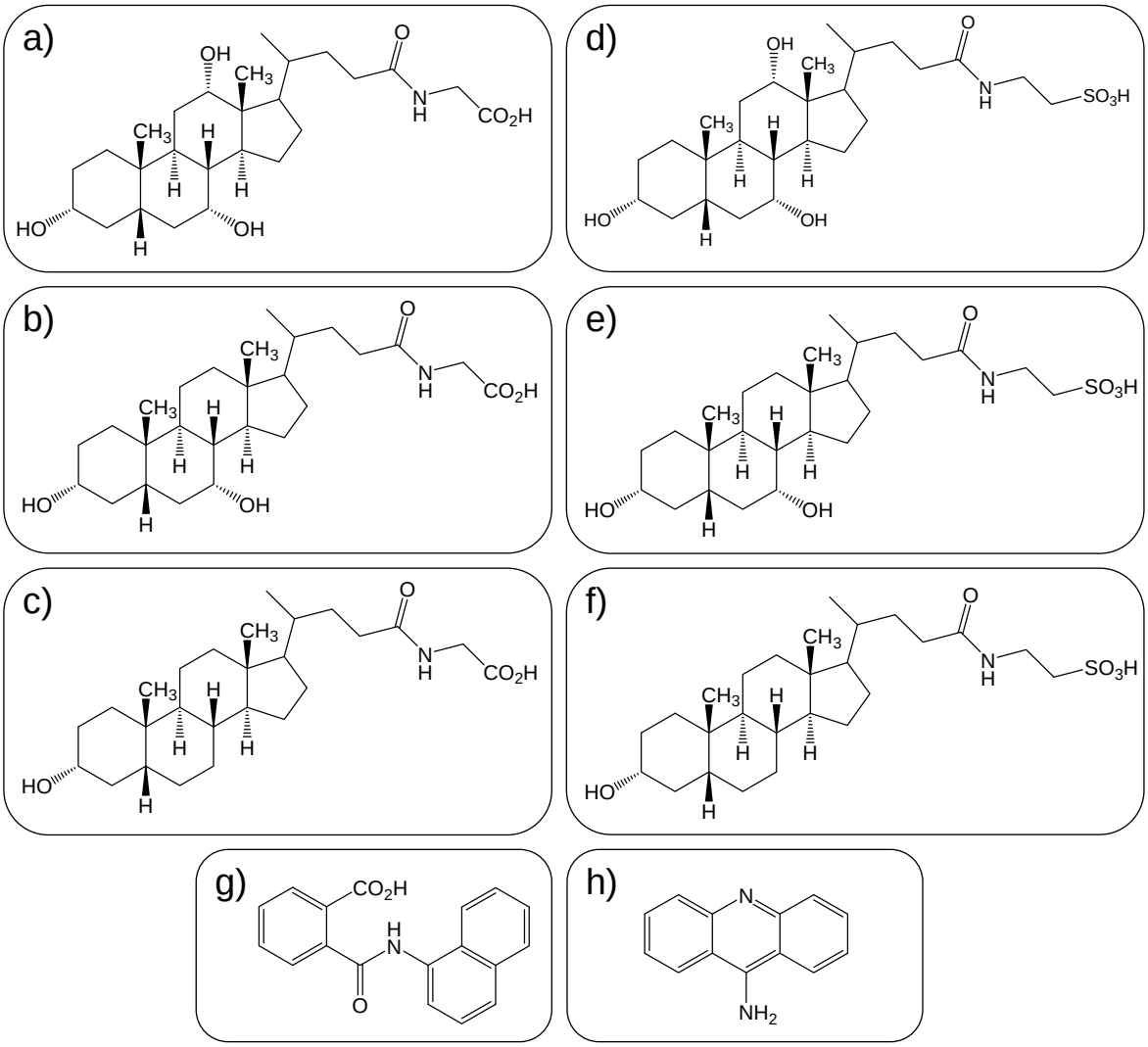
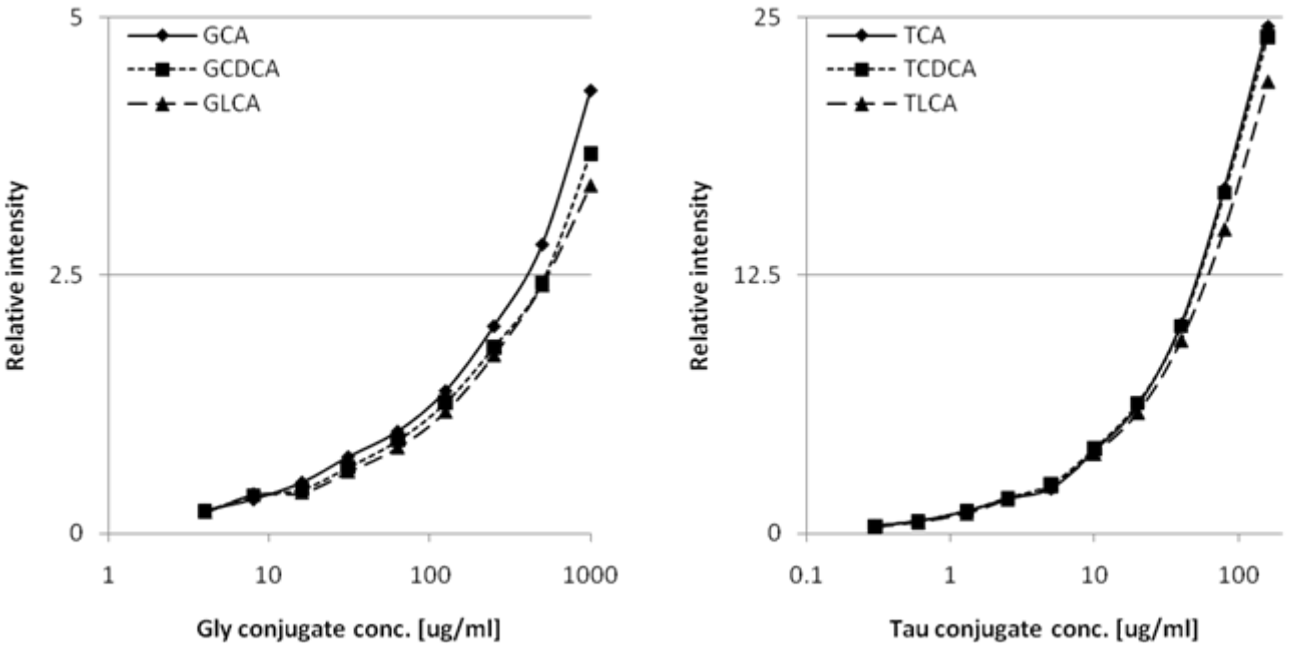
Supplementary figure 1



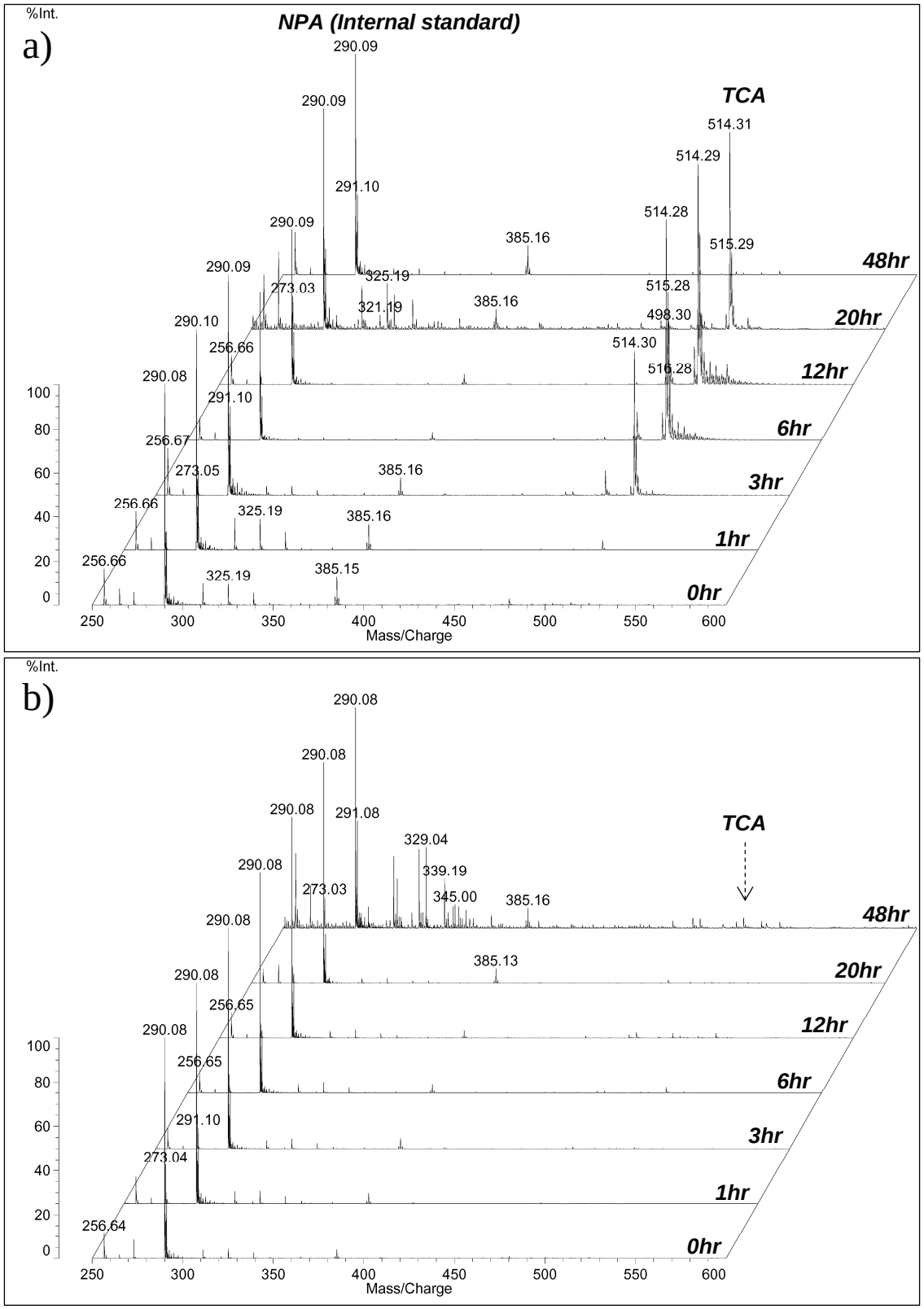
Supplementary figure 1. Chemical structure of bile acid and other reagents for MS.
Six bile acid standard of
a) GCA (glycocholic acid, MW=465.62),
b) GCDCA (glycochenodeoxycholic acid, MW=449.62),
c) GLCA (glycolithocholic acid, MW=433.62),
d) TCA (taurocholic acid, MW=515.70),
e) TCDCA (taurochenodeoxycholic acid, MW=499.70) and
f) TLCA (taurolithocholic acid, MW=483.71) are shown.
g) NPA (N-1-naphthylphthalamic acid, MW=291.30) as internal standard.
h) 9-AA (9-aminoacridine, MW=194.23) as MALDI matrix.

Supplementary figure 2



Supplementary figure 2. Calibration curve of six bile acids.
Bile acid calibration curve are shown.
Left panel of GCA (solid), GCDCA (dotted), GLCA (wide dotted),
and right of TCA (solid), TCDCA (dotted) and TLCA (wide dotted).
Each bile acid calibration curve is on secondary function with $R^2 > 0.99$:
GCA; $Y = 0.1141\ X^{0.5216}$ ($R^2 = 0.998$),
GCDCA; $Y = 0.1162\ X^{0.4957}$ ($R^2 = 0.996$),
GLCA; $Y = 0.1118\ X^{0.492}$ ($R^2 = 0.992$),
TCA; $Y = 0.8405\ X^{0.6713}$ ($R^2 = 0.998$),
TCDCA; $Y = 0.8564\ X^{0.6676}$ ($R^2 = 0.999$),
TLCA; $Y = 0.7646\ X^{0.6776}$ ($R^2 = 0.997$).

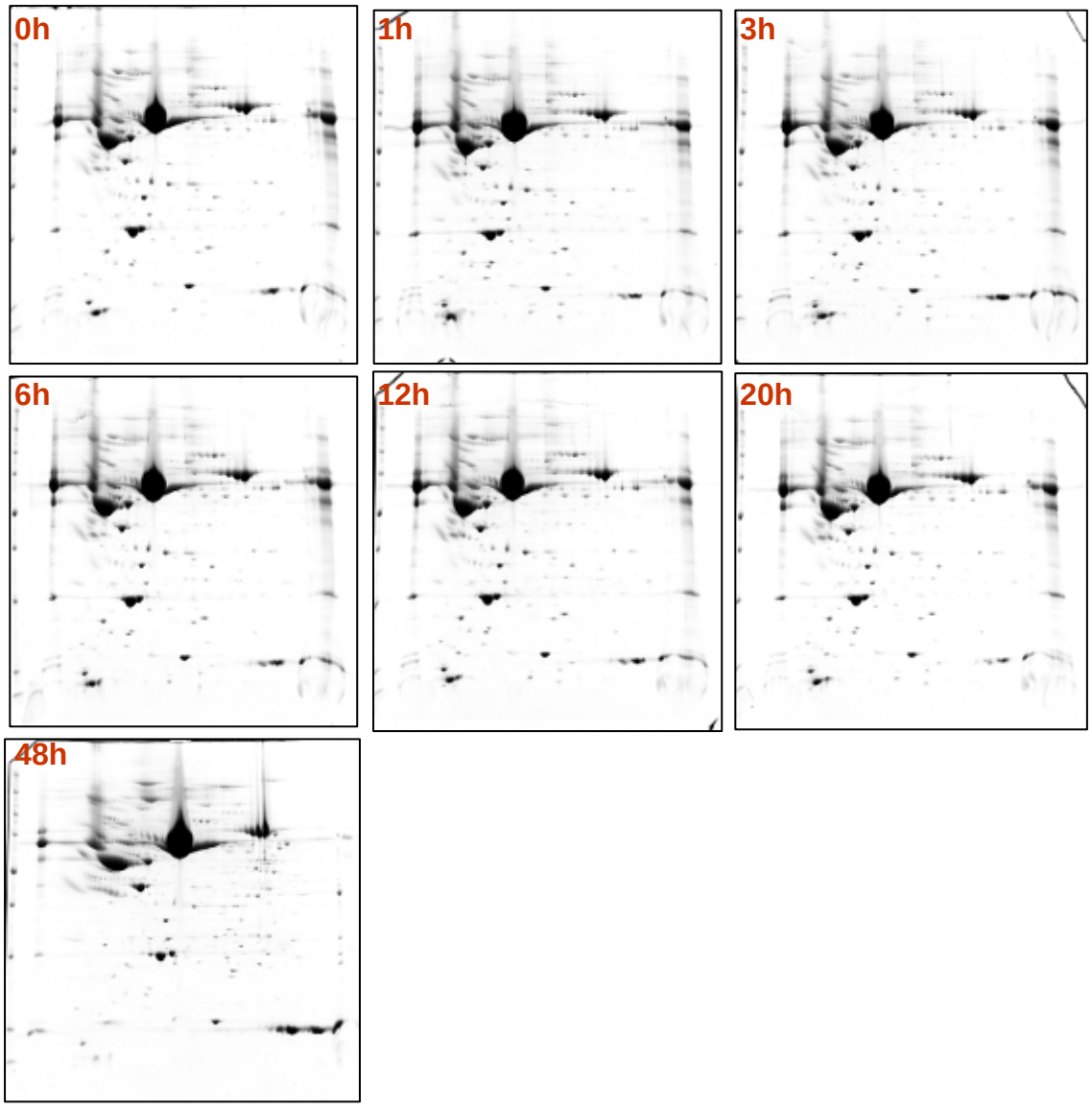
Supplementary figure 3



Supplementary figure 3. Representative SPE-MALDI-MS spectra from serum bile acid. Raw MS spectra of serum bile acid profile are shown in this figure from 0 to 48 hrs after a) CCl_4 i.p. and b) mineral oil i.p. control. Significant change of MS signal from TCA (m/z 514.3) was obtained in CCl_4 i.p. group, but no change was observed in control.

Supplementary figure 4

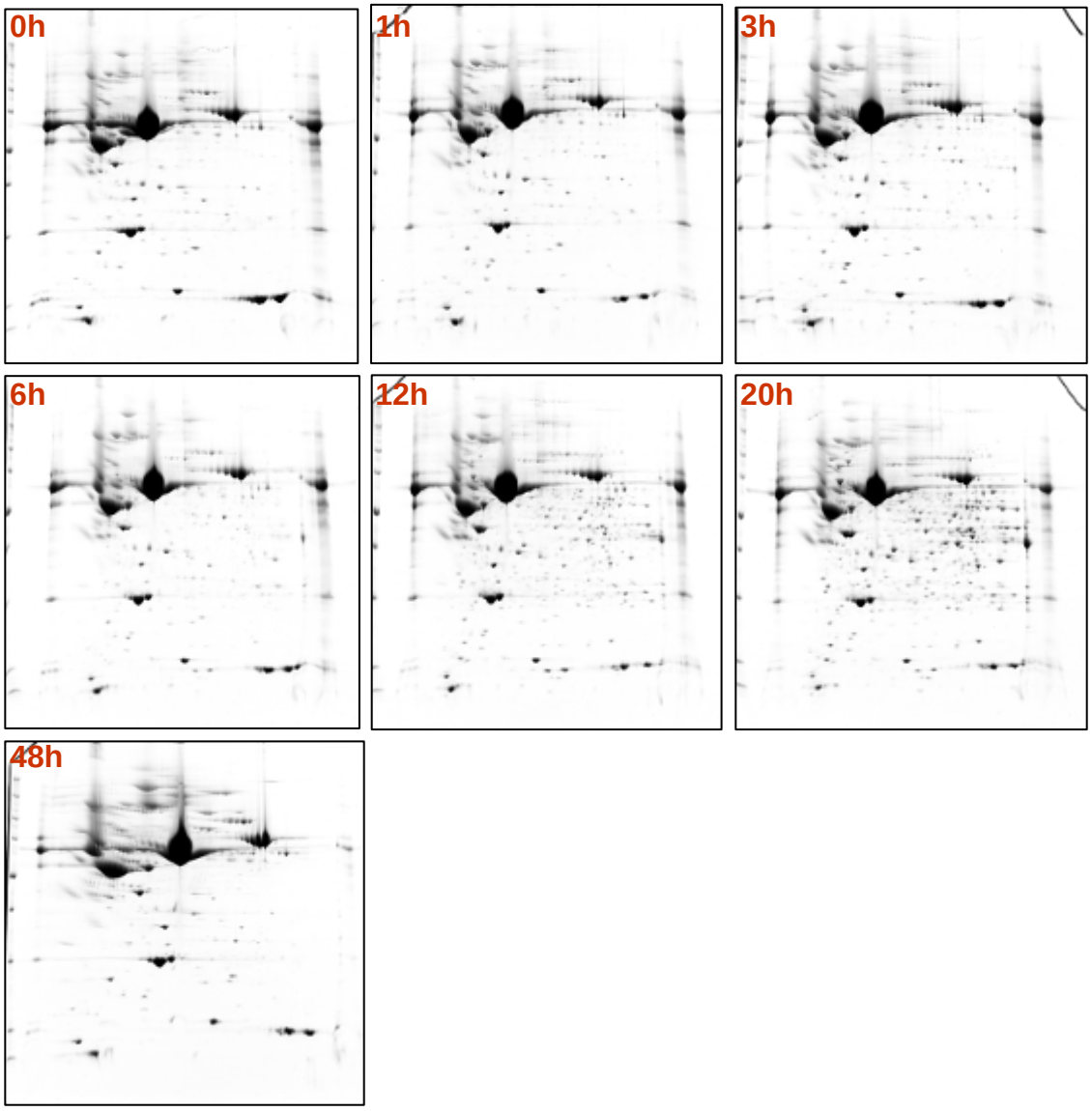
a)



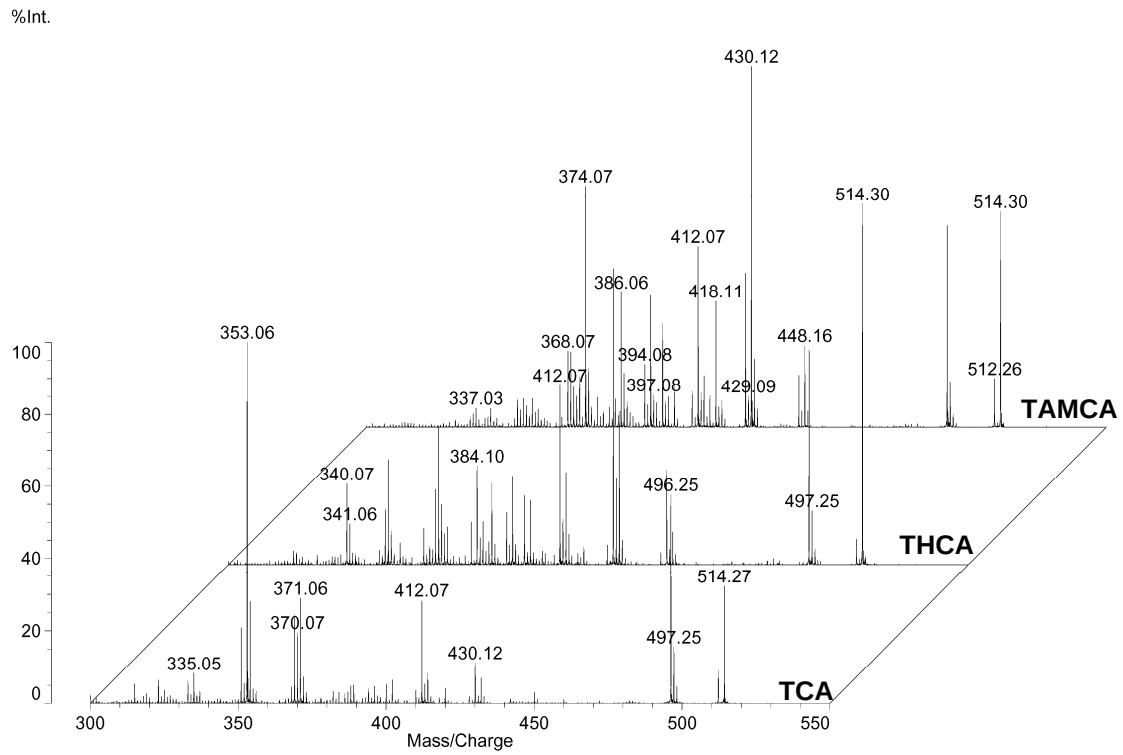
Supplementary figure 4. Representative image of time-dependent serum proteome on CBB G250-stained 2D-PAGE gel.
Collected serum at each time point was developed on 2D-PAGE gel.
a) control group (6 samples) and b) CCl_4 administration group (7 samples)

Supplementary figure 4

b)



Supplementary figure 5

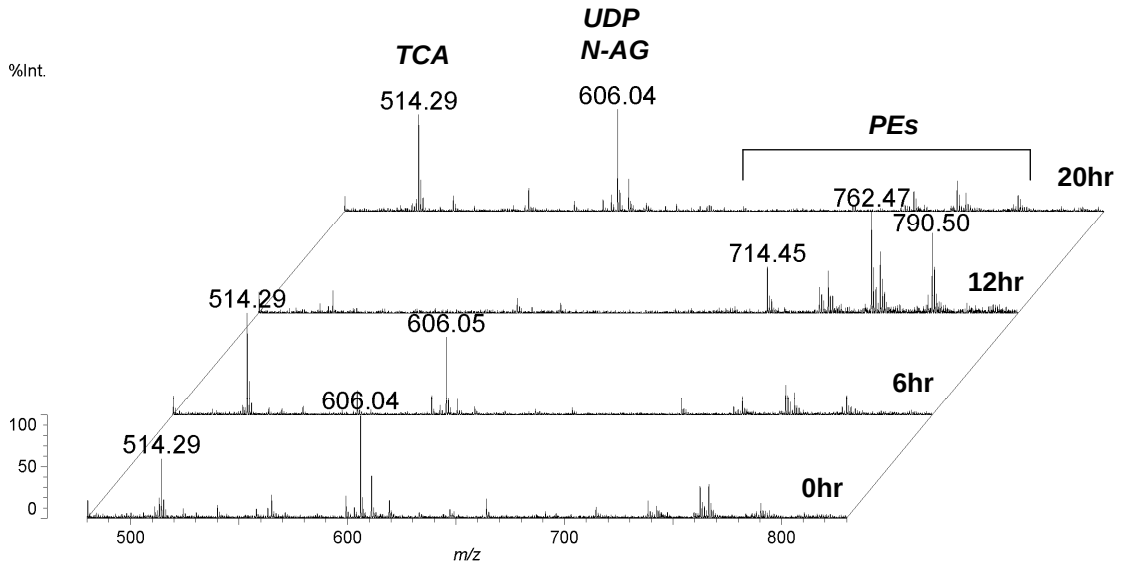


Supplementary figure 5. MS/MS fragment pattern of structural isomers of TCA. From the bottom, TCA, Taurohyocholic acid (THCA) and Tauro-α-muricholic acid (TAMCA) were indicated.

Structural isomers of TCA, Taurohyocholic acid and Tauro-α-muricholic acid, were analyzed by MS/MS fragment assignment using AXIMA QIT.

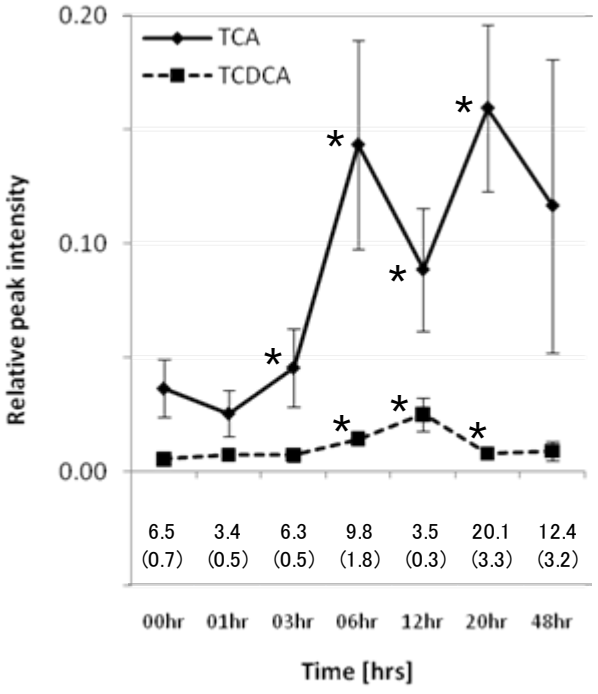
MS/MS fragment peaks indicated individual patterns by the vicinal hydroxyl group. Major and secondary fragment peak pattern suggested that MS/MS peaks on liver tissue was possible to TCA, not to other structural isomers.

Supplementary figure 6



Supplementary figure 6. MS spectra of TCA and other metabolite profile on liver section. Major MS spectra of TCA, UDP-N-acetyl glucosamine (UDP-N-AG) and phosphatidylethanolamine (PEs) were obtained from liver section at 0, 6, 12 and 20 hrs. At 12 hrs, ionization suppression effect occurred by large amount of signals such as m/z 762 possibly from PEs, for example appeared on surface of the liver reflecting massive necrosis.

Supplementary figure 7



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Supplementary figure 7. Time-dependent semi-quantitative profile of bile acids on liver section.
In order to evaluate the peak intensity for six bile acids at each time point, direct measurement was performed for eight matrix deposits onto each liver section. Matrix solution was micro dispensed using CHIP-1000 as described in manuscript. Eight deposit areas of m/z 514 and m/z 498 with 25% trim-mean were normalized by a peak area of NPA in same spectrum. TCA and TCDCA profile on liver section were shown at 0, 1, 3, 6, 12, 20, 48 hrs after CCl_4 administration.
Number shows the ratio of TCA/TCDCA intensity on liver.
* Significant change from previous time point of each group ($p < 0.05$)