Aspects of transition cow metabolomics - Part III: Alterations in the metabolome of liver and blood throughout the transition period in cows with different liver metabotypes.

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SUPPLEMENTAL MATERIAL

RESULTS

Univariate Analysis of Metabolomics Data

Amino acids. In liver as well as plasma samples for most AA a significant influence of the metabotype, the sampling day and/or their interaction was observed (Appendix Figure 1A). Almost throughout all AA in the liver an initial increase at 7 d p.p. and a subsequent decrease at 28 d p.p. was observed (exceptions: Gln and His with a.p. higher levels than p.p., and Orn exhibiting only an increase between 7 and 28 d p.p.), with generally lower concentrations in metabotype B and in some cases metabotype A (already present a.p.). In plasma AA lower a.p. levels and a subsequent p.p. increase at 7 d p.p. or 28 d p.p was observed. Exceptions form Gln, His, Ile, Leu and Orn with a.p. higher levels and a decrease at 7 d p.p, and subsequent increase at 28 d p.p., and Asn and Asp exhibiting an p.p. increase at 7 d p.p. compared to a.p., but decreased thereafter again at 28 d p.p. Also in blood lower AA concentrations were observed in metabotype B and in some cases metabotype A, compared to metabotype C.

Biogenic amines. Of the liver biogenic amines eight of ten showed a significant sampling day or metabotype ×sampling day effect (Appendix Figure 1B). A stand-alone effect of the metabotype was only observed in five of the metabolites. Overall in most metabolites (Creatinine, Dopamine, Serotonin, t4-OH-Pro, Taurine, SDMA) concentrations remained unaltered or increased from a.p. to 7 d p.p. and decreased thereafter at 28 d p.p. Alpha-AAA and Carnosine increased after calving, whereas Histamine and Ac-Orn remained unchanged. The pattern is however different when the metabotype are considered separately. In metabotype C only four, respectively two, metabolites were altered between 14 d a.p. and 7 d p.p. (alpha-AAA increasing and Serotonin, Creatinine and

SDMA decreasing) and p.p. between day 7 and 28 (Ac-Orn and Carnosine increasing), whereas in metabotype A and metabotype B the above described general effects were more prominent. From 17 measured biogenic amines, only five showed a significant effect of the metabotype, 13 were influenced by the sampling day and nine showed a metabotype ×sampling day interaction. The observed effects were very heterogenous with no alteration across the sampling days (c4-OH-Pro, Creatinine, DOPA, Putrescine), an increase from a.p. to 7 d p.p. and a subsequent decrease (Nitro-Tyr, t4-OH-Pro) or no alteration (Ac-Orn, Met-SO), a decrease from a.p. to 7 d p.p. and a subsequent increase (alpa-AAA, Carnosine, Kyn, SDMA) or no alteration (ADMA), no alterations between a.p. and 7 d p.p. and a subsequent increase (Serotonin) or decrease (Histamine and Sarcosine), or a continuous increase over the three sampling days (Taurine). Relevant influences of the metabotype were observed for plasma Carnosine and Creatinine, observing the above described effect of a p.p. decrease and subsequent increase in metabotype C, whereas in metabotype B and metabotype A no significant difference between the sampling days was observed. Furthermore, Kyn and Serotonin showed lower plasma concentrations ins metabotype B, compared to metabotype C. For the biogenic amines that were measured in liver as well as plasma alpha-AAA, Carnosine, t4-OH-Pro showed similar patterns over the sampling days, whereas for Ac-Orn, Creatinine, Histamine, Serotonin, Taurine and SDMA different patterns were observed.

The blood ratio of Kyn and Trp (**Kyn/Trp**) only showed a significant influence of the sampling day, with a decrease between 14 d a.p. (0.26 ± 0.1) to 7 d p.p. (0.13 ± 0.1) and a subsequent increase to 28 d p.p. (0.20 ± 0.1; LSMean ± SE, F-Test: metabotype : P = 0.493, Sampling Day (SD): P < 0.001, Treatment: P = 0.682, metabotype ×SD: P = 0.574, SD×Treatment: P = 0.830, metabotype ×Treatment: P = 0.333, metabotype ×SD×Treatment = 0.655, Dev: P = 0.284).

Acylcarnitines. Described in the main text.

Lysophosphatidylcholines. For almost all lysoPC an effect of the metabotype, the sampling day or their interaction was observed, with a pattern similar to the liver acylcarnitines (Appendix Figure 1E). In metabotype B generally lower concentrations were observed in both matrices. The concentrations increased from a.p. to p.p., with the lysoPC in the liver exhibiting a direct p.p. increase (at 7 d p.p.), whereas in plasma the higher levels were observed only 28 d p.p. An exception form plasma lysoPC a C14:0, C17:0, C20:4, C24:0, C26:0 and C28:0 which decreased at 7 d p.p. and increased thereafter again.

Phosphatidylcholines. Compared to the other metabolite groups, liver PC were much less influenced by the analyzed effects (Appendix Figure 1F and Appendix Figure 1G). Generally, the highest levels were observed in metabotype A at 7 d p.p., leading to a significant effect of the metabotype in 14 of the 75 metabolites. In the 31 metabolites influenced by the sampling day or its interaction with the metabotype, a p.p. increase was observed with three exceptions: PC aa C24:0, 26:0 and PC ae C40:1 exhibiting a p.p. decrease. In plasma all PC showed an influence of the sampling day with generally a p.p. increase, except for 14 metabolites which decreased after calving (PC aa C38:0, C38:1, C40:2, C40:3, C40:4, C42:1, C42:4, C42:5, C42:6, and PC ae C36:0, C38:1, C40:1, C42:1 and C42:2; Appendix Figure 1H and Appendix Figure 1I). In the 41 metabolites influenced by the metabotype or its interaction with the sampling day, generally lower concentrations in metabotype B compared to metabotype C were observed. Phosphatidylcholine aa C38:0 and PC ae C42:2 were lower a.p. in metabotype B compared to metabotype C.

Sphingomyelins. In the liver only five resp. six of twelve sphingomyelins were influenced by the metabotype, sampling time or their interaction (Appendix Figure 1J). As for acylcarnitines and lysoPC the sphingomyelins concentrations were generally lower in metabotype B. Further, generally lower concentrations a.p. with a p.p. step-wise increase was observed. Plasma sphingomyelins showed a different pattern. Only for one resp. four sphingomyelins a significant influence of the metabotype resp. an interaction metabotype×sampling day was observed, whereas the sampling day had a significant effect on almost all sphingomyelins. Also in plasma lower a.p. levels were present, however with a either comparable low or lower levels 7 d p.p. and a subsequent increase at 28 d p.p.

Hexoses. The hexoses in the liver were significantly influenced by the metabotype, with lower concentrations in metabotype A and metabotype B. In metabotype A a p.p. increase at 7 d p.p. and a subsequent decrease at 28 d p.p. was observed, whereas in metabotype B and metabotype C the concentrations were not altered significantly over the three sampling time points (Appendix Figure 1J). The plasma hexose concentrations remained unaltered over the three sampling days in metabotype A, decreased in metabotype B p.p. and decreased at 7 d p.p. with a subsequent increase at 28 d p.p. in metabotype C.

DISCUSSION

Biogenic Amines

Acetylornithine. Ac-Orn is an intermediate metabolite in the ornithine metabolism and thereby is connected to the urea cycle and gluconeogenesis. Only little is found on its metabolomic relevance in literature, especially in ruminants (Ghaffari et al., 2019b). Comparable to the study of Ghaffari et al. (2019b) we observed a p.p. increase in blood Ac-Orn concentration. In liver however, the p.p. concentrations only increased in metabotype C between 7 and 28 p.p.. Ghaffari et al. (2019b), Zhang et al. (2017) and Dervishi et al. (2018) observed an increase in blood Ac-Orn concentrations in highly lipomobilizing, ketotic or animals exhibiting retained placenta, respectively. This is in line with our study showing higher Ac-Orn concentrations in the metabotype B animals in the liver.

Carnosine. Carnosine is highly concentrated in muscle and brain tissue (Quinn et al., 1992), which has been confirmed by Ghaffari et al. (2019b), reporting carnosine as being the most abundant biogenic amine in muscle tissue of dairy cows. The systemic increase after calving in our study can therefore most likely be attributed to the post partum muscle tissue mobilization and is in line with the results of previous studies (Huber et al., 2016, Zhang et al., 2017, Ghaffari et al., 2019b). Boldyrev et al. (2013) hypothesize that skeletal muscle serves as a depot for carnosine, which is mobilized under certain circumstances, such as exercise, delivering a fast-accessible source of L-histidine or alanine. Transition cow physiology, characterized by a strong p.p. nutrient deficit, being compensated by massive tissue mobilization, supports this assumption. Furthermore, carnosine exhibits anti-oxidative properties (Quinn et al., 1992, Boldyrev et al., 2013). It can therefore be hypothesized that the higher p.p. systemic concentrations execute a protective function, in this period characterized by tissue degradative and pro-inflammatory processes. Ghaffari et al. (2019b) report cows with higher BCS exhibiting lower carnosine concentrations in muscle a.p., and a.p. as well as p.p. in blood. In this line Huber et al. (2016) show an association of elevated plasma concentrations of carnosine with increased productive lifespan. Also in our study, a different blood carnosine dynamic was observed in the different metabotypes, hinting towards a role of this metabolite transition cow health.

Creatinine. Creatinine is a breakdown product of creatine phosphate in muscle and is under normal circumstances produced a constant rate and due to its renal excretion used as an indicator for kidney function (Pasternack and Kuhlbäck, 1971, Perrone et al., 1992). In our study, similar to Ghaffari et al. (2019b), creatinine was the most abundant biogenic amine in blood. Many studies have reported alterations in blood creatinine concentrations across the transition period, with an initial p.p. increase and subsequent decrease (Graugnard et al., 2013, Pires et al., 2013, Osorio et al., 2014, Ghaffari et al., 2019b), suggesting its initial increase being an indicator for increased muscle catabolism during the NEB p.p. (Bruckmaier et al., 1998, Schröder and Staufenbiel, 2006, Pires et al., 2013), but also in heat-stressed animals (Fan et al., 2018). Ghaffari et al. (2019b) hypothesize that the initial p.p. increase and subsequent decrease of blood creatinine most likely reflects an altered kidney function, not being followed by in an increase in glomerular filtration rate upon the onset of lactation, citing Perrone et al. (1992) and Maltz and Silanikove (1996). Furthermore, referencing a work of Pires et al. (2013), showing lower plasma creatinine and a greater 3-methylhistidine to creatinine ratio in cows with low BCS as compared with medium and high BCS, pointing to less muscle mass but more intense mobilization of muscle protein in lean cows. Contrary to these studies, our results however show a decrease between a.p. to 7 d.p. and a subsequent increase in plasma in the metabotype C, whereas no alterations throughout the three sampling points was observed in metabotype A and metabotype B, and a decrease between 7 d and 28 d p.p. in the liver samples. We attribute this to a possible interaction with other confounding factors such as alimentation and exercise (Pasternack and Kuhlbäck, 1971, Perrone et al., 1992, Baxmann et al., 2008, Schären et al., 2016) which are altered when changing the environment from the dry cow to the fresh-cow pen.

DOPA and Dopamine. Dihydroxyphenylalanine or L-DOPA is formed by the conversion of tyrosine by the cytosolic enzyme tyrosine hydroxylase and is further decarboxylated to form dopamine (Elsworth and Roth, 1997). L-DOPA itself is not only a precursor of dopamine but also participates in a number of enzymatic reactions as well (Hornykiewicz, 2002). Dopamine is a neurotransmitter and a precursor to the catecholamines epinephrine and norepinephrine, but also has a role in various other metabolic and biological processes (e.g. sodium extraction and electrolyte balance; Drożak et al. (2005), Björklund and Dunnett (2007)). In regard to lactation physiology dopamine plays an important role in the suppression of the prolactin secretion (Fitzgerald and Dinan, 2008). Recent studies have given new insights on prolactin and dopamine function in ruminants, showing for example that the dopamine antagonist domperidone increases prolactin concentration and enhances milk production in dairy cows (Lacasse and Ollier, 2015, Lacasse et al., 2016). In our study DOPA concentrations in blood were not altered across sampling time points and remained relatively uninfluenced by the metabotype. In the liver however dopamine concentrations decreased after calving, indicating a role of liver dopamine in the peripartum and/or p.p. metabolism.

Histamine. Histamine is a short-acting amine and an important mediator in inflammatory processes (Wrenn et al., 1963, Wang et al., 2016). In dairy cows a systemic increase during metritis, mastitis, laminitis and endotoxemia, and its possible role in abomasal dislocation pathomechanisms have been described (Vermunt and Greenough, 1994, Plaizier et al., 2008, Wang et al., 2016, Al-Rawashdeh et al., 2017). Fuquay et al. (1969) describe an increase of plasma histamine shortly after calving and a subsequent decrease. This observation is similar to ours, observing a decrease between 7 d and 28 d p.p. and in line with the concept of an increase in pro-inflammatory processes in the peripartum period (Bradford et al., 2015, Drong et al., 2017b). We further observed no influence of the sampling day on liver histamine and no clear pattern regarding the metabotype (only higher histamine concentrations in the liver in metabotype A compared to metabotype B and C).

Kynurenine. Kynurenine is a metabolite of Trp and their ratio depicts the activity of the enzyme indoleamine 2,3-dioxygenase, which is increased during inflammatory processes (de Jong et al., 2009, Hüther et al., 2016, Bochniarz et al., 2018). Furthermore, Kyn and its degradation intermediates are associated with insulin resistance in humans (Oxenkrug, 2013). Recent studies in dairy cows describe a connection between the Kyn-Trp metabolism and ketosis (Zhang et al., 2017), increased production life span (Huber et al., 2016), mastitis (Bochniarz et al., 2018) and endotoxemia (Humer et al., 2018). Furthermore, Drong et al. (2017a) observed an increased Kyn-Trp ratio shortly after calving and Ghaffari et al. (2019b) describe no influence of the sampling day but a significantly higher ratio in high BCS animals 84 d p.p. Furthermore, Ghaffari et al. (2019b) observed an initial decrease and a subsequent increase after calving until 84 d p.p. of Kyn itself. This is in line with our study showing a decrease between 14 d a.p. and 7 d p.p. and a subsequent increase until 28 d p.p. Additionally, we observed lower Kyn concentrations in plasma in metabotype B than metabotype C. The Kyn-Trp ratio however remained unaltered by the metabotype and only showed a decrease from a.p. to 7 d p.p. with a subsequent increase. This data is in line with the studies of Drong et al. (2017a) and Huber et al. (2016), showing a marked increase from a.p. to 3 d p.p., followed by a strong decrease at 7 d p.p. and a subsequent increase at 21 d p.p., but does not confirm their and Ghaffari et al. (2019b)´s observation of an effect of the health status (lower in animals with a lower NEB, longer production life span and lipomobilization) on the blood Kyn/Trp. No Kyn concentrations above the lower limit of quantification (LLQ) were observed in liver samples.

Methionine sulfoxide and nitrotyrosine. Met-SO and Nitro-Tyr are both indicators for oxidative stress (Boschi-Muller et al., 2008, Luo and Levine, 2009, Cigliano et al., 2014). Both metabolites were only detected in plasma samples in our study and increased after calving, uninfluenced of the metabotype. As discussed with some of the other biogenic amines, the transition period is characterized by pro-inflammatory processes and increased oxidative stress. The increase of these metabolites in this period therefore is plausible and complemented by a study of Cigliano et al. (2014) showing higher levels of plasma concentration of protein-bound carbonyls, Nitro-Tyr, and lipid hydroperoxides in early lactating cows.

Polyamines. The polyamines putrescine, spermidine and spermine are found in plants, microorganisms and animal cells. They are responsible for specific (pungent) odours, but also play a key role in different biological processes, such as cell division (Igarashi and Kashiwagi, 2010, Hussain et al., 2016). Putrescine is formed from Orn and converted into spermidine, which is then used so synthesize spermine (Igarashi and Kashiwagi, 2010). Ghaffari et al. (2019b) report increased blood concentrations of putrescine in higher conditioned cows at 84 d p.p., and an increase in blood spermine concentrations at 21 d p.p. and higher levels of muscle spermidine p.p. (3, 21 and 84 d p.p.), irrespective of the body conditioning. The authors attribute the latter to the p.p. anabolic state. Furthermore, Huber et al. (2016) show an association of elevated plasma concentrations of spermidine with increased productive lifespan. In our trial putrescine was only detected in the blood samples and was uninfluenced by the sampling and metabotype.

Sarcosine. Sarcosine is an intermediate in the generation and degradation of glycine (Cernei et al., 2013). Only little is found in the literature on its specific role as a biological marker in metabolomics studies, especially in regard to ruminants. Humer et al. (2016) report no alterations in blood sarcosine levels in dairy cows experiencing high lipomobilization around parturition, whereas Zhang et al. (2017) observed a 3.4 and 4.4-fold change in blood sarcosine concentrations in ketosis vs. control cows at 4 and 8 weeks p.p., respectively. Furthermore, in the study of Huber et al. (2016) an association with sarcosine and an increased productive lifespan is described. In our study no association with the nutritional status (the metabotype) and sarcosine levels was observed, but the blood concentrations decreased between 7 and 28 d p.p. in all animals. In a study by Cabrita et al. (2011), investigating the effects of dietary protein concentration and balance of absorbable AA on dairy cow production and metabolome a significant influence of the main protein source in the ration (feeding a concentrate of either mainly soybean meal or a mixture of corn byproducts, dried corn distillers grains, and corn gluten meal) on blood sarcosine concentration was observed. The heterogenous results between studies investigating transition cow pathophysiology and the results of the latter study suggest that systemic sarcosine levels are influenced by different metabolic processes as well as nutritional factors most likely exhibiting various interactions.

Hydroxyproline. The AA Pro and its derivative OH-Pro constitute one-third of the AA in collagen proteins and play a key role in tissue stability. Hydroxyproline is formed by the post-translational hydroxylation of proline under influence of hypoxia, collagen and other protein degradation (Wu et al., 2011). In the transition cow a p.p. systemic increase is observed most likely due to uterus involution and tissue mobilization (Kaidi et al., 1991, Ghaffari et al., 2019b), which is also reflected in our data. Ghaffari et al. (2019b) observed higher OH-Pro concentrations in a.p. muscle samples (d -49) of higher conditioned animals, followed by increased blood OH-Pro concentrations p.p. (d +3, 21 and 84, also observed by Ghaffari et al. (2019a)).

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TABLES AND ILLUSTRATIONS

Table S1A. Acylcarnitines, AA and biogenic amines analyzed by the AbsoluteIDQ p180 kit

Abbreviation	**Metabolite**	**Abbreviation**	**Metabolite**
		Acylcarnitines	
C0	Carnitine	C10:1	Decenoylcarnitine
C2	Acetylcarnitine	C10:2	Decadienylcarnitine
C3	Propionylcarnitine	C12	Dodecanoylcarnitine
C3:1	Propenoylcarnitine	C12:1	Dodecenoylcarnitine
C3-OH	Hydroxypropionylcarnitine	C12-DC	Dodecanedioylcarnitine
C4	Butyrylcarnitine	C14	Tetradecanoylcarnitine
C4:1	Butenoylcarnitine	C14:1	Tetradecenoylcarnitine
C4-OH (C3-DC)	Hydroxybutyrylcarnitine	C14:1-OH	Hydroxytetradecenoylcarnitine
C5	Valerylcarnitine	C14:2	Tetradecadienylcarnitine
C5:1	Tiglylcarnitine	C14:2-OH	Hydroxytetradecadienylcarnitine
C5:1-DC	Glutaconylcarnitine	C16	Hexadecanoylcarnitine
C5-DC (C6-OH)	Glutarylcarnitine (Hydroxyhexanoylcarnitine)	C16:1	Hexadecenoylcarnitine
C5-M-DC	Methylglutarylcarnitine	C16:1-OH	Hydroxyhexadecenoylcarnitine
C5-OH (C3-DC-M)	Hydroxyvalerylcarnitine (Methylmalonylcarnitine)	C16:2	Hexadecadienylcarnitine
C6 (C4:1-DC)	Hexanoylcarnitine (Fumarylcarnitine)	C16:2-OH	Hydroxyhexadecadienylcarnitine
C6:1	Hexenoylcarnitine	C16-OH	Hydroxyhexadecanoylcarnitine
C7-DC	Pimelylcarnitine	C18	Octadecanoylcarnitine
C8	Octanoylcarnitine	C18:1	Octadecenoylcarnitine
C8:1	Octenoylcarnitine	C18:1-OH	Hydroxyoctadecenoylcarnitine
C9	Nonanoylcarnitine	C18:2	Octadecadienylcarnitine
C10	Decanoylcarnitine		
		Amino Acids	
Ala	Alanine	Lys	Lysine
Arg	Arginine	Met	Methionine
Asn	Asparagine	Orn	Ornithine
Asp	Aspartate	Phe	Phenylalanine
Cit	Citrulline	Pro	Proline
Gln	Glutamine	Ser	Serine
Glu	Glutamate	Thr	Threonine
Gly	Glycine	Trp	Tryptophan
His	Histidine	Tyr	Tyrosine
Ile	Isoleucine	Val	Valine
Leu	Leucine		

Table S1A. continued

Abbreviation	**Metabolite**	**Abbreviation**	**Metabolite**
		Biogenic Amines	
Ac-Orn	Acetylornithine	PEA	Phenylethylamine
ADMA	Asymmetric dimethylarginine	cis-OH-Pro	cis-4-Hydroxyproline
alpha-AAA	alpha-Aminoadipic acid	trans-OH-Pro	trans-4-Hydroxyproline
Carnosine	Carnosine	Putrescine	Putrescine
Creatinine	Creatinine	Sarcosine	Sarcosine
DOPA	DOPA	SDMA	Symmetric dimethylarginine
Dopamine	Dopamine	Serotonin	Serotonin
Histamine	Histamine	Spermidine	Spermidine
Kynurenine	Kynurenine	Spermine	Spermine
Met-SO	Methionine sulfoxide	Taurine	Taurine
Nitro-Tyr	Nitrotyrosine		

Table S1B. Glycerophospholipids, sphingolipids and hexoses analyzed by the AbsoluteIDQ p180 kit

Glycerophospholipids, PC = phosphatidylcholine			
lysoPC a C14:0	PC aa C34:1	PC aa C42:0	PC ae C38:2
lysoPC a C16:0	PC aa C34:2	PC aa C42:1	PC ae C38:3
lysoPC a C16:1	PC aa C34:3	PC aa C42:2	PC ae C38:4
lysoPC a C17:0	PC aa C34:4	PC aa C42:4	PC ae C38:5
lysoPC a C18:0	PC aa C36:0	PC aa C42:5	PC ae C38:6
lysoPC a C18:1	PC aa C36:1	PC aa C42:6	PC ae C40:1
lysoPC a C18:2	PC aa C36:2	PC ae C30:0	PC ae C40:2
lysoPC a C20:3	PC aa C36:3	PC ae C30:1	PC ae C40:3
lysoPC a C20:4	PC aa C36:4	PC ae C30:2	PC ae C40:4
lysoPC a C24:0	PC aa C36:5	PC ae C32:1	PC ae C40:5
lysoPC a C26:0	PC aa C36:6	PC ae C32:2	PC ae C40:6
lysoPC a C26:1	PC aa C38:0	PC ae C34:0	PC ae C42:0
lysoPC a C28:0	PC aa C38:1	PC ae C34:1	PC ae C42:1
lysoPC a C28:1	PC aa C38:3	PC ae C34:2	PC ae C42:2
PC aa C24:0	PC aa C38:4	PC ae C34:3	PC ae C42:3
PC aa C26:0	PC aa C38:5	PC ae C36:0	PC ae C42:4
PC aa C28:1	PC aa C38:6	PC ae C36:1	PC ae C42:5
PC aa C30:0	PC aa C40:1	PC ae C36:2	PC ae C44:3
PC aa C30:2	PC aa C40:2	PC ae C36:3	PC ae C44:4
PC aa C32:0	PC aa C40:3	PC ae C36:4	PC ae C44:5
PC aa C32:1	PC aa C40:4	PC ae C36:5	PC ae C44:6
PC aa C32:2	PC aa C40:5	PC ae C38:0	
PC aa C32:3	PC aa C40:6	PC ae C38:1	
Sphingolipids, SM = sphingomyelin			
SM (OH) C14:1	SM C18:0	SM (OH) C22:1	SM (OH) C24:1
SM C16:0	SM C18:1	SM (OH) C22:2	SM C26:0
SM C16:1	SM C20:2	SM C24:0	SM C26:1
SM (OH) C16:1	SM C22:3	SM C24:1	
Monosaccharides			
Sum of Hexoses (including Glucose)			

		F-Test			LSMeans: Metabotype			LSMeans: Sampling Day		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp
Liver	Ala	**0.009**	**0.000**	**0.000**	3680 A	2752 B	3542 A	3462 B	4331 A	2181 C
Liver	Asn	**0.000**	**0.000**	**0.000**	435 A	282 B	430 A	367 B	569 A	211 C
Liver	Cit	**0.000**	**0.000**	**0.000**	174 A	100 B	101 B	103 B	193 A	78 B
Liver	Gln	0.470	**0.000**	0.621	1605	1676	1728	1862 A	1632 B	1515 B
Liver	Glu	**0.027**	**0.000**	**0.000**	7343 AB	6361 B	7282 A	6930 B	8157 A	5900 B
Liver	Gly	**0.000**	**0.000**	0.187	4593 B	4716 B	5862 A	3582 C	6721 A	4869 B
Liver	His	0.367	**0.000**	**0.018**	292	282	301	332 A	276 B	266 B
Liver	Ile	**0.000**	**0.000**	**0.000**	109 B	93 B	134 A	103 B	124 A	110 B
Liver	Leu	**0.000**	**0.000**	**0.000**	184 B	159 B	250 A	182 B	237 A	175 B
Liver	Lys	**0.000**	**0.000**	**0.002**	84 B	66 B	117 A	87 B	111 A	70 B
Liver	Met	**0.000**	**0.000**	**0.000**	38 B	32 B	53 A	34 B	59 A	30 B
Liver	Orn	**0.001**	**0.000**	**0.041**	190 AB	162 B	219 A	178 B	176 B	217 A
Liver	Phe	**0.000**	**0.000**	**0.000**	63 B	55 B	96 A	62 B	93 A	59 B
Liver	Pro	**0.000**	**0.000**	0.075	157 B	151 B	212 A	133 C	220 A	167 B
Liver	Ser	0.188	**0.000**	0.212	737	845	937	798 B	1036 A	683 B
Liver	Thr	**0.000**	**0.000**	**0.000**	538 A	310 B	521 A	425 B	617 A	328 C
Liver	Trp	**0.000**	0.124	**0.000**	19.8 B	17.7 B	24.0 A	19.4	21.1	21.1
Liver	Tyr	**0.000**	**0.000**	**0.001**	58 B	51 B	84 A	55 B	82 A	55 B
Liver	Val	**0.000**	**0.000**	**0.001**	197 B	176 B	245 A	192 B	228 A	198 B
Plasma	Ala	**0.002**	**0.001**	**0.000**	173 AB	164 B	192 A	166 B	166 B	197 A
Plasma	Arg	**0.045**	**0.000**	**0.003**	48 AB	46 B	52 A	47 B	43 C	56 A
Plasma	Asn	0.246	**0.000**	**0.000**	58	52	52	19 C	116 A	27 B
Plasma	Asp	**0.002**	**0.001**	**0.002**	4.3 B	5.9 B	8.8 A	4.9 B	9.3 A	4.7 B
Plasma	Cit	0.136	**0.000**	**0.001**	56	53	60	51 B	48 B	71 A
Plasma	Gln	**0.014**	**0.000**	**0.016**	239 B	243 B	270 A	270 A	218 B	263 A
Plasma	Glu	**0.012**	0.577	**0.039**	63 A	51 B	55 AB	57	57	54
Plasma	Gly	0.322	**0.000**	**0.004**	365	366	395	266 B	418 A	442 A
Plasma	His	0.920	**0.000**	**0.001**	46	45	46	51 A	42 B	45 AB
Plasma	Ile	0.603	**0.000**	0.629	95	83	98	92 AB	75 B	108 A
Plasma	Leu	0.492	**0.003**	0.484	117	98	99	99 A	87 B	128 AB
Plasma	Lys	0.185	**0.003**	**0.008**	65	63	68	58 B	66 A	71 A
Plasma	Met	**0.000**	**0.000**	**0.000**	12 B	13 B	16 A	3 B	19 A	19 A
Plasma	Orn	**0.015**	**0.000**	**0.001**	26 AB	25 B	28 A	31 A	19 B	29 A
Plasma	Phe	**0.000**	**0.002**	**0.030**	36 B	41 B	45 A	37 B	41 A	44 A
Plasma	Pro	**0.000**	**0.000**	**0.000**	55 B	54 B	65 A	46 C	58 B	70 A
Plasma	Ser	0.110	**0.000**	**0.000**	73	69	78	62 B	78 A	80 A
Plasma	Thr	**0.001**	**0.000**	**0.000**	63 A	51 B	62 A	53 B	47 B	75 A
Plasma	Trp	**0.011**	**0.000**	**0.016**	32 AB	29 B	34 A	30 B	27 C	39 A
Plasma	Tyr	**0.048**	**0.000**	0.084	37 B	40 AB	42 A	38 B	33 C	48 A
Plasma	Val	**0.009**	**0.000**	0.051	154 B	159 B	179 A	170 A	140 B	183 A

		LSMeans: Metabotype*Sampling Day								
		Metabotype A			Metabotype B			Metabotype C		
	Metabolite	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Liver	Ala	1781 C	6746 A	2512 BC	2283 C	4242 B	1733 C	6323 A	2004 C	2299 C
Liver	Asn	178 CD	910 A	218 CD	207 CD	478 B	159 D	715 A	319 BC	257 C
Liver	Cit	67 CDE	340 A	114 CD	57 DE	181 B	62 E	185 BC	58 DE	60 E
Liver	Gln	1846	1485	1483	1895	1666	1468	1844	1745	1595
Liver	Glu	5962 CD	9947 A	6119 BCD	6008 CD	7758 ABC	5318 D	8819 AB	6764 BCD	6261 CD
Liver	Gly	2769	6678	4332	3652	6001	4495	4324	7483	5779
Liver	His	310 ABC	277 BC	289 ABC	355 A	258 C	232 C	332 AB	294 ABC	278 C
Liver	Ile	88 E	137 AB	103 CDE	99 DE	87 E	94 DE	120 BCD	149 A	134 ABC
Liver	Leu	139 C	270 AB	142 C	169 C	162 C	147 C	237 AB	278 A	235 B
Liver	Lys	73 BCD	129 AB	51 D	79 BCD	68 CD	51 D	108 ABC	135 A	107 ABC
Liver	Met	24 EF	69 AB	22 EF	29 DEF	42 CDE	25 F	50 BC	66 A	44 CD
Liver	Orn	169 BC	192 ABC	210 ABC	173 BC	136 C	176 BC	191 BC	200 B	266 A
Liver	Phe	43 DE	98 AB	46 DE	55 DE	64 CD	47 E	88 B	117 A	83 BC
Liver	Pro	105	219	146	126	176	152	167	266	202
Liver	Ser	641	953	616	909	1006	619	845	1150	815
Liver	Thr	200 BC	1044 A	370 B	262 BC	465 B	203 C	813 A	341 BC	410 B
Liver	Trp	18.0 CD	21.9 ABC	19.3 BCD	18.8 CD	15.1 D	19.3 CD	21.2 BC	26.2 A	24.6 AB
Liver	Tyr	40 D	90 AB	43 D	49 D	57 CD	46 D	76 BC	100 A	75 BC
Liver	Val	166 CD	247 AB	178 CD	183 BCD	170 D	174 CD	227 ABC	265 A	242 A
Plasma	Ala	150 C	181 BC	188 ABC	160 BC	167 BC	165 BC	189 B	149 C	239 A
Plasma	Arg	47 BC	45 BC	52 ABC	45 BC	43 BC	51 ABC	49 B	40 C	66 A
Plasma	Asn	19 D	135 A	22 CD	19 D	116 AB	20 D	20 D	97 B	40 C
Plasma	Asp	4.9 BC	6.8 ABC	1.1 C	5.6 BC	8.4 ABC	3.6 C	4.3 C	12.6 A	9.3 AB
Plasma	Cit	50 BC	54 BC	65 ABC	51 BC	45 C	64 AB	51 BC	46 C	83 A
Plasma	Gln	262 ABC	216 BC	237 ABC	258 AB	223 BC	248 ABC	291 A	215 C	304 A
Plasma	Glu	58 AB	73 A	57 AB	55 AB	52 AB	47 B	58 AB	48 B	57 AB
Plasma	Gly	237 D	449 AB	409 ABC	264 CD	426 AB	409 AB	296 CD	379 B	509 A
Plasma	His	50 A	44 AB	44 AB	51 A	45 AB	40 AB	51 A	38 B	51 A
Plasma	Ile	85	76	125	81	73	94	111	76	107
Plasma	Leu	96	81	173	99	92	104	103	89	106
Plasma	Lys	58 B	68 AB	69 AB	55 B	68 AB	64 AB	62 B	62 B	81 A
Plasma	Met	1 C	18 B	15 B	2 C	21 AB	17 B	6 C	18 B	25 A
Plasma	Orn	31 AB	19 C	27 ABC	29 AB	19 C	26 BC	32 AB	18 C	35 A
Plasma	Phe	35 B	38 B	36 B	37 B	42 B	43 AB	40 B	42 B	52 A
Plasma	Pro	45 C	61 B	61 BC	44 C	57 B	60 BC	50 BC	56 B	89 A
Plasma	Ser	59 C	87 AB	73 ABC	61 C	78 ABC	69 BC	66 BC	70 BC	97 A
Plasma	Thr	53 BCD	55 CD	81 AB	52 CD	45 CD	55 BCD	54 C	42 D	89 A
Plasma	Trp	30 BC	29 BC	38 AB	28 BC	25 C	35 B	31 BC	26 C	45 A
Plasma	Tyr	38	32	41	37	35	48	39	33	55
Plasma	Val	173	131	158	163	141	173	173	147	217

Figure S1A.

		F-Test			LSMeans																	
					Metabotype			Sampling Day			Metabotype*Sampling Day											
											Metabotype A			Metabotype B			Metabotype C					
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp			
Liver	Ac-Orn	**0.011**	0.342	**0.000**	3.9 AB	4.8 A	3.5 B	4.4	3.1	4.7	4.9 ABC	3.3 ABC	3.7 ABC	5.3 AB	3.4 ABC	5.7 A	3.0 BC	2.6 C	4.8 A			
Liver	alpha-AAA	**0.029**	**0.020**	**0.000**	10.0 A	12.0 A	11.9 A	11.6 AB	8.5 B	13.8 A	14.0 A	2.6 B	13.3 A	14.2 A	9.3 AB	12.4 A	6.5 B	13.6 A	15.5 A			
Liver	Carnosine	0.125	**0.000**	**0.000**	194	161	161	156 B	114 C	246 A	167 BCDEF	102 EF	313 A	177 BCD	95 F	211 ABC	124 DEF	145 CDE	214 AB			
Liver	Creatinine	0.051	**0.000**	**0.000**	123	80	131	148 A	142 A	44 B	72 BC	249 A	49 C	76 BC	129 B	35 C	296 A	48 C	48 C			
Liver	Dopamine	**0.000**	**0.000**	**0.000**	3.0 A	1.4 B	1.2 B	2.4 A	1.5 AB	1.7 B	3.6 A	3.1 AB	2.2 AB	2.2 AB	0.4 B	1.6 B	1.3 B	1.1 B	1.2 B			
Liver	Histamine	**0.000**	0.934	0.441	36 A	19 B	15 B	24	23	24	37	33	40	18	22	15	16	13	16			
Liver	Serotonin	**0.018**	**0.000**	**0.000**	4.1 A	2.8 B	3.8 AB	3.3 B	5.1 A	2.3 B	1.6 CD	8.5 A	2.4 D	1.5 D	4.9 BC	2.0 D	7.0 AB	1.9 D	2.5 D			
Liver	t4-OH-Pro	0.225	**0.000**	0.613	48	64	45	45 B	61 A	50 B	40	53	49	59	73	61	36	57	41			
Liver	Taurine	0.179	**0.000**	**0.000**	1185	1345	1378	1059 B	1799 A	1050 B	612 C	1978 A	964 BC	955 BC	1987 A	1093 BC	1610 A	1433 AB	1092 BC			
Liver	SDMA	0.615	**0.000**	**0.000**	3.2	2.7	3.4	3.3 A	4.3 A	1.7 B	1.6 BCD	5.8 AB	2.1 BC	2.0 BCD	5.0 A	1.1 D	6.4 A	2.0 BCD	1.9 C			
Plasma	Ac-Orn	0.211	**0.000**	0.077	4.6	4.3	3.8	3.1 B	4.6 A	4.9 A	2.9	5.0	5.8	3.3	4.5	5.1	3.2	4.3	3.9			
Plasma	ADMA	**0.020**	**0.000**	**0.035**	0.27 B	0.41 A	0.37 AB	0.70 A	0.24 B	0.12 B	0.73 A	0.07 BC	0.00 C	0.76 A	0.29 BC	0.19 BC	0.60 A	0.36 B	0.16 BC			
Plasma	alpha-AAA	0.178	**0.000**	0.382	1.9	1.5	1.9	2.3 A	0.4 B	2.7 A	2.4	0.4	3.0	2.2	0.2	2.1	2.3	0.5	3.0			
Plasma	c4-OH-Pro	0.361	0.374	0.153	0.08	0.11	0.05	0.04	0.12	0.07	0.02	0.17	0.04	0.04	0.16	0.14	0.07	0.03	0.03			
Plasma	Carnosine	0.565	**0.000**	**0.013**	8.2	7.8	8.4	7.9 B	6.9 C	9.6 A	7.6 BC	7.5 BC	9.3 ABC	7.8 BC	6.9 BC	8.7 ABC	8.3 B	6.2 C	10.8 A			
Plasma	Creatinine	0.177	0.347	**0.002**	69	61	65	67	64	64	63 AB	68 AB	76 AB	69 AB	65 AB	48 AB	69 A	60 B	67 AB			
Plasma	DOPA	**0.003**	0.075	**0.008**	0.50 A	0.37 AB	0.27 B	0.41	0.31	0.43	0.53 A	0.33 AB	0.63 A	0.30 AB	0.29 AB	0.54 AB	0.39 AB	0.31 AB	0.10 B			
Plasma	Histamine	0.894	**0.000**	0.433	0.13	0.11	0.13	0.17 A	0.16 A	0.03 B	0.11	0.23	0.04	0.16	0.12	0.04	0.24	0.13	0.00			
Plasma	Kynurenine	**0.020**	**0.000**	**0.027**	5.6 AB	5.7 B	6.8 A	6.9 A	3.5 B	7.7 A	5.6 BC	3.7 CD	7.5 AB	6.9 AB	3.3 D	6.8 AB	8.2 A	3.5 CD	8.8 A			
Plasma	Met-SO	0.992	**0.003**	0.447	1.31	1.30	1.31	1.17 B	1.40 A	1.36 AB	1.21	1.48	1.24	1.19	1.41	1.31	1.10	1.32	1.53			
Plasma	Nitro-Tyr	0.187	**0.000**	**0.019**	0.22	0.29	0.22	0.14 B	0.58 A	0.01 C	0.03 BCD	0.63 A	0.00 D	0.18 BC	0.67 A	0.03 CD	0.21 B	0.44 A	0.00 D			
Plasma	Putrescine	0.676	0.157	**0.043**	0.05	0.03	0.02	0.03	0.06	0.01	0.03 A	0.13 A	0.00 A	0.01 A	0.06 A	0.03 A	0.05 A	0.00 A	0.01 A			
Plasma	Sarcosine	0.277	**0.000**	0.147	0.56	0.68	0.62	0.87 A	0.84 A	0.15 B	0.87	0.69	0.11	0.93	0.87	0.24	0.81	0.96	0.09			
Plasma	Serotonin	**0.039**	**0.000**	0.529	4.4 AB	3.9 B	5.2 A	3.2 B	4.1 B	6.3 A	3.7	4.2	5.4	2.2	3.3	6.1	3.6	4.7	7.3			
Plasma	t4-OH-Pro	0.487	**0.000**	**0.000**	11.2	11.9	11.0	9.4 C	13.5 A	11.3 B	8.5 D	15.3 A	9.8 BCD	9.9 CD	13.9 AB	11.9 ABCD	9.7 D	11.2 BCD	12.2 ABC			
Plasma	Taurine	**0.003**	**0.000**	**0.026**	26 B	32 AB	35 A	17 C	29 B	46 A	16 D	24 CD	37 BC	18 D	31 C	47 AB	18 D	33 C	55 A			
Plasma	SDMA	0.333	**0.000**	0.086	0.28	0.29	0.32	0.41 A	0.04 B	0.44 A	0.37	0.04	0.43	0.44	0.03	0.39	0.41	0.05	0.49			

Figure S1B.

		F-Test			LSMeans														
											Metabotype*Sampling Day								
					Metabotype			Sampling Day			Metabotype A			Metabotype B			Metabotype C		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Liver	C0	0.000	0.000	0.000	87 B	48 C	134 A	40 C	96 B	132 A	39 B	65 B	156 A	41 B	60 B	44 B	42 B	162 A	197 A
	C10	0.000	0.000	0.000	8.3 B	0.9 C	14.2 A	0.8 C	7.7 B	14.8 A	0.8 B	3.2 B	20.7 A	0.8 B	1.0 B	0.8 B	0.9 C	18.9 A	22.9 A
	C10:1	0.000	0.000	0.000	2.32 B	0.53 C	3.56 A	0.52 C	2.19 B	3.70 A	0.53 B	1.46 B	4.98 A	0.47 B	0.57 B	0.54 B	0.56 B	4.55 A	5.58 A
	C10:2	0.000	0.000	0.000	2.08 B	0.34 C	3.33 A	0.35 C	1.72 B	3.69 A	0.36 C	0.73 C	5.16 AB	0.31 C	0.35 C	0.36 C	0.36 C	4.07 B	5.56 A
	C12	0.000	0.000	0.000	3.83 B	0.56 C	6.27 A	0.56 C	3.53 B	6.57 A	0.57 B	1.91 B	9.01 A	0.55 B	0.58 B	0.56 B	0.57 B	8.09 A	10.14 A
	C12-DC	0.000	0.000	0.000	5.94 B	2.51 C	8.88 A	2.55 C	5.78 B	9.01 A	2.49 C	4.13 C	11.21 AB	2.42 C	2.68 C	2.44 BC	2.73 C	10.52 A	13.38 A
	C12:1	0.000	0.000	0.000	2.85 B	0.59 C	4.18 A	0.60 C	2.47 B	4.55 A	0.63 BC	1.22 BC	6.70 A	0.54 C	0.64 BC	0.60 BC	0.62 B	5.56 A	6.36 A
	C14	0.000	0.000	0.000	5.04 B	0.40 C	8.31 A	0.41 C	5.08 B	8.26 A	0.41 B	3.36 B	11.34 A	0.40 B	0.42 B	0.38 B	0.42 B	11.45 A	13.05 A
	C14:1	0.000	0.000	0.000	1.22 B	0.12 C	2.02 A	0.13 C	1.27 B	1.95 A	0.14 B	0.86 B	2.65 A	0.13 B	0.12 B	0.11 B	0.13 B	2.84 A	3.10 A
	C14:1-OH	0.000	0.000	0.000	1.85 B	0.15 C	2.96 A	0.16 C	1.85 B	2.96 A	0.15 BC	1.41 BC	4.00 A	0.14 C	0.18 BC	0.14 BC	0.17 B	3.97 A	4.73 A
	C14:2	0.000	0.000	0.000	1.27 B	0.11 C	2.00 A	0.13 B	1.32 A	1.93 A	0.15 C	0.98 BC	2.67 AB	0.11 C	0.11 C	0.11 C	0.13 C	2.87 A	3.00 A
	C14:2-OH	0.000	0.000	0.000	1.56 B	0.14 C	2.67 A	0.15 C	1.58 B	2.64 A	0.14 B	0.93 B	3.61 A	0.14 B	0.14 B	0.14 B	0.16 B	3.68 A	4.18 A
	C16	0.000	0.000	0.000	1.98 A	0.21 B	2.88 A	0.21 B	2.02 A	2.84 A	0.24 C	2.17 ABC	3.54 B	0.20 C	0.23 C	0.19 C	0.18 C	3.68 AB	4.79 A
	C16-OH	0.000	0.000	0.000	2.33 A	0.16 B	3.46 A	0.18 B	2.53 A	3.24 A	0.19 C	2.76 ABC	4.03 B	0.17 C	0.14 C	0.17 C	0.19 C	4.68 AB	5.51 A
	C16:1	0.000	0.000	0.000	1.03 A	0.18 B	1.42 A	0.18 B	1.01 A	1.44 A	0.18 C	0.95 BC	1.95 AB	0.18 C	0.18 C	0.17 C	0.18 C	1.89 AB	2.19 A
	C16:1-OH	0.000	0.000	0.000	1.73 B	0.16 C	2.64 A	0.17 C	1.77 B	2.59 A	0.19 C	1.44 BC	3.55 AB	0.16 C	0.17 C	0.15 C	0.17 C	3.69 AB	4.06 A
	C16:2	0.000	0.000	0.000	1.79 B	0.19 C	3.03 A	0.18 C	1.94 B	2.89 A	0.18 CD	1.54 BCD	3.66 AB	0.16 D	0.24 CD	0.16 CD	0.20 C	4.02 AB	4.85 A
	C16:2-OH	0.000	0.000	0.000	1.02 B	0.29 C	1.56 A	0.27 C	1.11 B	1.49 A	0.24 C	0.91 BC	1.91 AB	0.27 C	0.32 C	0.27 C	0.28 C	2.10 A	2.30 A
	C18	0.000	0.000	0.000	0.97 A	0.21 B	1.24 A	0.22 B	0.94 A	1.25 A	0.26 C	1.02 ABC	1.62 A	0.21 C	0.23 BC	0.19 C	0.18 C	1.59 AB	1.94 A
	C18:1	0.000	0.000	0.000	0.97 B	0.20 C	1.53 A	0.18 C	0.97 B	1.55 A	0.19 C	0.82 BC	1.91 AB	0.19 C	0.21 C	0.20 C	0.17 C	1.87 AB	2.54 A
	C18:1-OH	0.000	0.000	0.000	1.04 A	0.25 B	1.29 A	0.29 B	0.98 A	1.33 A	0.33 C	1.12 ABCD	1.68 A	0.29 CD	0.22 BCD	0.26 CD	0.25 D	1.59 AB	2.04 A
	C18:2	0.000	0.000	0.000	1.21 B	0.15 C	1.84 A	0.14 B	1.31 A	1.75 A	0.15 C	1.35 ABC	2.14 B	0.13 C	0.18 C	0.13 C	0.15 C	2.41 AB	2.97 A
	C2	0.000	0.000	0.000	4.88 A	2.77 B	6.00 A	3.38 B	3.96 B	6.31 A	4.23 CD	3.46 BCDE	6.94 B	3.79 CD	2.12 DE	2.39 DE	2.11 E	6.29 BC	9.60 A
	C3	0.025	0.000	0.000	2.77 AB	3.07 A	2.44 B	3.36 A	2.07 B	2.85 A	4.12 ABC	1.47 E	2.74 ABCD	4.27 A	2.32 CDE	2.63 BCD	1.70 DE	2.42 BCDE	3.19 AB
	C3-OH	0.000	0.000	0.000	0.72 B	0.28 C	1.16 A	0.26 C	0.75 B	1.15 A	0.27 C	0.48 C	1.43 B	0.24 C	0.33 C	0.27 C	0.27 C	1.44 B	1.76 A
	C3:1	0.000	0.000	0.000	0.50 B	0.20 C	0.84 A	0.18 C	0.52 B	0.83 A	0.17 C	0.33 C	0.99 B	0.17 C	0.23 C	0.19 C	0.20 C	1.01 B	1.31 A
	C4	0.000	0.000	0.000	0.87 B	0.47 C	1.23 A	0.52 C	0.80 B	1.24 A	0.59 C	0.54 CD	1.48 B	0.58 C	0.46 CD	0.36 D	0.39 D	1.41 B	1.88 A
	C3-DC (C4-OH)	0.000	0.000	0.000	0.68 B	0.30 C	1.02 A	0.29 C	0.66 B	1.05 A	0.28 C	0.47 C	1.29 B	0.29 C	0.32 C	0.28 C	0.29 C	1.19 B	1.58 A
	C4:1	0.000	0.000	0.000	0.59 B	0.26 C	0.89 A	0.27 C	0.59 B	0.87 A	0.24 D	0.44 CD	1.08 B	0.25 D	0.30 CD	0.25 CD	0.32 C	1.04 B	1.30 A
	C5	0.000	0.000	0.000	1.49 B	0.59 C	2.21 A	0.68 C	1.36 B	2.26 A	0.72 BC	0.81 BC	2.95 A	0.75 B	0.53 BC	0.49 BC	0.57 C	2.74 A	3.33 A
	C5-M-DC	0.000	0.000	0.000	1.40 B	0.47 C	2.39 A	0.44 C	1.42 B	2.39 A	0.44 C	0.95 C	2.81 B	0.43 C	0.58 C	0.40 C	0.47 C	2.73 B	3.98 A
	C5-OH (C3-DC-M)	0.000	0.000	0.000	3.72 B	0.86 C	6.28 A	0.86 C	3.70 B	6.30 A	0.77 C	2.36 C	8.03 B	0.78 C	1.11 C	0.68 C	1.02 C	7.63 B	10.18 A
	C5:1	0.000	0.000	0.000	1.11 B	0.29 C	1.80 A	0.29 C	1.06 B	1.85 A	0.29 C	0.59 C	2.46 AB	0.28 C	0.31 C	0.28 C	0.30 C	2.28 B	2.81 A
	C5:1-DC	0.000	0.000	0.000	1.38 B	0.32 C	2.07 A	0.33 C	1.22 B	2.21 A	0.34 C	0.66 C	3.14 AB	0.34 C	0.31 C	0.30 C	0.32 C	2.70 B	3.19 A
	C6 (C4:1-DC)	0.000	0.000	0.000	5.46 B	0.83 C	9.35 A	0.79 C	5.05 B	9.80 A	0.74 B	1.50 B	14.14 A	0.76 B	0.93 B	0.80 B	0.87 B	12.72 A	14.47 A
	C5-DC (C6-OH)	0.000	0.000	0.000	2.15 B	0.43 C	3.28 A	0.42 C	1.87 B	3.56 A	0.40 C	0.94 C	5.10 AB	0.40 C	0.49 C	0.40 C	0.45 C	4.19 B	5.19 A
	C6:1	0.000	0.000	0.000	2.51 B	0.39 C	4.56 A	0.38 C	2.53 B	4.56 A	0.36 B	0.77 B	6.39 A	0.36 B	0.44 B	0.38 B	0.42 B	6.38 A	6.89 A
	C7-DC	0.000	0.000	0.000	1.15 B	0.26 C	1.61 A	0.24 C	1.03 B	1.73 A	0.24 B	0.65 B	2.56 A	0.26 B	0.28 B	0.23 B	0.23 B	2.17 A	2.41 A
	C8	0.000	0.000	0.000	5.45 B	0.93 C	7.14 A	0.91 C	4.43 B	8.19 A	0.89 C	2.22 C	13.24 A	0.88 C	1.07 C	0.85 C	0.94 C	10.01 B	10.46 B
	C9	0.000	0.000	0.000	2.51 B	0.46 C	3.74 A	0.49 C	2.37 B	3.86 A	0.50 C	1.88 BC	5.15 A	0.48 C	0.45 C	0.46 C	0.48 C	4.78 AB	5.97 A

Figure S1C.

Plasma

				LSMeans																													
																Metabotype*Sampling Day																	
	F-Test			Metabotype						Sampling Day						Metabotype A						Metabotype B						Metabotype C					
Metabolite	FP	SD	FPxSD	A		B		C		14ap		7pp		28pp		14ap		7pp		28pp		14ap		7pp		28pp		14ap		7pp		28pp	
C0	0.469	0.000	0.149	3.1		3.1		3.2		3.9	A	2.3	C	3.2	B	3.7		2.3		3.3		3.9		2.3		3.0		4.2		2.3		3.2	
C10	0.001	0.000	0.000	0.136	A	0.134	A	0.127	B	0.130	B	0.148	A	0.120	C	0.139	BC	0.140	ABCD	0.130	CDE	0.126	DE	0.154	A	0.122	E	0.125	E	0.148	AB	0.109	F
C10:1	0.067	0.002	0.565	0.071		0.066		0.067		0.070	A	0.070	A	0.063	B	0.075		0.072		0.066		0.068		0.068		0.062		0.069		0.072		0.061	
C10:2	0.156	0.463	0.000	0.056		0.054		0.052		0.053		0.055		0.053		0.058	AB	0.050	ABC	0.060	A	0.051	BC	0.056	AB	0.054	AB	0.051	BC	0.059	A	0.046	C
C12	0.327	0.000	0.085	0.073		0.071		0.070		0.071	B	0.075	A	0.068	B	0.075		0.073		0.070		0.070		0.077		0.067		0.068		0.075		0.068	
C12-DC	0.060	0.000	0.022	0.387		0.375		0.371		0.404	A	0.363	B	0.366	B	0.422	A	0.361	DEF	0.379	BCDE	0.396	ABC	0.361	E	0.368	BCDE	0.393	ABD	0.368	CEF	0.350	E
C12:1	0.020	0.000	0.205	0.090	AB	0.083	B	0.090	A	0.084	B	0.094	A	0.085	B	0.085		0.099		0.085		0.080		0.090		0.080		0.087		0.092		0.091	
C14	0.000	0.000	0.226	0.065	A	0.058	B	0.049	C	0.060	B	0.065	A	0.047	C	0.070		0.068		0.057		0.059		0.069		0.046		0.051		0.059		0.038	
C14:1	0.000	0.002	0.020	0.021	A	0.020	A	0.018	B	0.021	A	0.019	B	0.019	B	0.023	A	0.019	BC	0.021	AB	0.021	AB	0.020	AB	0.020	AB	0.019	B	0.019	BC	0.016	C
C14:1-OH	0.001	0.235	0.000	0.023	A	0.021	B	0.020	B	0.022		0.021		0.020		0.023	AB	0.020	ABC	0.024	A	0.021	AB	0.021	AB	0.020	BC	0.021	AB	0.021	AB	0.017	C
C14:2	0.000	0.756	0.000	0.017	A	0.015	B	0.013	C	0.015		0.015		0.015		0.016	AB	0.015	BC	0.019	A	0.014	BC	0.016	AB	0.015	B	0.014	B	0.014	B	0.011	C
C14:2-OH	0.000	0.000	0.178	0.018	A	0.018	A	0.016	B	0.017	A	0.018	A	0.016	B	0.019		0.018		0.018		0.017		0.020		0.016		0.015		0.018		0.014	
C16	0.000	0.161	0.020	0.043	A	0.038	AB	0.035	B	0.037		0.040		0.038		0.042	AB	0.041	AB	0.045	A	0.035	BC	0.043	AB	0.037	ABC	0.036	ABC	0.037	ABC	0.031	C
C16-OH	0.000	0.000	0.000	0.039	A	0.033	B	0.030	C	0.042	A	0.029	B	0.031	B	0.048	A	0.030	CD	0.038	BC	0.039	B	0.029	D	0.031	D	0.038	B	0.029	D	0.023	E
C16:1	0.094	0.000	0.407	0.022		0.022		0.021		0.021	B	0.023	A	0.020	C	0.022		0.023		0.021		0.022		0.024		0.020		0.021		0.023		0.019	
C16:1-OH	0.000	0.000	0.017	0.026	A	0.022	B	0.021	C	0.027	A	0.022	B	0.020	C	0.030	A	0.023	BCD	0.024	BCD	0.026	B	0.021	CD	0.020	D	0.025	BC	0.021	CD	0.016	E
C16:2	0.000	0.008	0.000	0.017	A	0.017	A	0.014	B	0.017	A	0.017	A	0.015	B	0.019	A	0.016	AB	0.017	AB	0.017	A	0.018	A	0.017	A	0.015	B	0.017	A	0.011	C
C16:2-OH	0.000	0.000	0.000	0.022	A	0.021	A	0.019	B	0.023	A	0.020	B	0.019	B	0.025	A	0.019	C	0.023	ABC	0.023	AB	0.020	BC	0.021	BC	0.022	BC	0.020	C	0.014	D
C18	0.484	0.019	0.370	0.046		0.047		0.044		0.040	B	0.048	A	0.049	A	0.044		0.048		0.046		0.038		0.052		0.052		0.039		0.044		0.049	
C18:1	0.004	0.000	0.003	0.052	A	0.047	AB	0.041	B	0.040	B	0.060	A	0.040	B	0.051	AB	0.063	A	0.041	BCD	0.038	CD	0.066	A	0.038	BCD	0.030	D	0.051	ABC	0.041	BCD
C18:1-OH	0.000	0.000	0.000	0.034	A	0.029	B	0.026	C	0.033	A	0.029	B	0.027	B	0.038	A	0.029	BCD	0.034	AB	0.031	BC	0.030	BCD	0.026	D	0.030	BCD	0.028	CD	0.021	E
C18:2	0.000	0.140	0.008	0.016	A	0.015	A	0.013	B	0.015		0.015		0.014		0.017	A	0.015	AB	0.016	AB	0.015	AB	0.016	AB	0.015	AB	0.013	B	0.014	AB	0.011	C
C2	0.282	0.068	0.714	0.844		0.969		0.950		1.009		0.872		0.882		0.934		0.806		0.793		1.097		0.933		0.878		0.997		0.877		0.976	
C3	0.019	0.000	0.157	0.160	B	0.179	AB	0.195	A	0.164	B	0.161	B	0.210	A	0.143		0.158		0.180		0.176		0.157		0.204		0.172		0.167		0.245	
C3-OH	0.526	0.714	0.016	0.043		0.044		0.041		0.043		0.040		0.044		0.043	AB	0.038	AB	0.049	A	0.043	AB	0.045	AB	0.043	AB	0.044	AB	0.038	AB	0.039	B
C3:1	0.072	0.000	0.008	0.034		0.034		0.032		0.035	A	0.028	B	0.036	A	0.036	AB	0.027	C	0.039	A	0.035	AB	0.028	C	0.038	AB	0.035	AB	0.028	C	0.032	BC
C4	0.045	0.000	0.049	0.098	A	0.110	A	0.109	A	0.125	A	0.092	B	0.100	B	0.115	AB	0.084	C	0.096	BC	0.135	A	0.093	BC	0.102	BC	0.123	A	0.101	BC	0.104	BC
C3-DC (C4-OH)	0.164	0.000	0.001	0.051		0.048		0.047		0.048	B	0.045	B	0.054	A	0.048	B	0.043	B	0.061	A	0.048	B	0.046	B	0.051	B	0.048	B	0.046	B	0.049	B
C4:1	0.009	0.000	0.007	0.043	A	0.041	AB	0.039	B	0.044	A	0.037	B	0.042	A	0.045	A	0.036	B	0.047	A	0.045	A	0.038	B	0.042	AB	0.044	A	0.037	B	0.037	B
C5	0.423	0.000	0.419	0.073		0.075		0.076		0.084	A	0.067	C	0.074	B	0.083		0.063		0.074		0.086		0.068		0.071		0.083		0.070		0.076	
C5-M-DC	0.000	0.000	0.000	0.062	A	0.057	A	0.054	B	0.064	A	0.052	C	0.057	B	0.069	A	0.050	CD	0.066	A	0.063	AB	0.053	CD	0.056	BC	0.061	AB	0.052	CD	0.047	D
C5-OH (C3-DC-M)	0.301	0.000	0.004	0.096		0.094		0.091		0.105	A	0.079	B	0.098	A	0.104	AB	0.079	C	0.105	A	0.104	A	0.077	C	0.102	A	0.106	A	0.082	C	0.086	BC
C5:1	0.000	0.000	0.002	0.057	B	0.056	B	0.063	A	0.054	C	0.063	A	0.058	B	0.053	C	0.060	ABC	0.060	ABC	0.052	C	0.064	AB	0.051	C	0.057	BC	0.067	A	0.064	A
C5:1-DC	0.000	0.003	0.000	0.080	A	0.066	B	0.062	B	0.074	A	0.065	B	0.068	AB	0.083	AB	0.063	C	0.094	A	0.070	BC	0.067	C	0.061	CD	0.069	BC	0.066	C	0.050	D
C6 (C4:1-DC)	0.071	0.000	0.000	0.100		0.105		0.099		0.116	A	0.096	B	0.092	B	0.118	A	0.084	CD	0.099	BC	0.118	A	0.097	BC	0.098	BC	0.111	AB	0.105	AB	0.079	D
C5-DC (C6-OH)	0.628	0.000	0.002	0.044		0.044		0.043		0.047	A	0.042	B	0.042	B	0.047	ABC	0.039	CD	0.046	ABC	0.048	A	0.042	ABCD	0.041	BCD	0.047	AB	0.044	ABC	0.038	D
C6:1	0.082	0.000	0.000	0.053		0.054		0.052		0.057	A	0.053	B	0.049	C	0.057	ABC	0.048	CD	0.054	ABC	0.058	A	0.054	ABC	0.051	BC	0.055	AB	0.058	A	0.042	D
C7-DC	0.000	0.000	0.000	0.047	B	0.047	B	0.059	A	0.034	C	0.075	A	0.045	B	0.034	B	0.070	A	0.037	B	0.033	B	0.079	A	0.029	B	0.035	B	0.076	A	0.068	A
C8	0.870	0.000	0.001	0.156		0.157		0.158		0.132	B	0.202	A	0.137	B	0.136	BC	0.191	A	0.141	BC	0.133	BC	0.210	A	0.129	BC	0.129	C	0.203	A	0.143	B
C9	0.064	0.000	0.021	0.073		0.070		0.068		0.063	B	0.075	A	0.072	A	0.065	BCD	0.075	AB	0.078	A	0.061	D	0.076	A	0.073	AB	0.064	D	0.075	AC	0.066	BD

Figure S1D.

		F-Test			LSMeans					
					Metabotype			Sampling Day		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp
Liver	lysoPC a C14:0	**0.000**	**0.000**	**0.000**	32.2 A	28.4 B	34.0 A	28.0 B	32.3 A	34.4 A
Liver	lysoPC a C16:0	0.059	**0.000**	**0.002**	25.9	14.4	23.3	10.4 B	29.4 A	23.8 A
Liver	lysoPC a C16:1	**0.010**	**0.000**	**0.026**	3.35 A	2.54 B	3.29 A	1.81 B	3.85 A	3.53 A
Liver	lysoPC a C17:0	0.054	**0.000**	**0.000**	4.40	0.96	2.92	1.15 B	4.15 AB	2.98 A
Liver	lysoPC a C18:0	**0.000**	**0.000**	**0.006**	15.40 A	7.84 B	19.18 A	8.71 B	16.62 A	17.09 A
Liver	lysoPC a C18:1	**0.001**	**0.000**	**0.000**	22.0 A	16.7 B	21.4 A	11.2 C	26.7 A	22.2 B
Liver	lysoPC a C18:2	**0.003**	**0.000**	**0.001**	14.6 A	11.5 B	15.0 A	6.1 B	18.6 A	16.3 A
Liver	lysoPC a C20:3	**0.000**	**0.000**	**0.000**	6.14 A	3.30 B	5.57 A	3.43 B	5.66 A	5.93 A
Liver	lysoPC a C20:4	**0.000**	**0.000**	**0.000**	8.33 A	5.49 B	8.12 A	6.22 B	8.28 A	7.44 AB
Liver	lysoPC a C24:0	**0.036**	**0.000**	**0.009**	2.24 A	0.56 B	1.55 AB	0.63 B	2.03 AB	1.70 A
Liver	lysoPC a C26:0	**0.047**	**0.000**	**0.000**	2.67 A	0.43 B	1.56 AB	0.59 B	2.22 AB	1.84 A
Liver	lysoPC a C26:1	**0.030**	**0.000**	**0.000**	1.44 A	0.22 B	1.15 AB	0.27 B	1.50 AB	1.04 A
Liver	lysoPC a C28:0	**0.002**	**0.000**	**0.000**	2.82 A	0.61 B	2.43 A	0.81 B	2.21 AB	2.84 A
Liver	lysoPC a C28:1	**0.000**	**0.000**	**0.000**	1.85 A	0.42 B	2.10 A	0.50 B	1.66 A	2.21 A
Plasma	lysoPC a C14:0	**0.000**	**0.000**	**0.000**	4.6 A	4.3 C	4.5 B	4.5 B	4.3 C	4.6 A
Plasma	lysoPC a C16:0	0.936	**0.000**	**0.000**	14.1	13.8	13.9	10.2 C	14.1 B	17.5 A
Plasma	lysoPC a C16:1	**0.042**	**0.000**	**0.030**	1.19 A	1.02 B	1.08 AB	0.87 B	0.88 B	1.54 A
Plasma	lysoPC a C17:0	0.079	**0.000**	**0.001**	0.94	0.80	0.90	0.97 A	0.66 B	1.01 A
Plasma	lysoPC a C18:0	0.180	**0.000**	**0.000**	12.52	11.34	12.28	10.79 B	10.83 B	14.52 A
Plasma	lysoPC a C18:1	0.226	**0.000**	**0.031**	11.3	10.4	11.3	8.7 B	8.8 B	15.5 A
Plasma	lysoPC a C18:2	0.059	**0.000**	0.140	13.1	12.8	14.9	7.1 C	10.1 B	23.5 A
Plasma	lysoPC a C20:3	**0.002**	**0.000**	**0.020**	0.98 A	0.77 B	1.01 A	0.85 B	0.51 C	1.40 A
Plasma	lysoPC a C20:4	**0.003**	**0.000**	0.055	0.98 A	0.82 B	0.98 A	1.09 A	0.57 B	1.12 A
Plasma	lysoPC a C24:0	**0.006**	**0.000**	**0.001**	0.07 A	0.06 B	0.07 AB	0.07 A	0.05 B	0.07 A
Plasma	lysoPC a C26:0	0.110	**0.000**	0.297	0.09	0.08	0.09	0.08 B	0.08 B	0.10 A
Plasma	lysoPC a C26:1	**0.003**	**0.000**	0.271	0.05 A	0.04 B	0.04 AB	0.04 C	0.04 B	0.05 A
Plasma	lysoPC a C28:0	**0.012**	**0.000**	**0.002**	0.16 A	0.14 B	0.16 A	0.14 B	0.12 C	0.20 A
Plasma	lysoPC a C28:1	**0.009**	**0.000**	**0.001**	0.34 A	0.26 B	0.31 AB	0.23 B	0.21 B	0.47 A

		LSMeans								
		Metabotype*Sampling Day								
		Metabotype A			Metabotype B			Metabotype C		
	Metabolite	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Liver	lysoPC a C14:0	28.3 B	31.4 AB	37.1 A	27.7 B	28.9 B	28.6 B	28.1 B	36.7 A	37.4 A
Liver	lysoPC a C16:0	9.5 CD	42.9 ABCD	25.3 AB	8.9 D	20.1 ABCD	14.1 BCD	12.7 C	25.1 ABCD	32.0 A
Liver	lysoPC a C16:1	1.68 CD	4.86 AB	3.51 AB	1.69 D	3.12 ABCD	2.81 BC	2.04 CD	3.57 AB	4.26 A
Liver	lysoPC a C17:0	1.11 B	8.31 AB	3.78 A	1.00 B	1.08 AB	0.81 B	1.33 B	3.06 AB	4.37 A
Liver	lysoPC a C18:0	8.57 CD	15.71 ABCD	21.92 A	6.40 D	10.62 ABCD	6.49 CD	11.15 BC	23.54 AB	22.86 A
Liver	lysoPC a C18:1	10.0 C	31.9 A	24.0 AB	10.9 C	23.2 AB	16.2 BC	12.8 C	25.0 A	26.5 A
Liver	lysoPC a C18:2	5.3 C	22.8 A	15.6 AB	6.0 C	15.3 AB	13.1 B	7.1 C	17.7 AB	20.1 A
Liver	lysoPC a C20:3	3.01 C	8.76 A	6.66 AB	3.09 C	3.36 BC	3.46 BC	4.18 B	4.86 ABC	7.67 A
Liver	lysoPC a C20:4	5.58 CD	11.37 A	8.04 ABCD	5.48 D	5.79 CD	5.21 CD	7.59 BC	7.68 ABCD	9.08 AB
Liver	lysoPC a C24:0	0.68 B	3.93 AB	2.10 AB	0.58 B	0.54 AB	0.57 B	0.63 B	1.61 AB	2.42 A
Liver	lysoPC a C26:0	0.72 B	4.86 ABC	2.42 A	0.56 BC	0.32 ABC	0.39 BC	0.49 C	1.48 ABC	2.72 A
Liver	lysoPC a C26:1	0.31 B	2.67 AB	1.34 AC	0.24 B	0.21 AB	0.20 BC	0.26 B	1.61 AB	1.59 A
Liver	lysoPC a C28:0	0.97 B	3.50 ABC	3.97 A	0.82 BC	0.44 ABC	0.58 BC	0.63 C	2.69 ABC	3.97 A
Liver	lysoPC a C28:1	0.62 C	2.14 ABCD	2.79 AB	0.45 CD	0.38 BCD	0.43 CD	0.42 D	2.47 ABCD	3.42 A
Plasma	lysoPC a C14:0	4.5 ABC	4.6 ABC	4.7 AB	4.4 CD	4.1 E	4.3 CDE	4.4 BC	4.2 DE	4.7 A
Plasma	lysoPC a C16:0	9.5 EF	16.4 AB	16.4 ABC	9.4 F	13.7 BCD	18.2 A	11.8 DE	12.1 CDEF	17.8 A
Plasma	lysoPC a C16:1	0.91 B	1.00 B	1.65 A	0.79 B	0.85 B	1.42 A	0.91 B	0.78 B	1.55 A
Plasma	lysoPC a C17:0	0.99 AB	0.81 BC	1.00 AB	0.87 AB	0.62 CD	0.92 AB	1.04 AB	0.56 D	1.11 A
Plasma	lysoPC a C18:0	10.44 CDE	13.08 ABCD	14.04 ABC	9.89 E	10.02 DE	14.11 AB	12.05 BCD	9.40 E	15.41 A
Plasma	lysoPC a C18:1	8.9 BC	9.7 BC	15.2 A	7.8 C	8.6 BC	14.8 A	9.4 B	7.9 BC	16.6 A
Plasma	lysoPC a C18:2	7.3	10.4	21.5	6.5	9.9	21.9	7.6	10.0	27.0
Plasma	lysoPC a C20:3	0.87 C	0.60 DE	1.47 AB	0.78 CD	0.43 E	1.09 BC	0.90 C	0.49 E	1.65 A
Plasma	lysoPC a C20:4	1.17	0.64	1.15	0.94	0.53	0.98	1.17	0.55	1.24
Plasma	lysoPC a C24:0	0.08 AB	0.06 DEF	0.08 ABC	0.07 BCD	0.05 EF	0.06 CDE	0.07 BC	0.05 F	0.08 A
Plasma	lysoPC a C26:0	0.09	0.08	0.12	0.08	0.08	0.10	0.09	0.07	0.10
Plasma	lysoPC a C26:1	0.04	0.04	0.06	0.03	0.04	0.05	0.04	0.04	0.06
Plasma	lysoPC a C28:0	0.14 CD	0.14 CDE	0.21 AB	0.14 CDE	0.11 DE	0.17 BC	0.14 C	0.11 E	0.23 A
Plasma	lysoPC a C28:1	0.24 BC	0.27 B	0.50 A	0.22 BC	0.18 CD	0.39 A	0.23 BD	0.19 C	0.51 A

Figure S1E.

					LSMeans														
											Metabotype*Sampling Day								
		F-Test			Metabotype			Sampling Day			Metabotype A			Metabotype B			Metabotype C		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Liver	PC aa C24:0	0.175	**0.001**	**0.004**	0.96	0.22	0.22	0.27 A	0.93 AB	0.20 B	0.33 A	2.39 AB	0.16 B	0.27 AB	0.18 AB	0.21 B	0.23 B	0.21 AB	0.24 AB
	PC aa C26:0	0.171	**0.000**	**0.000**	3.70	2.16	1.80	2.16 A	3.70 AB	1.79 B	2.21 A	7.38 AB	1.51 B	2.17 A	2.11 AB	2.19 A	2.11 A	1.62 AB	1.66 B
	PC aa C28:1	0.092	**0.005**	0.516	1.09	0.58	0.57	0.50 B	1.06 AB	0.68 A	0.56	1.93	0.77	0.44	0.72	0.57	0.48	0.54	0.69
	PC aa C30:0	0.149	0.344	0.614	2.26	0.82	0.97	0.94	2.00	1.11	1.07	4.49	1.23	0.82	0.75	0.87	0.93	0.74	1.24
	PC aa C30:2	**0.041**	0.097	0.231	0.67 A	0.40 AB	0.32 B	0.33	0.66	0.40	0.37	1.25	0.40	0.30	0.45	0.43	0.32	0.28	0.36
	PC aa C32:0	0.291	0.276	0.713	3.34	0.97	2.23	1.09	3.21	2.23	1.12	6.28	2.60	0.93	0.82	1.18	1.24	2.54	2.92
	PC aa C32:1	0.134	**0.000**	0.732	7.94	5.51	6.73	3.37 B	8.78 A	8.03 A	3.62	9.53	10.67	3.01	7.61	5.91	3.50	9.19	7.52
	PC aa C32:2	**0.031**	**0.000**	0.295	3.48 A	1.96 B	2.33 AB	1.34 B	3.59 A	2.85 A	1.47	5.26	3.72	1.20	2.70	1.97	1.35	2.80	2.86
	PC aa C32:3	0.057	**0.000**	0.257	1.42	0.90	0.96	0.67 B	1.30 A	1.32 AB	0.74	1.79	1.75	0.59	1.14	0.96	0.67	0.97	1.24
	PC aa C34:1	0.665	**0.006**	0.945	29.2	22.8	29.0	13.3 B	37.0 A	30.7 AB	11.7	41.5	34.4	13.0	30.7	24.6	15.1	38.7	33.3
	PC aa C34:2	0.526	**0.000**	0.890	29.3	20.8	25.4	8.5 B	39.9 A	27.0 A	7.9	47.9	32.0	8.3	32.7	21.4	9.2	39.2	27.7
	PC aa C34:3	0.372	**0.000**	0.844	8.71	6.95	7.41	3.81 C	11.74 A	7.51 B	3.94	12.99	9.19	3.42	11.07	6.36	4.07	11.16	6.99
	PC aa C34:4	**0.007**	**0.000**	0.134	2.19 A	1.40 B	1.32 B	1.11 C	2.29 A	1.52 B	1.19	3.34	2.03	1.01	1.95	1.25	1.13	1.57	1.27
	PC aa C36:0	**0.044**	**0.015**	0.305	2.01 A	1.19 B	1.60 AB	1.16 A	1.90 A	1.74 A	1.15	2.94	1.94	1.08	1.29	1.20	1.24	1.48	2.08
	PC aa C36:1	0.811	0.520	0.891	13.0	11.2	15.4	9.8	13.5	16.2	7.3	15.7	16.0	9.5	11.8	12.1	12.6	13.0	20.5
	PC aa C36:2	0.873	**0.004**	0.858	26.8	22.0	24.9	10.5 B	34.6 A	28.6 AB	8.5	40.9	31.0	10.7	32.3	23.0	12.2	30.6	31.8
	PC aa C36:3	0.542	**0.000**	0.721	20.6	15.6	16.7	7.9 B	25.5 A	19.5 AB	7.3	30.8	23.7	7.3	24.0	15.4	8.9	21.6	19.4
	PC aa C36:4	0.108	**0.000**	0.467	17.6	11.8	13.0	7.2 B	21.0 A	14.1 A	7.2	27.6	18.1	6.3	18.0	11.1	8.2	17.6	13.2
	PC aa C36:5	**0.007**	**0.000**	0.194	9.33 A	5.95 B	6.39 B	4.54 C	10.52 A	6.60 B	4.84	14.07	9.08	3.80	8.88	5.16	4.97	8.62	5.57
	PC aa C36:6	**0.003**	**0.025**	0.106	2.03 A	1.22 B	1.18 B	1.18 B	2.02 A	1.22 AB	1.27	3.22	1.59	1.02	1.61	1.04	1.24	1.24	1.05
	PC aa C38:0	0.300	0.517	0.597	0.53	0.22	0.31	0.26	0.52	0.28	0.23	1.07	0.29	0.23	0.24	0.20	0.33	0.26	0.34
	PC aa C38:1	0.220	0.664	0.855	0.40	0.26	0.44	0.39	0.29	0.43	0.36	0.38	0.47	0.27	0.22	0.29	0.54	0.26	0.52
	PC aa C38:3	0.636	0.786	0.611	7.99	4.65	7.64	5.33	6.04	8.91	4.26	9.58	10.13	4.55	4.02	5.37	7.19	4.51	11.22
	PC aa C38:4	0.416	0.540	0.533	14.76	8.97	12.37	10.08	13.81	12.21	8.84	21.03	14.40	8.42	9.92	8.56	12.97	10.49	13.66
	PC aa C38:5	0.089	**0.007**	0.360	20.26	13.02	15.08	11.36 B	21.62 A	15.38 AB	11.11	29.68	20.00	9.41	17.81	11.84	13.57	17.36	14.30
	PC aa C38:6	**0.050**	**0.001**	0.217	11.14 A	4.71 A	5.20 A	3.28 B	12.44 A	5.33 A	3.41	23.02	7.00	2.78	7.13	4.22	3.64	7.17	4.79
	PC aa C40:1	0.099	0.443	0.177	1.01	0.86	0.85	0.87	0.99	0.86	0.89	1.23	0.92	0.86	0.84	0.88	0.86	0.90	0.79
	PC aa C40:2	0.482	0.689	0.846	0.11	0.09	0.10	0.09	0.11	0.10	0.09	0.15	0.10	0.09	0.09	0.09	0.09	0.10	0.11
	PC aa C40:3	0.200	0.603	0.513	0.27	0.11	0.12	0.13	0.25	0.12	0.11	0.58	0.13	0.11	0.11	0.10	0.15	0.07	0.13
	PC aa C40:4	0.485	0.919	0.681	1.11	0.65	0.99	1.02	0.87	0.86	0.82	1.63	0.88	0.83	0.55	0.58	1.42	0.43	1.11
	PC aa C40:5	0.603	0.752	0.570	5.53	3.77	4.71	4.32	5.39	4.30	3.69	7.96	4.93	3.47	4.51	3.35	5.81	3.70	4.63
	PC aa C40:6	0.101	0.193	0.474	6.10	3.08	3.30	2.79	6.38	3.30	2.67	11.84	3.78	2.47	4.07	2.70	3.24	3.22	3.43
	PC aa C42:0	0.194	0.147	0.220	0.61	0.17	0.19	0.17	0.60	0.19	0.18	1.43	0.23	0.17	0.16	0.17	0.17	0.22	0.18
	PC aa C42:1	0.143	0.465	0.106	0.32	0.12	0.15	0.16	0.29	0.15	0.17	0.65	0.13	0.14	0.10	0.12	0.16	0.11	0.19
	PC aa C42:2	0.178	0.308	0.407	0.84	0.43	0.38	0.42	0.83	0.40	0.43	1.71	0.37	0.44	0.42	0.44	0.40	0.35	0.38
	PC aa C42:4	0.167	**0.003**	**0.007**	0.25	0.06	0.09	0.06 B	0.24 AB	0.10 A	0.06 B	0.60 AB	0.10 AB	0.06 B	0.06 AB	0.06 B	0.07 B	0.06 AB	0.14 A
	PC aa C42:5	0.166	0.054	0.232	0.29	0.11	0.16	0.11	0.31	0.14	0.10	0.62	0.14	0.11	0.11	0.10	0.11	0.19	0.17
	PC aa C42:6	0.102	**0.000**	**0.003**	1.09	0.43	0.66	0.48 B	1.06 AB	0.64 A	0.49 B	1.95 AB	0.83 A	0.47 B	0.42 AB	0.41 B	0.49 B	0.81 AB	0.69 A

Figure S1F.

					LSMeans														
											Metabotype*Sampling Day								
		F-Test			Metabotype			Sampling Day			Metabotype A			Metabotype B			Metabotype C		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Liver	PC ae C30:0	0.099	0.150	0.683	0.65	0.32	0.32	0.41	0.55	0.34	0.47	1.09	0.38	0.37	0.29	0.31	0.38	0.26	0.33
	PC ae C30:1	0.287	0.363	0.639	0.96	0.25	0.20	0.27	0.83	0.31	0.32	2.24	0.31	0.25	0.24	0.26	0.25	0.01	0.35
	PC ae C30:2	0.163	0.271	0.340	0.45	0.17	0.15	0.15	0.45	0.16	0.16	1.00	0.17	0.14	0.20	0.17	0.16	0.16	0.14
	PC ae C32:1	**0.042**	**0.019**	0.257	1.45 A	0.52 B	0.81 AB	0.57 B	1.21 AB	1.00 A	0.66	2.29	1.40	0.51	0.52	0.55	0.55	0.84	1.04
	PC ae C32:2	**0.027**	**0.001**	0.243	1.62 A	0.73 B	1.10 AB	0.59 B	1.61 A	1.25 A	0.60	2.68	1.56	0.51	0.92	0.74	0.64	1.21	1.43
	PC ae C34:0	0.210	0.782	0.604	1.06	0.37	0.68	0.58	0.85	0.67	0.56	1.84	0.77	0.52	0.24	0.35	0.66	0.48	0.91
	PC ae C34:1	0.248	0.157	0.820	3.59	2.21	3.05	2.21	3.22	3.41	2.27	4.20	4.28	1.91	2.55	2.17	2.45	2.92	3.77
	PC ae C34:2	0.095	**0.000**	0.756	1.82	1.17	1.50	0.93 B	1.76 A	1.79 A	1.00	2.07	2.39	0.83	1.48	1.20	0.97	1.73	1.79
	PC ae C34:3	0.148	**0.025**	0.517	1.55	0.62	0.89	0.50 B	1.50 AB	1.06 A	0.54	2.74	1.36	0.43	0.75	0.69	0.52	1.02	1.12
	PC ae C36:0	0.125	0.201	0.471	1.68	0.72	0.99	0.80	1.75	0.86	0.87	3.09	1.09	0.73	0.83	0.62	0.79	1.32	0.86
	PC ae C36:1	0.582	0.851	0.688	3.34	1.96	2.88	2.36	2.81	3.02	2.03	4.55	3.45	2.15	1.94	1.80	2.89	1.94	3.82
	PC ae C36:2	0.415	**0.007**	0.668	2.89	2.04	2.35	1.56 B	2.95 A	2.77 AB	1.53	3.68	3.45	1.44	2.76	1.93	1.71	2.41	2.93
	PC ae C36:3	0.122	**0.031**	0.476	1.89	0.98	1.10	0.79 A	1.93 A	1.24 A	0.83	3.27	1.57	0.72	1.32	0.90	0.83	1.20	1.26
	PC ae C36:4	**0.007**	0.053	0.187	1.06 A	0.60 B	0.68 B	0.62	0.95	0.78	0.65	1.46	1.08	0.52	0.73	0.55	0.68	0.66	0.70
	PC ae C36:5	0.217	0.200	0.541	1.27	0.57	0.72	0.58	1.32	0.66	0.62	2.43	0.78	0.45	0.73	0.53	0.67	0.81	0.67
	PC ae C38:0	**0.027**	**0.000**	0.280	1.78 A	1.03 B	1.15 AB	0.74 B	1.93 A	1.29 A	0.80	3.00	1.54	0.65	1.38	1.06	0.77	1.41	1.26
	PC ae C38:1	0.124	0.734	0.477	0.83	0.28	0.37	0.40	0.69	0.38	0.36	1.63	0.49	0.34	0.26	0.23	0.49	0.19	0.42
	PC ae C38:2	0.242	0.496	0.546	0.94	0.41	0.55	0.47	0.80	0.63	0.43	1.58	0.80	0.43	0.42	0.40	0.54	0.40	0.70
	PC ae C38:3	0.291	0.560	0.540	1.22	0.62	0.88	0.72	0.99	1.00	0.68	1.68	1.30	0.63	0.62	0.60	0.85	0.66	1.11
	PC ae C38:4	**0.036**	0.816	0.347	1.81 A	1.02 B	1.02 AB	1.26	1.47	1.13	1.29	2.68	1.47	1.13	1.04	0.89	1.35	0.69	1.03
	PC ae C38:5	0.108	0.317	0.470	2.12	0.90	1.04	1.05	1.99	1.01	1.10	3.92	1.34	0.90	1.02	0.77	1.16	1.04	0.92
	PC ae C38:6	0.166	0.232	0.518	1.41	0.58	0.64	0.52	1.46	0.64	0.52	3.00	0.69	0.43	0.77	0.54	0.60	0.62	0.69
	PC ae C40:1	**0.042**	**0.005**	**0.001**	0.48 A	0.42 AB	0.33 B	0.39 A	0.51 A	0.32 B	0.40 A	0.73 A	0.29 AB	0.37 A	0.45 AB	0.42 A	0.41 A	0.36 AB	0.24 B
	PC ae C40:2	0.145	0.315	0.312	0.53	0.14	0.15	0.16	0.49	0.18	0.15	1.19	0.25	0.14	0.15	0.13	0.17	0.12	0.17
	PC ae C40:3	0.464	0.473	0.665	0.41	0.17	0.25	0.20	0.42	0.21	0.19	0.83	0.22	0.17	0.15	0.17	0.24	0.28	0.24
	PC ae C40:4	0.081	0.687	0.472	0.60	0.35	0.42	0.40	0.51	0.45	0.39	0.85	0.54	0.37	0.35	0.32	0.45	0.33	0.47
	PC ae C40:5	0.101	0.541	0.455	1.33	0.55	0.77	0.74	1.18	0.73	0.73	2.34	0.91	0.61	0.60	0.45	0.89	0.59	0.81
	PC ae C40:6	0.209	0.149	0.383	1.39	0.55	0.44	0.68	1.25	0.45	0.67	3.04	0.46	0.63	0.55	0.45	0.74	0.14	0.43
	PC ae C42:0	**0.000**	**0.000**	**0.000**	2.38 A	1.90 B	2.49 A	1.87 B	2.32 A	2.58 A	1.89 B	2.22 AB	3.04 A	1.88 B	1.92 B	1.91 B	1.85 B	2.83 A	2.80 A
	PC ae C42:1	0.146	**0.033**	0.110	0.70	0.33	0.45	0.36 A	0.70 A	0.43 A	0.35	1.29	0.47	0.36	0.31	0.33	0.36	0.50	0.49
	PC ae C42:2	0.066	**0.017**	0.338	0.30	0.17	0.20	0.17 A	0.30 A	0.20 A	0.17	0.51	0.21	0.15	0.18	0.17	0.18	0.22	0.21
	PC ae C42:3	0.176	0.317	0.454	0.46	0.15	0.17	0.16	0.47	0.16	0.18	1.06	0.16	0.15	0.15	0.16	0.16	0.21	0.15
	PC ae C42:5	0.264	0.074	0.302	1.90	1.69	1.65	1.70	1.91	1.62	1.69	2.46	1.56	1.71	1.69	1.68	1.71	1.59	1.64
	PC ae C44:3	0.426	0.190	0.057	0.19	0.12	0.14	0.11	0.21	0.13	0.11	0.37	0.09	0.12	0.13	0.11	0.11	0.14	0.17
	PC ae C44:4	0.143	0.342	0.292	0.59	0.25	0.24	0.25	0.57	0.26	0.26	1.23	0.28	0.23	0.25	0.25	0.25	0.23	0.23
	PC ae C44:5	0.158	**0.003**	**0.008**	0.48	0.19	0.28	0.20 B	0.47 AB	0.29 A	0.21 B	0.98 AB	0.27 AB	0.20 B	0.17 AB	0.20 AB	0.19 B	0.27 AB	0.40 A
	PC ae C44:6	0.080	**0.005**	0.142	0.27	0.14	0.17	0.14 B	0.25 AB	0.18 A	0.15	0.43	0.22	0.13	0.14	0.14	0.14	0.18	0.18

Figure S1G.

		F-Test			LSMeans														
											Metabotype*Sampling Day								
					Metabotype			Sampling Day			Metabotype A			Metabotype B			Metabotype C		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Plasma	**PC aa C24:0**	0.503	**0.000**	0.121	0.032	0.030	0.031	0.021 C	0.030 B	0.042 A	0.021	0.031	0.044	0.021	0.032	0.038	0.021	0.027	0.044
	PC aa C26:0	0.442	**0.000**	**0.020**	0.32	0.32	0.32	0.29 C	0.33 B	0.35 A	0.29 D	0.33 BC	0.34 ABC	0.29 D	0.33 BC	0.35 AB	0.29 D	0.32 C	0.36 A
	PC aa C28:1	0.782	**0.000**	**0.001**	1.53	1.49	1.55	0.98 C	1.22 B	2.37 A	0.93 C	1.39 B	2.27 A	0.98 C	1.16 BC	2.32 A	1.02 C	1.10 C	2.52 A
	PC aa C30:0	0.086	**0.000**	0.146	1.87	1.97	2.14	1.47 B	1.62 B	2.90 A	1.44	1.62	2.56	1.44	1.57	2.91	1.53	1.65	3.23
	PC aa C30:2	0.600	**0.000**	0.412	0.56	0.51	0.52	0.42 B	0.34 C	0.83 A	0.41	0.39	0.87	0.41	0.32	0.79	0.43	0.30	0.84
	PC aa C32:0	**0.007**	**0.000**	**0.004**	3.76 B	3.91 B	4.52 A	3.42 B	3.17 B	5.60 A	3.37 B	3.26 B	4.66 AB	3.20 B	3.13 B	5.38 A	3.70 B	3.11 B	6.75 A
	PC aa C32:1	0.860	**0.000**	0.078	5.70	5.56	5.49	4.22 B	4.36 B	8.18 A	4.10	4.82	8.18	4.13	4.35	8.20	4.42	3.91	8.15
	PC aa C32:2	0.503	**0.000**	0.188	6.33	5.74	6.17	5.35 B	4.02 C	8.87 A	5.52	4.52	8.96	5.26	3.85	8.10	5.28	3.68	9.53
	PC aa C32:3	0.545	**0.000**	0.312	9.86	9.48	10.54	6.61 B	5.69 C	17.58 A	6.97	6.29	16.33	6.54	5.35	16.55	6.32	5.43	19.86
	PC aa C34:1	0.313	**0.000**	0.066	70.2	77.7	73.7	57.1 C	65.6 B	99.0 A	52.4	66.6	91.6	56.4	69.9	106.8	62.3	60.2	98.6
	PC aa C34:2	0.109	**0.000**	0.094	104.0	117.4	113.5	64.4 C	93.7 B	176.8 A	60.1	93.8	158.2	64.4	96.9	190.8	68.7	90.5	181.3
	PC aa C34:3	0.980	**0.000**	**0.012**	16.00	15.79	15.91	13.74 B	11.19 C	22.77 A	13.45 BC	12.45 BC	22.10 A	12.85 BC	11.35 C	23.17 A	14.92 B	9.77 C	23.03 A
	PC aa C34:4	0.233	**0.000**	0.264	2.54	2.25	2.58	2.37 B	1.37 C	3.63 A	2.49	1.56	3.58	2.25	1.25	3.24	2.37	1.30	4.09
	PC aa C36:0	**0.043**	**0.000**	**0.009**	4.61 AB	4.19 B	5.16 A	5.86 A	2.28 B	5.81 A	5.63 A	2.73 B	5.46 A	5.02 A	1.99 B	5.55 A	6.93 A	2.14 B	6.42 A
	PC aa C36:1	0.711	**0.000**	0.161	75.8	77.0	79.2	73.1 B	58.9 C	100.0 A	70.9	62.4	94.1	71.8	58.9	100.2	76.6	55.5	105.6
	PC aa C36:2	0.729	**0.000**	0.521	130.5	134.1	135.4	98.4 B	105.7 B	195.8 A	97.1	108.0	186.2	97.0	105.7	199.5	101.2	103.3	201.7
	PC aa C36:3	0.238	**0.000**	**0.039**	53.2	54.5	58.3	41.1 B	38.9 B	86.1 A	40.3 BC	40.9 BC	78.4 A	39.3 BC	39.0 BC	85.2 A	43.5 B	36.7 C	94.7 A
	PC aa C36:4	0.187	**0.000**	**0.008**	18.6	19.2	20.7	16.1 B	13.4 C	28.9 A	15.6 BC	14.1 C	26.1 A	14.8 BC	13.6 C	29.2 A	18.1 B	12.5 C	31.4 A
	PC aa C36:5	0.717	**0.000**	**0.012**	5.44	5.16	5.21	5.10 B	3.91 C	6.80 A	4.99 BCD	4.51 CD	6.84 AB	4.69 CD	3.85 DE	6.95 A	5.63 ABC	3.39 E	6.61 AB
	PC aa C36:6	0.438	**0.000**	0.510	1.81	1.59	1.70	1.73 B	1.19 C	2.19 A	1.84	1.37	2.23	1.66	1.10	2.01	1.68	1.10	2.33
	PC aa C38:0	**0.004**	**0.000**	**0.004**	1.43 AB	1.29 B	1.73 A	2.25 A	0.63 C	1.57 B	2.09 AB	0.71 C	1.50 B	1.86 B	0.54 C	1.45 B	2.80 A	0.63 C	1.74 B
	PC aa C38:1	0.334	**0.000**	0.276	4.08	3.79	4.38	6.88 A	1.74 C	3.63 B	6.64	2.03	3.58	6.25	1.57	3.56	7.74	1.62	3.77
	PC aa C38:3	**0.027**	**0.000**	0.116	21.92 AB	18.99 B	22.55 A	23.79 B	11.10 C	28.57 A	23.76	13.04	28.96	22.63	9.55	24.79	24.98	10.70	31.95
	PC aa C38:4	**0.048**	**0.000**	0.084	22.47 AB	20.84 B	23.82 A	25.18 A	14.31 B	27.64 A	24.73	15.90	26.76	23.80	13.16	25.58	27.02	13.88	30.57
	PC aa C38:5	0.494	**0.000**	0.091	15.75	14.81	15.77	14.99 B	12.02 C	19.32 A	14.54	13.47	19.24	13.97	11.49	18.95	16.46	11.10	19.76
	PC aa C38:6	0.677	**0.000**	**0.035**	2.83	2.68	2.81	2.34 B	2.37 B	3.61 A	2.34 D	2.67 BCD	3.48 ABC	2.25 D	2.32 D	3.46 AB	2.43 CD	2.12 D	3.88 A
	PC aa C40:1	**0.012**	**0.000**	0.403	0.21 AB	0.20 B	0.21 A	0.23 A	0.17 B	0.22 A	0.23	0.17	0.21	0.22	0.16	0.21	0.24	0.17	0.23
	PC aa C40:2	**0.020**	**0.000**	**0.037**	0.16 AB	0.14 B	0.18 A	0.24 A	0.07 C	0.17 B	0.24 AB	0.08 C	0.17 B	0.21 AB	0.06 C	0.16 B	0.27 A	0.07 C	0.20 AB
	PC aa C40:3	0.096	**0.000**	0.289	1.74	1.44	1.83	2.93 A	0.43 C	1.64 B	3.03	0.54	1.64	2.55	0.35	1.43	3.22	0.40	1.86
	PC aa C40:4	**0.033**	**0.000**	**0.019**	5.39 AB	4.84 B	6.04 A	9.26 A	2.05 C	4.96 B	9.55 A	2.27 D	4.37 C	7.94 AB	1.85 D	4.72 C	10.28 A	2.05 D	5.78 BC
	PC aa C40:5	0.399	**0.000**	0.281	10.77	10.34	11.16	12.09 A	7.90 B	12.28 A	12.20	8.30	11.81	11.19	7.74	12.07	12.89	7.65	12.95
	PC aa C40:6	0.872	**0.000**	0.157	2.98	2.86	2.92	2.66 B	2.62 B	3.49 A	2.69	2.83	3.42	2.64	2.63	3.32	2.65	2.39	3.73
	PC aa C42:0	0.350	**0.000**	0.436	0.07	0.07	0.07	0.07 B	0.05 C	0.09 A	0.07	0.05	0.09	0.06	0.05	0.09	0.07	0.05	0.09
	PC aa C42:1	**0.000**	**0.000**	**0.001**	0.16 A	0.12 B	0.11 C	0.15 A	0.13 B	0.11 C	0.18 A	0.14 B	0.14 B	0.14 BC	0.13 BCD	0.10 E	0.12 CD	0.12 D	0.08 F
	PC aa C42:2	**0.002**	**0.000**	0.203	0.13 A	0.12 AB	0.11 B	0.13 A	0.10 B	0.13 A	0.15	0.10	0.14	0.13	0.10	0.13	0.13	0.09	0.12
	PC aa C42:4	**0.033**	**0.000**	**0.039**	0.08 AB	0.07 B	0.10 A	0.15 A	0.04 C	0.07 B	0.15 AB	0.04 EF	0.06 CDE	0.12 ABC	0.03 F	0.07 D	0.17 A	0.04 EF	0.08 BCD
	PC aa C42:5	0.076	**0.000**	0.097	0.53	0.43	0.54	0.98 A	0.15 C	0.37 B	1.05	0.18	0.35	0.79	0.14	0.36	1.08	0.15	0.40
	PC aa C42:6	0.329	**0.000**	0.053	0.25	0.23	0.25	0.37 A	0.13 C	0.23 B	0.40	0.15	0.22	0.34	0.12	0.22	0.38	0.12	0.24

Figure S1H.

		F-Test			LSMeans												Metabotype*Sampling Day																	
					Metabotype						Sampling Day						Metabotype A						Metabotype B						Metabotype C					
	Metabolite	FP	SD	FPxSD	A		B		C		14ap		7pp		28pp		14ap		7pp		28pp		14ap		7pp		28pp		14ap		7pp		28pp	
Plasma	PC ae C30:0	0.544	**0.000**	**0.028**	0.39		0.38		0.40		0.35	B	0.30	C	0.52	A	0.34	BC	0.33	BC	0.50	A	0.34	BC	0.29	C	0.51	A	0.36	B	0.29	C	0.55	A
	PC ae C30:1	0.633	**0.000**	0.566	0.97		0.92		0.99		0.78	B	0.68	C	1.42	A	0.79		0.75		1.36		0.75		0.63		1.39		0.79		0.67		1.51	
	PC ae C30:2	0.157	**0.000**	0.131	0.22		0.20		0.22		0.18	B	0.13	C	0.32	A	0.18		0.15		0.32		0.17		0.12		0.29		0.19		0.13		0.35	
	PC ae C32:1	0.078	**0.000**	**0.040**	1.88		1.73		1.94		1.47	B	1.38	B	2.71	A	1.50	BC	1.52	BC	2.63	A	1.37	BC	1.30	BC	2.53	A	1.53	B	1.32	C	2.97	A
	PC ae C32:2	0.243	**0.000**	0.139	3.29		3.12		3.54		2.77	B	2.19	C	4.99	A	2.70		2.36		4.80		2.68		2.05		4.64		2.93		2.17		5.52	
	PC ae C34:0	**0.001**	**0.000**	**0.000**	1.41	AB	1.26	B	1.60	A	1.59	B	0.80	C	1.86	A	1.69	B	0.89	C	1.65	AB	1.45	B	0.74	C	1.58	B	1.65	B	0.78	C	2.36	A
	PC ae C34:1	0.261	**0.000**	**0.005**	8.23		7.91		8.55		7.84	B	5.79	C	11.06	A	7.90	C	6.35	DE	10.44	AB	7.38	CD	5.73	E	10.61	A	8.25	BC	5.29	E	12.13	A
	PC ae C34:2	0.062	**0.000**	0.051	11.45		10.76		12.27		8.63	B	7.69	C	18.15	A	8.77		8.47		17.09		8.10		7.17		17.02		9.02		7.44		20.34	
	PC ae C34:3	**0.011**	**0.000**	**0.034**	11.29	AB	10.50	B	13.24	A	6.44	C	7.44	B	21.14	A	6.57	B	8.06	B	19.24	A	6.00	B	6.67	B	18.82	A	6.76	B	7.60	B	25.37	A
	PC ae C36:0	**0.045**	**0.000**	**0.030**	1.00	AB	0.87	B	1.03	A	1.25	A	0.55	C	1.10	B	1.26	AB	0.62	C	1.12	AB	1.11	AB	0.51	C	0.99	B	1.38	A	0.52	C	1.19	AB
	PC ae C36:1	0.394	**0.000**	**0.029**	9.99		9.29		9.91		10.82	B	6.15	C	12.21	A	11.39	AB	6.77	C	11.79	AB	10.28	B	6.15	C	11.44	AB	10.79	B	5.54	C	13.41	A
	PC ae C36:2	0.121	**0.000**	**0.031**	12.25		11.88		13.53		10.71	B	7.67	C	19.29	A	11.17	B	8.25	CD	17.35	A	10.34	BC	7.54	D	17.77	A	10.61	B	7.22	D	22.74	A
	PC ae C36:3	0.135	**0.000**	**0.050**	5.30		4.97		5.60		4.50	B	3.44	C	7.92	A	4.73	B	3.82	CD	7.34	A	4.23	BC	3.24	D	7.43	A	4.55	BC	3.26	D	8.97	A
	PC ae C36:4	0.112	**0.000**	**0.041**	4.06		3.91		4.49		2.87	B	2.95	B	6.63	A	2.92	B	3.28	B	5.97	A	2.68	B	2.73	B	6.32	A	3.02	B	2.85	B	7.60	A
	PC ae C36:5	0.051	**0.000**	**0.034**	2.79		2.59		2.99		2.41	B	2.09	C	3.87	A	2.39	CD	2.31	CD	3.68	AB	2.19	CD	1.94	D	3.63	A	2.64	BC	2.03	D	4.30	A
	PC ae C38:0	**0.050**	**0.000**	**0.020**	0.97	AB	0.85	B	1.00	A	1.09	A	0.61	B	1.13	A	1.09	A	0.70	BC	1.13	A	0.96	AB	0.54	C	1.04	A	1.22	A	0.58	C	1.21	A
	PC ae C38:1	0.105	**0.000**	0.258	1.11		0.92		1.06		1.56	A	0.45	C	1.08	B	1.68		0.53		1.11		1.46		0.40		0.91		1.55		0.41		1.22	
	PC ae C38:2	0.138	**0.000**	**0.040**	1.74		1.55		1.72		1.78	B	0.93	C	2.29	A	1.92	B	1.07	C	2.23	AB	1.70	B	0.89	C	2.04	AB	1.73	B	0.83	C	2.60	A
	PC ae C38:3	**0.047**	**0.000**	**0.035**	2.21	AB	1.96	B	2.26	A	2.36	B	1.15	C	2.92	A	2.47	B	1.31	C	2.84	AB	2.24	B	1.09	C	2.54	AB	2.36	B	1.06	C	3.36	A
	PC ae C38:4	**0.024**	**0.000**	**0.008**	2.24	AB	2.09	B	2.44	A	2.67	A	1.39	B	2.71	A	2.72	AB	1.50	C	2.51	AB	2.48	B	1.33	C	2.45	AB	2.82	AB	1.34	C	3.16	A
	PC ae C38:5	**0.024**	**0.000**	**0.025**	2.03	AB	1.91	B	2.23	A	2.08	B	1.48	C	2.61	A	2.07	B	1.62	CD	2.41	AB	1.93	BC	1.39	D	2.42	AB	2.23	B	1.44	D	3.01	A
	PC ae C38:6	0.344	**0.000**	0.203	2.19		2.01		2.23		1.67	B	1.80	B	2.97	A	1.68		1.97		2.92		1.57		1.70		2.77		1.74		1.72		3.23	
	PC ae C40:1	0.168	**0.000**	0.325	0.25		0.22		0.25		0.32	A	0.13	C	0.26	B	0.34		0.15		0.26		0.29		0.12		0.24		0.33		0.13		0.29	
	PC ae C40:2	**0.018**	**0.000**	**0.010**	0.58	AB	0.55	B	0.63	A	0.67	A	0.38	B	0.71	A	0.67	AB	0.40	C	0.66	AB	0.62	B	0.36	C	0.67	AB	0.73	AB	0.37	C	0.78	A
	PC ae C40:3	**0.019**	**0.000**	0.073	0.46	AB	0.39	B	0.46	A	0.51	A	0.25	B	0.56	A	0.52		0.29		0.57		0.48		0.23		0.48		0.52		0.24		0.62	
	PC ae C40:4	**0.010**	**0.000**	**0.028**	0.54	AB	0.48	B	0.57	A	0.64	A	0.30	B	0.65	A	0.66	AB	0.34	C	0.63	AB	0.60	B	0.27	C	0.56	B	0.65	AB	0.30	C	0.76	A
	PC ae C40:5	0.116	**0.000**	0.159	1.17		1.05		1.21		1.27	A	0.79	B	1.37	A	1.32		0.85		1.33		1.18		0.75		1.24		1.31		0.77		1.54	
	PC ae C40:6	0.317	**0.000**	0.050	0.68		0.64		0.69		0.63	B	0.54	C	0.83	A	0.65		0.59		0.78		0.61		0.51		0.79		0.64		0.51		0.92	
	PC ae C42:0	**0.041**	**0.000**	**0.012**	0.31	AB	0.30	B	0.32	A	0.30	B	0.29	B	0.33	A	0.30	BCDEF	0.30	DEFG	0.33	ABC	0.30	CEFG	0.29	EF	0.32	ABD	0.31	BCDE	0.29	F	0.35	A
	PC ae C42:1	**0.000**	**0.000**	**0.003**	0.22	A	0.19	B	0.18	B	0.22	A	0.18	B	0.19	B	0.26	A	0.20	BC	0.22	AB	0.21	B	0.18	CD	0.17	CD	0.19	BC	0.17	D	0.19	BCD
	PC ae C42:2	**0.016**	**0.000**	**0.004**	0.18	A	0.15	B	0.17	AB	0.21	A	0.11	C	0.17	B	0.22	AB	0.13	CD	0.19	AB	0.17	BC	0.11	DE	0.16	BC	0.24	A	0.10	E	0.17	B
	PC ae C42:3	**0.012**	**0.000**	**0.007**	0.13	AB	0.11	B	0.13	A	0.15	A	0.08	B	0.14	A	0.15	AB	0.09	C	0.14	AB	0.13	AB	0.07	C	0.13	B	0.17	A	0.07	C	0.15	AB
	PC ae C42:4	**0.005**	**0.000**	0.090	0.09	A	0.07	B	0.09	A	0.12	A	0.05	C	0.09	B	0.13		0.05		0.09		0.10		0.05		0.08		0.13		0.05		0.10	BD
	PC ae C42:5	0.062	**0.000**	0.774	0.41		0.38		0.40		0.42	A	0.34	B	0.42	A	0.44		0.35		0.43		0.41		0.32		0.40		0.43		0.33		0.44	
	PC ae C44:3	0.490	**0.000**	0.182	0.05		0.05		0.05		0.05	B	0.04	C	0.06	A	0.06		0.04		0.06		0.05		0.04		0.06		0.05		0.04		0.07	
	PC ae C44:4	0.484	**0.000**	0.803	0.07		0.07		0.07		0.07	A	0.05	B	0.07	A	0.07		0.05		0.08		0.07		0.06		0.07		0.07		0.06		0.07	
	PC ae C44:5	**0.006**	**0.000**	0.067	0.06	AB	0.05	B	0.06	A	0.06	A	0.05	B	0.06	A	0.06		0.05		0.06		0.06		0.05		0.06		0.07		0.05		0.07	
	PC ae C44:6	0.436	**0.000**	0.563	0.06		0.06		0.06		0.06	B	0.05	C	0.07	A	0.06		0.05		0.07		0.06		0.05		0.07		0.07		0.05		0.07	

Figure S1I.

		F-Test			LSMeans						Metabotype*Sampling Day								
					Metabotype			Sampling Day			Metabotype A			Metabotype B			Metabotype C		
	Metabolite	FP	SD	FPxSD	A	B	C	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp	14ap	7pp	28pp
Liver	SM (OH) C14:1	0.000	0.000	0.000	4.3 A	1.0 B	4.9 A	1.26 C	3.26 B	5.69 A	1.49 B	1.65 B	9.80 A	1.02 B	1.15 B	0.89 B	1.27 B	6.98 A	6.37 A
Liver	SM (OH) C16:1	0.012	0.001	0.000	2.1 AB	0.5 B	2.7 A	0.65 B	1.32 A	3.23 A	0.71 B	0.66 B	4.82 AB	0.57 B	0.41 B	0.43 AB	0.68 B	2.89 A	4.43 AB
Liver	SM (OH) C22:1	0.443	0.515	0.851	3.5	0.7	4.5	0.80	3.06	4.81	0.61	4.95	4.86	0.82	0.48	0.85	0.99	3.75	8.72
Liver	SM (OH) C22:2	0.499	0.437	0.820	0.5	0.1	0.5	0.12	0.53	0.43	0.09	0.85	0.47	0.12	0.07	0.10	0.15	0.67	0.73
Liver	SM (OH) C24:1	0.494	0.405	0.696	0.6	0.1	0.5	0.16	0.47	0.61	0.11	0.93	0.72	0.17	0.09	0.13	0.19	0.39	0.99
Liver	SM C16:0	0.000	0.000	0.002	36.6 A	8.0 B	45.9 A	9.1 B	28.8 AB	52.7 A	10.0 BC	14.3 BC	85.5 A	8.4 C	7.8 C	8.0 C	8.9 C	64.3 AB	64.5 AB
Liver	SM C16:1	0.000	0.000	0.000	3.4 A	0.8 B	3.0 A	0.81 B	2.89 A	3.41 A	0.91 C	3.84 ABC	5.32 A	0.70 C	0.88 BC	0.73 C	0.81 C	3.96 ABC	4.16 AB
Liver	SM C18:0	0.040	0.065	0.412	2.2 AB	0.5 B	3.1 A	0.47	1.97	3.34	0.42	1.60	4.60	0.45	0.40	0.51	0.54	3.90	4.91
Liver	SM C18:1	0.205	0.013	0.213	1.0	0.1	0.8	0.12 B	1.08 AB	0.70 A	0.14	1.85	1.00	0.10	0.15	0.11	0.12	1.24	1.00
Liver	SM C24:0	0.662	0.551	0.782	2.7	0.8	3.6	0.96	2.06	3.98	0.69	3.78	3.54	0.93	0.56	0.85	1.26	1.86	7.56
Liver	SM C26:0	0.136	0.061	0.249	0.4	0.1	0.2	0.06	0.25	0.33	0.05	0.62	0.41	0.07	0.03	0.06	0.07	0.10	0.52
Liver	SM C26:1	0.189	0.008	0.013	0.6	0.1	0.3	0.14 B	0.58 AB	0.31 A	0.15 B	1.40 AB	0.34 AB	0.14 B	0.07 AB	0.11 B	0.15 B	0.25 AB	0.47 A
Liver	H1	0.000	0.002	0.000	15560 B	15819 B	21065 A	17087 AB	20143 A	15214 B	10934 C	25148 A	10597 C	16202 BC	15925 BC	15332 BC	24125 A	19355 AB	19714 AB
Plasma	SM (OH) C14:1	0.159	0.000	0.009	6.26	5.85	6.49	5.83 B	4.46 C	8.31 A	5.77 CD	4.99 DE	8.01 AB	5.58 CD	4.20 E	7.77 AB	6.15 BC	4.19 E	9.13 A
Plasma	SM (OH) C16:1	0.240	0.000	0.019	3.84	3.66	4.06	3.76 B	2.58 C	5.23 A	3.78 B	2.88 C	4.88 AB	3.76 B	2.41 C	4.82 AB	3.74 B	2.45 C	6.00 A
Plasma	SM (OH) C22:1	0.757	0.000	0.187	8.45	8.25	8.59	5.71 C	6.86 B	12.73 A	5.46	7.42	12.48	5.59	6.51	12.66	6.07	6.66	13.06
Plasma	SM (OH) C22:2	0.490	0.000	0.121	3.66	3.46	3.63	3.30 B	2.73 C	4.72 A	3.23	3.00	4.74	3.17	2.59	4.62	3.49	2.59	4.81
Plasma	SM (OH) C24:1	0.587	0.000	0.291	0.69	0.71	0.73	0.64 B	0.54 C	0.94 A	0.63	0.55	0.88	0.66	0.53	0.93	0.63	0.54	1.02
Plasma	SM C16:0	0.605	0.000	0.038	56.0	55.8	58.3	45.7 B	44.3 B	80.1 A	44.1 B	48.1 B	75.9 A	45.2 B	43.1 B	79.0 A	47.9 B	41.8 B	85.3 A
Plasma	SM C16:1	0.231	0.000	0.054	5.42	5.22	5.73	5.37 B	3.53 C	7.48 A	5.41	3.89	6.97	5.15	3.36	7.16	5.56	3.35	8.30
Plasma	SM C18:0	0.036	0.000	0.007	6.07 A	6.18 A	6.83 A	5.15 B	5.08 B	8.84 A	5.04 B	5.31 B	7.84 A	5.01 B	4.99 B	8.54 A	5.40 B	4.95 B	10.15 A
Plasma	SM C18:1	0.257	0.000	0.141	2.17	2.15	2.31	2.06 B	1.69 C	2.89 A	2.06	1.78	2.66	2.01	1.64	2.80	2.10	1.64	3.19
Plasma	SM C20:2	0.800	0.077	0.368	0.02	0.02	0.02	0.013	0.020	0.026	0.007	0.027	0.020	0.016	0.015	0.029	0.016	0.018	0.030
Plasma	SM C22:3	0.073	0.000	0.038	0.01	0.02	0.03	0.005 B	0.012 B	0.041 A	0.002 B	0.014 B	0.016 AB	0.003 B	0.014 B	0.037 AB	0.009 B	0.007 B	0.071 A
Plasma	SM C24:0	0.193	0.000	0.147	12.88	11.86	13.33	12.67 B	7.39 C	18.01 A	13.38	8.26	17.00	11.43	6.85	17.31	13.20	7.06	19.72
Plasma	SM C24:1	0.059	0.000	0.162	3.29	3.94	3.89	2.41 C	3.75 B	4.96 A	2.15	3.63	4.11	2.48	3.96	5.38	2.61	3.67	5.39
Plasma	SM C26:0	0.089	0.000	0.581	0.18	0.21	0.19	0.20 B	0.15 C	0.23 A	0.19	0.15	0.21	0.22	0.17	0.25	0.18	0.15	0.24
Plasma	SM C26:1	0.325	0.412	0.123	0.220	0.214	0.199	0.219	0.203	0.211	0.237	0.205	0.218	0.237	0.209	0.195	0.182	0.195	0.220
Plasma	H1	0.170	0.000	0.000	2506	2674	2732	2840 A	2333 B	2738 A	2709 ABC	2350 CD	2457 BCD	3036 AB	2477 CD	2508 BCD	2774 BC	2173 D	3249 A

Figure S1J.

Figure S1. Results of F-test (p-values) as well as the associated LSMeans and test of the differences (Tukey-test, letter representation of significances) of metabotype, sampling day and their interaction, on transition cow liver and blood metabolome across the transition period. A: AA, B: biogenic amines, C-D: acylcarnitines, E: lysophophatidylcholines, F-I: phosphatidylcholines, J: sphingomyelins and hexoses. Size of bar in relation to greatest value within respective comparison (sampling day, metabotype or sampling day×metabotype). All values in µmol/L and presented as LSMeans. Different letters indicate a significant difference with P ≤ 0.05 within respective comparison. P-values in F-Test ≤ 0.0009 are presented as 0.000.