

Supplementary information

1. Animal modeling method [1]

All adult male Wistar rats (2 months) weighing 200 ± 20 g were housed in a 12/12 h light/dark cycle at an ambient temperature of 20 ± 2 °C and relative humidity of 60% - 65%. The normal control group were fed with normal diet. The MetS model group were fed with high-sugar-fat-diet (50% of normal diet, 18% sugar, 10% lard, 12% egg yolk powder, 2% cholesterol, 7.5% salt and 0.5% bile salt). After 15 weeks, MetS model group were fed with high-fat emulsion (ingredients: 10% of cholesterol, 30% of lard, 2% of sodium cholate, 0.5% of propylthiouracil, 10% of tween 80 and 10% of propylene glycol) by intragastric at a dose of 10 mL/kg/d for 2 weeks. The metabolic disorder of the animals was assessed by measuring abdominal perimeters, serum levels of HDL-C and insulin, and insulin-resistances (HOMA-IR, estimated using the homeostasis model assessment) according to the WHO definition [2]. After 17 weeks, all these parameters of MetS group were significantly different from that of normal control group, the specific result can be seen in Figure S1. Data were presented as the mean \pm standard error. Statistical significance ($P < 0.05$) was determined using Two-sample T-test in SPSS software 20.0.

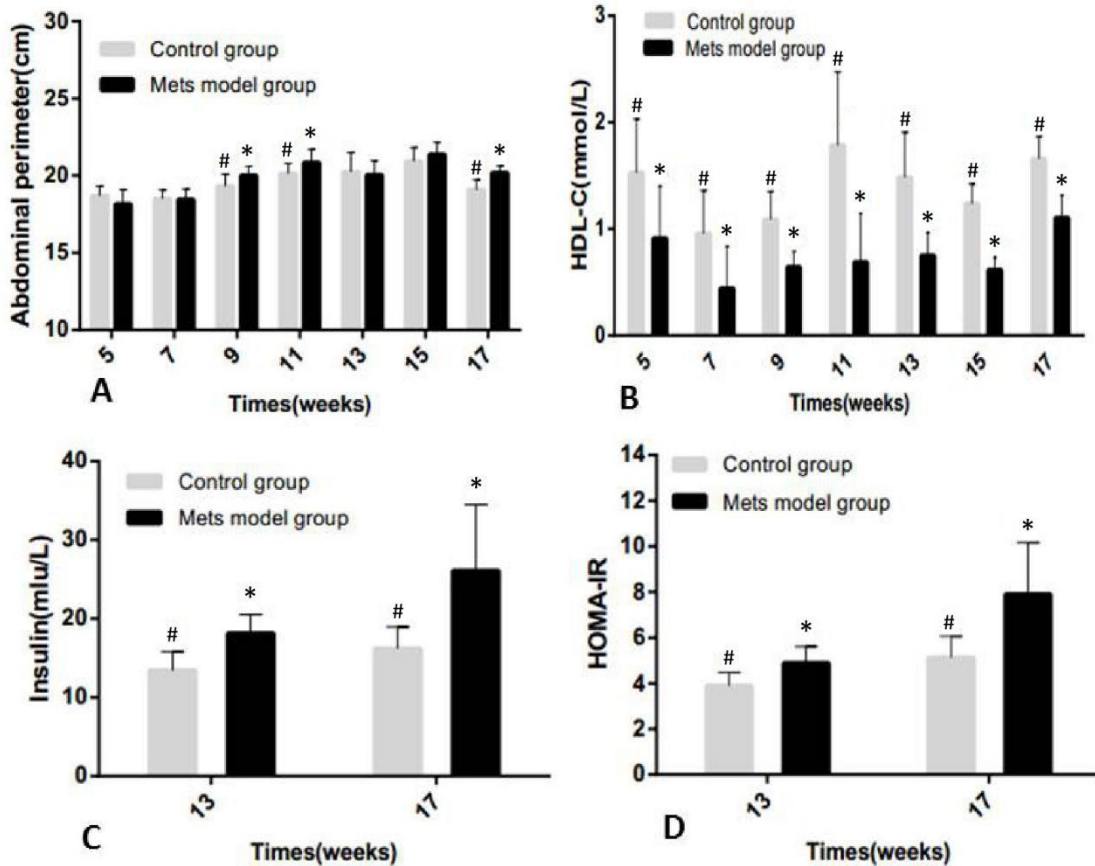


Figure S1. Biochemistry values of Wistar rats during 17 weeks diet feeding: (A) abdominal perimeter; (B) serum HDL level; (C) serum insulin level; (D) HOMA-IR. # $P < 0.05$ vs. Mets model group, * $P < 0.05$ vs. control group by t-test.

1. Z. Chen, H. Gan, J. Kang, Y. Guo, J. Zhang, M. Chen, Study on modeling method of sputum syndrome of metabolic syndrome in rats [J]. J. Liaoning Univ. Tradit. Chin. Med., 2017, 19(11):75-78.
2. WHO. Definition, diagnosis and classification of diabetes mellitus and its complications. diabetic medicine,

1999.

2. iTRAQ Labeling

After digested with sequence-grade modified trypsin (Promega, Madison, WI) at 37 ° C for 12 hours, the resultant peptide mixture was labeled using chemicals from the iTRAQ8Plex reagent kit (AB Sciex, CA, USA) according to the manufacturer's protocol. The MetS samples were labelled with isobaric tags 113, 114 and 115. The control samples were labelled with isobaric tags 116, 118 and 119. Internal standard (equivalent MetS and control) was labelled with isobaric tag 121.

3. Data Analysis

MS/MS spectra were searched using MASCOT engine (Matrix Science, London, UK; version 2.3.2) embedded into Proteome Discoverer 1.4. The following parameters were set.

| Item | Value |
|------------------------|--|
| Fixed modifications | Carbamidomethyl (C), iTRAQ 8plex (K), iTRAQ 8plex (N-term) |
| Variable modifications | Oxidation (M) ; iTRAQ 8plex (Y) |
| Peptide Mass Tolerance | 10 ppm |
| MS/MS Tolerance | 50mmu |
| Max missed cleavages | 2 |
| Enzyme | Trypsin |
| Database | UniprotKB Swiss-Prot (Rattus norvegicus (Rat)) |
| Protein Quantification | The protein ratios are calculated as the median of only unique peptides of the protein |
| Experimental Bias | Normalizes all peptide ratios by the median protein ratio. The median protein ratio should be 1 after the normalization. |

Table S1. Differential metabolites in liver tissue samples of rats between normal and MetS groups

| Metabolites | Abundance variation | Metabolites | Abundance variation |
|-------------------------------|---------------------|-----------------------------|---------------------|
| 2-Ketobutyric Acid | up | D-Glucoheptose | down |
| N-Methyl-DL-Alanine | down | Oleic Acid | down |
| Malonic Acid | up | Linolenic Acid | up |
| 3-Methylamino-1,2-Propanediol | down | Cis-Gondoic Acid | down |
| Valine | up | Xanthosine | up |
| Hydroxyurea | up | Guanosine | up |
| Guaiacol | up | Palatinose | down |
| Ethanolamine | up | 5-Alpha-Dihydroprogesterone | down |
| Nicotinic Acid | up | Alpha-Tocopherol | up |
| Isoleucine | up | 4-Cholesten-3-One | down |
| Proline | up | Pyruvic Acid | up |
| Maleic Acid | down | Oxalic Acid | up |
| Itaconic Acid | up | 2-Hydroxybutanoic Acid | up |

| | | | |
|---------------------------|------|-----------------------------|------|
| Fumaric Acid | down | Sulfuric Acid | up |
| Pyrrole-2-Carboxylic Acid | up | Phosphate | down |
| Tartronic Acid | up | Serine | up |
| 4-Methyl-5-Thiazolethanol | up | Cycloleucine | up |
| Threonine | up | 1-Indanol | up |
| Hydroquinone | down | Beta-Alanine | up |
| Thymine | up | 3-Methylthiopropylamine | up |
| Biuret | up | Phosphoglycolic Acid | down |
| Maleamate | down | Threo-Beta-Hydroxyaspartate | up |
| Nicotinamide | up | Beta-Glutamic Acid | up |
| Threitol | up | 5-Aminovaleric Acid | down |
| Methionine | up | Creatine | up |
| Oxoproline | down | Taurine | up |
| Phenylalanine | up | Flavin Adenine | down |
| Allose | up | Fructose | down |
| Pyrophosphate | down | Gluconic Lactone | down |
| Xylose | down | Mannose | down |
| Phthalic Acid | down | Guanidinosuccinic Acid | down |
| D-(Glycerol 1-Phosphate) | down | Myo-Inositol | down |
| Dehydroshikimic Acid | up | Cellobiose | down |
| Hypoxanthine | up | 2-Monoolein | up |
| Ornithine | up | Prunin | up |
| 1,5-Anhydroglucitol | up | Adrenosterone | up |
| Beta-Mannosylglycerate | up | 21-Hydroxypregnenolone | down |
| Pantothenic Acid | up | 5-Dihydrocortisol | down |
| L-Dopa | down | Zymosterol | up |
| N,N-Dimethylarginine | down | Luteolin | up |
| Glucoheptonic Acid | down | Stigmasterol | up |

Table S2. Differential proteins in liver tissue samples of rats between normal and MetS groups

| Symbol | Protein name | Fold change | P-value |
|---------|---|-------------|---------|
| Dhcr7 | 7-Dehydrocholesterol Reductase | 1.835 | 0.0004 |
| Nap111 | Nucleosome Assembly Protein 1-Like 1 | 0.805 | 0.0059 |
| Fads2 | Fatty Acid Desaturase 2 | 1.345 | 0.0049 |
| Tpmt | Thiopurine S-Methyltransferase | 1.217 | 0.0083 |
| Mpeg1 | Macrophage-Expressed Gene 1 Protein | 0.802 | 0.0173 |
| Vamp8 | Vesicle-Associated Membrane Protein 8 | 0.675 | 0.0124 |
| Epb4111 | Band 4.1-Like Protein 1 | 0.821 | 0.0210 |
| Crym | Ketimine Reductase Mu-Crystallin | 0.754 | 0.0006 |
| Ccs | Copper Chaperone For Superoxide Dismutase | 1.244 | 0.0015 |
| Ebp | 3-Beta-Hydroxysteroid-Delta(8),Delta(7)-Isomerase | 1.280 | 0.0474 |
| Hrg | Histidine-Rich Glycoprotein | 0.788 | 0.0414 |

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|------------|---|-------|--------|
| Acot12 | Acyl-Coenzyme A Thioesterase 12 | 0.832 | 0.0019 |
| Vmp1 | Vacuole Membrane Protein 1 | 0.780 | 0.0142 |
| Retsat | All-Trans-Retinol 13,14-Reductase | 0.832 | 0.0024 |
| Higd1a | Hig1 Domain Family Member 1A, Mitochondrial | 0.819 | 0.0347 |
| Dcps | m7Gpppx Diphosphatase | 0.808 | 0.0387 |
| Pgpep1 | Pyroglutamyl-Peptidase 1 | 1.308 | 0.0013 |
| Sdhd | Succinate Dehydrogenase [Ubiquinone] Cytochrome b Small Subunit, Mitochondrial | 0.797 | 0.0424 |
| Hsd17b11 | Estradiol 17-Beta-Dehydrogenase 11 | 0.685 | 0.0044 |
| Echdc1 | Ethylmalonyl-Coa Decarboxylase | 1.433 | 0.0019 |
| Stn1 | Cst Complex Subunit Stn1 | 0.743 | 0.0286 |
| Hbs1l | Hbs1-Like Protein | 0.797 | 0.0219 |
| Pla2g15 | Group Xv Phospholipase A2 | 0.778 | 0.0076 |
| Cyp51a1 | Lanosterol 14-Alpha Demethylase | 2.016 | 0.0002 |
| Ugt1a5 | Udp-Glucuronosyltransferase 1-5 | 0.694 | 0.0246 |
| Cyp3a18 | Cytochrome P450 3A18 | 0.719 | 0.0006 |
| Ugt1a1 | Udp-Glucuronosyltransferase 1-1 | 0.722 | 0.0000 |
| Ptgs1 | Prostaglandin G/H Synthase 1 | 0.803 | 0.0012 |
| Azgp1 | Zinc-Alpha-2-Glycoprotein | 0.824 | 0.0136 |
| Gbp2 | Guanylate-Binding Protein 1 | 0.753 | 0.0136 |
| Lbp | Lipopolysaccharide-Binding Protein | 1.695 | 0.0246 |
| Mvd | Diphosphomevalonate Decarboxylase | 1.555 | 0.0001 |
| Hsd17b7 | 3-Keto-Steroid Reductase | 1.618 | 0.0028 |
| Ugt2b7 | Udp-Glucuronosyltransferase 2B7 | 0.623 | 0.0038 |
| Tomm20 | Mitochondrial Import Receptor Subunit Tom20 Homolog | 1.210 | 0.0070 |
| Cd81 | Cd81 Antigen | 1.227 | 0.0002 |
| Rap1b | Ras-Related Protein Rap-1b | 1.266 | 0.0111 |
| Gadd45gip1 | Growth Arrest And Dna Damage-Inducible Proteins-Interacting Protein 1 | 1.329 | 0.0111 |
| Letm1 | Mitochondrial Proton/Calcium Exchanger Protein | 1.288 | 0.0000 |
| Ghitm | Growth Hormone-Inducible Transmembrane Protein | 0.767 | 0.0038 |
| Eepd1 | Endonuclease/Exonuclease/Phosphatase Family Domain-Containing Protein 1 | 1.261 | 0.0328 |
| Acat2 | Acetyl-Coa Acetyltransferase, Cytosolic | 1.999 | 0.0041 |
| Tmem97 | Sigma Intracellular Receptor 2 | 1.264 | 0.0341 |
| Ryden | Repressor Of Yield Of Denv Protein Homolog | 0.724 | 0.0111 |
| Aox3 | Aldehyde Oxidase 3 | 1.253 | 0.0003 |
| Pycr3 | Pyrroline-5-Carboxylate Reductase 3 | 0.770 | 0.0028 |
| Rsrc1 | Serine/Arginine-Related Protein 53 | 1.283 | 0.0377 |
| Uqcrh | Cytochrome b-c1 Complex Subunit 6, Mitochondrial | 1.338 | 0.0071 |
| Fgl1 | Fibrinogen-Like Protein 1 | 0.820 | 0.0190 |
| Sit1 | Signaling Threshold-Regulating Transmembrane Adapter 1 | 0.338 | 0.0236 |
| Cnrip1 | Cb1 Cannabinoid Receptor-Interacting Protein 1 | 0.732 | 0.0307 |
| Cd302 | Cd302 Antigen | 0.830 | 0.0252 |

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| Stbd1 | Starch-Binding Domain-Containing Protein 1 | 0.814 | 0.0021 |
| Rab18 | Ras-Related Protein Rab-18 | 0.738 | 0.0007 |
| Slc25a18 | Mitochondrial Glutamate Carrier 2 | 1.325 | 0.0069 |
| Dhtkd1 | Probable 2-Oxoglutarate Dehydrogenase E1 Component Dhkbd1, Mitochondrial | 1.268 | 0.0017 |
| Serpinb1a | Leukocyte Elastase Inhibitor A | 0.773 | 0.0122 |
| Acsf2 | Acyl-Coa Synthetase Family Member 2, Mitochondrial | 1.860 | 0.0017 |
| Anxa2 | Annexin A2 | 0.781 | 0.0198 |
| Fdft1 | Squalene Synthase | 2.018 | 0.0005 |
| Enpp3 | Ectonucleotide Pyrophosphatase/Phosphodiesterase Family Member 3 | 0.803 | 0.0135 |
| Slc27a2 | Very Long-Chain Acyl-Coa Synthetase | 0.813 | 0.0043 |
| Pgd | 6-Phosphogluconate Dehydrogenase, Decarboxylating | 1.384 | 0.0000 |
| Fscn1 | Fascin | 0.824 | 0.0003 |
| H3f3b | Histone H3.3 | 1.291 | 0.0225 |
| Fabp4 | Fatty Acid-Binding Protein, Adipocyte | 0.750 | 0.0285 |
| Mapk1 | Mitogen-Activated Protein Kinase 1 | 0.797 | 0.0499 |
| Tpt1 | Translationally-Controlled Tumor Protein | 1.246 | 0.0001 |
| Cycs | Cytochrome c, Somatic | 1.290 | 0.0004 |
| Cnbp | Cellular Nucleic Acid-Binding Protein | 1.214 | 0.0349 |
| Tmsb4x | Thymosin Beta-4 | 0.635 | 0.0004 |
| Pon1 | Serum Paraoxonase/Arylesterase 1 | 0.802 | 0.0126 |
| Aif1 | Allograft Inflammatory Factor 1 | 0.696 | 0.0077 |
| Pctp | Phosphatidylcholine Transfer Protein | 1.208 | 0.0379 |
| Aldh1a1 | Retinal Dehydrogenase 1 | 0.715 | 0.0011 |
| Abat | 4-Aminobutyrate Aminotransferase, Mitochondrial | 1.237 | 0.0029 |
| S100a8 | Protein S100-A8 | 0.792 | 0.0135 |
| Ste2 | Estrogen Sulfotransferase Ste2 | 1.327 | 0.0067 |
| Asns | Asparagine Synthetase [Glutamine-Hydrolyzing] | 0.597 | 0.0245 |
| Lss | Lanosterol Synthase | 1.335 | 0.0134 |
| Nrdc | Nardilysin | 1.205 | 0.0005 |
| Sec11a | Signal Peptidase Complex Catalytic Subunit Sec11A | 0.812 | 0.0177 |
| Psmb2 | Proteasome Subunit Beta Type-2 | 0.822 | 0.0137 |
| Crip2 | Cysteine-Rich Protein 2 | 0.823 | 0.0181 |
| Sdc2 | Syndecan-2 | 1.263 | 0.0084 |
| Cyp2c55 | Cytochrome P450 2C55 | 0.535 | 0.0319 |
| Slc25a1 | Tricarboxylate Transport Protein, Mitochondrial | 1.331 | 0.0004 |
| Vim | Vimentin | 0.795 | 0.0166 |
| Gls2 | Glutaminase Liver Isoform, Mitochondrial | 1.527 | 0.0002 |
| Hprt1 | Hypoxanthine-Guanine Phosphoribosyltransferase | 0.809 | 0.0235 |
| Ctsd | Cathepsin D | 0.752 | 0.0069 |
| Hal | Histidine Ammonia-Lyase | 1.210 | 0.0110 |
| Hpx | Hemopexin | 0.823 | 0.0017 |
| Cyp2c70 | Cytochrome P450 2C70 | 0.690 | 0.0272 |

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|---------|---|-------|--------|
| Cth | Cystathionine Gamma-Lyase | 1.277 | 0.0019 |
| Cyp7a1 | Cholesterol 7-Alpha-Monooxygenase | 0.777 | 0.0200 |
| Hmgcs1 | Hydroxymethylglutaryl-Coa Synthase, Cytoplasmic | 1.581 | 0.0003 |
| Acly | Atp-Citrate Synthase | 1.338 | 0.0002 |
| St2a1 | Bile Salt Sulfotransferase | 1.496 | 0.0031 |
| Anpep | Aminopeptidase N | 0.797 | 0.0022 |
| Anxa3 | Annexin A3 | 0.752 | 0.0430 |
| Cp | Ceruloplasmin | 0.826 | 0.0032 |
| Got1 | Aspartate Aminotransferase, Cytoplasmic | 1.497 | 0.0011 |
| Fasn | Fatty Acid Synthase | 1.361 | 0.0031 |
| Mt-atp8 | Atp Synthase Protein 8 | 1.343 | 0.0024 |
| Dbi | Acyl-Coa-Binding Protein | 1.536 | 0.0003 |
| Ces1c | Carboxylesterase 1C | 0.803 | 0.0007 |
| Cd74 | H-2 Class Ii Histocompatibility Antigen Gamma Chain | 0.696 | 0.0127 |
| Aldh4a1 | Delta-1-Pyrroline-5-Carboxylate Dehydrogenase, Mitochondrial | 1.222 | 0.0004 |
| Agxt | Serine--Pyruvate Aminotransferase, Mitochondrial | 1.236 | 0.0061 |
| Ass1 | Argininosuccinate Synthase | 1.378 | 0.0006 |
| Kngr1 | Kininogen-1 | 0.718 | 0.0118 |
| Lgals3 | Galectin-3 | 0.570 | 0.0445 |
| Cyp4a10 | Cytochrome P450 4A10 | 0.718 | 0.0016 |
| Cps1 | Carbamoyl-Phosphate Synthase [Ammonia], Mitochondrial | 1.290 | 0.0003 |
| Ephx1 | Epoxide Hydrolase 1 | 0.706 | 0.0009 |
| Pck1 | Phosphoenolpyruvate Carboxykinase, Cytosolic [Gtp] | 1.248 | 0.0062 |
| Atp1b1 | Sodium/Potassium-Transporting Atpase Subunit Beta-1 | 1.234 | 0.0011 |
| S100a6 | Protein S100-A6 | 0.706 | 0.0282 |
| S100a10 | Protein S100-A10 | 0.746 | 0.0060 |
| Mt-atp6 | Atp Synthase Subunit a | 0.685 | 0.0045 |
| G6pdx | Glucose-6-Phosphate 1-Dehydrogenase | 1.228 | 0.0005 |
| Fdps | Farnesyl Pyrophosphate Synthase | 1.988 | 0.0002 |
| Cyp3a2 | Cytochrome P450 3A2 | 0.717 | 0.0029 |
| Cyp2c7 | Cytochrome P450 2C7 | 1.332 | 0.0122 |
| Rbp4 | Retinol-Binding Protein 4 | 0.831 | 0.0018 |
| Cyp3a1 | Cytochrome P450 3A1 | 0.670 | 0.0001 |
| Apoa2 | Apolipoprotein A-Ii | 1.481 | 0.0091 |
| Oat | Ornithine Aminotransferase, Mitochondrial | 1.475 | 0.0005 |
| Cyp2b2 | Cytochrome P450 2B2 | 0.398 | 0.0421 |
| Gpx1 | Glutathione Peroxidase 1 | 1.287 | 0.0016 |
| Ttr | Transthyretin | 0.681 | 0.0014 |
| Orm1 | Alpha-1-Acid Glycoprotein | 0.771 | 0.0075 |
| Fgg | Fibrinogen Gamma Chain | 0.827 | 0.0169 |
| Map1 | T-Kininogen 1 | 0.742 | 0.0029 |
| Por | Nadph--Cytochrome P450 Reductase | 0.814 | 0.0095 |
| Marc2 | Mitochondrial Amidoxime Reducing Component 2 | 1.265 | 0.0026 |

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|---------|---|-------|--------|
| Ggcx | Vitamin K-Dependent Gamma-Carboxylase | 0.812 | 0.0021 |
| Aspg | 60 Kda Lysophospholipase | 1.241 | 0.0010 |
| Cacna1g | Voltage-Dependent T-Type Calcium Channel Subunit Alpha-1G | 1.252 | 0.0165 |
| Slco1a4 | Solute Carrier Organic Anion Transporter Family Member 1A4 | 0.822 | 0.0237 |
| Idi1 | Isopentenyl-Diphosphate Delta-Isomerase 1 | 2.036 | 0.0012 |
| Hsd3b7 | 3 Beta-Hydroxysteroid Dehydrogenase Type 7 | 0.757 | 0.0314 |
| Bhmt | Betaine--Homocysteine S-Methyltransferase 1 | 1.314 | 0.0039 |
| Phgdh | D-3-Phosphoglycerate Dehydrogenase | 0.542 | 0.0037 |
| Rnf123 | E3 Ubiquitin-Protein Ligase Rnf123 | 0.750 | 0.0126 |
| Gtpbp1 | Gtp-Binding Protein 1 | 0.827 | 0.0001 |
| Krtcap2 | Keratinocyte-Associated Protein 2 | 1.396 | 0.0104 |
| Reep5 | Receptor Expression-Enhancing Protein 5 | 0.679 | 0.0011 |
| Nceh1 | Neutral Cholesterol Ester Hydrolase 1 | 0.814 | 0.0135 |
| Cotl1 | Coactosin-Like Protein | 0.770 | 0.0314 |
| Aass | Alpha-Aminoadipic Semialdehyde Synthase, Mitochondrial | 1.296 | 0.0006 |
| Agmo | Alkylglycerol Monooxygenase | 0.727 | 0.0097 |
