**Table S1 Primer sequences designed in the experiment**

| Primers | Sequence (5'-3') | Serial number |
|---|---|---|
| CAT-F | GCCTGGGACCCAACTATCTT | NM_001002984.1 |
| CAT-R | TTGGAGCACCACCCTGATTG | |
| Trx1-F | AGAAGGGACAAAAGGTGGGTG | XM_038682416.1 |
| Trx1-R | ACAGCCATGGGCTGGTTATG | |
| Trx2-F | GGCCAAGGTGGATATTGATG | XM_038679978.1 |
| Trx2-R | TGGTCCTCGTCCTTGATACC | |
| GR-F | AGCTCTTCTCACTCCAGTTGC | XM_025420473.2 |
| GR-R | ACGACTGTGGGGATGTTGTC | |
| PRDX3-F | GAAGGTTCCTCCGGGCTTC | NM_001256485.1 |
| PRDX3-R | GTGGTAGGAGGAACTGGTGC | |
| G6PD-F | GCCTGCGTCATCCTCACTT | XM_025460546.2 |
| G6PD-R | CCTGCACCTCCGAGATACACT | |
| GPX1-F | GTTCGGGCATCAGGAAAACG | XM_025455854.1 |
| GPX1-R | GTGATGAACTTGGGGTCGGT | |
| GPX4-F | CATGGAAGAGCCCCTGGTAAT | XM_038429345.1 |
| GPX4-R | GCGGGCTGGTTTTTAGACAG | |
| SOD1-F | GCCATTGTGTCCATAGAAGA | XM_025449735.2 |
| SOD1-R | GCGTTTCCTGTCTGTGTGTA | |
| SOD2-F | TGAACAACCTGAACACCAT | XM_038654563.1 |
| SOD2-R | GAATGATTGATATGACCTCCTC | |

| | | |
|---|---|---|
| HO-1-F | CTCAAGAAGATTGCTCAGAAG | XM_025461329.2 |
| HO-1-R | CTGGTCCTCAGTGTCCTT | |
| GAPDH-F | AGATCCCGCCAACATCAAAT | NM_001003142.2 |
| GAPDH-R | TTCACGCCCATCACAAACAT | |
| CYP2E1-F | TTTCCACTGCCCATCATTG | NM_001003339.1 |
| CYP2E1-R | CTTCACCGCCTTGTAGCC | |

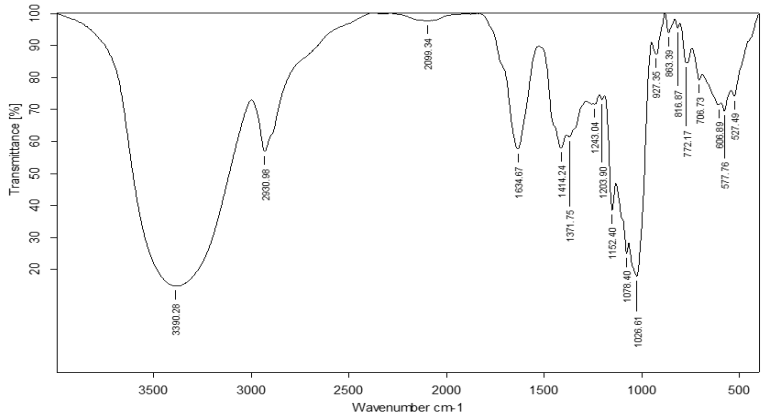



**Fig. S1 LBP infrared spectral structure diagram**

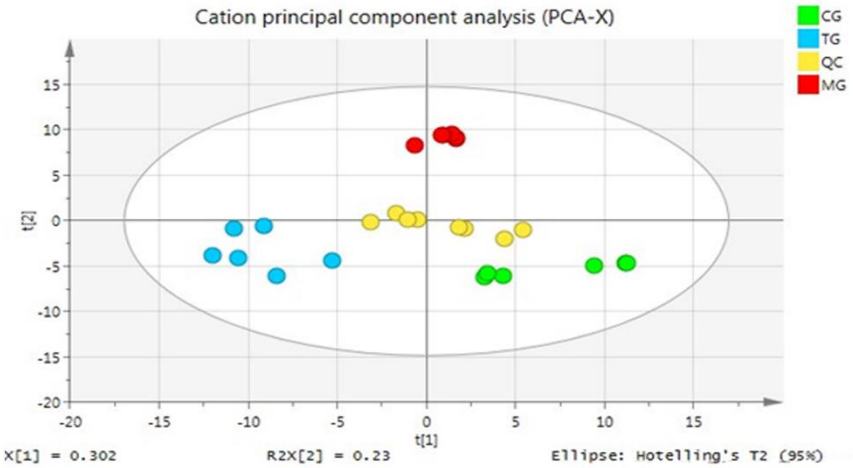



**Fig. S2 Cation principal component analysis scatter plot**

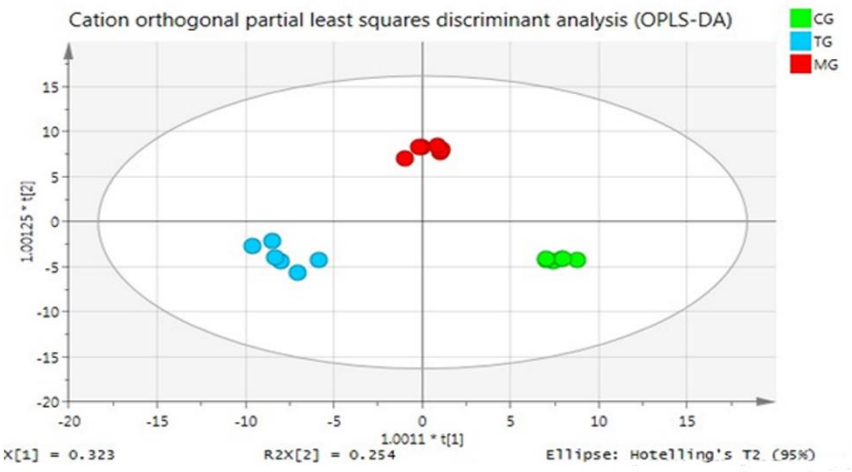



**Fig. S3 Cation orthogonal partial least square discriminant analysis scatter plot**

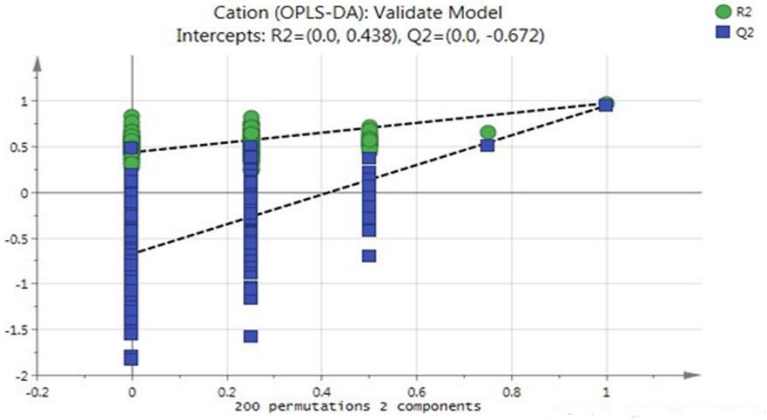



**Fig. S4 Cation permutation test**

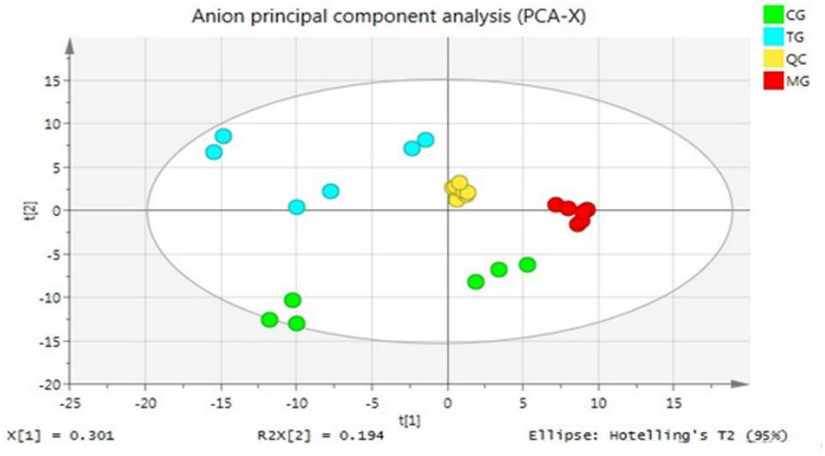



**Fig. S5 Anion principal component analysis scatter plot**

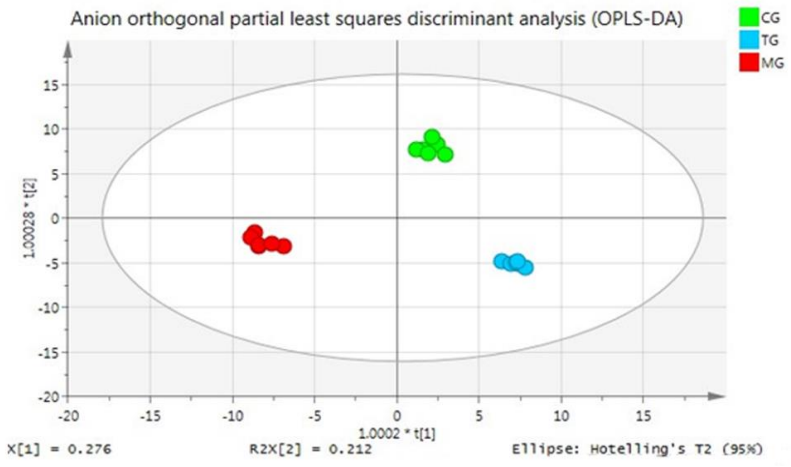



**Fig. S6 Anion orthogonal partial least square discriminant analysis scatter plot**

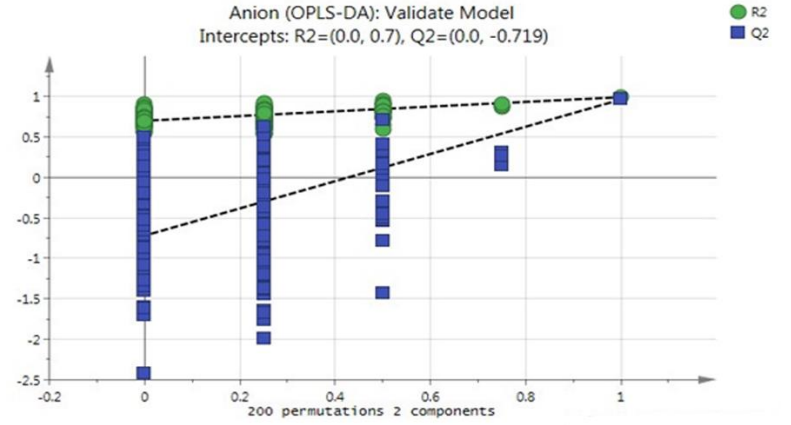



**Fig. S7 Anion permutation test**

## Materials and methods

Western blot analysis

The protein was extracted from liver tissue with RIPA buffer containing 1% phenylmethane sulfonyl fluoride (PMSF), and then the protein concentration was determined by BCA protein analysis kit (E112-01, Vazyme, China). The same amount of protein was transferred to polyvinylidene fluoride (PVDF) membrane by sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis (PAGE), incubated overnight with specific first antibody, washed and incubated

with second antibody labeled with homologous HRP, and displayed by enhanced chemiluminescence (ECL). Finally, the gray value of protein band was quantified by ImageJ software. The housekeeping proteins used in normalization analysis were glyceraldehyde-3-phosphate dehydrogenase (GAPDH), β-Actin and histone 3 (H3).

Quantitative real-time polymerase chain reaction

Take appropriate amount of liver tissue, add RNAiso Plus reagent (9108Q, TaKaRa, Japan), and extract total RNA from liver tissue homogenate. According to the instructions, HiScript II Q Select RT SuperMix for qPCR kit (R233-01, Vazyme, China) was used to reverse transcribe the extracted RNA into cDNA, and then quantitative real-time polymerase chain reaction (qPCR) was performed with qPCR instrument (Light Cyker 480 II, Roche, USA) to detect the mRNA expression level of oxidative stress related gene. The data were analyzed by $2^{-\Delta\Delta C_T}$ method and normalized to GAPDH/β-Actin expression.

Immunohistochemistry

The liver tissue sections were routinely dewaxed and dehydrated and put into citrate buffer (pH=6.0) for antigen repair. To inactivate the endogenous enzyme, the slices were soaked in 85% methanol and 30% hydrogen peroxide ($H_2O_2$), sealed with horse serum for 1 h, then incubated overnight with rabbit anti-p62 antibody (diluted by 1: 200), rabbit anti-Nrf2 antibody (diluted by 1: 200) and rabbit anti-4-HNE antibody (diluted by 1: 200) (bs-6313R, Bioss, China) at 4°C, and set a negative control with phosphate buffered saline (PBS), then incubated with HRP labeled secondary antibody (goat anti-rabbit, diluted by 1: 200) at room temperature for 1 h, and stained the slices with DAB. Then the nucleus was re-stained with hematoxylin for 1 min. Finally, the

slides were differentiated, dehydrated and transparent, sealed with neutral gum and observed under light microscope.

Masson staining

The slices were dewaxed to water conventionally, and placed in the incubator at 57℃–60℃ for 1 h for mordant dyeing, and then washed with running water for 10 min; the tissue was stained by azurol staining solution for 3 min, then water washing; hematoxylin dyeing solution is dripped for 3 min and washed with water; acidic ethanol differentiation solution differentiate for several seconds until the tissue turns completely red, then it is washed with water to stop differentiation and washed with distilled water for 10 min; the ponceau fuchsin dyeing solution was dripped for 10 min, and distilled water was washed twice; the tissue were treated with phosphomolybdic acid solution for about 10 min; add aniline blue dye solution for 5 min; after washing the aniline blue solution with weak acid solution, continue to drip weak acid working solution to cover the slices for 2 min; finally, the tissue was dehydrated with ethanol, transparent with xylene, sealed with resin, and the slices were observed under a microscope.

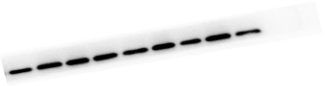
Non-targeted metabolomics detection

Take 150 μL serum into 1.5 mL EP tube, add 2 μL L-2-chloro-phenylalanine (300 μg/mL), add 450 μL organic solvent (methanol: acetonitrile=1: 9, precooled at −80℃), shaking, then store 30 min at -20°C, then vortex 2min, add 300 μL ultra-pure water to each EP tube, centrifuge 10 min (protein isolate) with 4°C and 12000 r/min, then get the supernatant. After being filtered by 0.22 μm filter membrane, the sample was detected by high resolution quadrupole mass spectrometer (TOF™ 5600, Thermo Fisher Scientific, USA) loaded with ACQUITY UPLC system. 100 μL liquid was extracted from each sample to obtain quality control (QC) samples to

evaluate the stability of the LC-MS system. The original data from the mass spectrometer were processed by Progenesis QI software to screen the differential metabolites. The selected metabolites were analyzed by multivariate statistical analysis with SIMCA 14.1, including principal component analysis (PCA) and orthogonal partial least square discriminant analysis (OPLS-DA), and the validity of the model was tested by permutation test. The selection criteria of final metabolites were $P<0.05$ and the VIP value (variable projection importance) of OPLS-DA model was greater than 1.

**Raw data of WB**

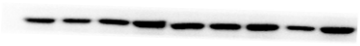
The order of sample addition from left to right is as follows: CG1, MG1, TG1, CG2, MG2, TG2, CG3, MG3, and TG3, and the sample was repeated 3 times.



**GAPDH**



**β -actin**



**GAPDH**



**GAPDH**

**P62 (the seventh hole is not added to the sample)**

**Keap1**

**Nucl-Nrf2 (on the far left is protein marker)**

**Cyto-Nrf2 (the seventh hole is not added to the sample)**

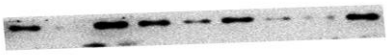
**Histone H3**



**HO-1**

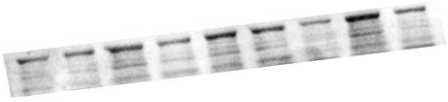
**SOD1**

**GPX4**



**Trx1**

**SOD2**



**8-OHDG**