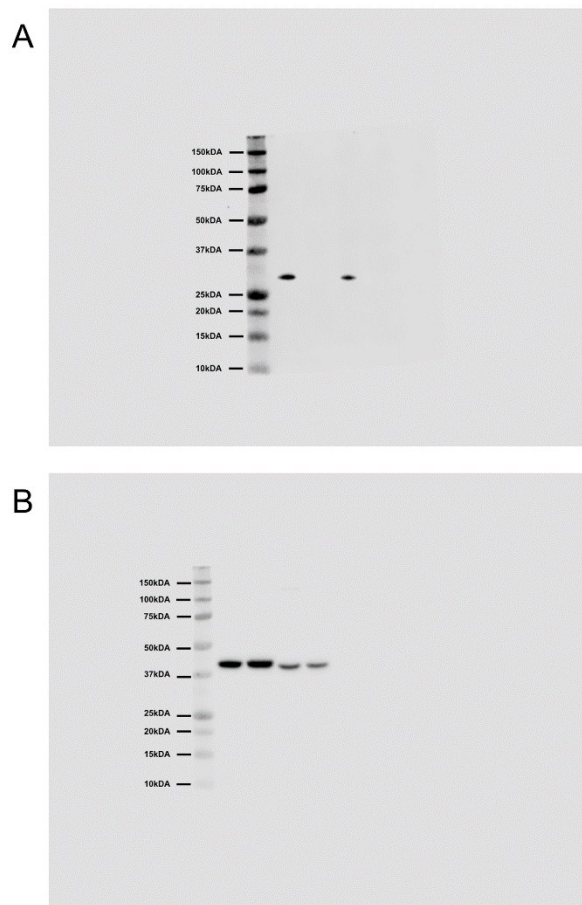
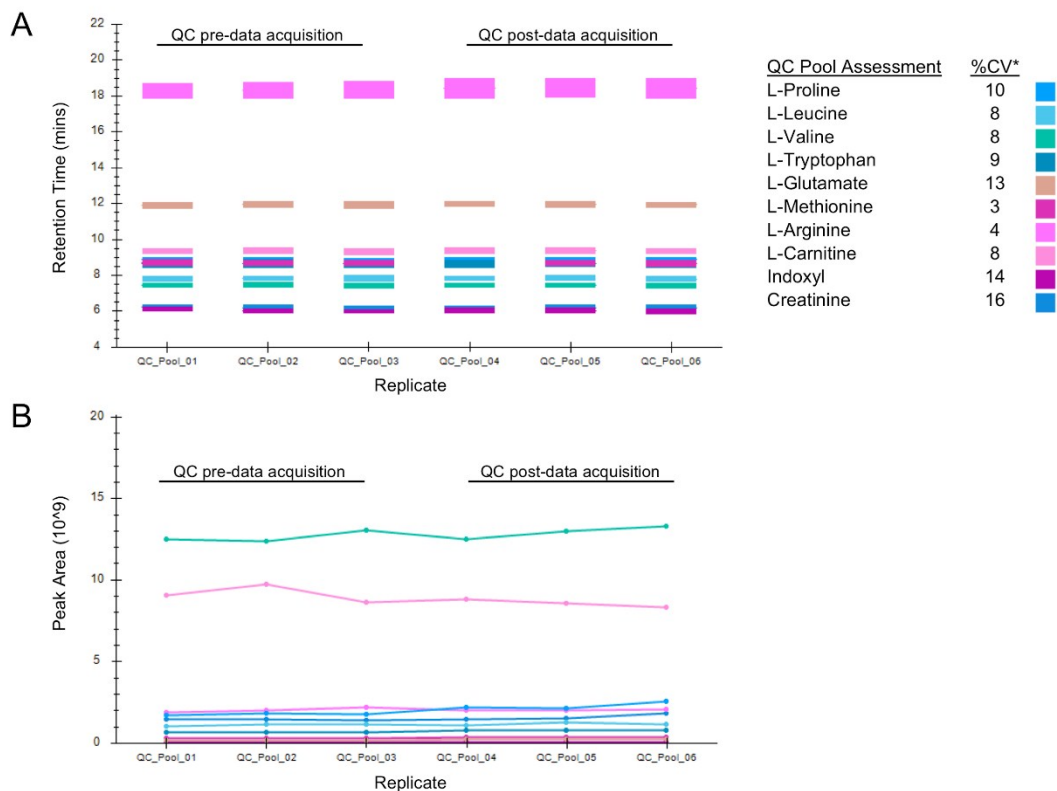


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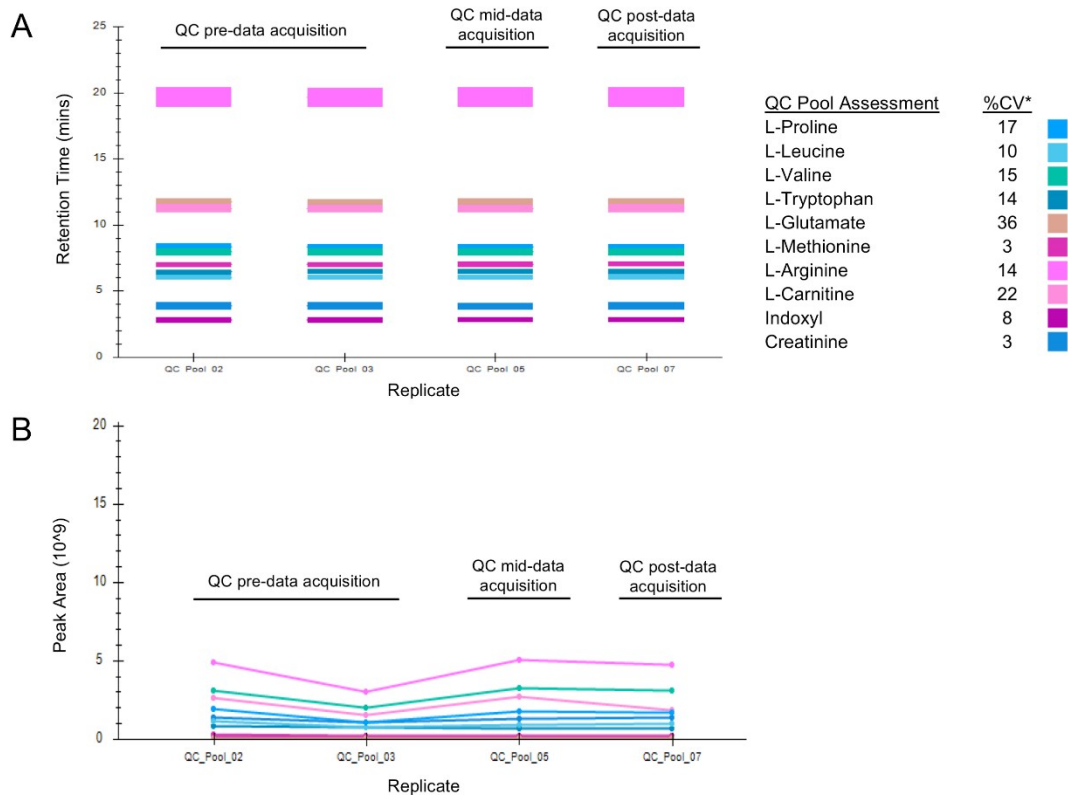


**Fig. S1:** Full immunoblots utilized for the generation of Fig. 1 to demonstrate loss of the specific Mblac1 immunoreactivity in KO mice. A. Full immunoblot for MBLAC1 1° antibody #4980. Left to right: cortex WT, cortex KO, liver WT, and liver KO. B. Full immunoblot for HRP-conjugated acting primary antibody. Left to right: cortex WT, cortex KO, liver WT, and liver KO.



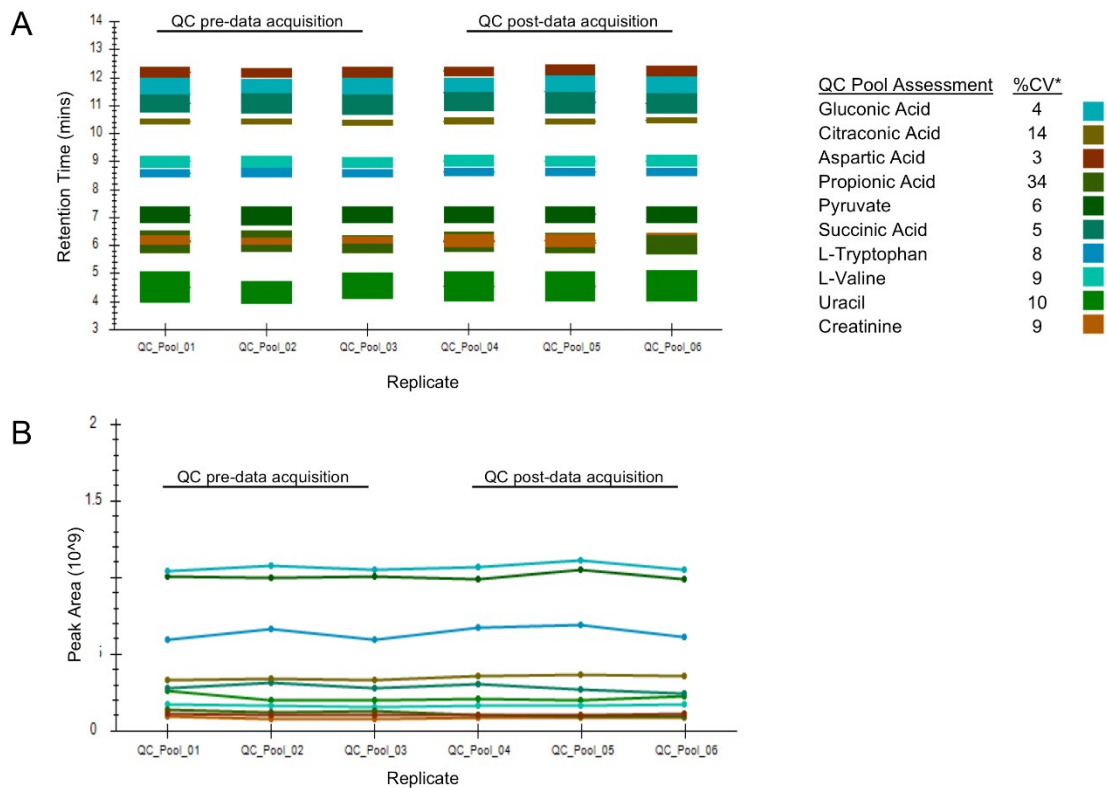
\* %CV was calculated within Progenesis QI by normalizing to all features.

**Fig. S2:** Comparison of ten endogenous molecules in replicate injections of a pooled sample for QC assessment prior to and after the experimental sample data acquisition for *HILIC-POS collection, discovery sample set*. (A) The retention time and (B) peak area for the ten endogenous compounds are reliable and reproducible (compound legend indicates respective %CVs). Figures were generated in Skyline software.



\* %CV was calculated within Progenesis QI by normalizing to all features.

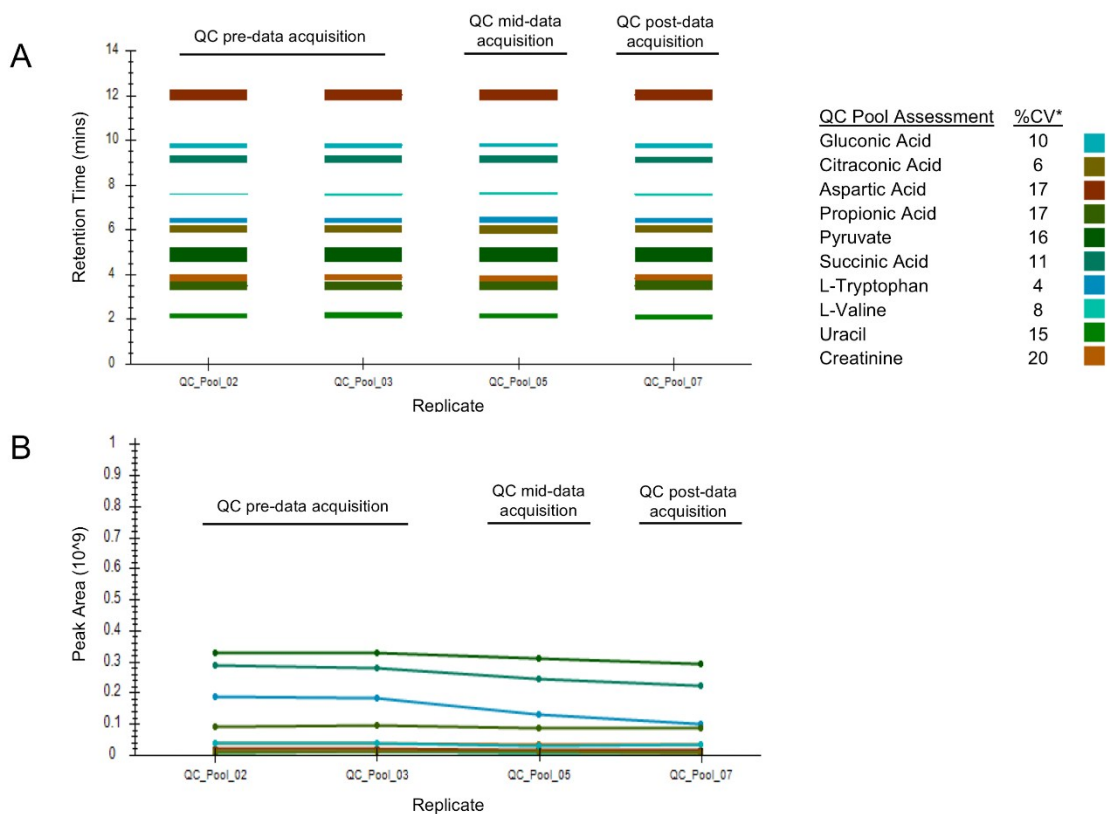
**Fig. S3:** Comparison of ten endogenous molecules in replicate injections of a pooled sample for QC assessment prior to, during, and after the experimental sample data acquisition for *HILIC-POS collection, validation sample set*. (A) The retention time and (B) peak area for the ten endogenous compounds are reliable and reproducible (compound legend indicates respective %CVs). Figures were generated in Skyline software.



\* %CV was calculated within Progenesis QI by normalizing to all features.

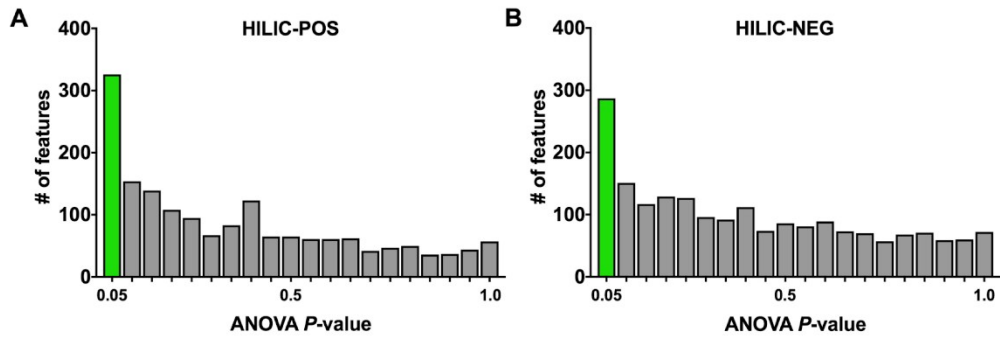
**Fig. S4:** Comparison of ten endogenous molecules in replicate injections of a pooled sample for QC assessment prior to and after the experimental sample data acquisition for *HILIC-NEG collection, discovery sample set*. (A) The retention time and (B) peak area for the ten endogenous compounds are reliable and reproducible (compound legend indicates respective %CVs). Figures were generated in Skyline software.

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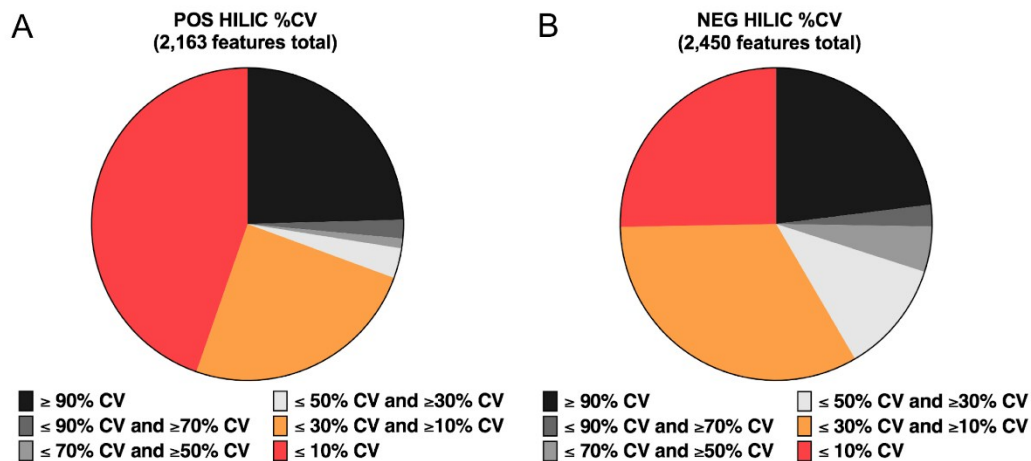


\* %CV was calculated within Progenesis Q1 by normalizing to all features.

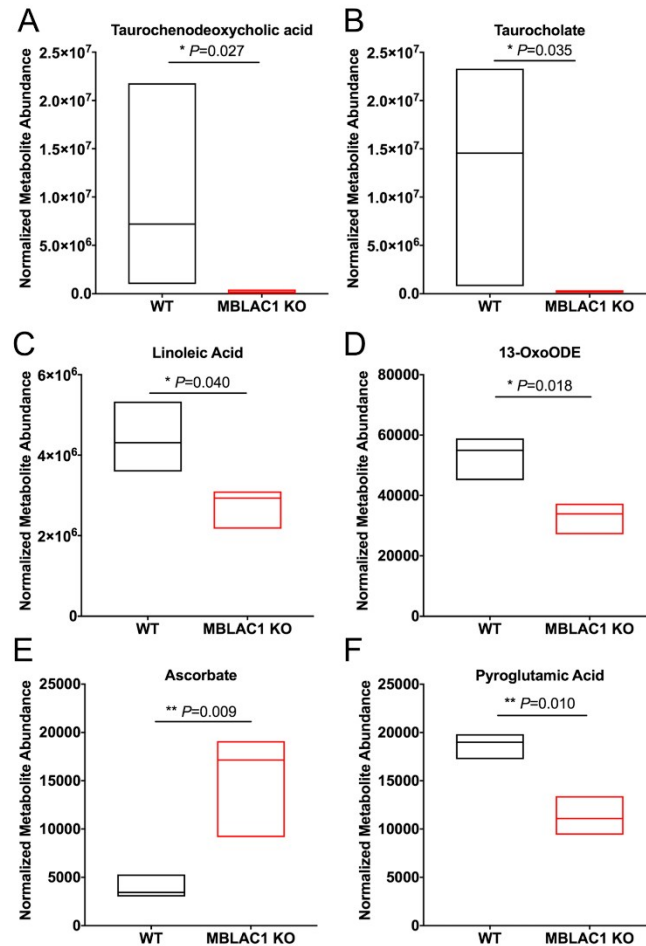
**Fig. S5:** Comparison of ten endogenous molecules in replicate injections of a pooled sample for QC assessment prior to, during, and after the experimental sample data acquisition for *HILIC-NEG collection, validation sample set*. (A) The retention time and (B) peak area for the ten endogenous compounds are reliable and reproducible (compound legend indicates respective %CVs). Figures were generated in Skyline software.



**Fig. S6:** Frequency histograms showing the distribution of nominal ANOVA  $P$ -values for the discovery datasets for A. HILIC-POS and B. HILIC-NEG. Green bar represents the total number of features declared to be significant with a nominal  $P$ -value  $\leq 0.05$ , 326 and 287 features for HILIC-POS and HILIC-NEG respectively.



**Fig. S7:** Features detected by untargeted UPLC-MS/MS approach binned according to minimum percent coefficient of variance (min %CV), A. HILIC-POS and B. HILIC-NEG. For both ion modes, about 60% of the detected features have a min %CV  $\leq 30\%$ .

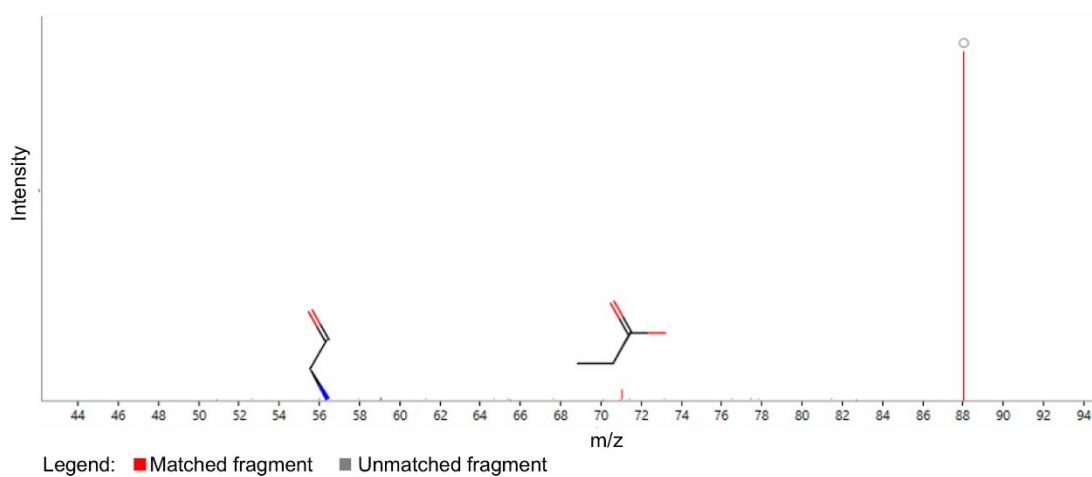


**Fig. S8:** Tentatively annotated features nominated in the discovery dataset as significantly impacted by loss of MBLAC1. A-B. Features within the taurine/primary bile acid pathway, A. taurochenodeoxycholic acid ( $P$ -value=0.027) and B. taurocholate ( $P$ -value=0.035) are both significantly reduced in MBLAC1 KO serum. C-D. Features within the linoleate metabolism pathway, C. linoleic acid ( $P$ -value=0.04) and D. 13-OxoODE ( $P$ -value=0.018). E-F. Features within the glutathione metabolism pathway, E. ascorbate ( $P$ -value=0.009) and F. pyroglutamic acid ( $P$ -value=0.01). Normalized metabolite abundances depicted in box plots with full range of variation (box with line at median with minimum-maximum), nominal  $P$ -value determined by Progenesis Q1 ANOVA analysis of the initial, discovery serum dataset.



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Experimental fragmentation data compared to spectral library match for level 2 (L2)  
putatively identified features in Table 1.

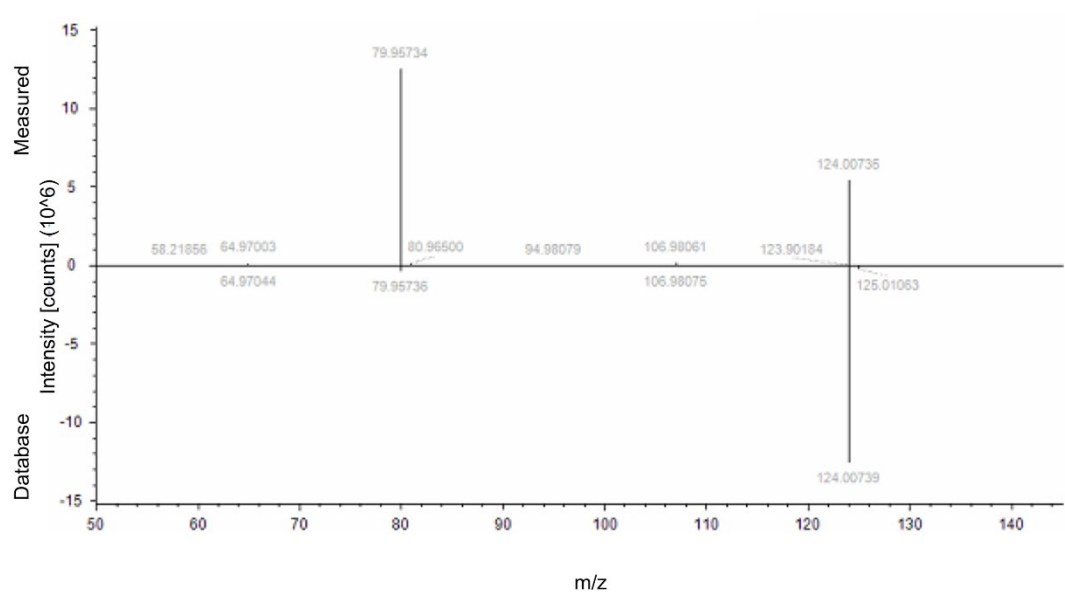


\* Instrument method scans low end of mass range at 70 Da, therefore we do not expect ions to be detected below 70 Da.

**Fig. S9:** Experimentally measured (shown above): Putative identification: **L-alanine**  
Progenesis Fragmentation Score: 17.7\*  
Reference (not shown) matched fragments in red): HMDB: **L-alanine**: C<sub>3</sub>H<sub>7</sub>NO<sub>2</sub>

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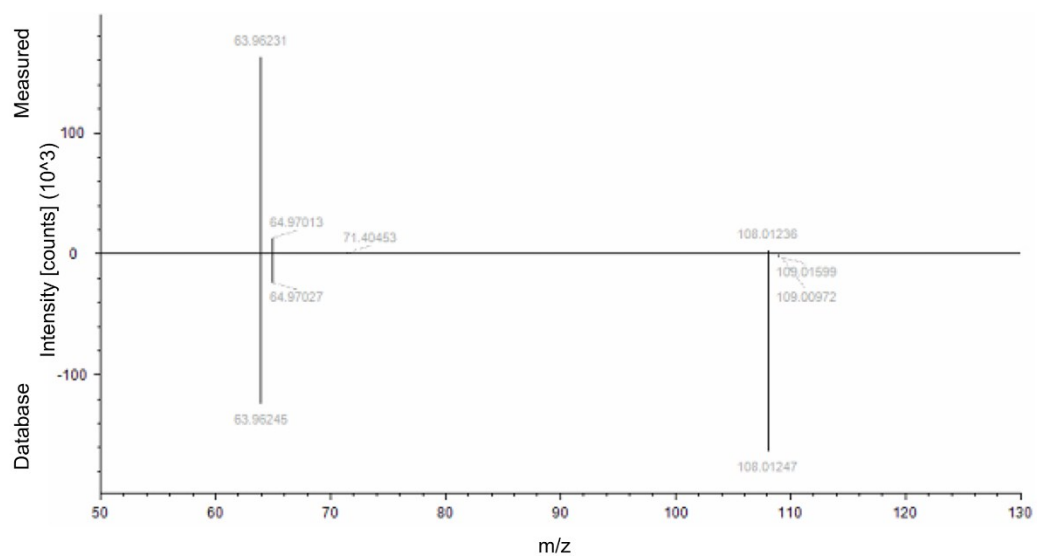
Experimental fragmentation data compared to spectral library match for level 2 (L2) putatively identified features in Table 1.



**Fig. S10:** Experimentally measured (Top): Putative identification: **Taurine**:  
Compound Discoverer Fragmentation Score: 92.4  
Reference (Bottom): mzCloud library: **Taurine**: C<sub>2</sub>H<sub>7</sub>NO<sub>3</sub>S

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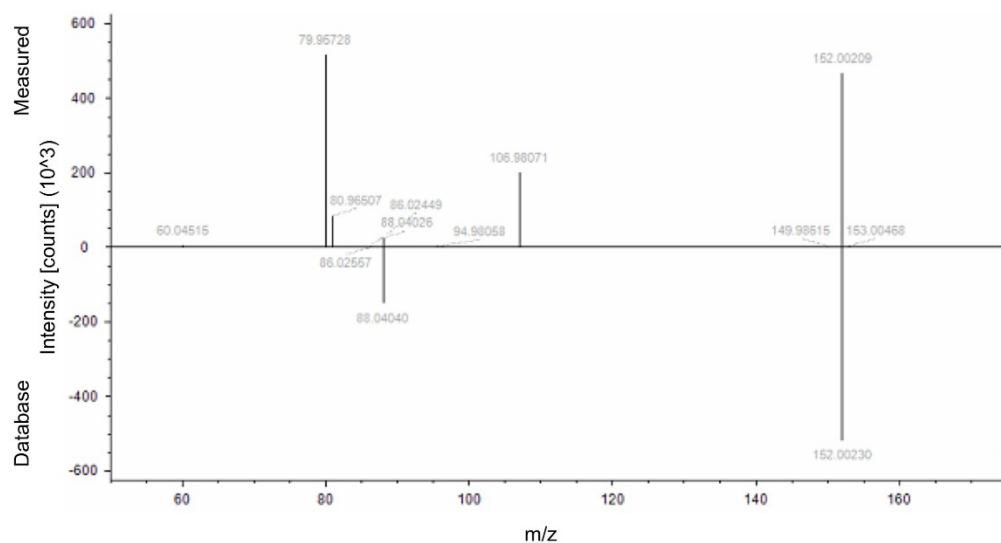
**Experimental fragmentation data compared to spectral library match for level 2 (L2) putatively identified features in Table 1.**



**Fig. S11:** Experimentally measured (Top); Putative identification: **Hypotaurine**:  
Compound Discoverer Fragmentation Score: 82.4  
Reference (Bottom): mzCloud library: **Hypotaurine**: C<sub>2</sub>H<sub>7</sub>NO<sub>2</sub>S

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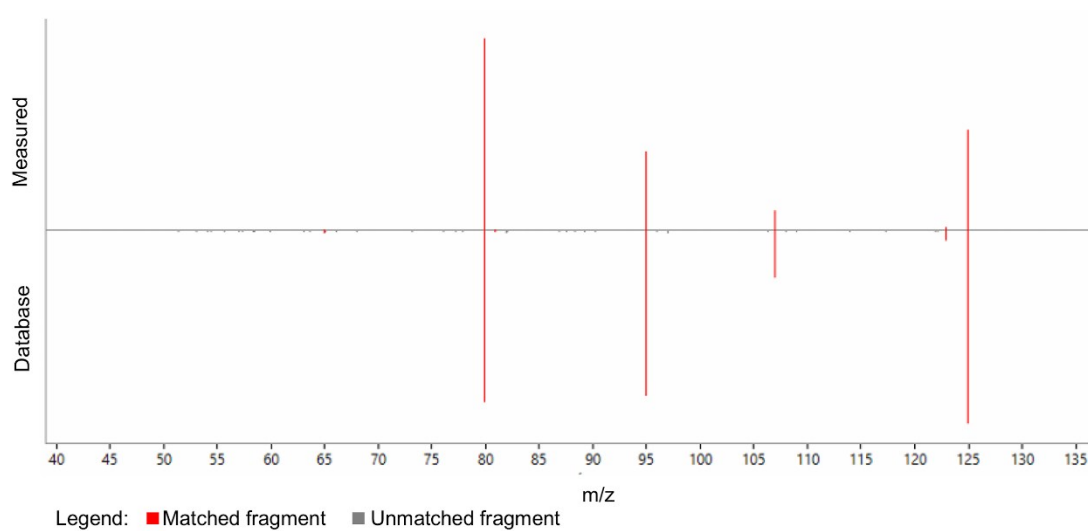
Experimental fragmentation data compared to spectral library match for level 2 (L2) putatively identified features in Table 1.



**Fig. S12:** Experimentally measured (Top): Putative identification: **3-Sulfinioalanine (syn: L-Cysteinesulfinic acid)**:  
Compound Discoverer Fragmentation Score: 60.1  
Reference (Bottom): mzCloud library: **L-Cysteinesulfinic acid**: C<sub>3</sub>H<sub>7</sub>NO<sub>4</sub>S

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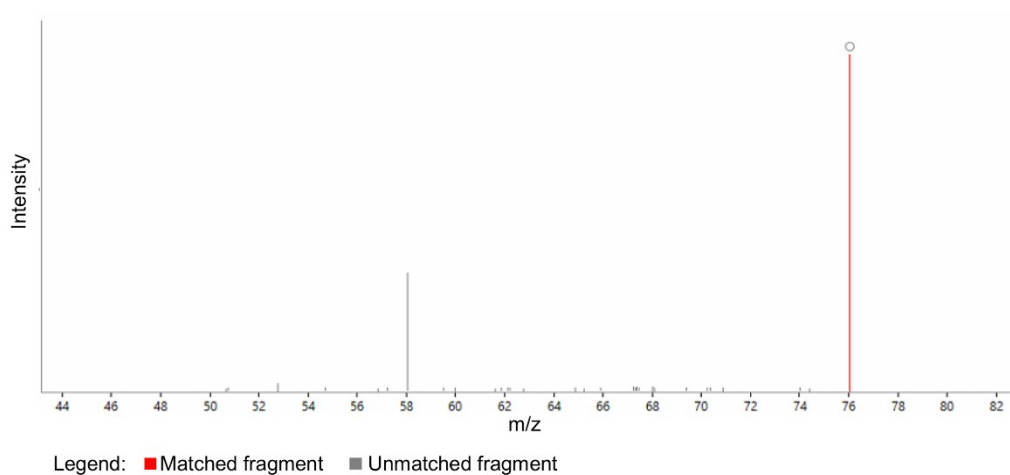
Experimental fragmentation data compared to spectral library match for level 2 (L2) putatively identified features in Table 1.



**Fig. S13:** Experimentally measured (Top): Putative identification: **2-Hydroxyethanesulfonate**: Progenesis Fragmentation Score: 92.6  
Reference (Bottom): In-house library: **2-Hydroxyethanesulfonate**: C<sub>2</sub>H<sub>6</sub>O<sub>4</sub>S

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Experimental fragmentation data compared to spectral library match for level 2 (L2) putatively identified features in Table 1.

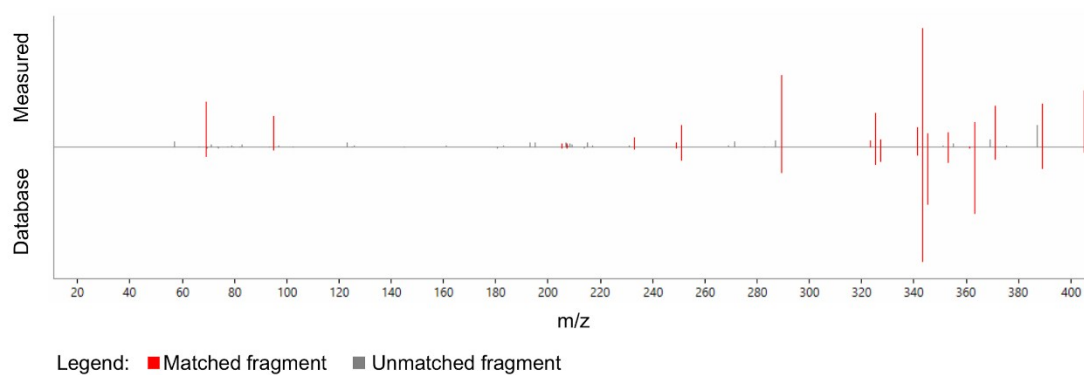


\* Instrument method scans low end of mass range at 70 Da, therefore we do not expect ions to be detected below 70 Da.

**Fig. S14:** Experimentally measured (shown above): Putative identification: **Glycine**  
Progenesis Fragmentation Score: 0.0\*  
Reference (not shown) matched fragments in red: HMDB: **Glycine**: C<sub>2</sub>H<sub>5</sub>NO<sub>2</sub>

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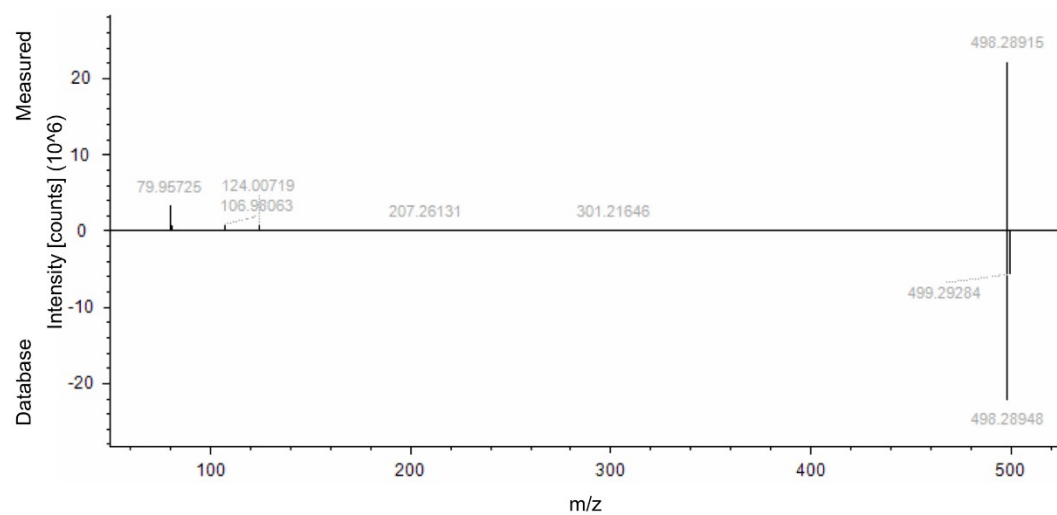
Experimental fragmentation data compared to spectral library match for level 2 (L2)  
putatively identified features in Table 1.



**Fig. S15:** Experimentally measured (Top): Putative identification: **Cholic Acid**:  
Progenesis Fragmentation Score: 82  
Reference (Bottom): In-house library: **Cholic Acid**: C<sub>24</sub>H<sub>40</sub>O<sub>5</sub>

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**Experimental fragmentation data compared to spectral library match for level 2 (L2)  
putatively identified features in Table 1.**

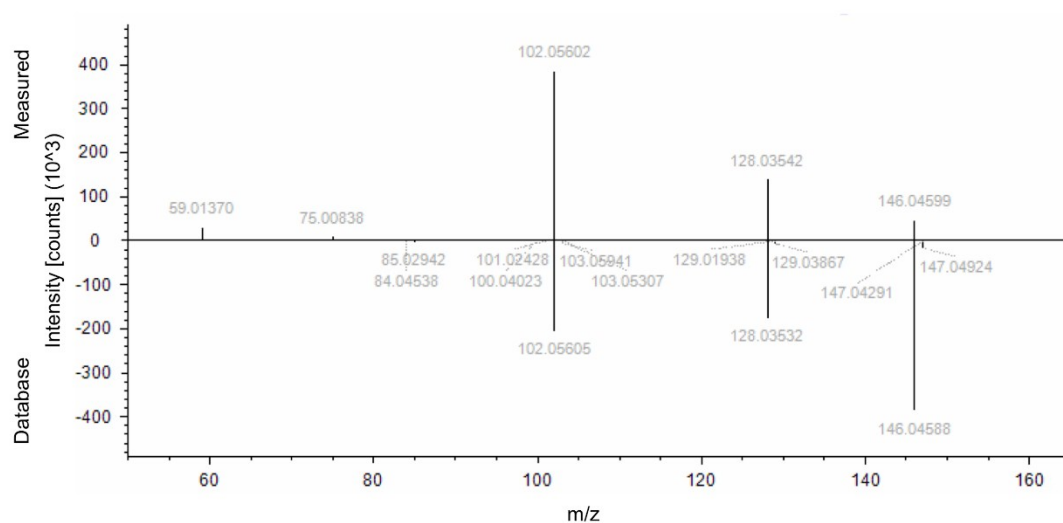


**Fig. S16:** Experimentally measured (Top): Putative identification: **Taurochenodeoxycholic acid**:  
Compound Discoverer Fragmentation Score: 81.3  
Reference (Bottom): mzCloud library: **Taurochenodeoxycholic acid**: C<sub>26</sub>H<sub>45</sub>NO<sub>6</sub>S



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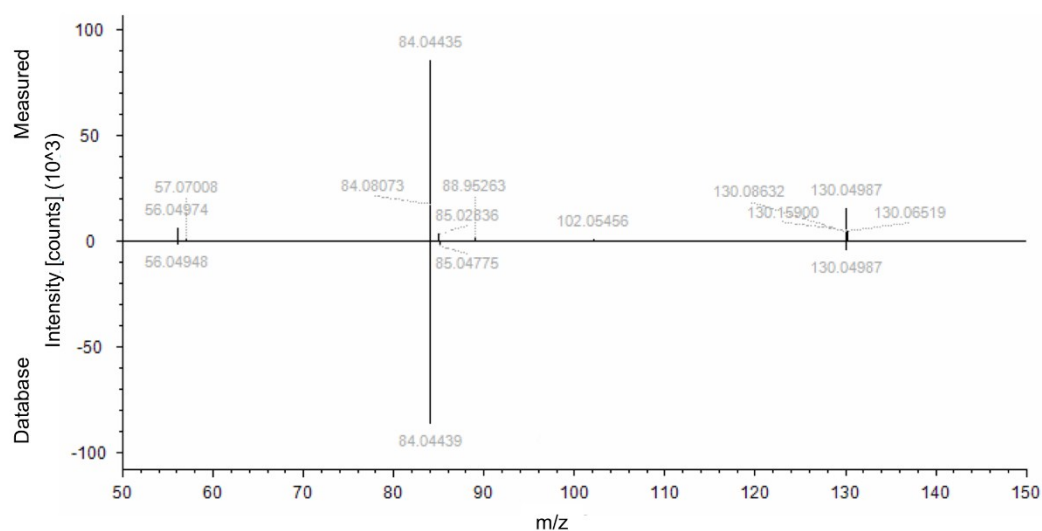
Experimental fragmentation data compared to spectral library match for level 2 (L2)  
putatively identified features in Table 1.



**Fig. S17:** Experimentally measured (Top); Putative identification: **L-Glutamate**:  
Compound Discoverer Fragmentation Score: 89.4  
Reference (Bottom): mzCloud library: **L-Glutamic acid**: C<sub>5</sub>H<sub>9</sub>NO<sub>4</sub>

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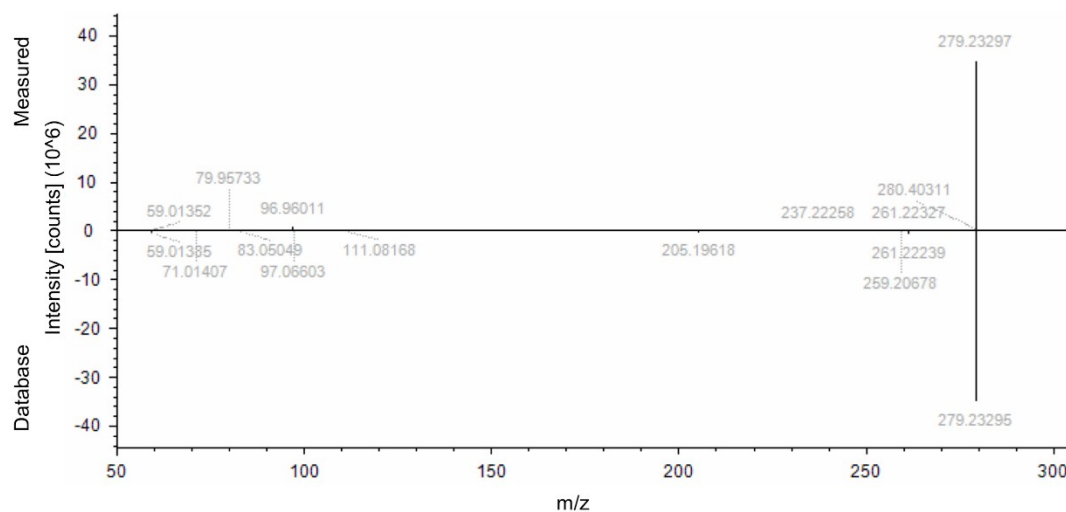
Experimental fragmentation data compared to spectral library match for level 2 (L2) putatively identified features in Table 1.



**Fig. S18:** Experimentally measured (Top): Putative identification: **Pyroglutamic acid**:  
Compound Discoverer Fragmentation Score: 83.0  
Reference (Bottom): mzCloud library: **Pyroglutamic acid**: C<sub>5</sub>H<sub>7</sub>NO<sub>3</sub>

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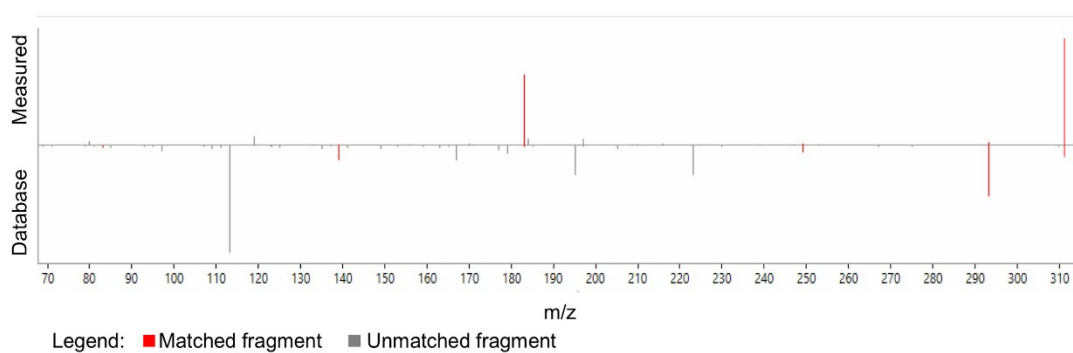
Experimental fragmentation data compared to spectral library match for level 2 (L2)  
putatively identified features in Table 1.



**Fig. S19:** Experimentally measured (Top): Putative identification: **Linoleic acid**:  
Compound Discoverer Fragmentation Score: 87.1  
Reference (Bottom): mzCloud library: **Linoleic acid**: C18H32O2

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Experimental fragmentation data compared to spectral library match for level 2 (L2)  
putatively identified features in Table 1.



**Fig. S20:** Experimentally measured (Top): Putative identification: **13(S)-HpODE**:  
Progenesis Fragmentation Score: 48.6  
Reference (Bottom): Metlin: **13(S)-HpODE**: C18H32O4

