

## *Supplementary Material*

**Supplemental Table 1. Patient characteristics shared by both California and Alabama cohorts**

Characteristic	California Cohort	Alabama Cohort
	Full-term (n=19)	Full-term (n=10)
Age, mean(SD)	32.2 (4.7)	26.(4.9)
GA @ Del, mean(SD)	39.5 (1.2)	38.2 (1.2)
Days, mean(SD)	2.9 (2.1)	2.4 (2.2)
Type of Membrane Rupture, N(%)		
AROM	11 (57.9)	6 (60)
SROM	8 (42.1)	4 (40)
How did labor begin?, N(%)		
Augmented	3 (15.8)	3 (30)
Induced	5 (26.3)	4 (40)
Spontaneous	9 (47.4)	3 (30)
SROM w/o contractions	1 (5.3)	0 (0)
NA	1 (5.3)	0 (0)
Mode of delivery, N(%)		
Cesarean	6 (31.6)	0 (0)
NSVD	12 (63.2)	10 (100)
Operative Vaginal delivery	1 (5.3)	0 (0)
Presentation @ Del, Vertex/cephalic	19 (100)	10 (100)
Beta blocker Use, No	19 (100)	10 (100)
GBS, N(%)		
Negative	16 (84.2)	7 (70)
Positive	3 (15.8)	3 (30)
Blood loss (>500mL for NSVD; >1,000mL for cesarean, N(%)		
No	17 (89.5)	10 (100)
Yes	2 (10.5)	0 (0)
Transfusion, N(%)		

No	18 (94.7)	10 (100)
Yes	1 (5.3)	0 (0)
<b>Antibiotic use, N(%)</b>		
No	12 (63.2)	7 (70)
Yes	7 (36.8)	3 (30)
<b>Preg Type, N(%)</b>		
IVF	1 (5.3)	0 (0)
Spontaneous	18 (94.7)	9 (90)
NA	0 (0)	1 (10)
<b>Race, N(%)</b>		
White	19 (100)	0 (0)
Black	0 (0)	10 (100)
<b>Ethnicity, Non-hispanic</b>	19 (100)	10 (100)
<b>BMI, median(IQR)</b>	21.8 (20.2,24.7)	29.8 (26.6,32.5)
<b>highest level of education, N(%)</b>		
Bachelor/undergraduate degree	5 (26.3)	0 (0)
High School diploma or equivalent (GED)	0 (0)	3 (30)
No high school (8th grade or less)	0 (0)	1 (10)
Post-undergraduate degree	12 (63.2)	0 (0)
Post-undergraduate degree/PhD	2 (10.5)	0 (0)
Some college	0 (0)	4 (40)
Some high school	0 (0)	2 (20)
<b>Smoker, N(%)</b>		
No	19 (100)	8 (80)
Yes	0 (0)	2 (20)
<b>Prev Pregs, median(IQR)</b>	1 (0,2)	3 (1,4)
<b>Hx of PTB, N(%)</b>		
NO	16 (84.2)	1 (10)
YES	3 (15.8)	9 (90)
<b>Progest Use, N(%)</b>		
YES	1 (5.3)	10 (100)
NA	18 (94.7)	0 (0)
<b>Mom Hgt (cm), mean(SD)</b>	166.9 (6.2)	162.9 (3)
<b>Hx of PE, N(%)</b>		

No	19 (100)	0 (0)
<b>Chorioamnionitis, N(%)</b>		
No	17 (89.5)	10 (100)
Yes	2 (10.5)	0 (0)
<b>Endometritis, N(%)</b>		
No	18 (94.7)	10 (100)
Yes	1 (5.3)	0 (0)
<b>Autoimmune Disorder, N(%)</b>		
No	18 (94.7)	10 (100)
Yes	1 (5.3)	0 (0)
<b>Multiple UTI, N(%)</b>		
No	17 (89.5)	10 (100)
Yes	2 (10.5)	0 (0)
<b>Psychiatric Dx (depression), N(%)</b>		
No	17 (89.5)	9 (90)
Yes	2 (10.5)	1 (10)
<b>Thyroid Dx, N(%)</b>		
No	18 (94.7)	10 (100)
Yes	1 (5.3)	0 (0)
<b>Asthma, N(%)</b>		
No	18 (94.7)	9 (90)
Yes	1 (5.3)	1 (10)
<b>Cancer, N(%)</b>		
No	18 (94.7)	10 (100)
Yes	1 (5.3)	0 (0)
<b>Epilepsy, N(%)</b>		
No	19 (100)	9 (90)
Yes	0 (0)	1 (10)
<b>Breast Dx, No</b>	19 (100)	10 (100)
<b>Gynecol surgery, N(%)</b>		
No	14 (73.7)	10 (100)
Yes	5 (26.3)	0 (0)
<b>HTN, N(%)</b>		
No	19 (100)	9 (90)

<b>Yes</b>	<b>0 (0)</b>	<b>1 (10)</b>
<b>Gest HTN, N(%)</b>		
<b>Mild gHTN</b>	<b>1 (5.3)</b>	<b>0 (0)</b>
<b>No</b>	<b>11 (57.9)</b>	<b>0 (0)</b>
<b>NA</b>	<b>7 (36.8)</b>	<b>10 (100)</b>
<b>EtOH, N(%)</b>		
<b>No</b>	<b>18 (94.7)</b>	<b>10 (100)</b>
<b>Yes</b>	<b>1 (5.3)</b>	<b>0 (0)</b>
<b>Recreational Drug Use, N(%)</b>		
<b>No</b>	<b>19 (100)</b>	<b>9 (90)</b>
<b>Yes</b>	<b>0 (0)</b>	<b>1 (10)</b>
<b>Sex, N(%)</b>	<b>0 (0)</b>	
<b>Female</b>	<b>8 (42.1)</b>	<b>5 (50)</b>
<b>Male</b>	<b>11 (57.9)</b>	<b>5 (50)</b>
<b>Wgt at Birth (kg), mean(SD)</b>	<b>3.4 (0.3)</b>	<b>3.1 (0.5)</b>
<b>Length at birth (cm), median(IQR)</b>	<b>51 (50,53)</b>	<b>49.5 (46.8,50.6)</b>

**Supplemental Table 2A. Patient characteristics of California cohort.**

Characteristic	California Cohort
	Full-term (n=19)
Age, mean(SD)	32.2 (4.7)
GA @ Del, mean(SD)	39.5 (1.2)
Days, mean(SD)	2.9 (2.1)
Type of Membrane Rupture, N(%)	
AROM	11 (57.9)
SROM	8 (42.1)
How did labor begin?, N(%)	
Augmented	3 (15.8)
Induced	5 (26.3)
Spontaneous	9 (47.4)
SROM w/o contractions	1 (5.3)
NA	1 (5.3)
Mode of delivery, N(%)	
Cesarean	6 (31.6)
NSVD	12 (63.2)
Operative Vaginal delivery	1 (5.3)
Presentation @ Del, Vertex/cephalic	19 (100)
Beta blocker Use, No	19 (100)
GBS, N(%)	
Negative	16 (84.2)
Positive	3 (15.8)
Blood loss (>500mL for NSVD; >1,000mL for cesarean, N(%)	
No	17 (89.5)
Yes	2 (10.5)
Transfusion, N(%)	
No	18 (94.7)
Yes	1 (5.3)
Antibiotic use, N(%)	
No	12 (63.2)

<b>Yes</b>	<b>7 (36.8)</b>
<b>Preg Type, N(%)</b>	
<b>IVF</b>	<b>1 (5.3)</b>
<b>Spontaneous</b>	<b>18 (94.7)</b>
<b>Race, N(%)</b>	
<b>White</b>	<b>19 (100)</b>
<b>Ethnicity, Non-hispanic</b>	<b>19 (100)</b>
<b>BMI, median(IQR)</b>	<b>21.8 (20.2,24.7)</b>
<b>highest level of education, N(%)</b>	
<b>Bachelor/undergraduate degree</b>	<b>5 (26.3)</b>
<b>High School diploma or equivalent (GED)</b>	<b>0 (0)</b>
<b>No high school (8th grade or less)</b>	<b>0 (0)</b>
<b>Post-undergraduate degree</b>	<b>12 (63.2)</b>
<b>Post-undergraduate degree/PhD</b>	<b>2 (10.5)</b>
<b>Smoker, N(%)</b>	
<b>No</b>	<b>19 (100)</b>
<b>Prev Pregs, median(IQR)</b>	<b>1 (0,2)</b>
<b>Hx of PTB, N(%)</b>	
<b>NO</b>	<b>16 (84.2)</b>
<b>YES</b>	<b>3 (15.8)</b>
<b>Progest Use, N(%)</b>	
<b>NA</b>	<b>18 (94.7)</b>
<b>YES</b>	<b>1 (5.3)</b>
<b>Mom Hgt (cm), mean(SD)</b>	<b>166.9 (6.2)</b>
<b>Mom Wgt (kg), median(IQR)</b>	<b>61 (57,66.7)</b>
<b>Hx of PE, N(%)</b>	
<b>No</b>	<b>19 (100)</b>
<b>Chorioamnionitis, N(%)</b>	
<b>No</b>	<b>17 (89.5)</b>
<b>Yes</b>	<b>2 (10.5)</b>
<b>Endometritis, N(%)</b>	
<b>No</b>	<b>18 (94.7)</b>
<b>Yes</b>	<b>1 (5.3)</b>

<b>Autoimmune Disorder, N(%)</b>	
No	18 (94.7)
Yes	1 (5.3)
<b>Multiple UTI, N(%)</b>	
No	17 (89.5)
Yes	2 (10.5)
<b>Psychiatric Dx (depression), N(%)</b>	
No	17 (89.5)
Yes	2 (10.5)
<b>Thyroid Dx, N(%)</b>	
No	18 (94.7)
Yes	1 (5.3)
<b>Asthma, N(%)</b>	
No	18 (94.7)
Yes	1 (5.3)
<b>Cancer, N(%)</b>	
No	18 (94.7)
Yes	1 (5.3)
<b>Epilepsy, N(%)</b>	
No	19 (100)
Yes	0 (0)
<b>Breast Dx, No</b>	
	19 (100)
<b>Gynecol surgery, N(%)</b>	
No	14 (73.7)
Yes	5 (26.3)
<b>HTN, N(%)</b>	
No	19 (100)
<b>Gest HTN, N(%)</b>	
Mild gHTN	1 (5.3)
No	11 (57.9)
NA	7 (36.8)
<b>EtOH, N(%)</b>	
No	18 (94.7)
Yes	1 (5.3)

<b>Recreational Drug Use, N(%)</b>	
<b>No</b>	<b>19 (100)</b>
<b>Sex, N(%)</b>	<b>0 (0)</b>
<b>Female</b>	<b>8 (42.1)</b>
<b>Male</b>	<b>11 (57.9)</b>
<b>Wgt at Birth (kg), mean(SD)</b>	<b>3.4 (0.3)</b>
<b>Length at birth (cm), median(IQR)</b>	<b>51 (50,53)</b>



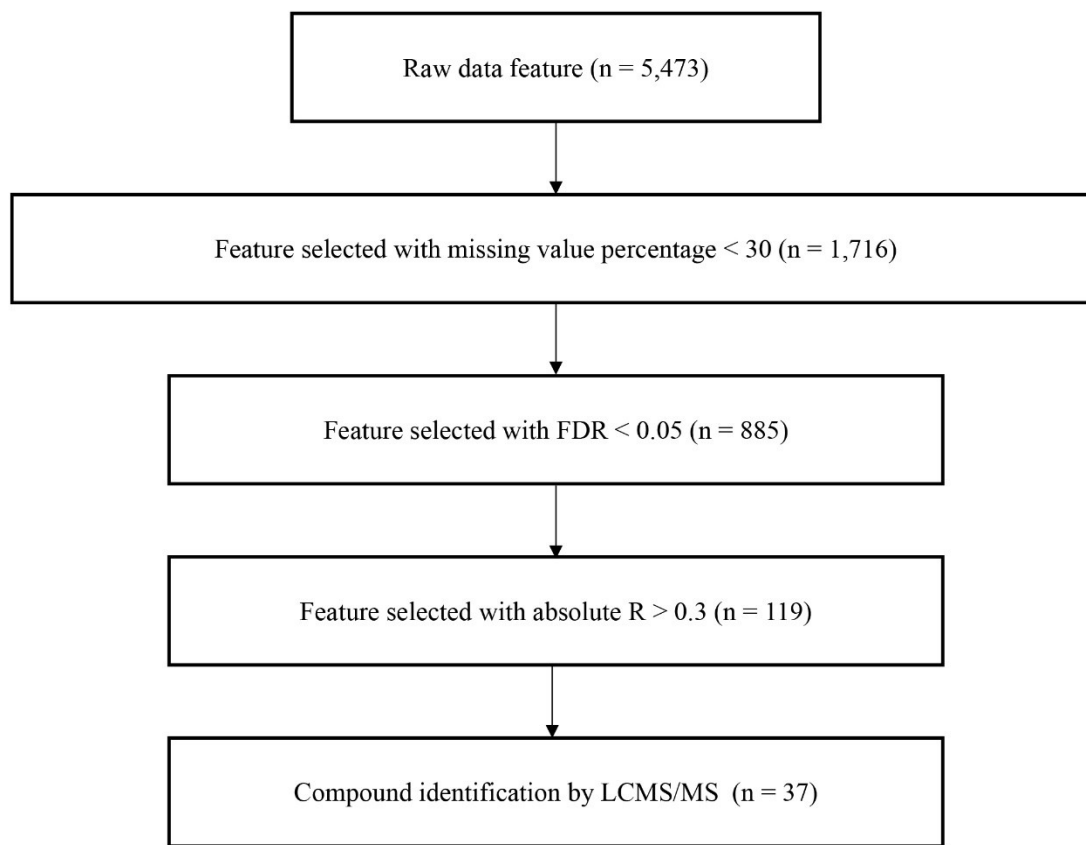
**Supplemental Table 2B. Patient characteristics of Alabama cohort.**

<b>Characteristic</b>	<b>Alabama Cohort</b>
	<b>Full-term (n=10)</b>
Age, mean(SD)	26.1 (4.9)
GA @ Del, mean(SD)	38.2 (1.2)
Days, mean(SD)	2.4 (2.2)
Type of Membrane Rupture, N(%)	
AROM	6 (60)
SROM	4 (40)
How did labor begin?, N(%)	
Augmented	3 (30)
Induced	4 (40)
Spontaneous	0 (0)
SROM w/o contractions	3 (30)
NA	0 (0)
Mode of delivery, N(%)	
Cesarean	0 (0)
NSVD	10 (100)
Operative Vaginal delivery	0 (0)
Presentation @ Del, Vertex/cephalic	10 (100)
Beta blocker Use, No	10 (100)
GBS, N(%)	
Negative	7 (70)
Positive	3 (30)
Blood loss (>500mL for NSVD; >1,000mL for cesarean, N(%)	
No	10 (100)
Yes	0 (0)
Transfusion, N(%)	
No	10 (100)
Yes	0 (0)

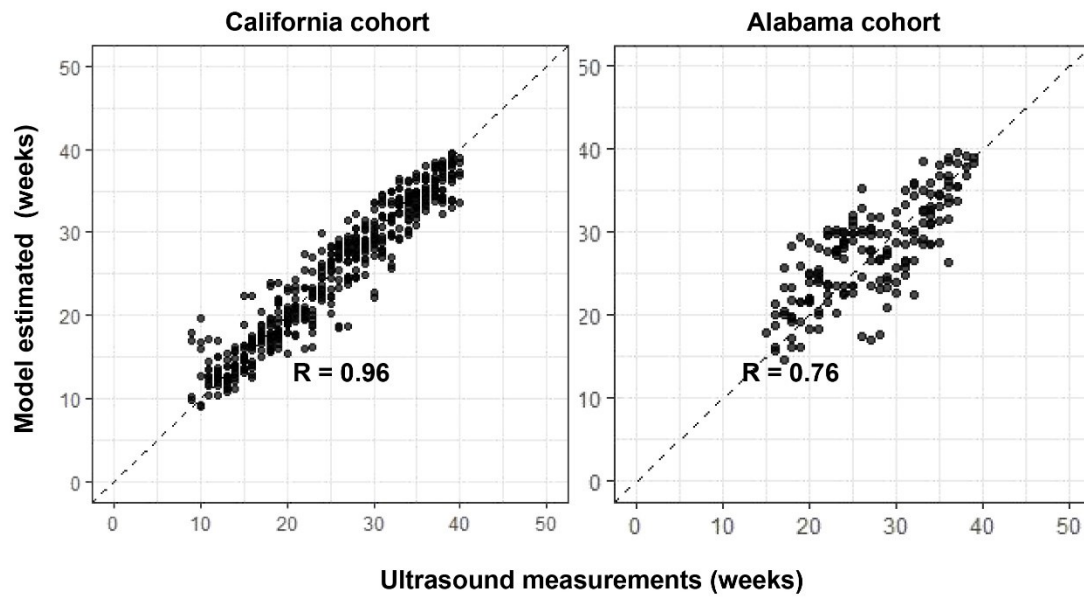
<b>Antibiotic use, N(%)</b>	
No	7 (70)
Yes	3 (30)
<b>Preg Type, N(%)</b>	
Spontaneous	9 (90)
NA	1 (10)
<b>Race, N(%)</b>	
Black	10 (100)
<b>Ethnicity, Non-hispanic</b>	10 (100)
<b>BMI, median(IQR)</b>	29.8 (26.6,32.5)
<b>highest level of education, N(%)</b>	
<b>High School diploma or equivalent (GED)</b>	3 (30)
No high school (8th grade or less)	1 (10)
Some college	4 (40)
Some high school	2 (20)
<b>Smoker, N(%)</b>	
No	8 (80)
Yes	2 (20)
<b>Prev Pregs, median(IQR)</b>	3 (1,4)
<b>Hx of PTB, N(%)</b>	
NO	1 (10)
YES	9 (90)
<b>Progest Use, N(%)</b>	
YES	10 (100)
<b>Mom Hgt (cm), mean(SD)</b>	162.9 (3)
<b>Mom Wgt (kg), median(IQR)</b>	78.8 (67.5,88)
<b>Hx of PE, N(%)</b>	
NA	10 (100)
<b>Chorioamnionitis, N(%)</b>	

No	10 (100)
<b>Endometritis, N(%)</b>	
No	10 (100)
<b>Autoimmune Disorder, N(%)</b>	
No	10 (100)
<b>Multiple UTI, N(%)</b>	
No	10 (100)
<b>Psychiatric Dx (depression), N(%)</b>	
No	9 (90)
Yes	1 (10)
<b>Thyroid Dx, N(%)</b>	
No	10 (100)
<b>Asthma, N(%)</b>	
No	9 (90)
Yes	1 (10)
<b>Cancer, N(%)</b>	
No	10 (100)
<b>Epilepsy, N(%)</b>	
No	9 (90)
Yes	1 (10)
<b>Breast Dx, No</b>	10 (100)
<b>Gynecol surgery, N(%)</b>	
No	10 (100)
<b>HTN, N(%)</b>	
No	9 (90)
Yes	1 (10)
<b>Gest HTN, N(%)</b>	
NA	10 (100)
<b>EtOH, N(%)</b>	
No	10 (100)
<b>Recreational Drug Use, N(%)</b>	
No	9 (90)
Yes	1 (10)
<b>Sex, N(%)</b>	0 (0)

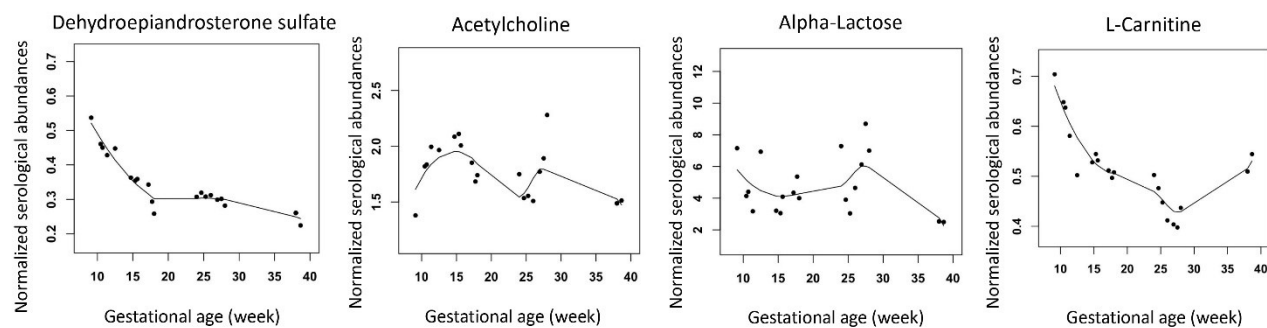
<b>Female</b>	<b>5 (50)</b>
<b>Male</b>	<b>5 (50)</b>
<b>Wgt at Birth (kg), mean(SD)</b>	<b>3.1 (0.5)</b>
<b>Length at birth (cm), median(IQR)</b>	<b>49.5 (46.8,50.6)</b>



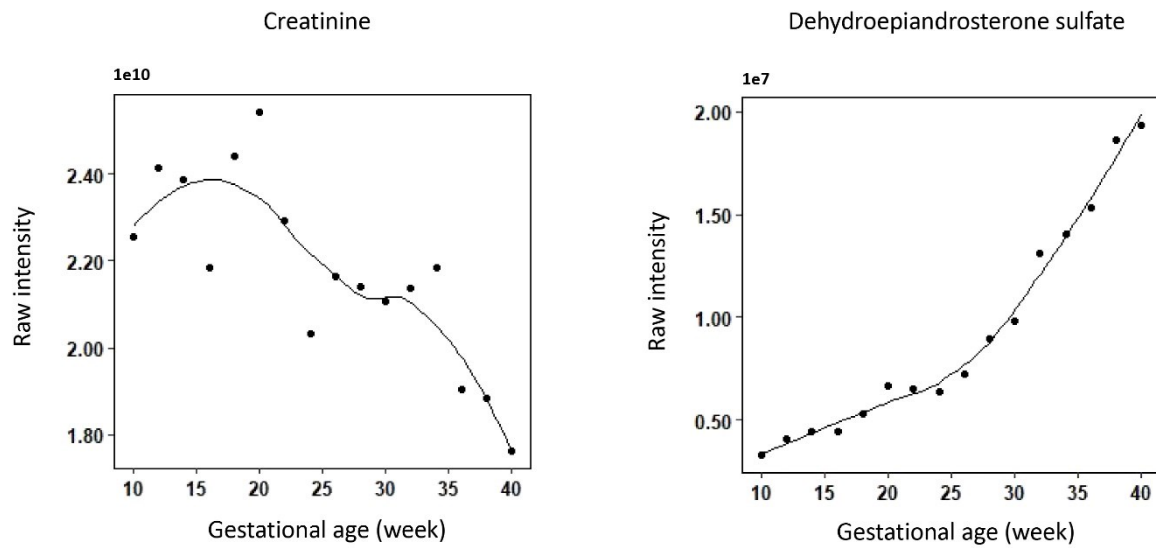
**Supplementary Figure 1. Data preprocessing and feature reduction.** A total of 5,473 metabolic features were identified by LC-MS-based untargeted metabolomics. Of these, 1,716 features were selected with missing value percentage less than 30% across all samples. 119 features were selected based on FDR and Pearson's screening. Finally, 37 compounds were annotated.



**Supplementary Figure 2. A pathway-based model to estimate GA.** X axis: GA measured by ultrasound at the first trimester. Y axis: model estimation. R: Pearson's correlation coefficient. Left: California cohort; Right: Alabama cohort.



**Supplementary Figure 3. Profile of dehydroepiandrosterone sulfate, acetylcholine,  $\alpha$ -lactose, and L-carnitine in maternal serum over the course of gestation on the California cohort. Loess regression lines were plotted.**



**Supplementary Figure 4. Intensity of creatinine (left) and dehydroepiandrosterone sulfate (right) in urine over the course of gestation on California cohort. Mean  $\pm$  standard error of the mean at each time point was plotted.**