

SUPPLEMENTARY DATA

**Supplementary Table 1.** UniPathway linear sub-pathways demonstrating differences for High v. Low FPG Mothers

<b>UniPathway Linear Sub-pathway (ULS) ULS ID: Name</b>	<b>FDR adj p</b>
<b>Amino acid metabolism</b>	
ULS00082: L-serine from 3-phospho-D-glycerate	<0.01
ULS00159: L-proline from L-ornithine	<0.01
ULS00170: L-glutamate from L-proline	<0.01
ULS00277: pyruvate from L-alanine	<0.01
ULS00045: L-ornithine and N-acetyl-L-glutamate from L-glutamate and N(2)-acetyl-L-ornithine	0.01
ULS00160: L-glutamate 5-semialdehyde from L-ornithine	0.01
ULS00424: 4-methyl-2-oxopentanoate from L-leucine	0.01
ULS00043: N(2)-acetyl-L-ornithine from L-glutamate	0.01
ULS00148: acetoacetate and fumarate from L-phenylalanine	0.01
ULS00434: L-methionine from S-methyl-5-thio-alpha-D-ribose 1-phosphate	0.03
ULS00419: glutaryl-CoA from L-lysine	0.03
ULS00425: 4-methyl-2-oxopentanoate from L-leucine (dehydrogenase route)	0.05
<b>Carbohydrate metabolism and / or organic acid metabolism</b>	
ULS00488: 2-oxoglutarate from isocitrate (NADP(+)) route)	0.01
ULS00293: (S)-lactate from pyruvate	0.03

UniPathway Linear Sub-pathways (ULSs) were evaluated for collective differences in high vs. low FPG mothers by comparing the median likelihood ratio test statistic for the set of constituent metabolites represented in the data set to the median test statistic for the same set of metabolites after random reshuffling of the sample covariate vectors 1000 times. Reported p-values represent the number of medians as or more extreme than the observed values. The ULSs reported here retain FDR-corrected  $p < 0.05$  and are organized according to amino acid or carbohydrate / organic acid metabolism involvement.

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**Supplementary Table 2.** Exploratory associations between HAPO newborn characteristics and maternal FPG non-targeted metabolite levels at 28 weeks' gestation

Newborn characteristics and Metabolites	Newborn association without adjustment for maternal high v. low FPG group	Newborn association including adjustment for maternal high v. low FPG group
	$\beta$ (p)	$\beta$ (p)
Newborn Sum of Skinfolds (per 1mm), n=92		
Glucose and other aldohexoses	0.08 (<0.001)	0.03 (0.31)
Alanine	0.06 (0.03)	0.05 (0.29)
Isoleucine	0.08 (0.03)	0.04 (0.46)
Campesterol	-0.28 (0.03)	-0.27 (0.29)
Proline	0.09 (0.03)	0.04 (0.46)
cis/trans-4-Hydroxyproline	0.07 (0.03)	0.06 (0.29)
Mannitol and other hexitols	-0.73 (0.04)	-0.88 (0.28)
Threonine	0.07 (0.05)	0.05 (0.31)
Citric acid	0.07 (0.05)	0.08 (0.26)
Newborn Cord C-peptide (per 1ug/l), n=100		
Glucose and other aldohexoses	.43 (<0.001)	0.18 (0.19)
2-Hydroxybutyric acid	0.43 (0.002)	0.41 (0.12)
Mannitol and other hexitols	-1.00 (0.006)	-0.96 (0.19)
beta-Sitosterol	4.98 (0.01)	6.64 (0.19)
alpha-Ketoglutaric acid	-0.15 (0.01)	-0.26 (0.19)
Pyruvic acid	1.79 (0.03)	1.55 (0.26)
cis/trans-4-Hydroxyproline	0.34 (0.03)	0.27 (0.26)
Threitol	0.25 (0.03)	-0.11 (0.26)
Proline	0.44 (0.03)	0.21 (0.50)
Ketoleucine	1.09 (0.03)	1.48 (0.12)
Isoleucine	0.36 (0.03)	0.13 (0.65)
Fructose and other ketohexoses	0.35 (0.03)	0.12 (0.65)
Oleic acid	0.29 (0.04)	0.25 (0.26)
Lauric acid	0.41 (0.04)	0.20 (0.56)
Xylitol and other pentitols	0.26 (0.04)	0.23 (0.26)
Pentadecanoic acid / 1-Hexadecanol	1.17 (0.05)	1.30 (0.19)

Mixture model parameter estimates ( $\beta$ ) for continuous associations between non-targeted metabolites with HAPO newborn characteristics (sum of skinfolds and cord C-peptide). Estimates of  $\beta$  represent a higher amount of the metabolite per newborn sum of skinfolds higher by 1mm, newborn birth weight higher by 100g or cord C-peptide higher by 1 ug/l. All estimates are adjusted for field center, parity, maternal and gestational age at OGTT and length of FPG sample storage time. Estimates of  $\beta$  are reported for associations with newborn characteristics, both with and without adjustment for maternal high v. low FPG group. Reported p-values include false discovery rate adjustment.

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**Supplementary Figure 1.** Amino acid metabolism UniPathway hierarchy. Enrichment analyses were performed using Unipathway ULSs to define the sets of compounds for joint analysis. Fourteen ULSs demonstrated collective differences in high v. low FPG mothers with FDR-corrected  $p < 0.05$ ; five ULSs related to amino acid metabolism are illustrated here. All pathway compounds demonstrated higher levels for high v. low FPG mothers.

