

## Supplementary Information

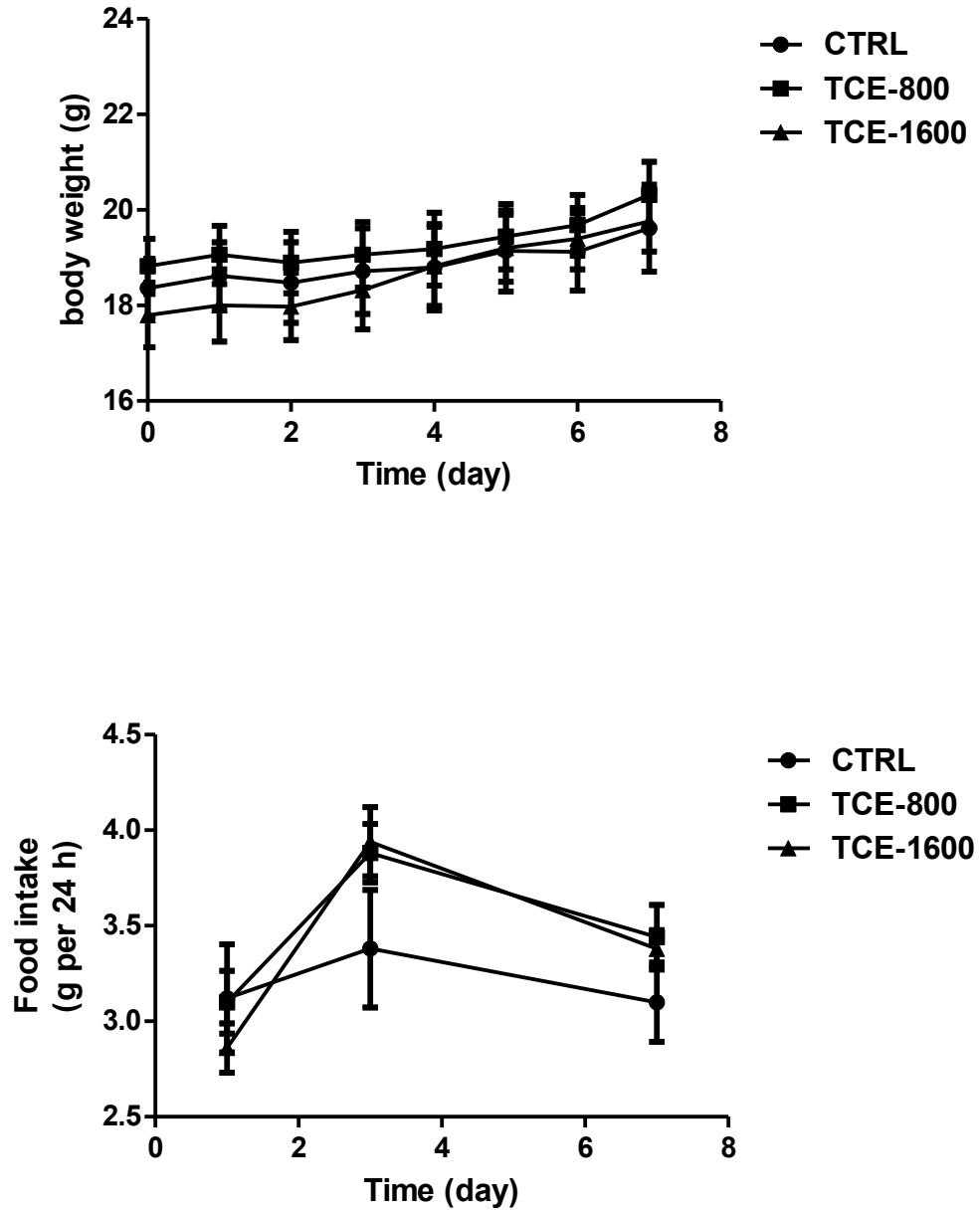
### **Metabolomics reveals trichloroacetate as a major contributor to trichloroethylene-induced metabolic alterations in mouse urine and serum**

Zhong-Ze Fang, Kristopher W Krausz, Naoki Tanaka, Fei Li, Aijuan Qu, Jeffrey R. Idle, Frank J Gonzalez

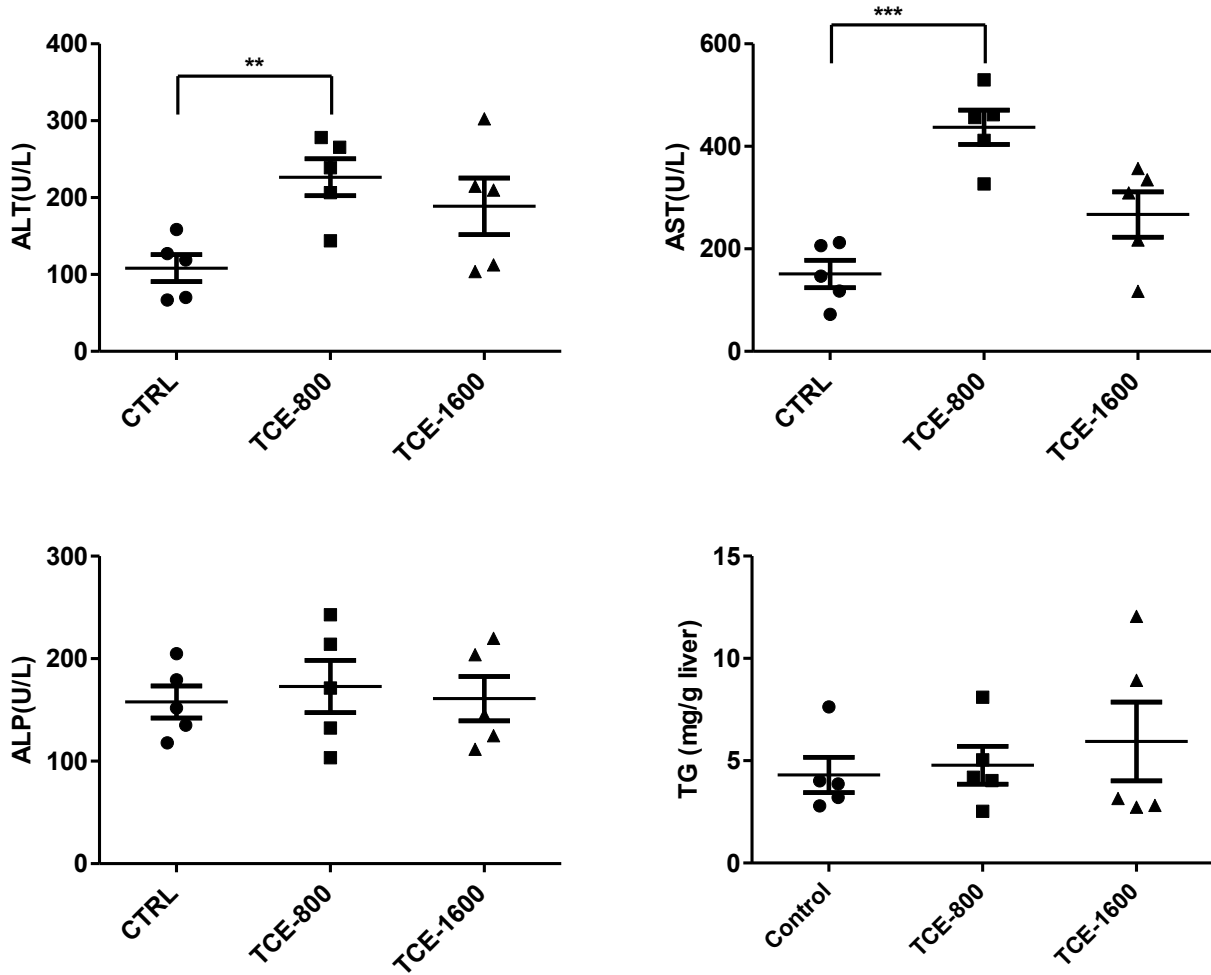
**Supplement table 1: Primer pairs used for qPCR**

Gene		Primer sequence
<i>Ppara</i>	F	5'-AGTTCGGGAACAAGACGTTG-3'
	R	5'-CAGTGGGGAGAGAGGACAGA-3'
<i>Acot1</i>	F	5'-CTGGCGCATGCAGGATC-3'
	R	5'-GGCACTTTTCTTGGATAGCTCC-3'
<i>Acox1</i>	F	5'-TCGCAGACCCTGAAGAAATC-3'
	R	5'-CCTGATTCAGCAAGGTAGGG-3'
<i>Acadm</i>	F	5'-AGCTCTAGACGAAGCCACGA-3'
	R	5'-GCGAGCAGAAATGAAACTCC-3'
<i>Acadl</i>	F	5'-TCTTGCGATCAGCTCTTTCA-3'
	R	5'-GGTACATGTGGGAGTACCCG-3'
<i>Ehhadh</i>	F	5'-CTATGATCCGCCTCTGCAA-3'
	R	5'-TGGCTCTAACCGTATGGTCC-3'
<i>Acaa1a</i>	F	5'-GTGGCATCAGAAATGGGTCT-3'
	R	5'-CGGGAAGAGATATTCCCAGG-3'
<i>Cpt1a</i>	F	5'-GCCCATGTTGTACAGCTTCC-3'
	R	5'-AGTGGCCTCACAGACTCCAG-3'
<i>Cpt2</i>	F	5'-ATGCACTACCAGGACAGGCT-3'
	R	5'-TGGCTGTCATTCAAGAGAGG-3'
<i>Cyp4a10</i>	F	5'-GATGGACGCTCTTTACCCAA-3'
	R	5'-AAGGGTCAAACACCTCTGGA-3'

**Supplementary figure 1.** Body weight change and food intake in control and TCE-treated mice. The data are given as mean±SEM (n=5).

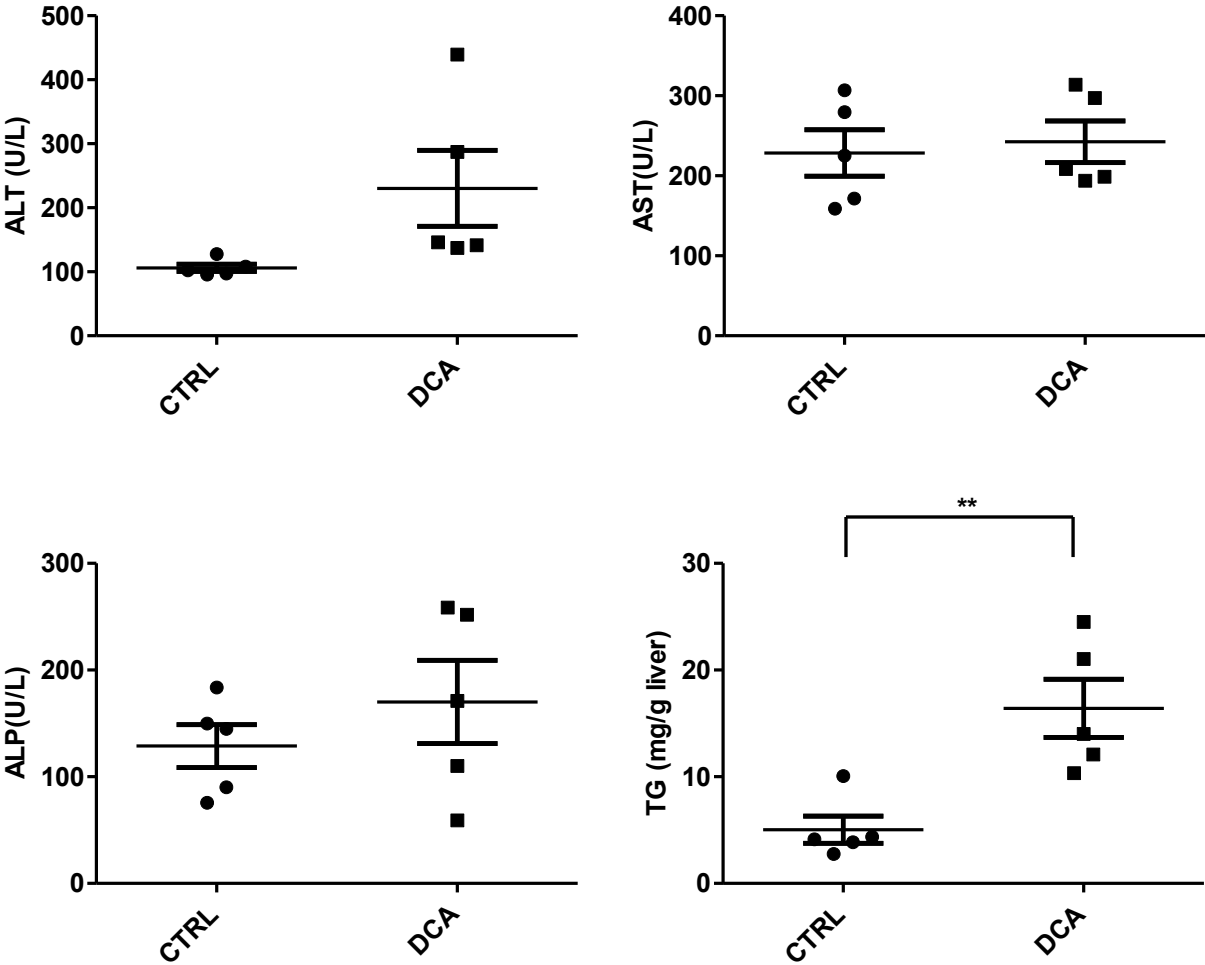


**Supplementary figure 2.** The influence of TCE exposure on alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) activities in serum, and triglyceride (TG) levels in liver. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

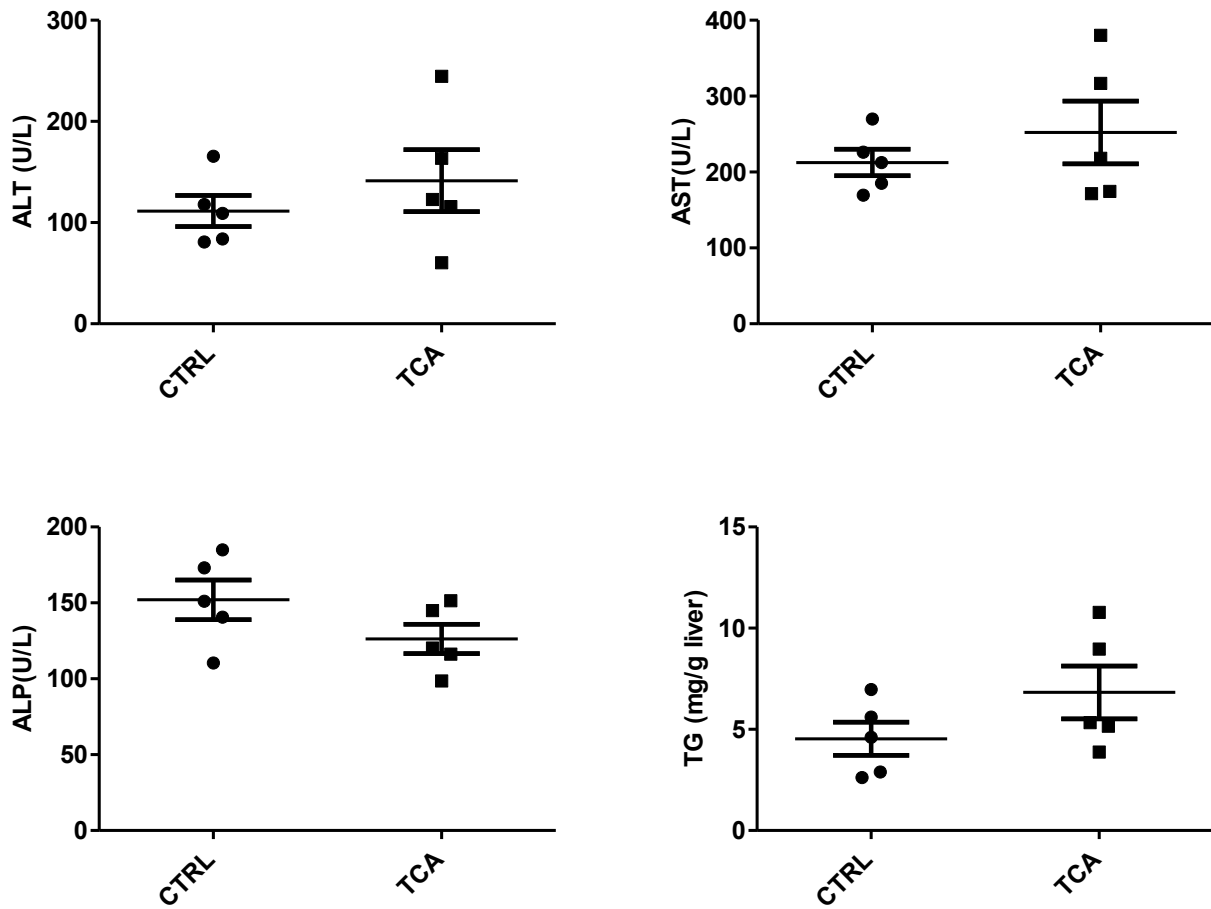




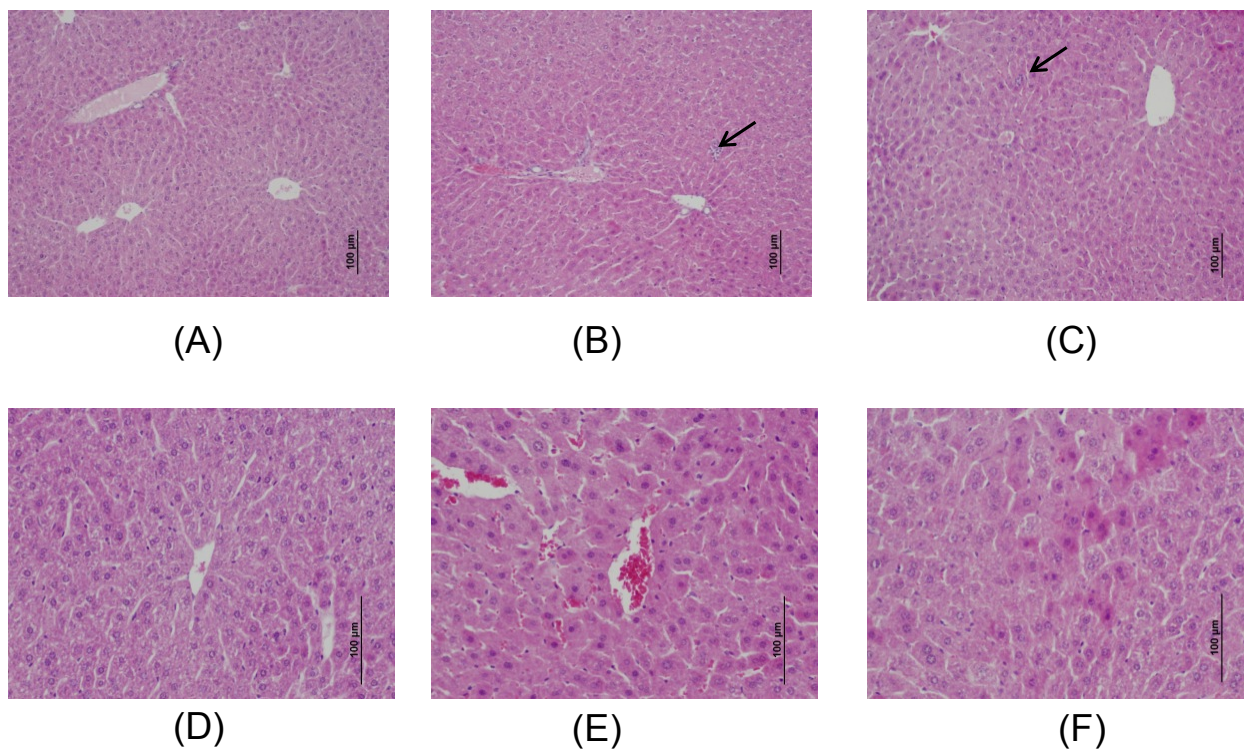
**Supplementary figure 3.** The influence of DCA exposure on alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) activities in serum, and triglyceride (TG) levels in liver. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.



**Supplementary figure 4.** The influence of TCA exposure on alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) activities in serum, and triglyceride (TG) levels in liver.

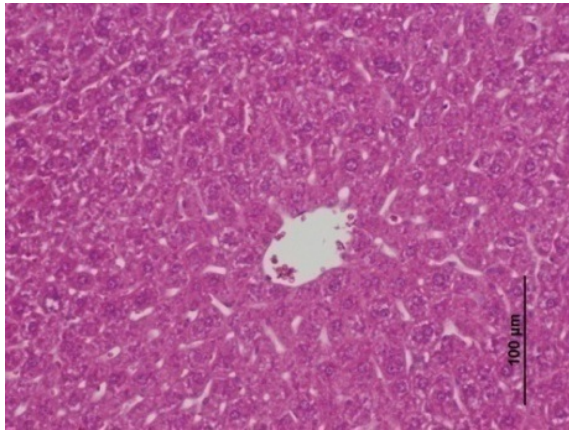


**Supplementary figure 5.** Histopathology (H&E staining) of livers from C57BL/6 treated with TCE. (A) TCE-ctrl; (B) TCE-800 mg/kg/day; (C) TCE-1600 mg/kg/day; (D) TCE-ctrl; (E) TCE-800 mg/kg/day; (F) TCE-1600 mg/kg/day. 100 X magnification.

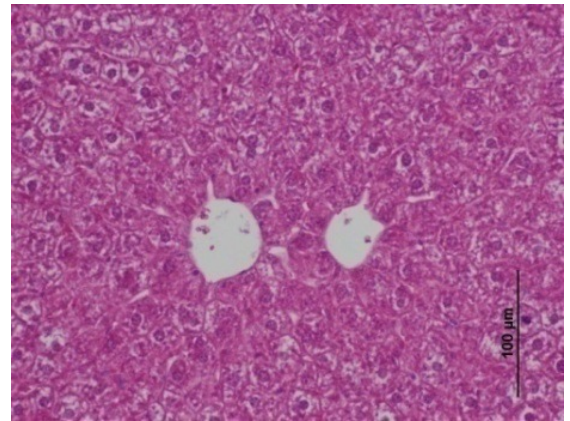




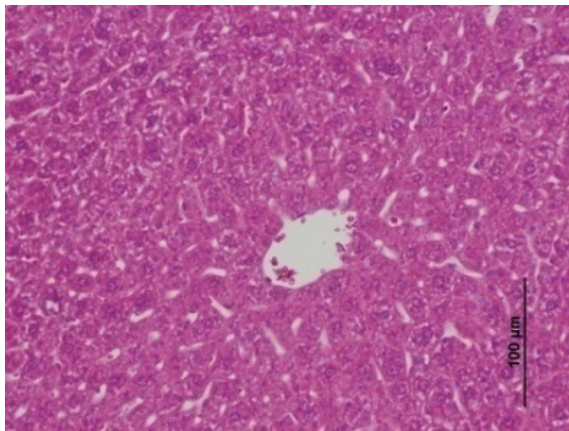
**Supplementary figure 6.** Histopathology (H&E staining) of livers after exposure of C57BL/6 mice to DCA and TCA. (A) DCA-ctrl; (B) DCA-treat; (C) TCA-ctrl; (D) TCA-treat.



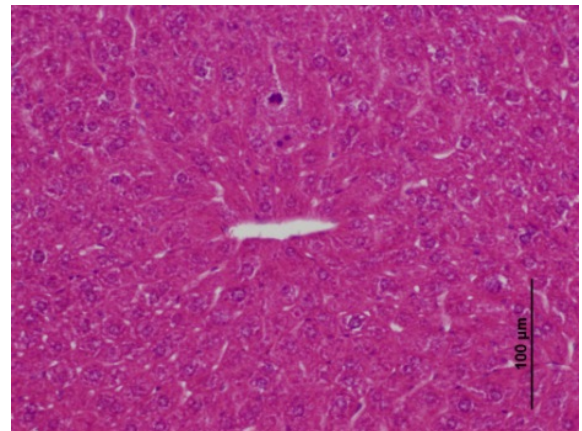
(A)



(B)



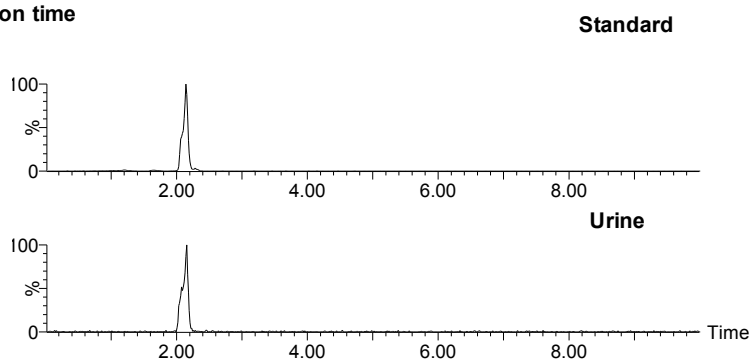
(C)



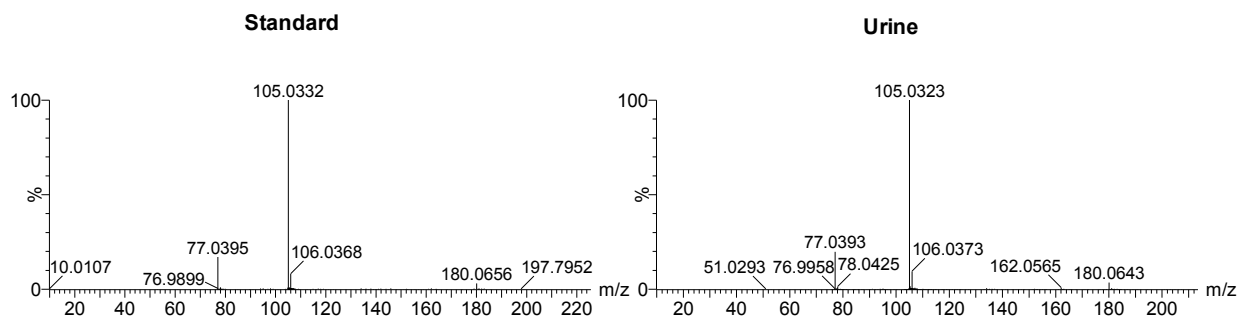
(D)

**Supplementary figure 7A.** UPLC-ESI-QTOFMS comparison of the authentic standard of hippuric acid with ions derived from urine obtained from C57BL/6 mice.

**Comparison of retention time**

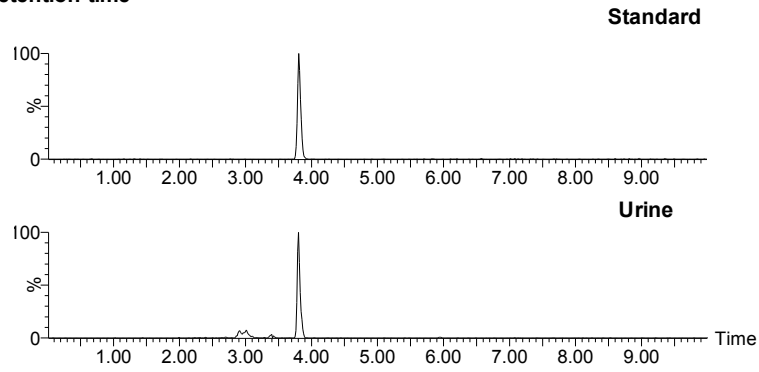


**Comparison of MS/MS fragmentation**

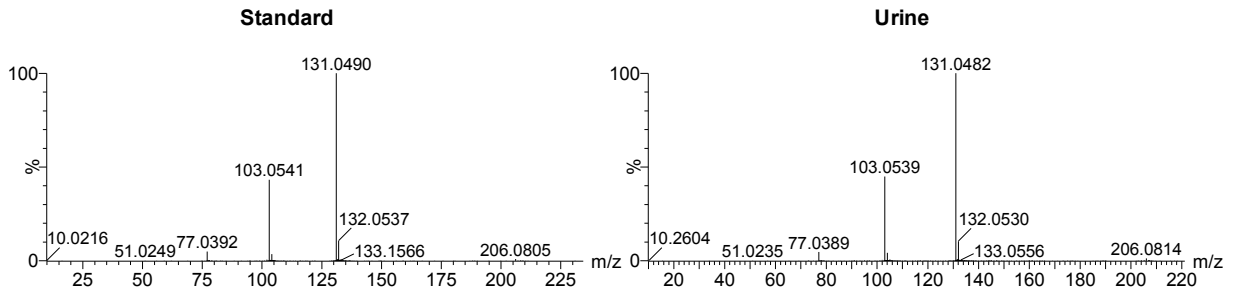


**Supplementary figure 7B.** UPLC-ESI-QTOFMS comparison of authentic standard of cinnamoylglycine with ions derived from urine obtained from C57BL/6 mice.

**Comparison of retention time**

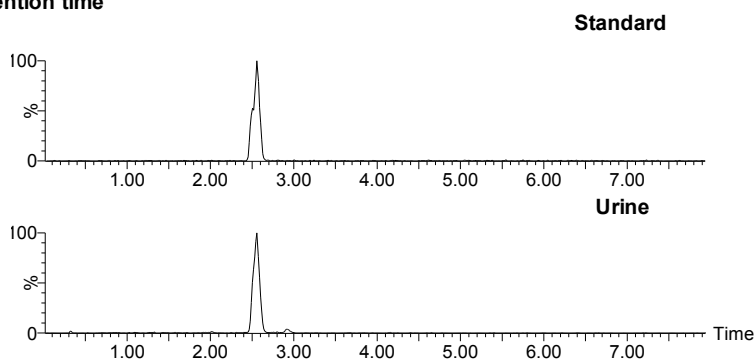


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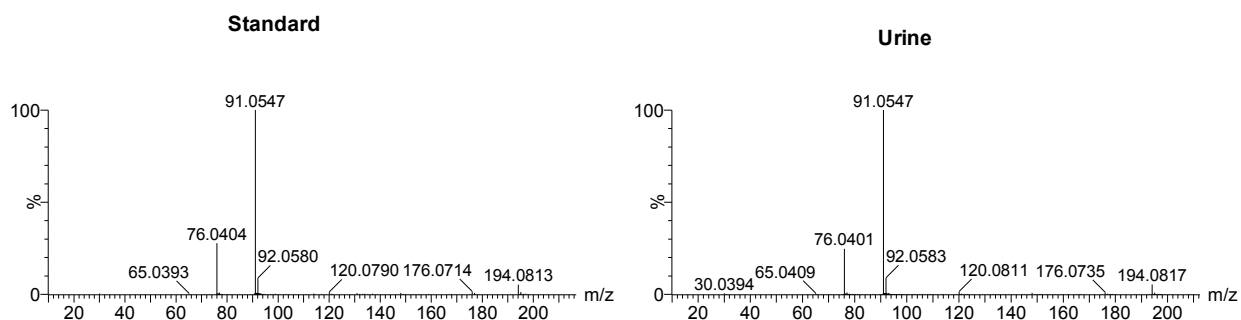


**Supplementary figure 7C.** UPLC-ESI-QTOFMS comparison of the authentic standard of phenylacetylglycine with ions derived from urine obtained from C57BL/6 mice.

**Comparison of retention time**

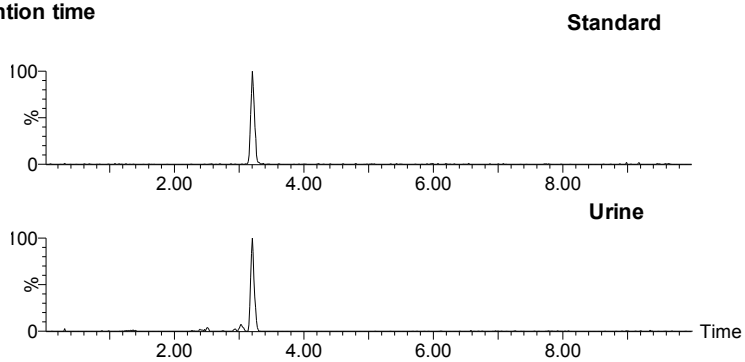


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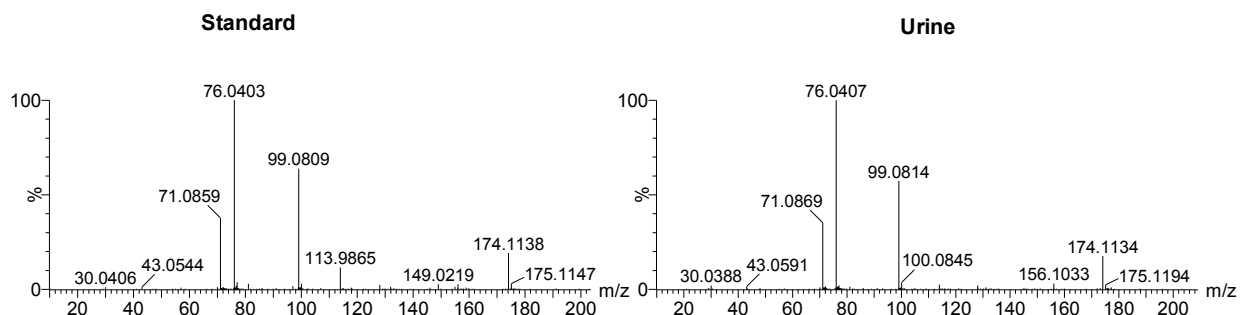


**Supplementary figure 7D.** UPLC-ESI-QTOFMS comparison of the authentic standard of hexanoylglycine with ions derived from urine obtained from C57BL/6 mice.

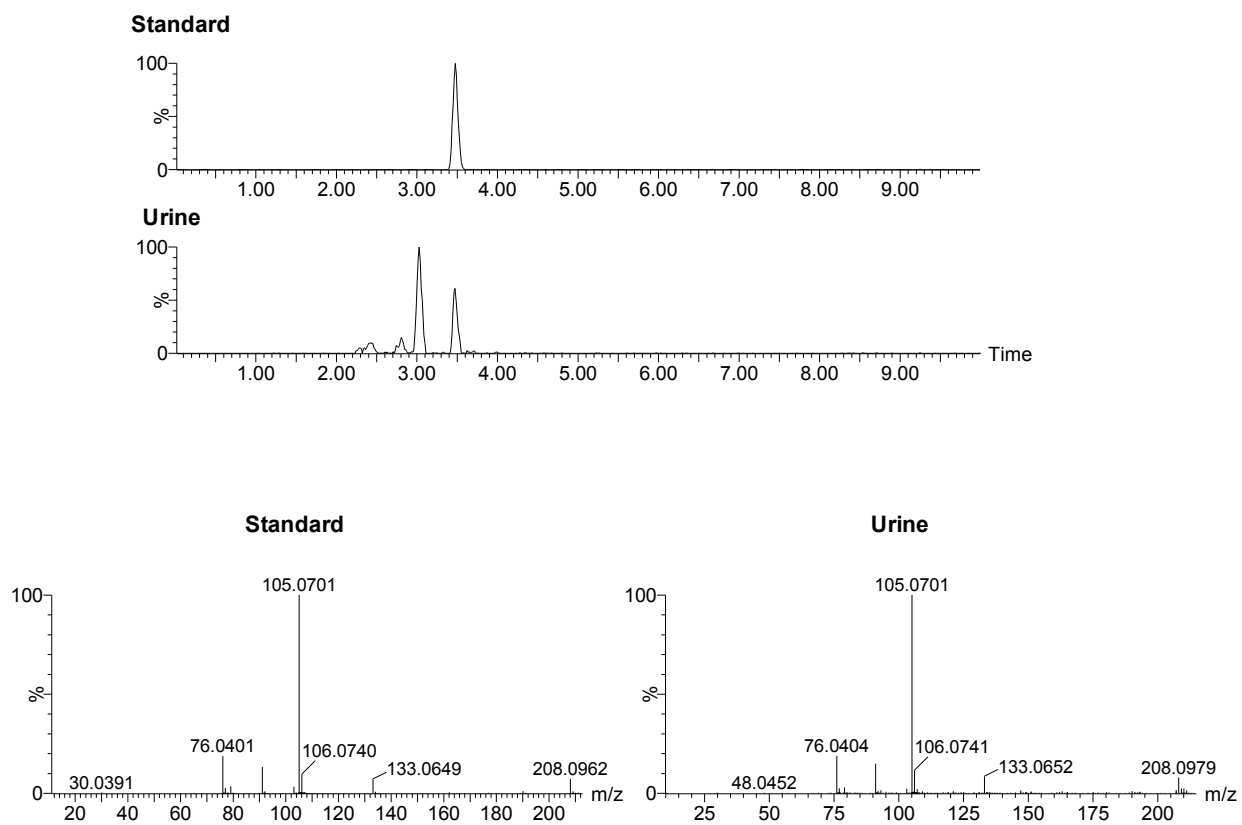
**Comparison of retention time**



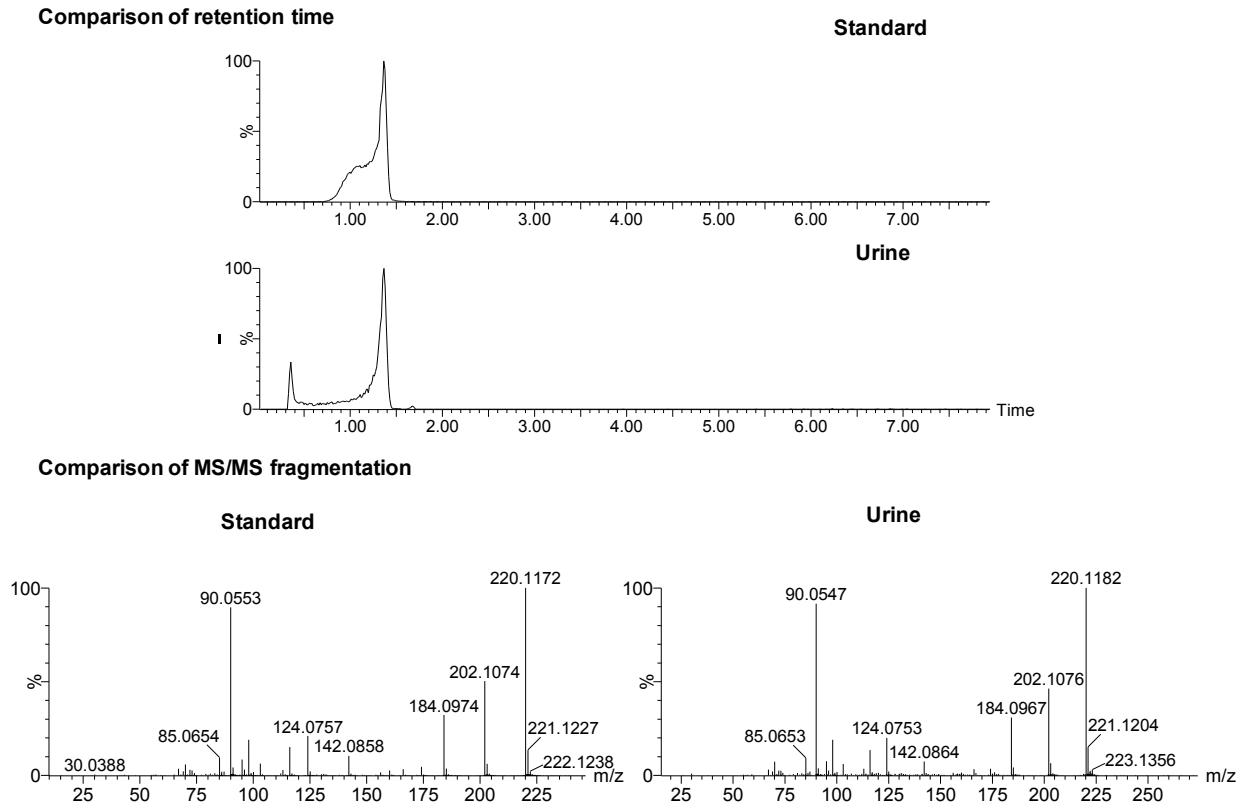
**Comparison of MS/MS fragmentation**



**Supplementary figure 7E.** UPLC-ESI-QTOFMS comparison of the authentic standard of phenylpropionylglycine with ions derived from urine obtained from C57BL/6 mice.

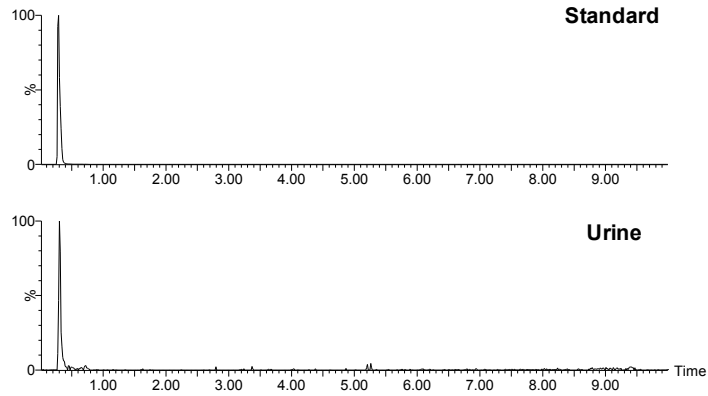


**Supplementary figure 7F.** UPLC-ESI-QTOFMS comparison of authentic standard of pantothenic acid with ions derived from urine obtained from C57BL/6 mice.

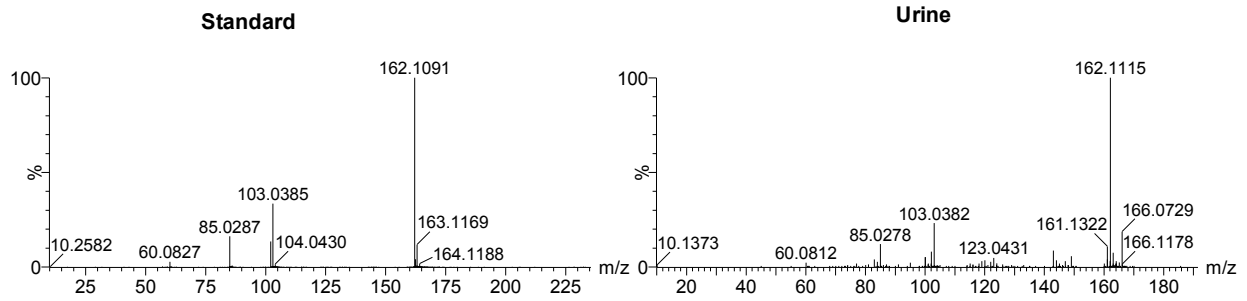


**Supplementary figure 7G.** UPLC-ESI-QTOFMS comparison of authentic standard of carnitine with ions derived from urine obtained from C57BL/6 mice.

**Comparison of retention time**

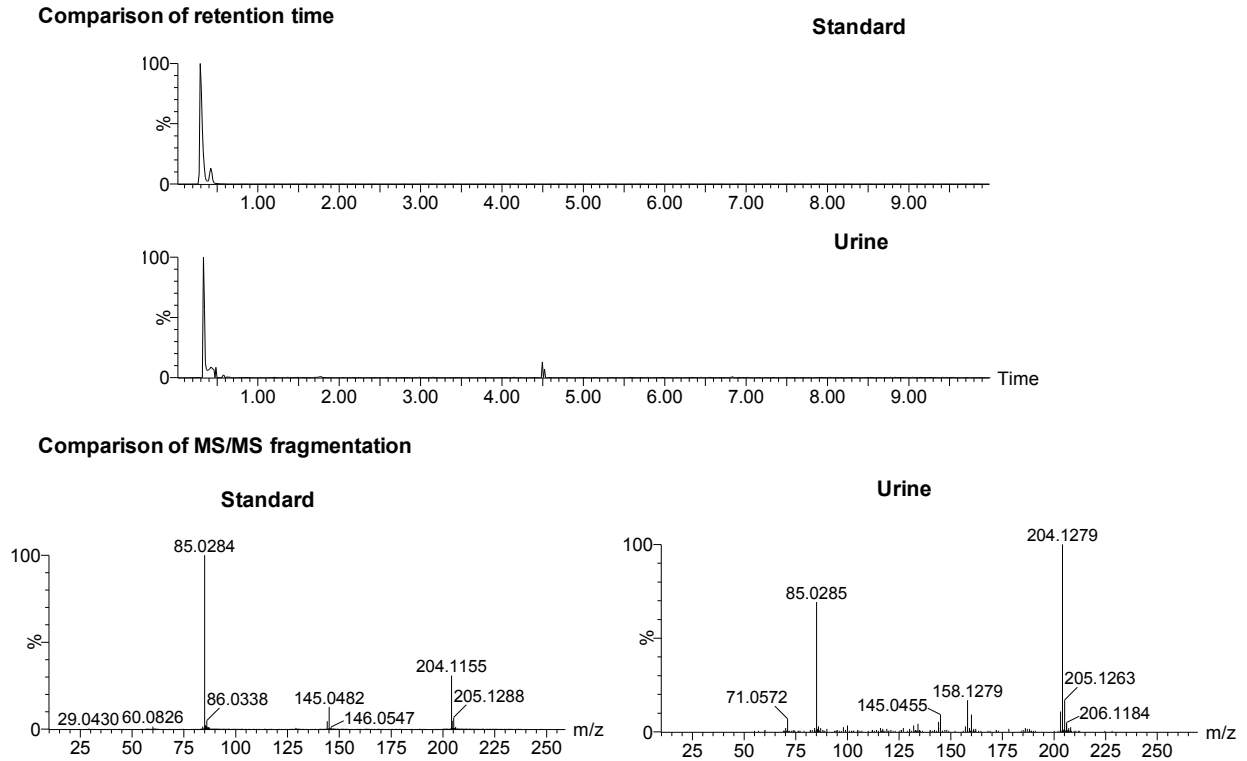


**Comparison of MS/MS fragmentation**



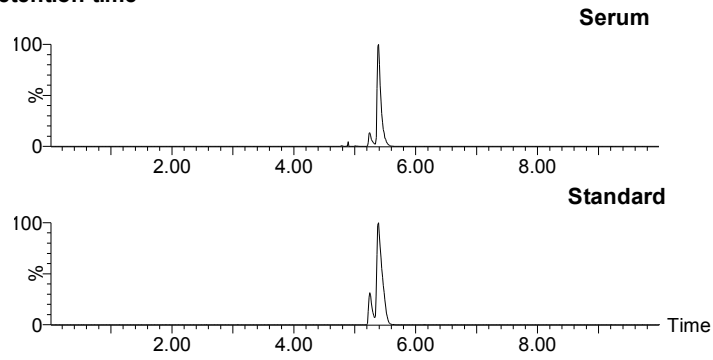


**Supplementary figure 7H.** UPLC-ESI-QTOFMS comparison of authentic standards of acetylcarnitine with ions derived from urine obtained from C57BL/6 mice.

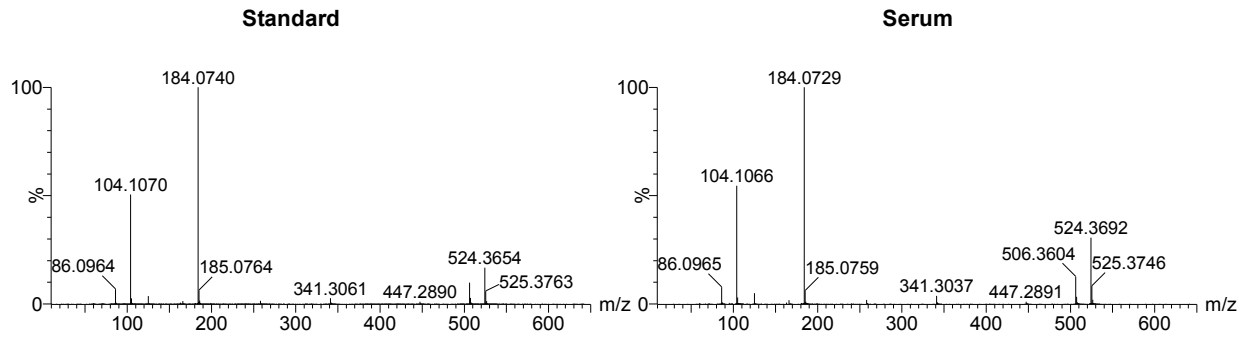


**Supplementary figure 7I.** UPLC-ESI-QTOFMS comparison of authentic standard of 1-octadecanoyl-*sn*-glycero-3-phosphocholine (LPC (18:0)) with ions derived from serum obtained from C57BL/6 mice.

**Comparison of retention time**

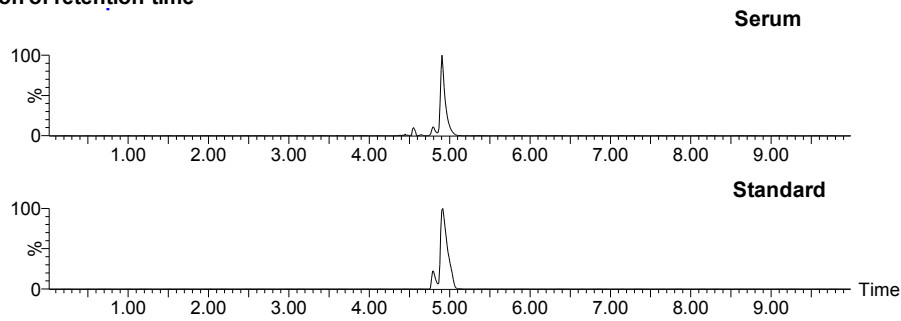


**Comparison of MS/MS fragmentation**

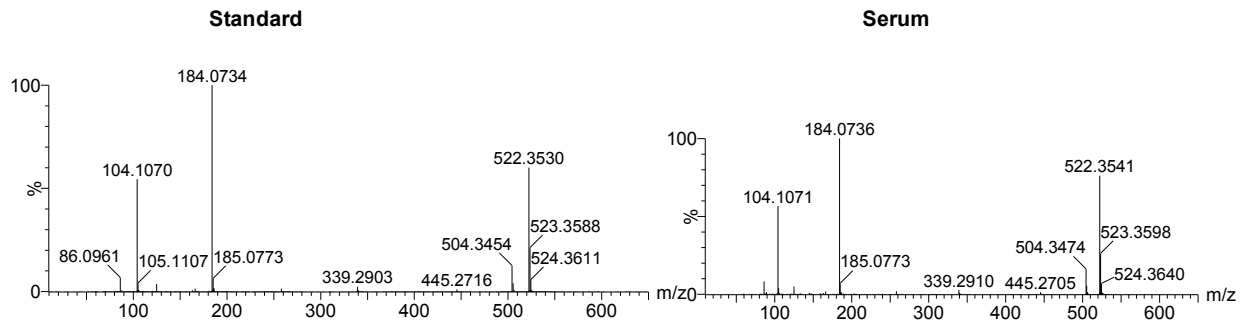


**Supplementary figure 7J.** UPLC-ESI-QTOFMS comparison of authentic standard of 1-oleoyl-2-hydroxy-*sn*-glycero-3-phosphocholine (LPC(18:1, 9Z)) with ions derived from serum obtained from C57BL/6 mice.

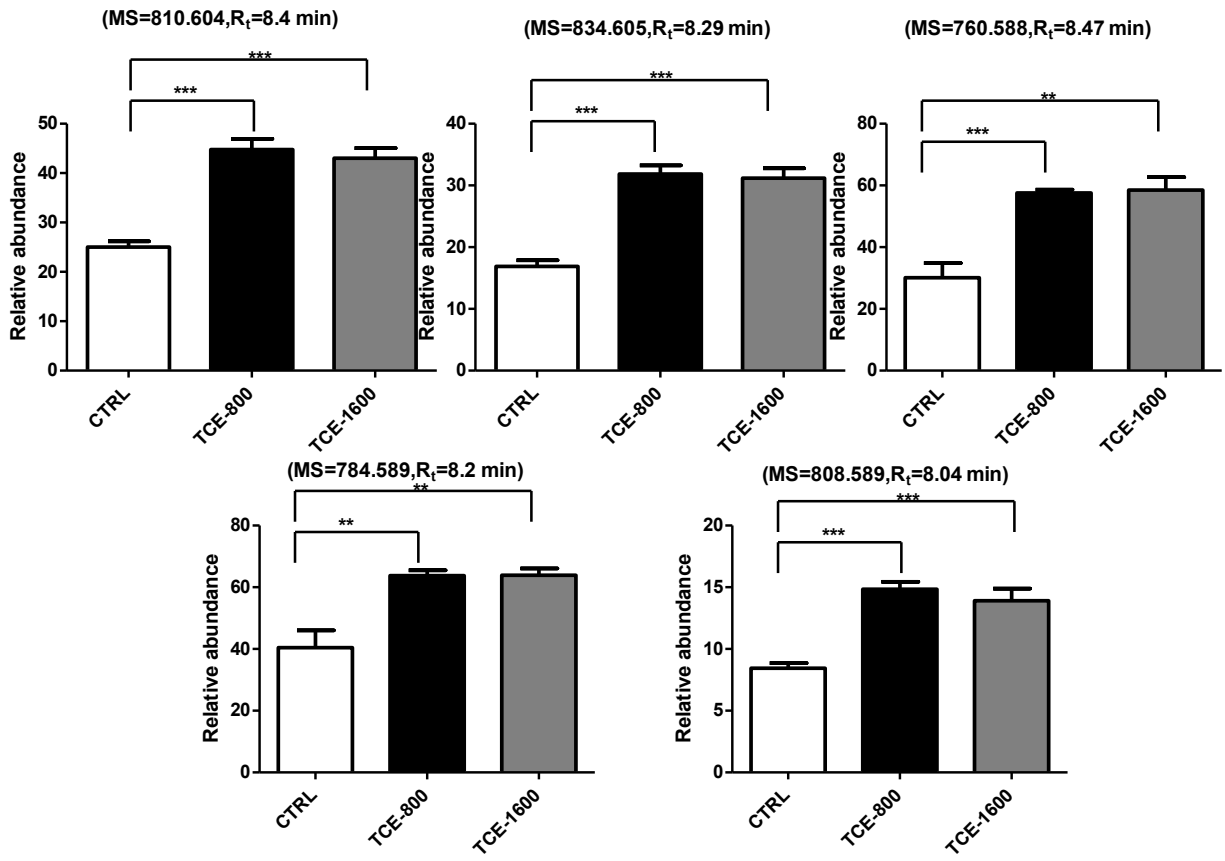
**Comparison of retention time**



**Comparison of MS/MS fragmentation**



**Supplementary figure 8.** Relative quantitation of PC components altered in serum from mice treated with TCE. The relative abundance (peak area of metabolites/internal standard) is given. The results were given as mean  $\pm$  SEM. \*,  $p < 0.05$ ; \*\*,  $p < 0.01$ ; \*\*\*,  $p < 0.001$ .



**Supplementary figure 9.** Comparison of the alteration of pantothenic acid and phenylacetyl-glycine in urine of mice treated with TCA and DCA.

