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# Alterations in the gut microbiome and metabolisms in pregnancies with fetal growth restriction

### Running title: Gut dysbiosis and metabolic disorders in FGR

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#### 33 Supplementary materials

34 Supplementary Table 1

	NP Group	FGR Group	
	(n=31)	(n=19)	Р
Maternal features			
Age (y)	$30.10 \pm 4.99$	$28.60 \pm 3.53$	0.3322
Gestational Age (w)	$39.80 \pm 1.18$	$37.20 \pm 1.77$	< 0.001
BMI ( $kg/m^2$ )	$26.80 \pm 3.00$	$26.30 \pm 3.97$	0.6154
SBP (mmHg)	117 (112-124)	124 (120-138)	0.0024
DBP (mmHg)	$68.90 \pm 7.97$	$77.42 \pm 8.25$	0.0009
PLT (× $10^{9}/L$ )	$229.6 \pm 59.76$	$250.8 \pm 54.14$	0.2025
ALT (U/L)	$10.27 \pm 2.97$	$11.87 {\pm} 4.98$	0.2157
AST (U/L)	14.9 (12.8-17.8)	17.5 (13.2-21.8)	0.1647
ALP (U/L)	158 (131-181)	139 (117-179)	0.4662
ALB (g/L)	$36.36 \pm 2.02$	$35.23 \pm 3.83$	0.2462
TBA (µmol/L)	3.3 (2.4-5.8)	3.1 (2.6-4.6)	0.6807
TBil (µmol/L)	8.0 (7.0-9.7)	6.6 (5.5-8.2)	0.0031
DBil (µmol/L)	1.4 (1.1-1.9)	1.1 (0.8-1.5)	0.0227
Cr (µmol/L)	45.0 (42.0-49.0)	51.0 (40.0-56.0)	0.3182
<b>Fetal features</b>			
NW (g)	$3310 \pm 301.6$	2151±239.2	< 0.0001
BPD (mm)	92.0 (86.0-95.0)	83.0 (75.0-87.0)	< 0.0001
HC (mm)	328 (317-334)	296 (274-311)	< 0.0001
AC (mm)	334 (325-345)	286 (269-303)	< 0.0001
FL (mm)	72 (69-73)	63 (58-67)	< 0.0001
AFV (mm)	48.8±11.6	$36.7 \pm 9.0$	0.0001

Data was assessed for normality using the Shapiro-Wilk normality test, and was presented as mean ± SD 35 36 or median (interquartile range). For normally distributed data, Student's t-test with Welch's correction 37 was performed between two groups. For non-normal distributed data, Mann-Whitney U test was 38 performed between two groups. BMI, body mass index; G, gravidity; P, parity; SBP, systolic blood 39 pressure; DBP, diastolic blood pressure; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate 40 aminotransferase; ALP, alkaline phosphatase; ALB, albumin; TBil, total bilirubin; DBil, direct bilirubin; 41 Cr, creatinine; NW, neonatal weight; BPD, biparietal diameter; HC, head circumference; AC, abdominal 42 circumference; FL, femur length; AFV, amniotic fluid volume.



44 Supplementary Figure 1 (A) Correlation heatmap of maternal gut microbiota and maternal

45 clinical manifestations. Data was processed by Spearman's correlation test. (B) KEGG

- 46 pathways predicted by PICRUSt analysis. (\* P < 0.05, \*\* P < 0.01, \*\*\* P < 0.001. NP, n = 35;
- 47 FGR, n = 35)



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49 **Supplementary Figure 2** (A) The top 25 abundant metabolites. (B) Correlation heatmap of 50 maternal gut metabolites and maternal clinical manifestations. Data was processed by 51 Spearman's correlation test. \* P < 0.05, \*\* P < 0.01, \*\*\* P < 0.001. NP, n = 35; FGR, n = 35.



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53 **Supplementary Figure 3** (A) The top 25 abundant metabolites. (B) Correlation heatmap of 54 maternal serum metabolites and maternal clinical manifestations. Data was processed by 55 Spearman's correlation test. \*P < 0.05, \*\*P < 0.01. NP, n = 31; FGR, n = 19.



57 **Supplementary Figure 4** The expression of glucose transporters (*Glut1* and *Glut3*), amino 58 acid transporters (*Slc38a1* and *Slc38a2*) and fatty acid transporters (*Cd36* and *Fabp3*) at the 59 mRNA level in the placenta, normalized to *18S*. Data was presented as mean  $\pm$  SEM. One-60 way ANOVA test was conducted followed by Bonferroni test. \**P* < 0.05, ns, not significant. n

61 = 6 /group.

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