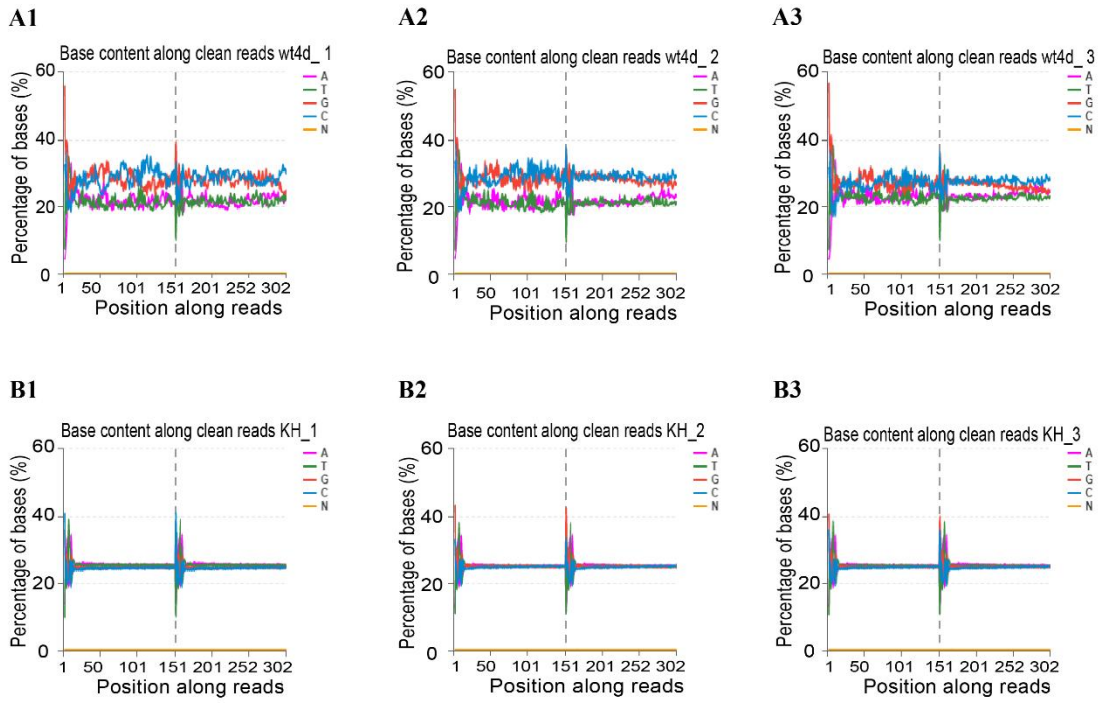
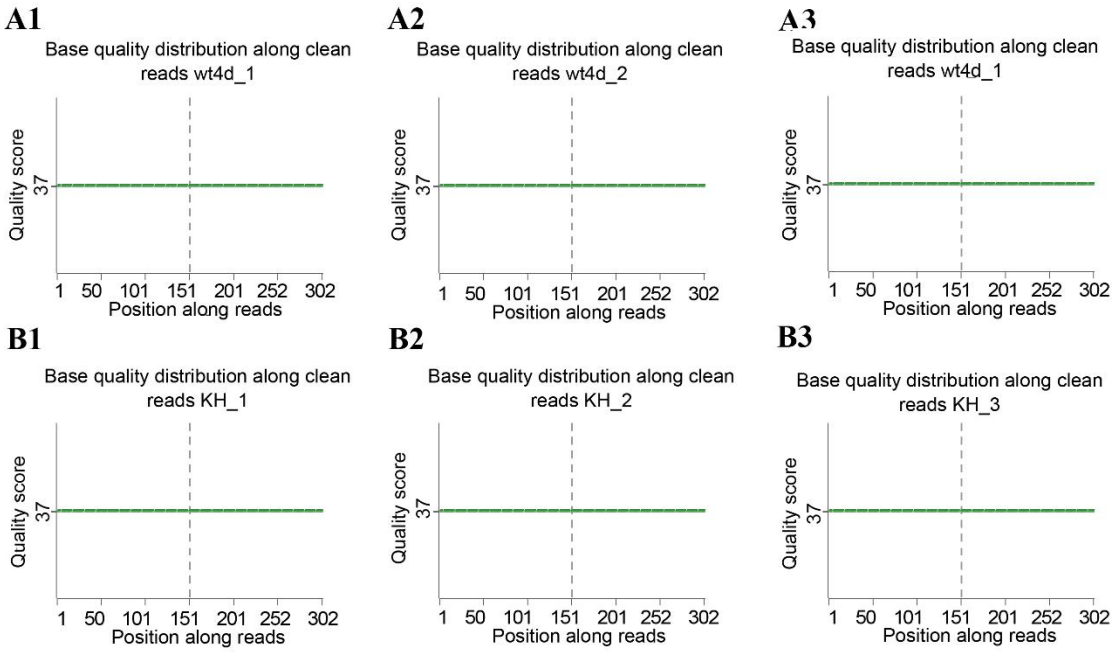
Supplementary Materials

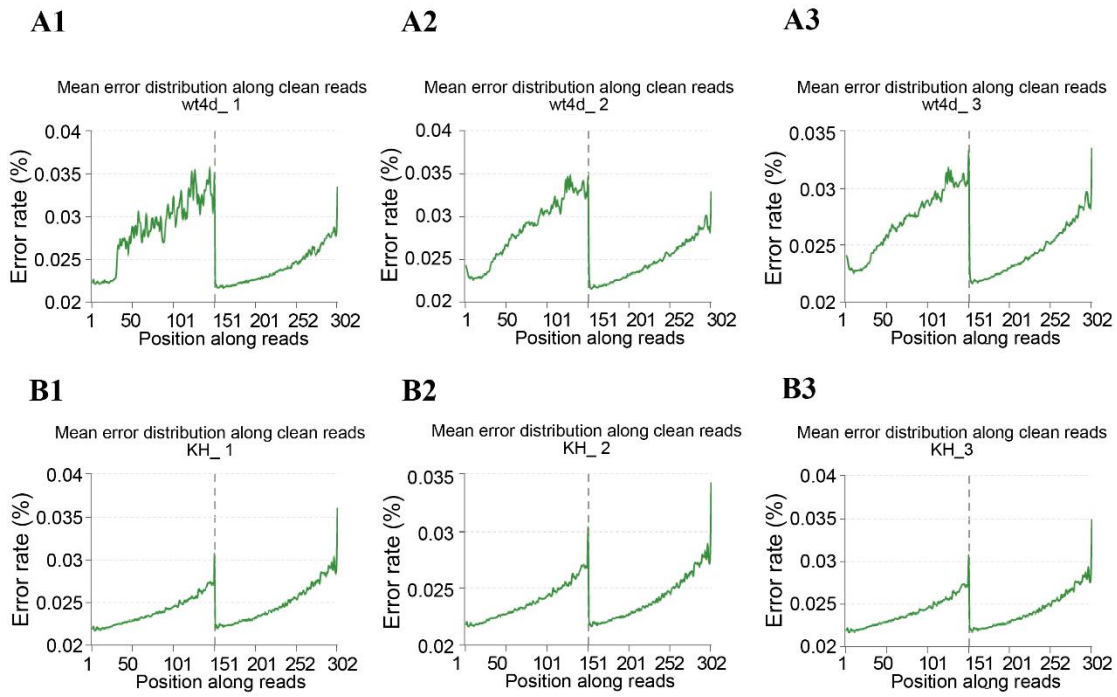


Supplementary Figure S1 Base content in raw reads (showing possible separation of AT and GC bases). Abscissa is bases of reads, and ordinate is all reads at sequencing position. Each base is a different color: A is purple; T is green; G is red; C is blue; N is orange. (A1)–(A3) are NZBD9 strain-infected group; (B1)–(B3) are *flgK*-RNAi strain-infected group.



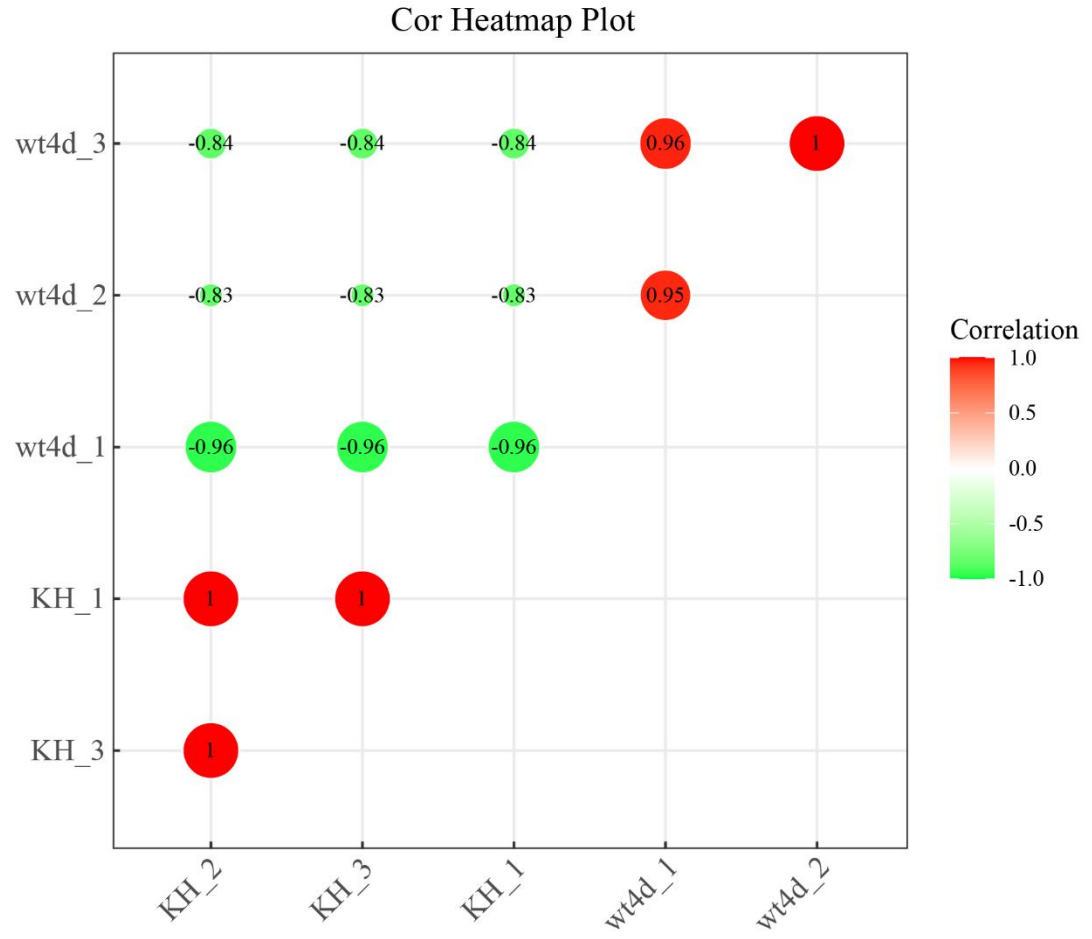
Supplementary Figure S2 Base quality distribution in raw reads

Abscissa is sequence of bases from 5' to 3' in reads and ordinate is base quality value of reads. Range specified by vertical green line "I" is the comprehensive base quality of all reads in this position, vertical green box is the range of quality quartile. (A1)–(A3) are NZBD9 strain-infected group; (B1)–(B3) are *flgK*-RNAi strain-infected group.



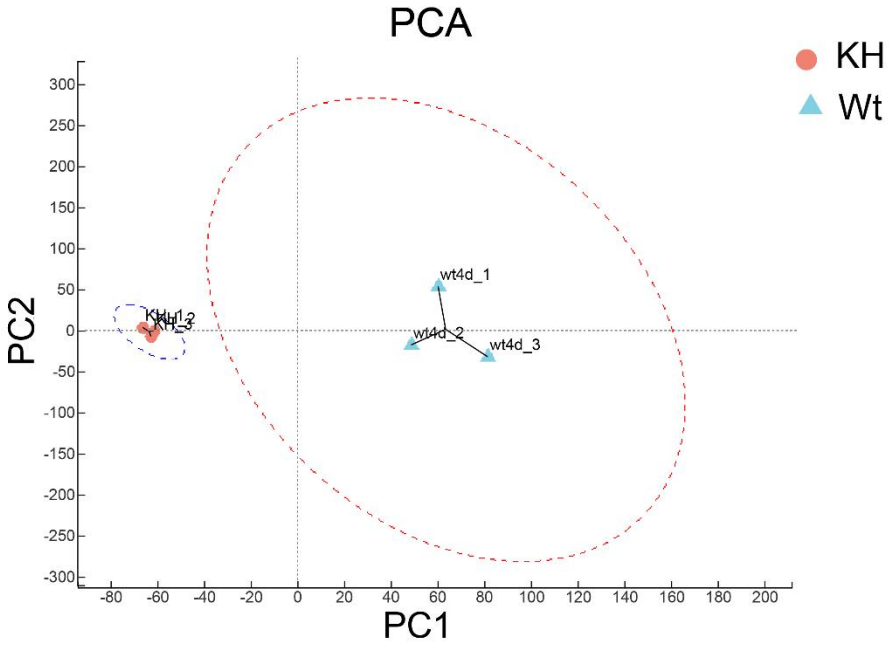
Supplementary Figure S3 Mean error distribution of raw reads

Abscissa is sequence of bases from 5' to 3' in reads and ordinate is the average error rate (%) of all reads at this site. Green line in graph corresponds to average base error rate, reflecting the distribution of the base error rate in the sequencing reads. (A1)–(A3) are NZBD9 strain-infected group; (B1)–(B3) are *flgK*-RNAi strain-infected group.



Supplementary Figure S4 Correlation of transcriptional data

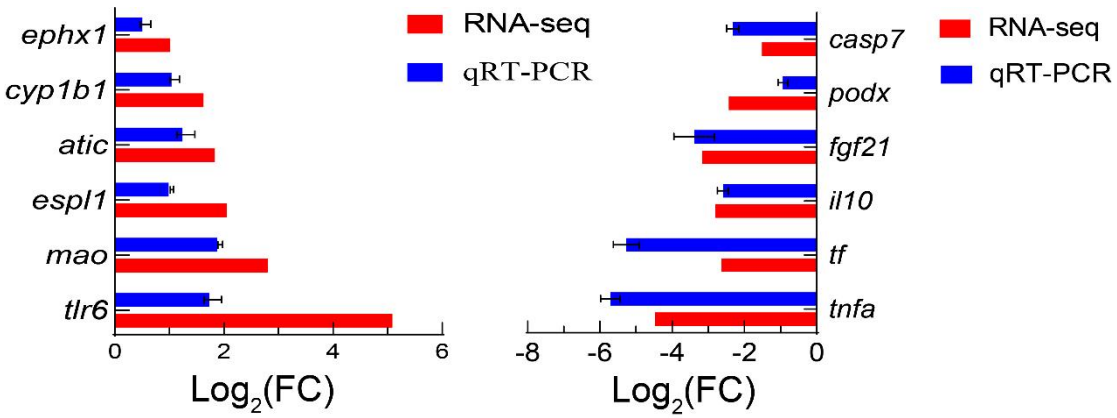
Value in circle indicates correlation coefficient between the corresponding two samples (based on Pearson correlation (-1,1)). Larger correlation coefficients (indicated in darker colors) indicate greater correlation between two samples.



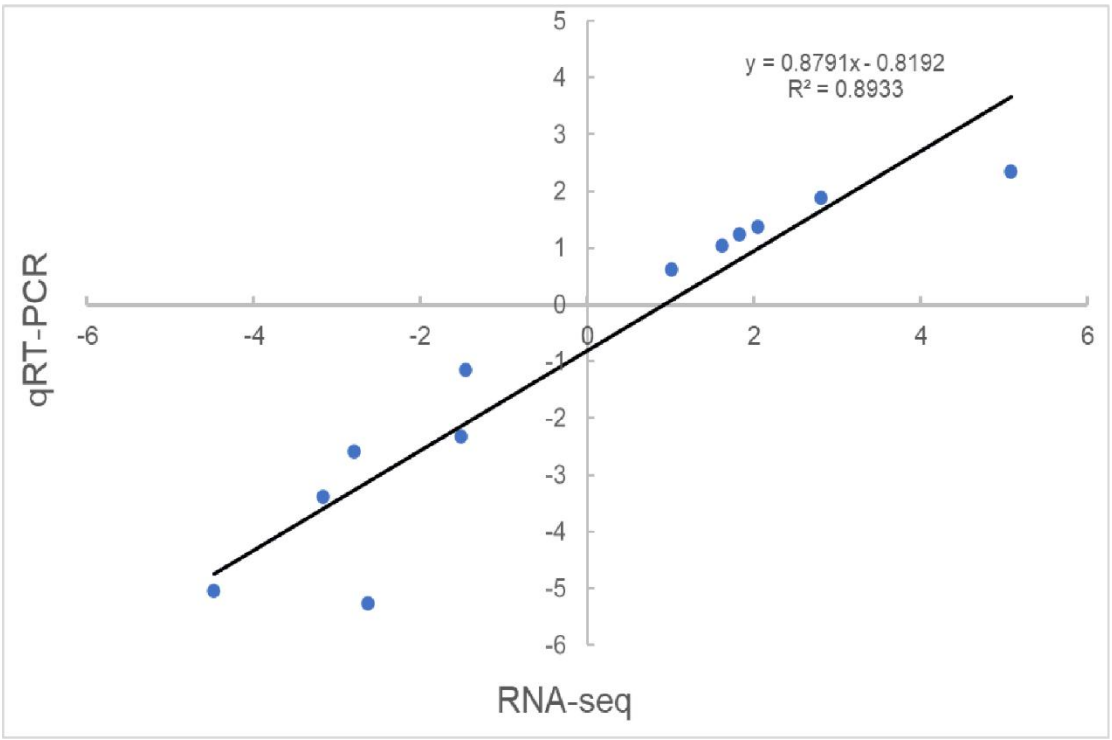
Supplementary Figure S5 PCA score plot

Abscissa represents the

contribution of principal component N (PCN) to distinguish samples in the two-dimensional graph. Ordinate represents the contribution of principal component M (PCM) to distinguish samples in the two-dimensional graph. Distance of each sample point represents the distance of the sample (the closer the distance, the higher the similarity between samples). 95% confidence ellipses.

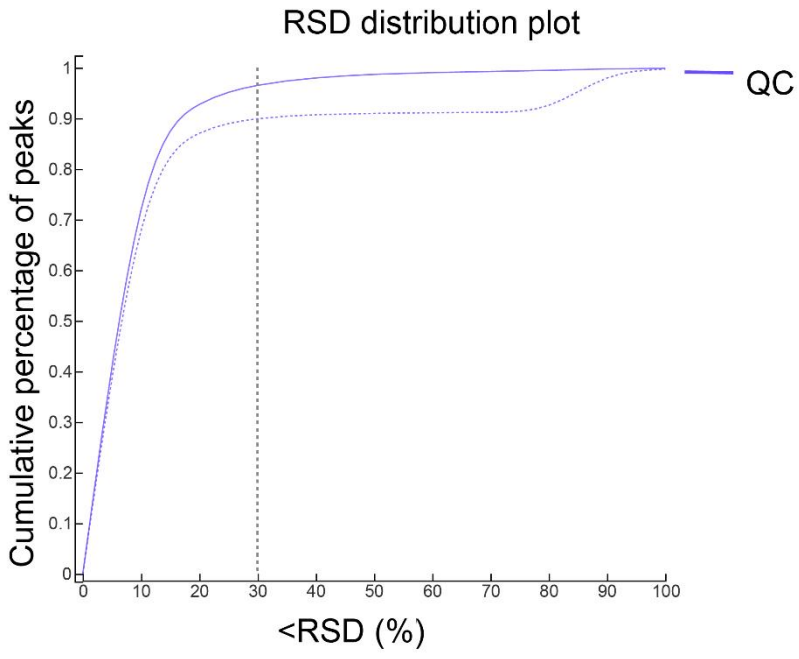


Supplementary Figure S6 qRT-PCR validation of selected candidate genes
RNA-seq data are in red and qRT-PCR data are in blue (geometric mean±geometric SD, *n*=3).



Supplementary Figure S7 Pearson correlation analysis between qRT-PCR and RNA-seq data

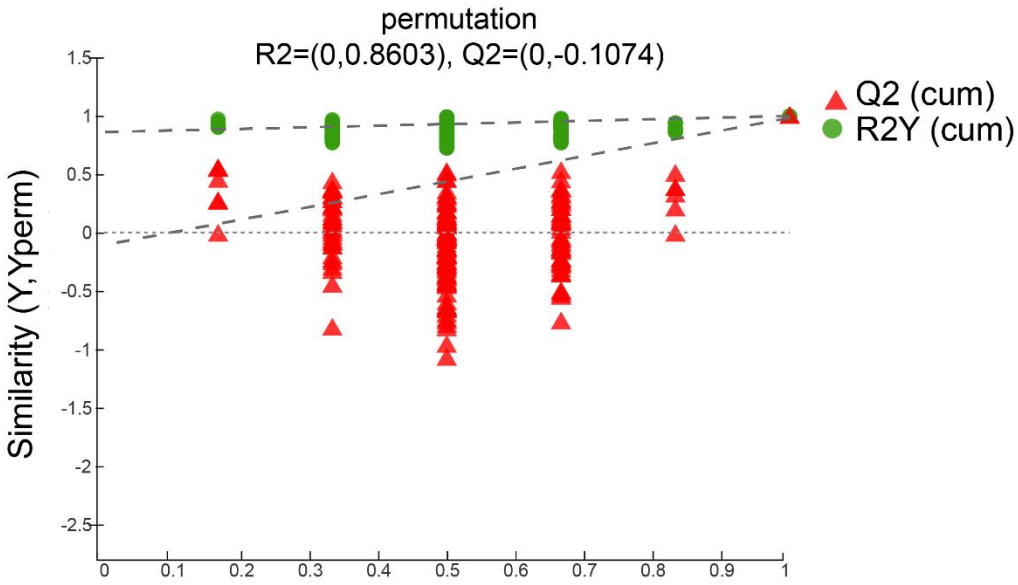
The qRT-PCR results showed strong correlation with RNA-seq (R^2 = 0.8933), indicating that RNA-seq interpretation in this study was reliable.



Supplementary Figure S8 Metabolomics QC sample evaluation chart

Abscissa is RSD (%), i.e., SD/mean, and ordinate is the cumulative proportion of ion peaks. For overall data, the RSD was 70%, indicating that the overall data were qualified

(virtual line represents data preprocessing, real line represents data preprocessing).



Supplementary Figure S9 Verification of OPLS-DA model

Abscissa represents displacement retention of the displacement test, and ordinate represents the values of the R2 (green dots) and Q2 (red triangle) displacement tests. Two dashed lines represent the regression lines of R2 and Q2, respectively. In the OPLS-DA model verification results, the value of Q2 increases as the abscissa increases. Longitudinal axis intercept of the regression line of Q2 is negative, and the values of R2Y and Q2 are greater than the longitudinal axis intercept of the regression lines of R2Y and Q2, thus the model could not be fit.

Supplementary Table S1 Sequences of four shRNAs for *flgK* gene

Name	Base sequence
***flgK*-shRNA-593**	F:5'-TGCGACTTGTTGATAGGCAAACTTCAAGAGAGTTTGCCTATCAACAAGTCGCTTTTTTT-3' R:5'-GTACAAAAAAAGCGACTTGTTGATAGGCAAACTCTCTTGAAGTTTGCCTATCAACAAGTCGCATGCA -3'
***flgK*-shRNA-687**	F:5'-TGCCAATGGTATCAGGACATACTTCAAGAGAGTATGTCCTGATACCATTGGCTTTTTTT-3' R:5'-GTACAAAAAAAGCCAATGGTATCAGGACATACTCTCTTGAAGTATGTCCTGATACCATTGGCATGCA -3'
***flgK*-shRNA-880**	F:5'-TGCACAAGCGTTGACGGAAATGTTCAAGAGACATTTCCGTCAACGCTTGTGCTTTTTTT-3' R:5'-GTACAAAAAAAGCACAAGCGTTGACGGAAATGTCTCTTGAACATTTCCGTCAACGCTTGTGCATGCA-3'
***flgK*-shRNA-1292**	F:5'-TGCAAGACAGTGCAGGCCAATATTCAAGAGATATTGGCCTGCACTGTCTTGCTTTTTTT-3' R:5'-GTACAAAAAAAGCAAGACAGTGCAGGCCAATATCTCTTGAATATTGGCCTGCACTGTCTTGCATGCA -3'

Supplementary Table S2 Reaction system and conditions for qRT-PCR

component	Volume (μL)
ddH_2O	4.00
2 x Taq Pro Universal SYBR qPCR Master Mix	5.00
Primer-F	0.25
Primer-R	0.25
cDNA	0.50

qRT-PCR was performed using a Taq Pro Universal SYBR qPCR Master Mix (Vazyme Biotech Co., Ltd, China), the reaction conditions: Initial denaturation step at 95 °C for 15 min followed by 40 cycles (20 s at 95 °C, 20 s at 57 °C, 72 °C at 20 s, 20 s at 78°C, the ramp speeds of the PCR steps was 1.6 °C/s).

Supplementary Table S3 Primer information for PCR and qRT-PCR

Gene Name	Acc Numbers	Base Sequence (From 5' to 3')	Target Sizes
gyrB	NZ_PHNR01000006	F:5'- TGCTGAAGGACGAGCGTTCG -3'	520
		R:5'- ATCATCTTGCCGACAACAGC - 3'	
tlr6	KM282521	R:5'- GACGGGTTTCAGTTTCGCAC - 3'	184
		R: 5'- CGGATAACAGGTTGCAGGGT -3'	
flgK	NZ_PHNR01000006	F:5'- ACTGTTGGAGGCACGAGAAC -3'	193
		R:5'- CTTATCAGCAAACGCCAGCC -3'	
16S rDNA	NZ_PHNR01000006	F: 5'- GAACACCGAGGTGATCGACG -3'	139
		R: 5'- ATAGTAGAACCCGTCGTGGC -3'	
β-actin	AY510710	F:5'- GGCTACTCCTTCACCACCACA-3'	185
		R: 5'- GGGCAACGGAACCTCTCAT -3'	
podx	XM_033612229	F:5'- CCACACCTTTTGCTGCTACG -3'	167
		R: 5'- AGGATTTCCAACAGCCGCTT -3'	
il10	XM_033625798	F:5'- TGCAACCCAATGTGCAACAA -3'	151
		R: 5'- GCGCAGCCTGTTAAGGTATG -3'	
tnfa	HQ011926	F:5'- ACCAGTCCCACTCTCAAGGA -3'	178
		R: 5'- GATTTGGACCAGCGCTTCAC -3'	
tf	JN540026	F:5'- GCTGAGACGGACAAGTGTGA -3'	200
		R: 5'- TACTGCTCCACCAAAGCAGG -3'	
atic	XM_033633415	F:5'- CCTGGCAACTGGTCAGAGAG -3'	231
		R: 5'- CCGACACAGCGATGAAGTCT -3'	
mao	XM_033641716	F:5'- CTCCGGTCTACAGCATCGAC -3'	193
		R: 5'- CACTTGATGACGGAGCCCAT -3'	
cyp1b1	XM_033613901	F:5'- CTCAGTCCACTGTCCGGATG -3'	182
		R: 5'- CACCGCGCTCATTATGTTGG -3'	
fgf21	XM_033612283	F: 5'- ACAGTGTGCTGGAGCTGAAA -3'	176
		R: 5'- TAGGAAGCGGGTGTATCCGT -3'	
espl1	XM_033625548	F: 5'- AGACGCCGCCTTGTATGAAA -3'	184
		R: 5'- AGCCACCATCTTCACAGAGC -3'	
ephx1	XM_033649438	F:5'- CGTCGCTTCCCTAAGCTGTT -3'	181
		R: 5'- AAATGTAGGCAGCCAGACCC -3'	
casp7	XM_033625548	F:5'- AGTGGGCAAGTGCATCATCA -3'	180
		R: 5'- GCCTCTCTGAGAAGACGCTC -3'	

Supplementary Table S4 Mobile phase elution gradient

Time （min）	Flow rate （mL/min）	A （%）	B （%）
0	0.4	100	0
3.5	0.4	75.5	24.5
5.5	0.4	0	100
7.4	0.6	0	100
7.6	0.6	48.5	51.5
7.8	0.5	100	0
9	0.4	100	0
10	0.4	100	0

During the LC-MS detection process, the flow rates and percentages of the two mobile phases A and B at the corresponding time points.

Supplementary Table S5 Mass spectrometry parameters.

mass spectrometric parameters	
Description	parameter
Scan type (m/z)	70-1050
Sheath gas flow rate (arb)	50
Aux gas flow rate (arb)	13
Heater temp (℃)	425
Capillary temp (℃)	325
Spray voltage (+) (V)	3500
Spray voltage (-) (V)	-3500
S-Lens RF Level	50
Normalized collision energy (eV)	20,40,60
Resolution (Full MS)	60000
Resolution (MS 2)	7500

Supplementary Table S6 OPLS-DA model parameters

	R2X	R2X(cum)	R2Y	R2Y(cum)	Q	Q2(cum)
p1	0.588	0.588	0.99	0.99	0.978	0.978
o1	0.101	0.689	0.008	0.008	0.0036	0.0036
sum	0	0.689	0	0.998	0	0.982

R2X and R2Y represent the explanatory rates of the established model for X and Y matrices, respectively, and R2X (cum) and R2Y (cum) represent the cumulative explanatory rates; Q2 indicates the prediction ability of the model. The closer these three indicators are to 1, the more stable and reliable the model is. Q2 > 0.5 indicates that the prediction ability of the model is good. Q2 < 0.5 indicates that the prediction ability of the model is poor. p1 represents the principal component; o1 Represents the first orthogonal component.