Supporting Information

Figure S1

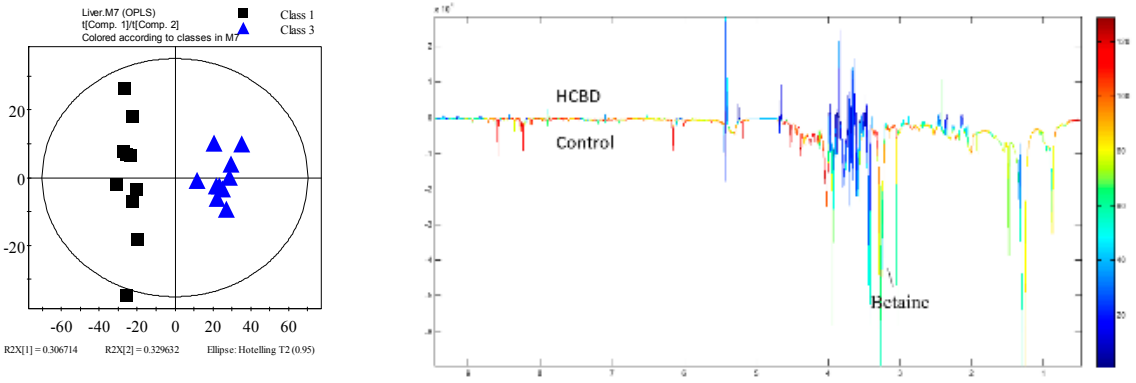

Figure S1. The significantly decreased r= 0.69 metabolites of betaine in liver between control and HCBD group by 1H NMR data analysis. OPLS-DA scores plots (left) and corresponding loading plots (right) derived from the 1H NMR data for liver from fish fed with HCD (blue triangle) and Control diet (black square).

Note: The colour code corresponds to the absolute value of the OPLS-DA correlation coefficient |r|, which indicates the contribution of the corresponding variable to the group separation. In these loadings plots, the hot-colored (the red end of the spectrum) metabolites contributed more significantly to the intergroup differences than the cold-colored (blue) ones.

Figure S2

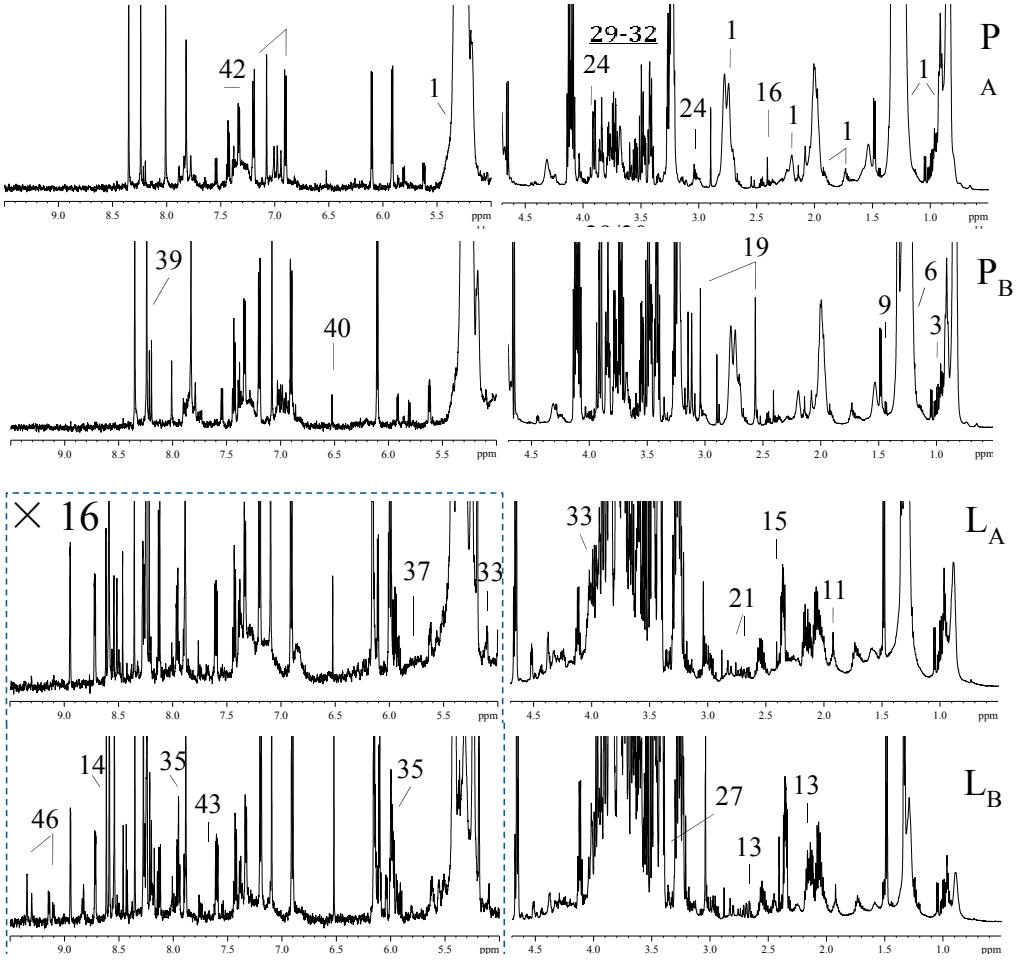

Figure S2. The 600 MHz ^{1}H NMR spectra of plasma (P) and liver (L) from control (A) and HCBD (B) groups. The dotted regions associated with our study were vertically expanded 16 times in the spectra of plasma and liver extracts. The keys for metabolites are given in Table S2.

Table S1. Primers designed for RT-qPCR

Gene	Primers sequences (5'-3')	Tm (ºC)
SOCS3-F	TTCAGTCTGCCTTTTCCTA	57
SOCS3-R	AAACGGGGTGGCTACTT	
INSR-F	TGAGGACATCACGCACTA	55
INSR-R	AGCATTGGCTACACCC	
IRS-F	CATTAGCGGCAGGTTGA	57
IRS-R	CGGTTACGGGACGATTT	
PI3K-F	GTGCGACCTCCTGCTCT	57
PI3K-R	GCTGCGCTTCCTACTCC	
PDK-F	GTTTAGAGCTGGGAACGA	60
PDK-R	GCTGGTAGGTAAGGGGTCA	
AKT-F	CCATTCAAACCGCAAGT	55
AKT-R	CGAACGGCTCCATACC	
GSK3β-F	TTCCTTTGGGATCTGC	53
GSK3β-R	GGCTCTGTAGTACCGTGA	
GYS-F	CCTCCAGTAACAACTCATAAC	55
GYS-R	CACAATCTTTACACGGTCA	
AMPK-F	TCATAGACAACCGCCGCATTA	55
AMPK-R	CCGCCGAACACCGAGAT	
ACC-F	CAGGCTGTCACCTAACTCT	55
ACC-R	AGCTGCTTCCGTCGTAT	
ChREBP-F	GACATGAGACGCCCTATA	55
ChREBP-R	AACATCCTCTTCCTGCTT	
IL6-F	GTAGTGGTGGTTTGCCTCA	53
IL6-R	GCAGCACGGCTTTGTC	
AP1-F	GCGGAGGGCTTTGTGA	55
AP1-R	GCTGATGGCRGGGTTG	
18s rRNA-F	CGGAGGTTCGAAGACGATCA (Tran *et al*., 2015) [72]	60
18s rRNA-R	GGGTCGGCATCGTTTACG (Tran *et al*., 2015) [72]	
Rpl13a-F	TCTGGAGGACTGTAAGAGGTATGC	50-57
Rpl13a-R	AGACGCACAATCTTGAGAGCAG	

Table S2. ^{1}H NMR signal assignments of metabolites in serum and liver extract of *Megalobrama amblycephala*

No.	Metabolites	δ ^{1}H (ppm)and multiplicity	Proton groups	^{13}C(ppm)	Samples
16	Succinate	2.41 (s)	a, β-C**H**$_2$	37.1	S, L
27	Betaine	3.27 (s)	-C**H**$_3$	56.1	S, L
		3.92 (s)	-C**H**$_2$	68.7	
29	β-Glucose	3.26 (dd)	2-C**H**	76.9	S, L
		3.41(dd)	4-C**H**	72.4	
		3.47 (ddd)	5-C**H**	78.7	
		3.74 (m)	3-C**H**	63.4	
		3.91 (m)	6-C**H**	63.5	
		4.65 (d)	1-C**H**	98.8	
31	α-Glucose	3.42 (t)	4-C**H**	78.7	S, L
		3.54 (dd)	2-C**H**	74.2	
		3.72 (t)	3-C**H**	75.4	
		3.77 (m)	6-C**H**	63.2	
		3.84 (ddd)	5-C**H**	74.1	
		5.24 (d)	1-C**H**	94.9	
32	Tyrosine	3.35 (dd)	-C**H**	56.1	S, L
		6.90 (d)	3,5- C**H**	118.6	
		7.20 (d)	2,6- C**H**	133.4	

Notes: s - singlet; d - doublet; t - triplet; q - quartet; m - multiplet; b - broad peak; dd - doublet of doublets; S - serum; L - liver.