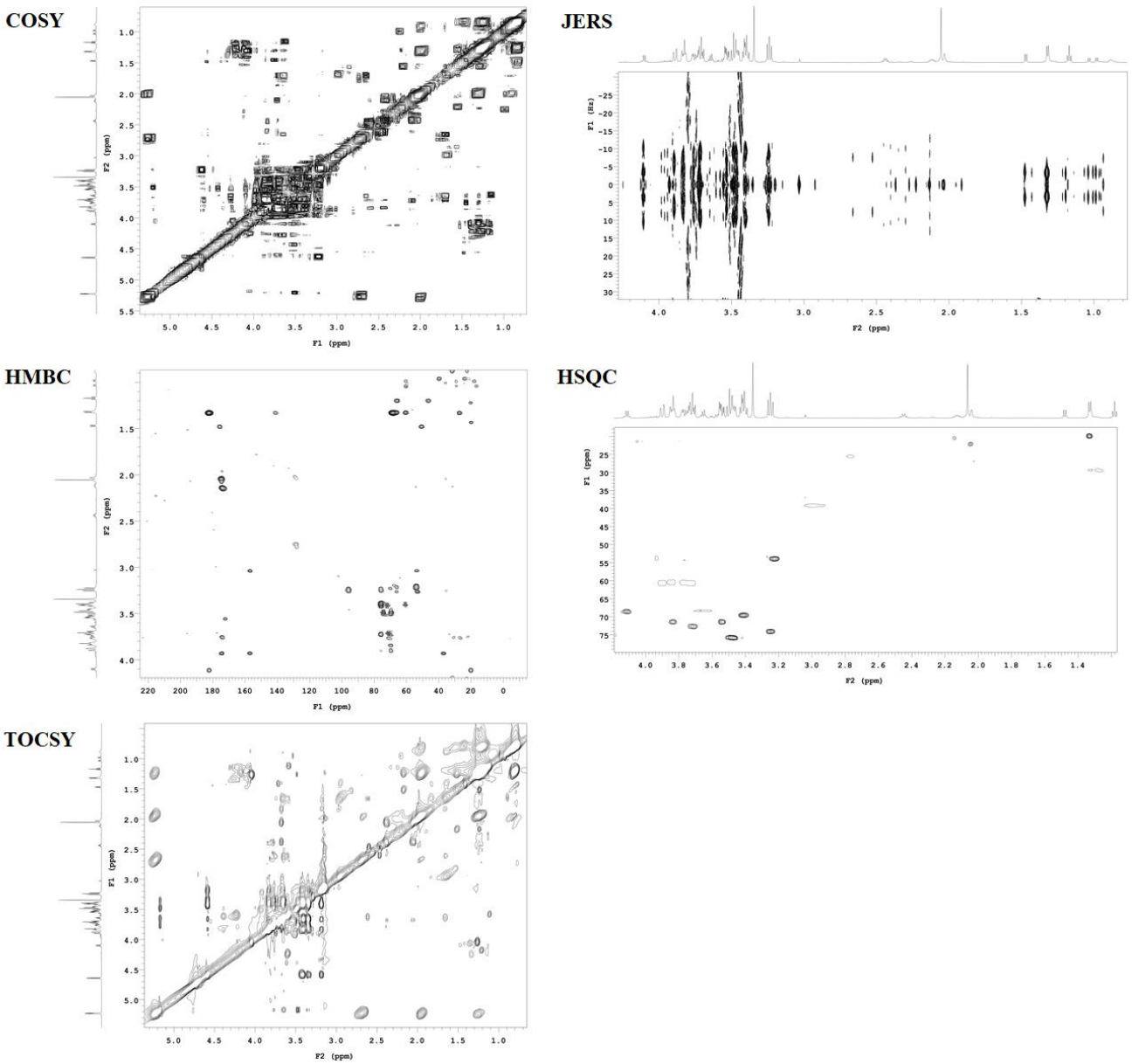

Figure S1 600 MHz 2D spectrum (^{1}H COSY, ^{1}H-^{13}C HMBC, ^{1}H-^{13}C HSQC, ^{1}H TOCSY, ^{1}H JRES) of rat serum sample measured at 298 K

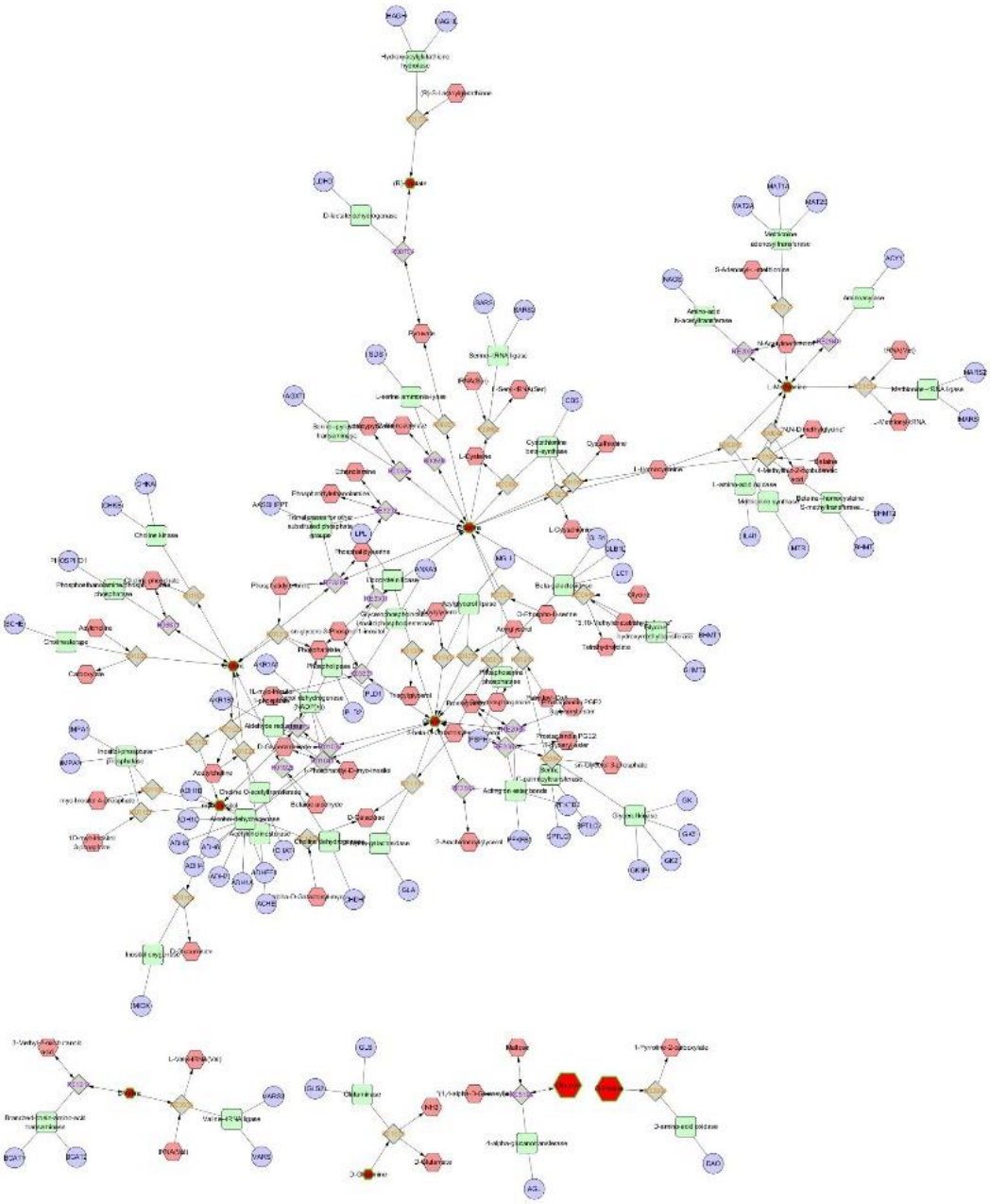

Figure S2 Metabolites-Reaction-Enzyme-protein Chart

Hexagon⬡: metabolites; round rectangle▭: enzyme; ellipse⬭: Gene; Diamond◇: reaction.

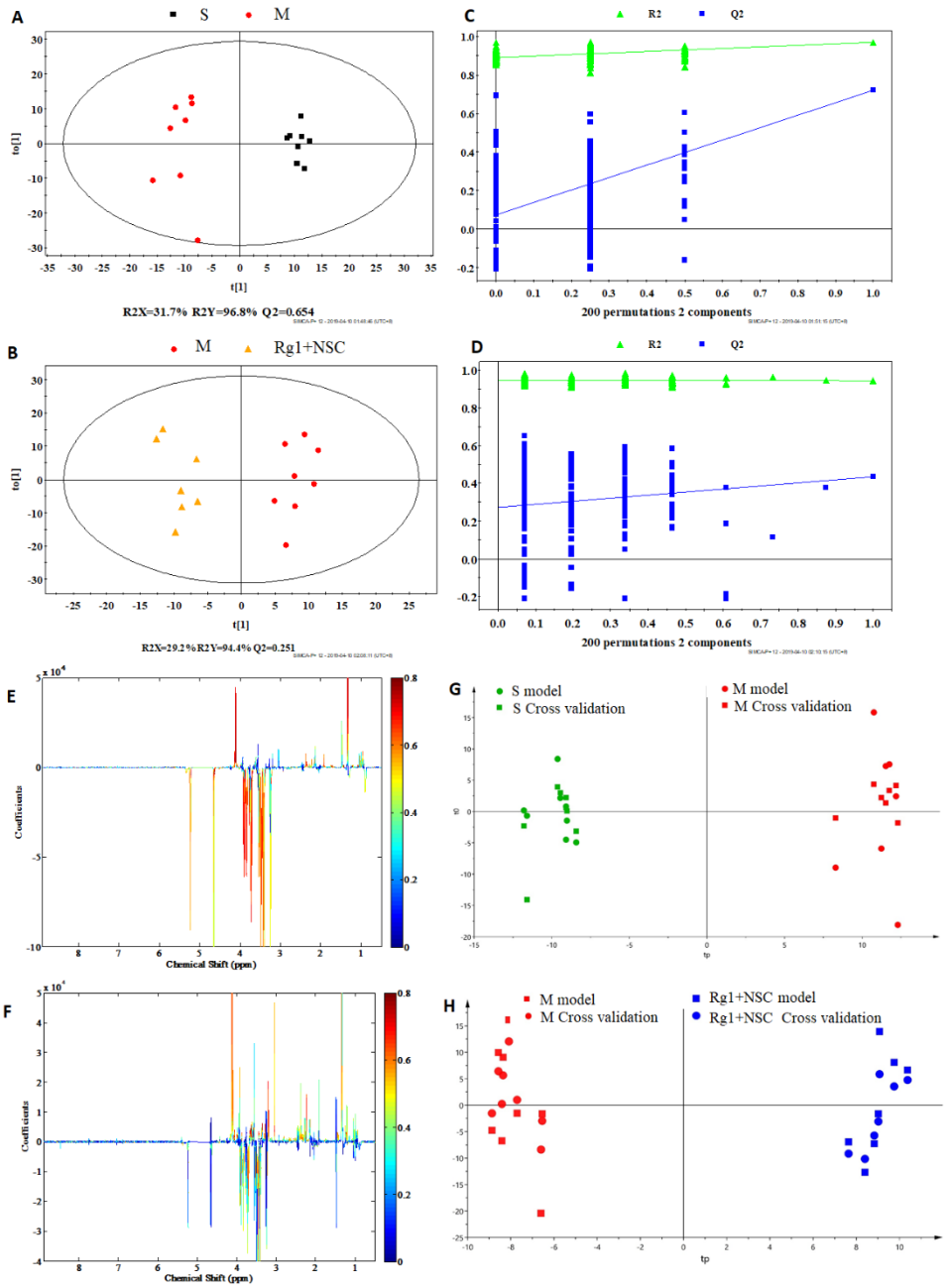

Figure S3 OPLS-DA scores plots (A and B), permutation test plots (C and D), corresponding coefficient loading plots (E and F) and cross-validated scores plots (G and H) (Rg1 vs M, NSC vs M)

(M: model group; NSC: NSCs transplantation group; Rg1: ginsenoside Rg1 treated group)

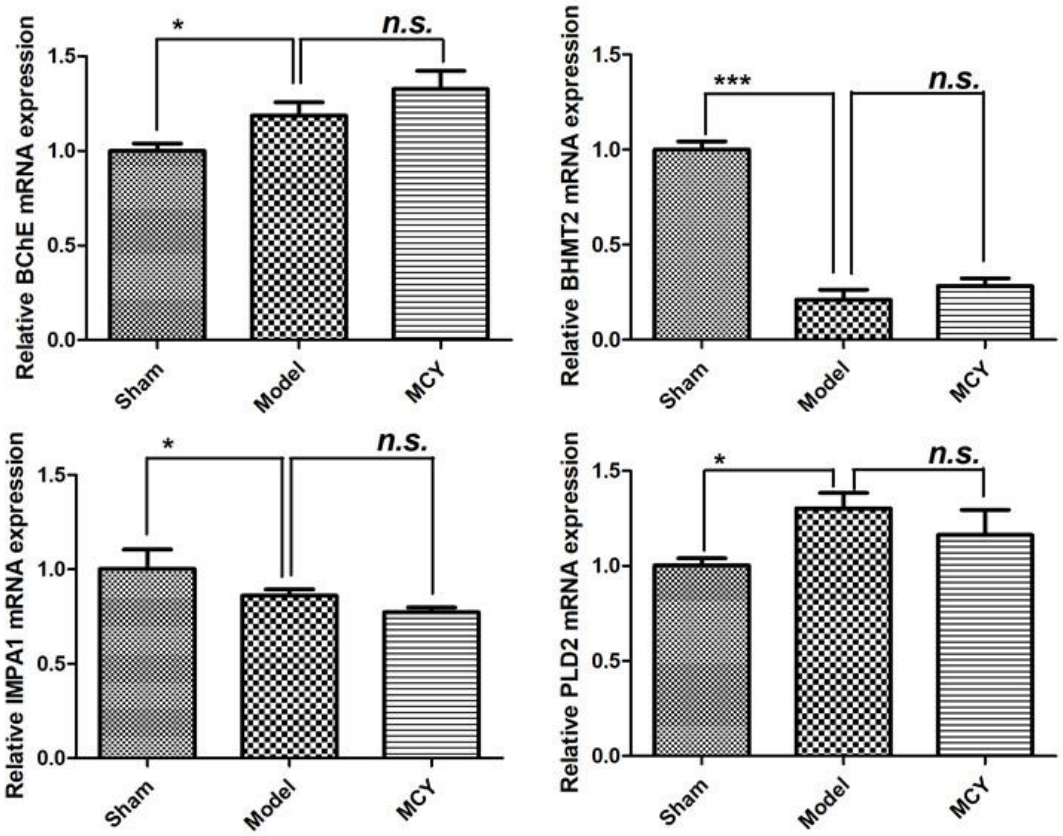

Figure S4 Quantitative real-time PCR (qRT-PCR) analysis to detect mRNA levels of potential targets

Data were expressed as the mean ± SD, and were analyzed by ANOVA. **p*<0.05, ***p*<0.01, **p*<0.001. *n.s.* no significance.

BChE: butyrylcholinesterase; IMPA1: inositol(myo)-1 (or 4)-monophosphatase 1; BHMT2: betaine-homocysteine methyltransferase 2; PLD2: phospholipase D2.

Table S1 The sequences of primers used for quantitative real-time PCR

Gene	Full Name	Sequences of primers (5'-3')	
		Sense	Antisense
AChE	acetylcholinesterase	GGGATTTCCTCAGTGACACGC	CACCGCACTCATGGCATCTC
ADH1	alcohol dehydrogenase 1	CCCATTCACCACTTCATCAGC	CGACAGACAGACCAACACCTCC
AKR1B1	aldo-keto reductase family 1, member B1 (aldose reductase)	ATCTGGAACTCAACAACGGCA	AAGGTAGAGGTCCAGGTAGTCCAG
ANXA3	annexin A3	ATCAACATTCTGACGGAGCGG	ATCTGCCTGCTTGTCCTGGTT
CBS	cystathionine-beta-synthase	GAAACTTGAAGCCTGGAGACACT	GATAATGCAGCGATAGCCCTT
ChAT	choline acetyltransferase	CAACCATCTTCTGGCACTGAGG	CGGGTCCATAACAGCAGAACAT
GLA	galactosidase, alpha	TGACTGCCAAGAAGAGCCTGAT	GTATTCATAACCCGCGTCCC
LPL	lipoprotein lipase	TTTGGCTCCAGAGTTTGACCG	CATACATTCCTGTCACCGTCCA
MTR	5-methyltetrahydrofolate-homocysteine methyltransferase	TAGTTGGTGGATGCTGTGGTTC	CGCTCAGGGCTTCTTCATAGTT
PLD1	phospholipase D1	ACCATCGCTTCGGCTCCTAC	CCTTGTTGTGCTTTCCGTTTGA
SHMT1	serine hydroxymethyltransferase 1 (soluble)	GTCCTAAGGGTACTGATGGCGG	CTCGGGATGTCAATGCTGGA
BChE	butyrylcholinesterase	TCTGAGGCTCCAGGAAACATG	CTGGCTTCCTCTGGATGCTTTA
IMPA1	inositol(myo)-1(or 4)-monophosphatase 1	GCTTTGCTCCATTCCTATCCA	GCCAGCCTCTATGACGATGAT
BHMT2	betaine-homocysteine methyltransferase 2	CGGATTTGAGCCCTACCACA	TGGCAACAGAGTTTCCCAGTAT
PLD2	phospholipase D2	GGCTCTGCAAACATCAACGAC	CCGCAGGGAACGAGTAGCAT

Table S2 Resonance Assignments with Chemical Shifts of Metabolites Identified in 600 MHz ^{1}H NMR Spectra of rats' serum sample

Metabolites	Chemical shift (ppm)(multiplicity)	Observed	Assignment
leucine	**0.97(d)**; 1.69(m)	JRES, COSY	***δ***-CH_3
valine	0.99(d); **1.05(d)**	JRES, COSY	CH_3
isobutyrate	**1.07(d)**	CPMG, JRES	CH3
methylmalonate	**1.22(d)**	JRES	CH3
threonine	1.32(d); **3.60(d)**	JRES	α-CH_3
lactate	**1.33(d)**; 4.13(q)	JRES, COSY, HSQC	CH_3
alanine	**1.48(d)**; 3.77(q)	CPMG, JRES, COSY, HMQC, TCOSY	CH_3
arginine	**1.70(m)**; 1.89(m)	CPMG, COSY	γ-CH_2
lysine	**1.46(m)**; 1.73(m)	CPMG, COSY	γ-CH_2
acetate	**1.93(s)**	JRES, CPMG	CH_3
proline	**1.99(m)**	COSY	γ-CH_2
glutamate	**2.13(m)**	JRES, COSY, HMQC, TCOSY	half β-CH_2
methionine	**2.14(s)**; 2.65(t)	JRES, CPMG	S-CH_3
pyruvate	**2.38(s)**	JRES, CPMG	CH_2
glutamine	2.18(m); **2.49(m)**	CPMG, JRES, COSY, HMQC, TCOSY	half β-CH_2
fatty acyl chain	**2.75(m)**	COSY, HMQC	C=CCH_2C=C
phenylalanine	3.98(m); **7.33(m)**	COSY, CPMG	H2, H6
choline	**3.20(s)**	JRES, HMQC	$N(CH_3)_3$
glucose	3.40(t); 3.90(dd); 4.65(d); **5.23(d)**	JRES, COSY, TCOSY, HMQC, CPMG	H1
myo-inositol	3.28(t); **3.63(t)**; 4.07(t)	JRES	H4, H6
betaine	**3.27(s)**; 3.91(s)	JRES	$N(CH_3)_3$
serine	**3.83(m)**; 3.96(m)	JRES	−CH_2
creatine	**3.05(s)**; 3.92(s)	JRES, CPMG	CH_3
ascorbate	3.89(m), 4.16(m), **4.52(d)**	COSY, CPMG	H5
glycerol	**3.57(dd)**; 3.66(m); 3.80(m)	JRES, COSY	half β-CH_2
glycerophosphocholine	**3.23(s)**; 3.35(m); 3.68(m); 4.33(m)	JRES, CPMG	$N(CH_3)_3$
formate	**8.46(s)**	CPMG	CH
3-Aminoisobutyrate	**1.19(d)**	JRES, CPMG	CH_3
Lipids	**1.95(br)**; 2.75(br)	COSY	CH_2C=C
citrulline	**3.16(t)**	JRES	γ-CH_2
3-hydroxybutyrate	**1.20(d)**; 2.31(m); 2.41(m); 4.19(m)	CPMG, JRES	γ-CH_3

Glutathione	**2.16(m)**; 2.64(m)	CPMG, JRES	$-CH_2$
aspartate	2.68(m); **2.83(dd)**	JRES	half β-CH_2
N,N-dimethylglycine	**2.93(s)**	CPMG, JERS	$N(CH_3)_3$

Table S3 Details of CV-ANOVA performed on OPLS-DA models with Entire NMR chemical shift data set or the screened integral segments with a VIP value>1

Model	Variable	CV-ANOVA (p value)
M/S	Entire NMR chemical shift data set	0.015
	The screened integral segments with a VIP value >1	0.002
NSC/M	Entire NMR chemical shift data set	0.076
	The screened integral segments with a VIP value >1	0.0017
Rg1/M	Entire NMR chemical shift data set	0.921
	The screened integral segments with a VIP value >1	0.023
Rg1+NSC/M	Entire NMR chemical shift data set	0. 071
	The screened integral segments with a VIP value >1	0.0016

(M: model group; NSC: NSCs transplantation group; Rg1: ginsenoside Rg1 treated group; Rg1+NSC: ginsenoside Rg1+NSCs transplantation- treated group)

Table S4. Differential metabolites derived from derived from ^{1}H NMR from ginsenoside Rg1 group and model group

Metabolites	**Chemical shift (ppm)(multiplicity)**	***p*[a]**	**FDR-p[b]**	**VIP**	**FC[c]**
3-Aminoisobutyrate	**1.19(d)**	0.002	0.0104	2.95	7.78
Lipids	**1.95(br)**; 2.75(br)	0.005	0.012	2.33	1.38
citrulline	**3.16(t)**	0.018	0.0206	2.05	0.71
choline	**3.20(s)**	0.0026	0.0104	2.07	0.73
glucose	3.40(t); 3.90(dd); 4.65(d); **5.23(d)**	0.0090	0.0133	2.21	0.64
glycerol	**3.57(dd)**; 3.66(m); 3.80(m)	0.006	0.012	2.33	1.85
3-hydroxybutyrate	**1.20(d)**; 2.31(m); 2.41(m); 4.19(m)	0.028	0.028	1.95	1.59
Glycerophosphocholine	3.23(s); **3.35(m)**; 3.68(m); 4.33(m)	0.01	0.0133	2.18	1.26

a The p values were obtained from student's t-test. The chemical shifts in boldface were that we used in calculating integrals and p values.

b The FDR p values were calculated from p values.

c FC: Fold change values, the increased and the decreased in each group.

Table S5. Differential metabolites derived from derived from ^{1}H NMR from NSC transplantation group and model group

Metabolites	Chemical shift (ppm)(multiplicity)	*p*[a]	FDR-p[b]	VIP	FC[c]
lactate	**1.33(d)**; 4.13(q)	0.0091	0.0273	1.77	0.69
alanine	**1.48(d)**; 3.77(q)	0.0191	0.0383	1.67	0.67
glutamate	**2.13(m)**	0.0221	0.0383	1.65	0.78
3-hydroxybutyrate	1.20(d); 2.31(m); **2.41(m)**; 4.19(m)	0.0382	0.0450	1.54	0.68
Glutathione	**2.16(m)**; 2.64(m)	0.0221	0.0383	1.66	0.62
methionine	**2.14(s)**; 2.65(t)	0.0451	0.0483	1.46	0.81
aspartate	2.68(m); **2.83(dd)**	0.0090	0.0273	1.79	0.17
fatty acyl chain	**2.75(m)**	0.0010	0.0075	2.17	0.20
N,N-dimethylglycine	**2.93(s)**	0.0390	0.0450	1.53	1.46
choline	**3.20(s)**	0.0260	0.0390	1.62	0.51
glucose	3.40(t); 3.90(dd); 4.65(d); **5.23(d)**	0.0010	0.0075	2.18	1.49
glycerol	**3.57(dd)**; 3.66(m); 3.80(m)	0.0020	0.0100	2.00	0.73
myo-Inositol	3.28(t); **3.63(t)**; 4.07(t)	0.0230	0.0383	1.60	0.75
glycerophosphocholine	3.23(s); **3.35(m)**; 3.68(m); 4.33(m)	0.170	0.1700	1.66	0.66
formate	8**.46(s)**	0.0293	0.0400	1.69	1.85

a The p values were obtained from student's t-test. The chemical shifts in boldface were that we used in calculating integrals and p values.

b The FDR p values were calculated from p values.

c FC: Fold change values, the increased and the decreased in each group.