H1-4 | 0.606 | 0.028 | down |
| Selenoprotein W | Selenow | 0.615 | 0.014 | down |
| Protein kinase domain-containing protein | Stk24 | 0.633 | 0.006 | down |
| D-glucuronyl C5-epimerase | Glce | 0.637 | 0.001 | down |
| NADPH-dependent 3-keto-steroid reductase Hsd3b5 | Hsd3b5 | 0.649 | 0.017 | down |
| Cationic amino acid transporter 2 | Slc7a2 | 0.664 | 0.012 | down |
| Deoxyguanosine kinase 3 | Dguok | 0.712 | 0.023 | down |
| Glutathione peroxidase 1 | Gpx1 | 0.713 | 0.017 | down |
| Sulfotransferase | Sult2a8 | 0.715 | 0.003 | down |
| Interferon regulatory factor 5 | Irf5 | 0.737 | 0.047 | down |
| Keratin intermediate filament 16a | K16 | 0.744 | 0.046 | down |
| Carbonic anhydrase 1 | Ca1 | 0.746 | 0.044 | down |
| N-acetyltransferase 8 | Nat8 | 0.747 | 0.035 | down |
| Predicted gene, 20730 | Gm20730 | 0.761 | 0.042 | down |
| Anti-HIV fusion peptide monocolonal anitbody light chain vFP5.01 (Fragment) | | 0.762 | 0.029 | down |
| Cell growth-regulating nucleolar protein | Lyar | 0.762 | 0.002 | down |
| Arpin | Arpin | 0.765 | 0.011 | down |
| Mediator of RNA polymerase II transcription subunit 12 | Med12 | 0.781 | 0.031 | down |
| Clat_adaptor_s domain-containing protein | Ap3s2 | 0.783 | 0.015 | down |
| Chromatin target of PRMT1 protein | Chtop | 0.785 | 0.028 | down |
| Ring finger and CHY zinc finger domain containing 1 | Rchy1 | 0.788 | 0.006 | down |
| TYR_PHOSPHATASE_2 domain-containing protein | Ptpmt1 | 0.789 | 0.036 | down |
| Chromobox protein homolog 8 | Cbx8 | 0.789 | 0.025 | down |
| Sulfotransferase family cytosolic 1B member 1 | Sult1b1 | 0.792 | 0.003 | down |
| Tyrosine aminotransferase | Tat | 0.796 | 0.030 | down |
| Uncharacterized protein | Mob3b | 0.800 | 0.043 | down |
| Fc receptor, IgG, low affinity IIb | Fcgr2b | 0.801 | 0.017 | down |
| Guanosine-3,5-bis(diphosphate) 3-pyrophosphohydrolase MESH1 | Hddc3 | 0.801 | 0.004 | down |
| MKIAA0737 protein (Fragment) | Tox4 | 0.802 | 0.002 | down |
| Histone H2A type 2-A | Hist2h2aa1 | 0.802 | 0.005 | down |
| Complement factor H-related protein | Gm4788 | 0.805 | 0.040 | down |
| E3 ubiquitin-protein ligase XIAP | Xiap | 0.805 | 0.002 | down |
| E3 ubiquitin-protein ligase PPP1R11 | Ppp1r11 | 0.809 | 0.049 | down |
| Uncharacterized protein | Rab10 | 0.809 | 0.018 | down |
| Sodium- and chloride-dependent taurine transporter | Slc6a6 | 0.811 | 0.018 | down |
| Syndecan | Sdc1 | 0.813 | 0.039 | down |
| Arf-GAP with GTPase, ANK repeat and PH domain-containing protein 3 | Agap3 | 0.813 | 0.015 | down |
| Uncharacterized protein | Tmem258 | 0.815 | 0.032 | down |
| Unconventional myosin-Id | Myo1d | 0.816 | 0.016 | down |
| Leucine-rich repeat flightless-interacting protein 1 | Lrrfip1 | 0.817 | 0.028 | down |
| Nuclear factor 1 B-type | Nfib | 0.823 | 0.022 | down |
| Cytochrome P450, family 2, subfamily d, polypeptide 40 | Cyp2d40 | 0.824 | 0.036 | down |
| RNA/DNA-binding protein | Rnps1 | 0.825 | 0.003 | down |
| Uncharacterized protein | Selenoo | 0.826 | 0.033 | down |
| Transcription elongation factor SPT4-A | Supt4h1a | 0.826 | 0.004 | down |
| Mid1ip1 protein | Mid1ip1 | 0.827 | 0.018 | down |
| CMP-sialic acid transporter | Slc35a1 | 0.827 | 0.006 | down |
| Selenide, water dikinase 2 | Sephs2 | 0.827 | 0.005 | down |
| Ankyrin repeat and SAM domain-containing protein 3 | Anks3 | 0.828 | 0.035 | down |

| | | | | |
|---|---|---|---|---|
| Multifunctional fusion protein | Fgf1 | 0.828 | 0.001 | down |
| Galectin-related protein | Lgalsl | 0.829 | 0.033 | down |
| Putative L-aspartate dehydrogenase | Aspdh | 0.832 | 0.006 | down |
| Rsrc1 protein (Fragment) | Rsrc1 | 0.832 | 0.019 | down |
| Shiftless antiviral inhibitor of ribosomal frameshifting protein homolog | Shfl | 0.833 | 0.035 | down |
| Oxidoreductase HTATIP2 | Htatip2 | 1.206 | 0.011 | up |
| Striatin-4 | Strn4 | 1.209 | 0.002 | up |
| Serum paraoxonase/arylesterase 1 | Pon1 | 1.209 | 0.021 | up |
| Ester hydrolase C11orf54 homolog | | 1.215 | 0.003 | up |
| Fat storage-inducing transmembrane protein 2 | Fitm2 | 1.220 | 0.030 | up |
| Cytochrome b5 | Cyb5a | 1.225 | 0.018 | up |
| Neutral cholesterol ester hydrolase 1 | Nceh1 | 1.225 | 0.022 | up |
| Cytochrome P450 2C70 | Cyp2c70 | 1.229 | 0.006 | up |
| Cell death-inducing p53-target protein 1 | Cdip1 | 1.230 | 0.025 | up |
| Cytochrome P450, family 2, subfamily c, polypeptide 65 | Cyp2c65 | 1.232 | 0.011 | up |
| NADPH--cytochrome P450 reductase | Por | 1.238 | 0.005 | up |
| NADH-ubiquinone oxidoreductase chain 4 | ND4 | 1.241 | 0.021 | up |
| Complement component 6 | C6 | 1.245 | 0.029 | up |
| MKIAA0205 protein (Fragment) | Lpgat1 | 1.251 | 0.013 | up |
| Ectonucleoside triphosphate diphosphohydrolase 5 | Entpd5 | 1.251 | 0.001 | up |
| RNA-binding protein PNO1 | Pno1 | 1.255 | 0.019 | up |
| Cytochrome P450 CYP4F15 | Cyp4f15 | 1.255 | 0.000 | up |
| UDP-glucuronosyltransferase | Ugt2b1 | 1.276 | 0.004 | up |
| Dimethylaniline monooxygenase [N-oxide-forming] 5 | Fmo5 | 1.279 | 0.012 | up |
| 26S proteasome non-ATPase regulatory subunit 4 | Psmd4 | 1.285 | 0.027 | up |
| Methyltransferase-like protein 7B | Mettl7b | 1.289 | 0.011 | up |
| Leukotriene-B4 omega-hydroxylase 3 | Cyp4f14 | 1.292 | 0.000 | up |
| Estradiol 17-beta-dehydrogenase 2 | Hsd17b2 | 1.294 | 0.036 | up |
| Plastin-1 | Pls1 | 1.310 | 0.011 | up |
| Solute carrier family 22 member 18 | Slc22a18 | 1.311 | 0.000 | up |
| UDP-glucuronosyltransferase | Ugt2b35 | 1.315 | 0.003 | up |
| UDP-glucuronosyltransferase | Ugt2b34 | 1.318 | 0.001 | up |
| Cytochrome P450 3A13 | Cyp3a13 | 1.336 | 0.001 | up |
| Pentaxin | Crp | 1.372 | 0.024 | up |
| Cytochrome P450 2C37 | Cyp2c37 | 1.387 | 0.003 | up |
| 3-oxo-5-alpha-steroid 4-dehydrogenase | Srd5a1 | 1.410 | 0.000 | up |
| Dynamin-1-like protein | Dnm1l | 1.419 | 0.013 | up |
| Pyrethroid hydrolase Ces2a | Ces2a | 1.425 | 0.017 | up |
| Perilipin-2 | Plin2 | 1.430 | 0.007 | up |
| Cytochrome P450 2C29 | Cyp2c29 | 1.442 | 0.001 | up |
| Proteasome subunit beta | Psmb9 | 1.450 | 0.007 | up |
| Epoxide hydrolase 1 | Ephx1 | 1.462 | 0.000 | up |
| Cytochrome P450 2E1 | Cyp2e1 | 1.467 | 0.002 | up |
| Ubiquitin-associated domain-containing protein 2 | Ubac2 | 1.508 | 0.001 | up |
| Cytochrome P450 2C54 | Cyp2c54 | 1.552 | 0.001 | up |
| Cytochrome P450 3A11 | Cyp3a11 | 1.556 | 0.007 | up |
| H-2K(D) antigen | | 1.699 | 0.008 | up |
| Mitochondrial 10-formyltetrahydrofolate dehydrogenase | Aldh1l2 | 1.868 | 0.009 | up |
| Cytochrome P450 2C50 | Cyp2c50 | 1.873 | 0.000 | up |
| Cytochrome P450 1A2 | Cyp1a2 | 1.887 | 0.005 | up |
| Cytochrome P450 2C55 | Cyp2c55 | 2.005 | 0.000 | up |
| Cytochrome P450 2B10 | Cyp2b10 | 3.107 | 0.000 | up |

**Table S6.** The DEPs between the low-dose group and the high-dose group.

| Protein | Gene | Fold Change | P value | Trend |
|---|---|---|---|---|
| Podocalyxin | Podxl | 0.494 | 0.009 | down |
| Vacuolar protein sorting-associated protein 8 homolog | Vps8 | 0.567 | 0.014 | down |
| InaD-like protein | Patj | 0.612 | 0.037 | down |
| NADPH-dependent 3-keto-steroid reductase Hsd3b5 | Hsd3b5 | 0.641 | 0.005 | down |
| Mediator of RNA polymerase II transcription subunit 20 | Med20 | 0.652 | 0.022 | down |
| p21-activated protein kinase-interacting protein 1 | Pak1ip1 | 0.661 | 0.001 | down |
| Uncharacterized protein | Amfr | 0.665 | 0.002 | down |
| Splicing regulatory glutamine/lysine-rich protein 1 | Srek1 | 0.676 | 0.017 | down |
| Uncharacterized protein (Fragment) | Hspa5 | 0.698 | 0.021 | down |
| Regulation of nuclear pre-mRNA domain-containing protein 2 | Rprd2 | 0.702 | 0.047 | down |
| Uncharacterized protein | Rab10 | 0.705 | 0.001 | down |
| 3-hydroxybutyrate dehydrogenase type 2 | Bdh2 | 0.706 | 0.025 | down |
| Histone H1.4 | H1-4 | 0.709 | 0.035 | down |
| Protein dopey-2 | Dop1b | 0.711 | 0.008 | down |
| TLC domain-containing protein 2 | Tlcd2 | 0.721 | 0.018 | down |
| Vacuolar protein sorting-associated protein 37C | Vps37c | 0.722 | 0.003 | down |
| Alpha-globin | Hbat1 | 0.726 | 0.027 | down |
| Aquaporin-9 | Aqp9 | 0.728 | 0.039 | down |
| N-acetyltransferase 8 | Nat8 | 0.733 | 0.020 | down |
| Ninjurin-1 | Ninj1 | 0.737 | 0.033 | down |
| N6-adenosine-methyltransferase subunit METTL3 | Mettl3 | 0.744 | 0.001 | down |
| Ubiquitin-associated protein 2 | Ubap2 | 0.744 | 0.002 | down |
| Hdc homolog, cell cycle regulator | Heca | 0.750 | 0.035 | down |
| HEAT repeat-containing protein 6 | Heatr6 | 0.753 | 0.010 | down |
| Serine/threonine-protein kinase ULK3 | Ulk3 | 0.753 | 0.003 | down |
| RNA helicase aquarius | Aqr | 0.753 | 0.008 | down |
| NEDD8-activating enzyme E1 regulatory subunit | Nae1 | 0.754 | 0.016 | down |
| Acp1 protein | Acp1 | 0.756 | 0.016 | down |
| Son of sevenless homolog 1 | Sos1 | 0.757 | 0.006 | down |
| Sulfotransferase | Sult2a8 | 0.760 | 0.010 | down |
| RNA binding protein fox-1 homolog 2 | Rbfox2 | 0.761 | 0.046 | down |
| RIKEN cDNA 2210010C04 gene | 2210010C04Rik | 0.764 | 0.036 | down |
| CMP-sialic acid transporter | Slc35a1 | 0.768 | 0.019 | down |
| Krt2 protein | Krt2 | 0.768 | 0.002 | down |
| Ras association domain-containing protein 8 | Rassf8 | 0.768 | 0.014 | down |
| Leucine-rich repeat-containing protein 3 | Lrrc3 | 0.770 | 0.029 | down |
| Cytochrome P450 4V2 | Cyp4v2 | 0.770 | 0.017 | down |
| Alpha-1-antitrypsin 1-1 | Serpina1a | 0.770 | 0.045 | down |
| Exosome complex component RRP41 | Exosc4 | 0.772 | 0.008 | down |
| Uncharacterized protein KIAA1143 homolog | | 0.774 | 0.009 | down |
| Oxysterol-binding protein | Osbpl2 | 0.774 | 0.002 | down |
| Hyccin | Fam126a | 0.777 | 0.020 | down |
| Protein FAM210A | Fam210a | 0.778 | 0.003 | down |
| Small cell adhesion glycoprotein | Smagp | 0.779 | 0.005 | down |
| Transmembrane protein 254c | Tmem254c | 0.779 | 0.033 | down |
| Rab3A | Rab3a | 0.782 | 0.006 | down |
| Probable C-mannosyltransferase DPY19L3 | Dpy19l3 | 0.782 | 0.030 | down |
| CRIB domain-containing protein | Cdc42ep4 | 0.783 | 0.039 | down |
| Fucose-1-phosphate guanylyltransferase | Fpgt | 0.784 | 0.018 | down |

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|---|---|---|---|---|
| Uncharacterized protein | Calu | 0.785 | 0.025 | down |
| Arrestin, beta 2 | Arrb2 | 0.786 | 0.000 | down |
| Sulfotransferase family cytosolic 1B member 1 | Sult1b1 | 0.787 | 0.007 | down |
| WD repeat domain phosphoinositide-interacting protein 3 | Wdr45b | 0.791 | 0.001 | down |
| Abscission/NoCut checkpoint regulator | Zfyve19 | 0.792 | 0.008 | down |
| E3 ubiquitin-protein ligase HECTD3 | Hectd3 | 0.794 | 0.001 | down |
| H-2 class II histocompatibility antigen, A-U beta chain | | 0.796 | 0.004 | down |
| Monofunctional C1-tetrahydrofolate synthase, mitochondrial | Mthfd1l | 0.797 | 0.035 | down |
| Cytochrome P450, family 2, subfamily d, polypeptide 40 | Cyp2d40 | 0.798 | 0.042 | down |
| E3 ubiquitin-protein ligase | Nedd4l | 0.799 | 0.015 | down |
| WASH complex subunit 3 | Washc3 | 0.800 | 0.030 | down |
| Carbonyl reductase [NADPH] 3 | Cbr3 | 0.800 | 0.028 | down |
| 39S ribosomal protein L42, mitochondrial | Mrpl42 | 0.800 | 0.004 | down |
| Phosphoglycerate kinase (Fragment) | Pgk1 | 0.801 | 0.021 | down |
| CMP-N-acetylneuraminate-beta-galactosamide-alpha-2,3-sialyltransferase 4 | St3gal4 | 0.802 | 0.003 | down |
| WD repeat-containing protein 18 | Wdr18 | 0.802 | 0.050 | down |
| Growth hormone-regulated TBC protein 1 | Grtp1 | 0.803 | 0.015 | down |
| Mid1ip1 protein | Mid1ip1 | 0.803 | 0.014 | down |
| Splicing factor 3b, subunit 3 | Sf3b3 | 0.804 | 0.007 | down |
| Protein transport protein Sec16A (Fragment) | Sec16a | 0.804 | 0.007 | down |
| Tdrkh protein | Tdrkh | 0.805 | 0.010 | down |
| Multifunctional fusion protein | Fgf1 | 0.805 | 0.001 | down |
| Replication protein A 32 kDa subunit | Rpa2 | 0.806 | 0.001 | down |
| DNA repair protein RAD50 | Rad50 | 0.806 | 0.029 | down |
| Gap junction beta-1 protein | Gjb1 | 0.806 | 0.004 | down |
| Sodium-dependent phosphate transporter 2 | Slc20a2 | 0.808 | 0.047 | down |
| E3 ubiquitin-protein ligase Praja-1 | Pja1 | 0.808 | 0.003 | down |
| RAS p21 protein activator 1 | Rasa1 | 0.809 | 0.005 | down |
| Nostrin | Nostrin | 0.809 | 0.016 | down |
| Uncharacterized protein | Abtb2 | 0.809 | 0.003 | down |
| Trafficking protein particle complex subunit 2-like protein | Trappc2l | 0.810 | 0.005 | down |
| Tuftelin | Tuft1 | 0.810 | 0.045 | down |
| Serpina1 DOM-7 | DOM-7 | 0.810 | 0.029 | down |
| Uncharacterized protein | Mrpl40 | 0.811 | 0.028 | down |
| Uncharacterized protein | Tmem258 | 0.811 | 0.009 | down |
| Vinexin | Sorbs3 | 0.811 | 0.002 | down |
| Eukaryotic translation initiation factor 4H | Eif4h | 0.813 | 0.003 | down |
| Acyl-CoA synthetase short-chain family member 3, mitochondrial | Acss3 | 0.814 | 0.020 | down |
| Uncharacterized protein | Ubqln1 | 0.815 | 0.009 | down |
| Uncharacterized protein (Fragment) | Rabgap1l | 0.815 | 0.010 | down |
| Complement component 7 | C7 | 0.817 | 0.039 | down |
| Casein kinase I isoform gamma-3 | Csnk1g3 | 0.818 | 0.002 | down |
| Beta-mannosidase | Manba | 0.819 | 0.011 | down |
| Plexin B1 | Plxnb1 | 0.819 | 0.045 | down |
| Breast cancer anti-estrogen resistance protein 3 | Bcar3 | 0.820 | 0.033 | down |
| Peptidase S1 domain-containing protein | Try5 | 0.820 | 0.005 | down |
| Glyceraldehyde-3-phosphate dehydrogenase | Gm3839 | 0.820 | 0.001 | down |
| Probable proline--tRNA ligase, mitochondrial | Pars2 | 0.821 | 0.004 | down |
| [F-actin]-monooxygenase MICAL3 | Mical3 | 0.821 | 0.004 | down |
| Conserved oligomeric Golgi complex subunit 3 | Cog3 | 0.821 | 0.004 | down |
| Chloride channel protein 2 | Clcn2 | 0.821 | 0.004 | down |

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|---|---|---|---|---|
| Ubiquitin carboxyl-terminal hydrolase 48 | Usp48 | 0.822 | 0.000 | down |
| Calmodulin-1 | Calm1 | 0.822 | 0.014 | down |
| Structural maintenance of chromosomes flexible hinge domain-containing protein 1 | Smchd1 | 0.823 | 0.011 | down |
| Carboxypeptidase D | Cpd | 0.823 | 0.014 | down |
| Non-lysosomal glucosylceramidase | Gba2 | 0.823 | 0.000 | down |
| Sin3 histone deacetylase corepressor complex component SDS3 | Suds3 | 0.824 | 0.009 | down |
| SEC22 vesicle trafficking protein homologe A (S. cerevisiae) | Sec22a | 0.824 | 0.043 | down |
| Unconventional myosin-Id | Myo1d | 0.825 | 0.013 | down |
| Uridine-cytidine kinase | Uck1 | 0.826 | 0.000 | down |
| SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily E member 1 | Smarce1 | 0.826 | 0.010 | down |
| Transmembrane anterior posterior transformation protein 1 | Tapt1 | 0.826 | 0.001 | down |
| Proteasome assembly chaperone 4 | Psmg4 | 0.827 | 0.018 | down |
| Dedicator of cytokinesis 8 | Dock8 | 0.827 | 0.040 | down |
| Leucine carboxyl methyltransferase 1 | Lcmt1 | 0.829 | 0.019 | down |
| Core histone macro-H2A.2 | H2afy2 | 0.829 | 0.002 | down |
| WD repeat-containing protein 5 | Wdr5 | 0.830 | 0.001 | down |
| SH3 domain-containing protein | Bcar1 | 0.830 | 0.003 | down |
| Cell cycle control protein 50A | Tmem30a | 0.830 | 0.004 | down |
| HDAg domain-containing protein | Nelfa | 0.830 | 0.022 | down |
| Thromboxane-A synthase | Tbxas1 | 0.830 | 0.025 | down |
| Serine--tRNA ligase, mitochondrial | Sars2 | 0.830 | 0.034 | down |
| 5-3 exonuclease PLD3 | Pld3 | 0.833 | 0.000 | down |
| UDP-glucuronosyltransferase | Ugt2b35 | 1.200 | 0.012 | up |
| Eukaryotic translation initiation factor 1A | Eif1a | 1.202 | 0.010 | up |
| Retinol dehydrogenase 13 | Rdh13 | 1.203 | 0.016 | up |
| Complement component receptor 1-like protein | Cr1l | 1.206 | 0.027 | up |
| Oxidoreductase HTATIP2 | Htatip2 | 1.206 | 0.017 | up |
| STE20-related kinase adapter protein beta | Stradb | 1.209 | 0.004 | up |
| Signal recognition particle 9 kDa protein | Srp9 | 1.211 | 0.013 | up |
| Glutathione S-transferase theta-1 | Gstt1 | 1.215 | 0.014 | up |
| GTP-binding protein SAR1b | Sar1b | 1.216 | 0.027 | up |
| 2-hydroxyacyl-CoA lyase 1 | Hacl1 | 1.216 | 0.010 | up |
| 6-pyruvoyl tetrahydrobiopterin synthase | Pts | 1.216 | 0.030 | up |
| Multifunctional procollagen lysine hydroxylase and glycosyltransferase LH3 | Plod3 | 1.219 | 0.043 | up |
| Protein cereblon | Crbn | 1.219 | 0.040 | up |
| Ubiquitin-associated domain-containing protein 2 | Ubac2 | 1.219 | 0.003 | up |
| Acylcarnitine hydrolase | Ces2c | 1.220 | 0.012 | up |
| Rnase4 protein | Rnase4 | 1.220 | 0.001 | up |
| Glutathione S-transferase Mu 1 | Gstm1 | 1.221 | 0.008 | up |
| Cytochrome b-c1 complex subunit 6, mitochondrial | Uqcrh | 1.222 | 0.002 | up |
| Cytochrome P450 CYP4F15 | Cyp4f15 | 1.223 | 0.034 | up |
| Ectonucleoside triphosphate diphosphohydrolase 5 | Entpd5 | 1.225 | 0.005 | up |
| Cytochrome P450 2C29 | Cyp2c29 | 1.226 | 0.048 | up |
| 39S ribosomal protein L53, mitochondrial | Mrpl53 | 1.228 | 0.001 | up |
| F-box/LRR-repeat protein 20 | Fbxl20 | 1.230 | 0.015 | up |
| Mitochondrial fission regulator 1-like | Mtfr1l | 1.230 | 0.001 | up |
| Phospholipid-transporting ATPase (Fragment) | Atp11b | 1.233 | 0.047 | up |
| Retinol-binding protein 1 | Rbp1 | 1.236 | 0.012 | up |
| Serine dehydratase-like | Sdsl | 1.237 | 0.036 | up |
| Malignant T-cell-amplified sequence 1 | Mcts1 | 1.238 | 0.013 | up |

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|---|---|---|---|---|
| Macrophage migration inhibitory factor | Mif | 1.240 | 0.042 | up |
| Translocation protein SEC62 | Sec62 | 1.243 | 0.044 | up |
| Predicted gene 4788 | Gm4788 | 1.246 | 0.026 | up |
| Delta(14)-sterol reductase TM7SF2 | Tm7sf2 | 1.246 | 0.007 | up |
| Protein spinster homolog 1 | Spns1 | 1.247 | 0.049 | up |
| Synaptophysin-like protein 1 | Sypl1 | 1.248 | 0.008 | up |
| Etoposide-induced protein 2.4 | Ei24 | 1.249 | 0.017 | up |
| Transmembrane protein 33 | Tmem33 | 1.252 | 0.001 | up |
| Sigma intracellular receptor 2 | Tmem97 | 1.255 | 0.027 | up |
| Glutathione S-transferase theta-3 | Gstt3 | 1.256 | 0.040 | up |
| Uncharacterized protein | Acaa1b | 1.256 | 0.020 | up |
| Glucose-6-phosphatase | G6pc | 1.258 | 0.020 | up |
| Cytochrome P450 2E1 | Cyp2e1 | 1.258 | 0.011 | up |
| Sorting nexin-21 | Snx21 | 1.260 | 0.033 | up |
| Ubiquitin carboxyl-terminal hydrolase MINDY-1 | Mindy1 | 1.260 | 0.015 | up |
| Rho guanine nucleotide exchange factor (GEF) 26 | Arhgef26 | 1.261 | 0.044 | up |
| Cytochrome P450 3A13 | Cyp3a13 | 1.262 | 0.005 | up |
| Protein phosphatase 1 regulatory subunit 3G | Ppp1r3g | 1.265 | 0.040 | up |
| Leukotriene-B4 omega-hydroxylase 3 | Cyp4f14 | 1.266 | 0.002 | up |
| Uncharacterized protein | Ghdc | 1.272 | 0.016 | up |
| Transmembrane protease serine 6 | Tmprss6 | 1.272 | 0.011 | up |
| Phosphatidylcholine transfer protein | Pctp | 1.282 | 0.034 | up |
| BolA-like protein 2 | Bola2 | 1.282 | 0.001 | up |
| Alpha-ketoglutarate-dependent dioxygenase FTO | Fto | 1.284 | 0.027 | up |
| Dimethylaniline monooxygenase [N-oxide-forming] 5 | Fmo5 | 1.286 | 0.021 | up |
| Mycophenolic acid acyl-glucuronide esterase, mitochondrial | Abhd10 | 1.289 | 0.002 | up |
| [Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial | Pdk2 | 1.290 | 0.030 | up |
| Pyrethroid hydrolase Ces2a | Ces2a | 1.290 | 0.047 | up |
| Cytochrome P450 3A25 | Cyp3a25 | 1.290 | 0.008 | up |
| NADH-ubiquinone oxidoreductase chain 4 | ND4 | 1.293 | 0.019 | up |
| Eukaryotic translation initiation factor 6 | Eif6 | 1.294 | 0.004 | up |
| Irgm1 | OTTMUSPW KG00059374 | 1.298 | 0.048 | up |
| Ester hydrolase C11orf54 homolog | | 1.298 | 0.000 | up |
| F-box only protein 6 | Fbxo6 | 1.304 | 0.004 | up |
| Kelch domain-containing protein 10 | Klhdc10 | 1.309 | 0.007 | up |
| Epoxide hydrolase 1 | Ephx1 | 1.309 | 0.001 | up |
| Solute carrier family 22 member 18 | Slc22a18 | 1.314 | 0.000 | up |
| DENN domain-containing protein 10 | Dennd10 | 1.317 | 0.001 | up |
| Lymphocyte antigen 6 complex, locus G2 | Ly6g2 | 1.318 | 0.001 | up |
| Programmed cell death protein 2 | Pdcd2 | 1.321 | 0.006 | up |
| Neuroplastin | Nptn | 1.324 | 0.017 | up |
| Perilipin-2 | Plin2 | 1.325 | 0.006 | up |
| Transmembrane protein 11, mitochondrial | Tmem11 | 1.328 | 0.028 | up |
| Hsp90 co-chaperone Cdc37-like 1 | Cdc37l1 | 1.328 | 0.007 | up |
| Plastin-1 | Pls1 | 1.329 | 0.011 | up |
| Disintegrin and metalloproteinase domain-containing protein 17 | Adam17 | 1.332 | 0.005 | up |
| Vitamin D-binding protein | Gc | 1.336 | 0.017 | up |
| Pentaxin | Crp | 1.338 | 0.026 | up |
| Mitochondrial import inner membrane translocase subunit Tim8 A | Timm8a1 | 1.340 | 0.005 | up |
| Oligosaccharyltransferase complex subunit OSTC | Ostc | 1.353 | 0.001 | up |

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|---|---|---|---|---|
| Tubulointerstitial nephritis antigen-like | Tinagl1 | 1.356 | 0.004 | up |
| Sodium- and chloride-dependent GABA transporter 2 | Slc6a13 | 1.356 | 0.002 | up |
| Cytochrome P450 3A11 | Cyp3a11 | 1.361 | 0.031 | up |
| Vitamin K epoxide reductase complex subunit 1-like protein 1 | Vkorc1l1 | 1.362 | 0.005 | up |
| NHP2-like protein 1 | Snu13 | 1.370 | 0.001 | up |
| Uncharacterized protein | Ndufs5 | 1.371 | 0.004 | up |
| Aldehyde dehydrogenase | Aldh3a2 | 1.374 | 0.014 | up |
| Mannose-P-dolichol utilization defect 1 | Mpdu1 | 1.379 | 0.004 | up |
| Dynein light chain Tctex-type 3 | Dynlt3 | 1.381 | 0.007 | up |
| NADH-ubiquinone oxidoreductase chain 3 | ND3 | 1.385 | 0.035 | up |
| Cytochrome P450 2C37 | Cyp2c37 | 1.388 | 0.002 | up |
| COX assembly mitochondrial protein (Fragment) | Cmc1 | 1.390 | 0.029 | up |
| Leptin receptor gene-related protein | Leprot | 1.392 | 0.025 | up |
| Cytochrome P450 1A2 | Cyp1a2 | 1.393 | 0.034 | up |
| Glutathione reductase, mitochondrial | Gsr | 1.395 | 0.004 | up |
| Lysosomal alpha-glucosidase | Gaa | 1.397 | 0.001 | up |
| Tetraspanin-31 | Tspan31 | 1.426 | 0.017 | up |
| 7-dehydrocholesterol reductase | Dhcr7 | 1.432 | 0.007 | up |
| SCAN domain containing 3 | Zbed5 | 1.434 | 0.009 | up |
| ADP-ribosylation factor-related protein 1 | Arfrp1 | 1.436 | 0.006 | up |
| Cytochrome P450 4A10 | Cyp4a10 | 1.448 | 0.037 | up |
| Mitochondrial intermembrane space import and assembly protein 40 | Chchd4 | 1.449 | 0.007 | up |
| TP53-regulated inhibitor of apoptosis 1 | Triap1 | 1.466 | 0.001 | up |
| Aspartylglucosaminidase | Aga | 1.466 | 0.004 | up |
| Uncharacterized protein | Igfbp7 | 1.468 | 0.002 | up |
| Glycine N-acyltransferase-like protein | Gm4952 | 1.478 | 0.049 | up |
| Coagulation factor IX | F9 | 1.478 | 0.005 | up |
| HECT domain E3 ubiquitin protein ligase 4 | Hectd4 | 1.484 | 0.022 | up |
| Solute carrier family 25 member 46 | Slc25a46 | 1.485 | 0.006 | up |
| Putative bifunctional UDP-N-acetylglucosamine transferase and deubiquitinase ALG13 | Alg13 | 1.497 | 0.012 | up |
| Glucose-6-phosphate isomerase | Gpi1 | 1.502 | 0.025 | up |
| Isoc2a protein | Isoc2a | 1.530 | 0.000 | up |
| BRISC and BRCA1-A complex member 2 | Babam2 | 1.537 | 0.003 | up |
| 1-acylglycerol-3-phosphate O-acyltransferase ABHD5 | Abhd5 | 1.543 | 0.009 | up |
| Tetraspanin-9 | Tspan9 | 1.554 | 0.001 | up |
| Fibulin-1 | Fbln1 | 1.558 | 0.041 | up |
| Sialin | Slc17a5 | 1.598 | 0.021 | up |
| T-cell immunoglobulin and mucin domain-containing protein 4 | Timd4 | 1.611 | 0.044 | up |
| Endonuclease/exonuclease/phosphatase family domain-containing protein 1 | Eepd1 | 1.615 | 0.006 | up |
| Vitamin K epoxide reductase complex subunit 1 | Vkorc1 | 1.630 | 0.002 | up |
| Cytochrome c oxidase assembly factor 4 homolog, mitochondrial | COA4 | 1.652 | 0.004 | up |
| Cytochrome P450 2C55 | Cyp2c55 | 1.675 | 0.000 | up |
| RING-type domain-containing protein (Fragment) | Rnf121 | 1.679 | 0.000 | up |
| Cytochrome P450 2C54 | Cyp2c54 | 1.679 | 0.000 | up |
| Squalene synthase | Fdft1 | 1.718 | 0.044 | up |
| Uncharacterized protein | | 1.726 | 0.002 | up |
| Uncharacterized protein | Psap | 1.791 | 0.035 | up |
| Cytochrome P450 2C50 | Cyp2c50 | 1.808 | 0.000 | up |
| Coiled-coil-helix-coiled-coil-helix domain-containing 10 | Chchd10 | 1.961 | 0.001 | up |
| Mitochondrial 10-formyltetrahydrofolate dehydrogenase | Aldh1l2 | 2.064 | 0.003 | up |

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|---|---|---|---|---|
| Glutamine synthetase | | 2.077 | 0.012 | up |
| Glutathione S-transferase | Gm10639 | 2.113 | 0.007 | up |
| Cytochrome P450 2B10 | Cyp2b10 | 2.206 | 0.000 | up |
| Uncharacterized protein | Grn | 2.639 | 0.019 | up |

**Table S7.** The major discussed DEPs after nutmeg exposure and their KEGG pathways.

| Protein | Group | Fold Change | P value | Trend | KEGG Pathway |
|---|---|---|---|---|---|
| CYP450 1A2 | Low-dose vs Control | 1.355 | 0.006 | up | Steroid hormone biosynthesis, Caffeine metabolism, Tryptophan metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolism of xenobiotics, Drug metabolism, Metabolic pathways, Chemical carcinogenesis |
| | High-dose vs Control | 1.887 | 0.005 | up | |
| | High-dose vs Low-dose | 1.393 | 0.034 | up | |
| CYP450 2B10 | Low-dose vs Control | 1.408 | 0.005 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Retinol metabolism, Metabolic pathways, Chemical carcinogenesis |
| | High-dose vs Control | 3.107 | 0.000 | up | |
| | High-dose vs Low-dose | 2.206 | 0.000 | up | |
| CYP450 2C29 | High-dose vs Control | 1.442 | 0.001 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channels, Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.226 | 0.048 | up | |
| CYP450 2C37 | High-dose vs Control | 1.387 | 0.003 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channel, Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.388 | 0.002 | up | |
| CYP450 2C50 | High-dose vs Control | 1.873 | 0.000 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channels, Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.808 | 0.000 | up | |
| CYP450 2C54 | High-dose vs Control | 1.552 | 0.001 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channels, Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.679 | 0.000 | up | |
| CYP450 2C55 | High-dose vs Control | 2.005 | 0.000 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channels, Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.675 | 0.000 | up | |
| CYP450 2C70 | Low-dose vs Control | 1.218 | 0.006 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channels, Chemical carcinogenesis |
| | High-dose vs Control | 1.229 | 0.006 | up | |
| CYP450 2E1 | High-dose vs Control | 1.467 | 0.002 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Metabolism of xenobiotics, Drug metabolism, Metabolic pathways, Non-alcoholic fatty liver disease (NAFLD), Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.258 | 0.011 | up | |
| CYP450 3A11 | High-dose vs Control | 1.556 | 0.007 | up | Steroid hormone biosynthesis, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Chemical car- |

| | | | | | |
|---|---|---|---|---|---|
| | High-dose vs Low-dose | 1.361 | 0.031 | up | cinogenesis |
| CYP450 3A13 | High-dose vs Control | 1.336 | 0.001 | up | Steroid hormone biosynthesis, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Chemical carcinogenesis |
| | High-dose vs Low-dose | 1.262 | 0.005 | up | |
| CYP450 3A25 | High-dose vs Low-dose | 1.290 | 0.008 | up | Steroid hormone biosynthesis, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Chemical carcinogenesis |
| CYP450 4A10 | High-dose vs Low-dose | 1.448 | 0.037 | up | Fatty acid degradation, Arachidonic acid metabolism, Retinol metabolism, Metabolic pathways, PPAR signaling pathway, Vascular smooth muscle contraction, Inflammatory mediator regulation of TRP channels |
| CYP450 4V2 | Low-dose vs Control | 1.220 | 0.032 | up | -- |
| | High-dose vs Low-dose | 0.770 | 0.017 | down | |
| CYP450 CYP4F15 | High-dose vs Control | 1.255 | 0.000 | up | -- |
| | High-dose vs Low-dose | 1.223 | 0.034 | up | |
| CYP450, family 2, subfamily c, polypeptide 65 | High-dose vs Control | 1.232 | 0.011 | up | Steroid hormone biosynthesis, Arachidonic acid metabolism, Linoleic acid metabolism, Retinol metabolism, Metabolic pathways, Serotonergic synapse, Inflammatory mediator regulation of TRP channels, Chemical carcinogenesis |
| CYP450, family 2, subfamily d, polypeptide 40 | High-dose vs Control | 0.824 | 0.036 | down | Steroid hormone biosynthesis, Serotonergic synapse |
| | High-dose vs Low-dose | 0.798 | 0.042 | down | |
| Glutathione peroxidase 1 | Low-dose vs Control | 0.787 | 0.042 | down | Glutathione metabolism, Arachidonic acid metabolism, Thyroid hormone synthesis |
| | High-dose vs Control | 0.713 | 0.017 | down | |
| Glutathione peroxidase 3 | Low-dose vs Control | 0.764 | 0.019 | down | Glutathione metabolism, Arachidonic acid metabolism, Thyroid hormone synthesis |
| Glutathione S-transferase | High-dose vs Low-dose | 2.113 | 0.007 | up | -- |
| Glutathione S-transferase Mu 1 | High-dose vs Low-dose | 1.221 | 0.008 | up | Glutathione metabolism, Metabolism of xenobiotics, Drug metabolism, Platinum drug resistance, Pathways in cancer, Chemical carcinogenesis, Hepatocellular carcinoma, Fluid shear stress and atherosclerosis |
| Glutathione S-transferase Mu 7 | Low-dose vs Control | 0.785 | 0.031 | down | Glutathione metabolism, Metabolism of xenobiotics, Drug metabolism, Platinum drug resistance, Pathways in cancer, Chemical carcinogenesis, Hepatocellular carcinoma, Fluid shear stress and atherosclerosis |
| Glutathione S-transferase theta-1 | High-dose vs Low-dose | 1.215 | 0.014 | up | Glutathione metabolism, Metabolism of xenobiotics, Drug metabolism, Platinum drug resistance, Pathways in cancer, Chemical carcinogenesis, Hepatocellular carcinoma, Fluid shear stress and atherosclerosis |
| Glutathione S-transferase theta-3 | High-dose vs Low-dose | 1.256 | 0.040 | up | Glutathione metabolism, Metabolism of xenobiotics, Drug metabolism, Platinum drug resistance, Pathways |

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|---|---|---|---|---|---|
| | | | | | in cancer, Chemical carcinogenesis, Hepatocellular carcinoma, Fluid shear stress and atherosclerosis |
| Selenoprotein W | Low-dose vs Control | 0.698 | 0.023 | down | -- |
| | High-dose vs Control | 0.615 | 0.023 | down | |
| Cytochrome b5 | High-dose vs Control | 1.225 | 0.018 | up | -- |
| Cytochrome b-c1 complex subunit 6, mitochondrial | Low-dose vs Control | 0.829 | 0.011 | down | Oxidative phosphorylation, Metabolic pathways, Cardiac muscle contraction, Non-alcoholic fatty liver disease (NAFLD), Alzheimer's disease, Parkinson's disease, Huntington's disease |
| | High-dose vs Low-dose | 1.222 | 0.002 | up | |
| Cytochrome c oxidase assembly factor 4 homolog, mitochondrial | Low-dose vs Control | 0.581 | 0.008 | down | -- |
| | High-dose vs Low-dose | 1.652 | 0.004 | up | |
| Cytochrome c oxidase assembly factor 6 homolog | Low-dose vs Control | 0.756 | 0.015 | down | -- |
| NADPH--CYP450 reductase | High-dose vs Control | 1.238 | 0.005 | up | -- |
| Leukotriene-B4 omega-hydroxylase 3 | High-dose vs Control | 1.292 | 0.000 | up | Arachidonic acid metabolism, Metabolic pathways |
| | High-dose vs Low-dose | 1.266 | 0.002 | up | |