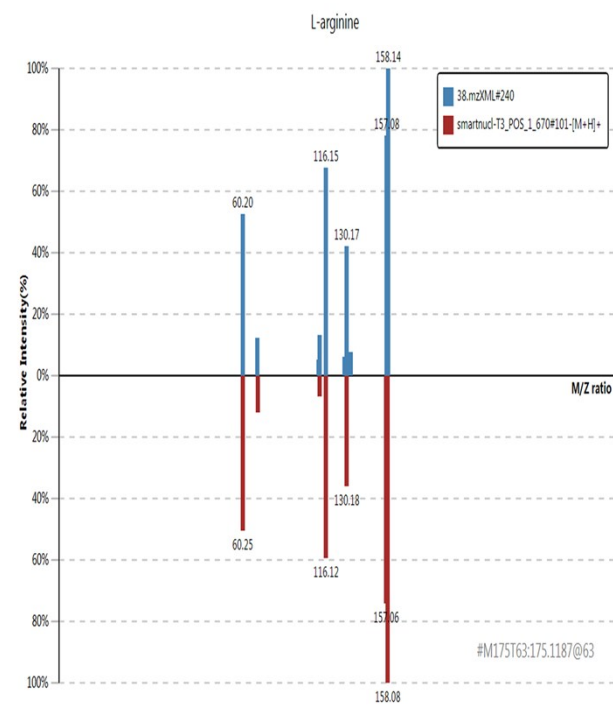
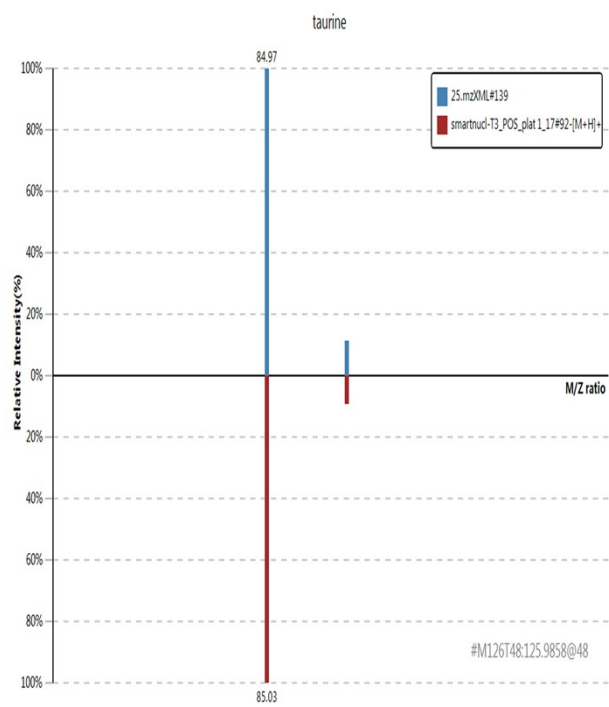
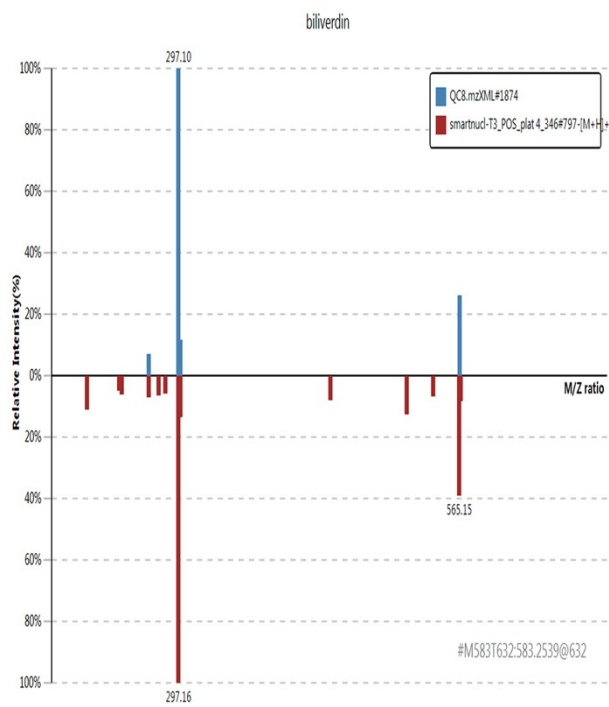


Supplementary Figure 1. PCA score plots and quality assurance (QA) results in the negative and positive ion modes.



Supplementary Figure 2. Identification graphs for biliverdin, taurine and L-Arginine.

Supplementary Table 1. Detected pathways between DN and DM groups.

	Total	Hits	Raw P	$-\log(P)$	Holm P	FDR	Impact
Taurine and hypotaurine metabolism	20	1	0.23566	1.4454	1	1	0.33094
Arginine and proline metabolism	77	4	0.01764	4.0376	1	0.82994	0.1644
Galactose metabolism	41	1	0.42499	0.85568	1	1	0.08543
Tyrosine metabolism	76	3	0.077976	2.5514	1	1	0.05976
Steroid hormone biosynthesis	99	1	0.74151	0.29906	1	1	0.02959
Butanoate metabolism	40	2	0.097725	2.3256	1	1	0.02251
Porphyrin and chlorophyll metabolism	104	1	0.75896	0.27581	1	1	0.01844
Citrate cycle (TCA cycle)	20	1	0.23566	1.4454	1	1	0.01684
Purine metabolism	92	2	0.3477	1.0564	1	1	0.01669
Valine, leucine and isoleucine degradation	27	1	0.30465	1.1886	1	1	0.01325
Cysteine and methionine metabolism	56	1	0.53151	0.63203	1	1	0.01289
Primary bile acid biosynthesis	47	1	0.47015	0.7547	1	1	0.00822
Ascorbate and aldarate metabolism	45	1	0.4555	0.78637	1	1	0.00802
Alanine, aspartate and glutamate metabolism	24	1	0.27586	1.2879	1	1	0.00285
Glutathione metabolism	38	1	0.40104	0.9137	1	1	0.0019
Glycine, serine and threonine metabolism	48	1	0.47734	0.73953	1	1	0.00071
Lysine degradation	47	1	0.47015	0.7547	1	1	0.0005
Synthesis and degradation of ketone bodies	6	1	0.07724	2.5608	1	1	0
D-Arginine and D-ornithine metabolism	8	1	0.10168	2.2859	1	1	0
D-Glutamine and D-glutamate metabolism	11	1	0.13716	1.9866	1	1	0
Nitrogen metabolism	39	1	0.40913	0.89372	1	1	0
Valine, leucine and isoleucine degradation	40	1	0.41711	0.8744	1	1	0
Nicotinate and nicotinamide metabolism	44	1	0.44802	0.80292	1	1	0
Phenylalanine metabolism	45	3	0.020749	3.8753	1	0.82994	0
Aminoacyl-tRNA biosynthesis	75	2	0.26303	1.3355	1	1	0

Total: total number of metabolites in objective metabolic pathways; Hits: number of differential metabolites in objective metabolic pathways; Raw P: Raw P values; $-\log(P)$: negative natural logarithm of P values; Holm P: P values after Holm Correction; FDR: P values after FDR Correction; Impact: impact values of metabolic pathways.