

Supplemental Table S1. Final metabolite model in the model-building dataset (n = 153,342) for prediction of gestational age from *Ryckman et al.*

| Metabolite | <u>Metabolite</u> | | <u>Metabolite Squared</u> | | <u>Metabolite Cubed</u> | |
|------------|-----------------------|----------------------|---------------------------|----------------------|-------------------------|-----------------------|
| | Coefficient | SE | Coefficient | SE | Coefficient | SE |
| TSH | 0.01 | 8.8×10 ⁻⁴ | -8.8×10 ⁻⁵ | 1.2×10 ⁻⁵ | 1.3×10 ⁻⁷ | 2.3×10 ⁻⁸ |
| 17-OHP | -0.05 | 5.2×10 ⁻⁴ | 1.1×10 ⁻⁴ | 3.5×10 ⁻⁶ | N/A | N/A |
| GALT | -0.07 | 0.01 | 3.5×10 ⁻³ | 7.5×10 ⁻⁴ | N/A | N/A |
| ALA | 9.6×10 ⁻³ | 2.7×10 ⁻⁴ | -1.3×10 ⁻⁵ | 6.3×10 ⁻⁷ | 5.3×10 ⁻⁹ | 3.7×10 ⁻¹⁰ |
| ARG | -0.02 | 1.5×10 ⁻³ | 2.9×10 ^{-5a} | 1.0×10 ⁻⁵ | N/A | N/A |
| LEU | -0.01 | 3.3×10 ⁻⁴ | 1.7×10 ⁻⁵ | 8.3×10 ⁻⁷ | -4.3×10 ⁻⁹ | 2.1×10 ⁻¹⁰ |
| MET | 0.03 | 1.2×10 ⁻³ | -2.3×10 ⁻⁴ | 1.2×10 ⁻⁵ | 3.5×10 ⁻⁷ | 1.8×10 ⁻⁸ |
| PHE | -0.01 | 8.3×10 ⁻⁴ | 4.2×10 ⁻⁵ | 4.7×10 ⁻⁶ | -2.9×10 ⁻⁸ | 3.9×10 ⁻⁹ |
| TYR | -5.3×10 ⁻³ | 1.2×10 ⁻⁴ | N/A | N/A | N/A | N/A |
| VAL | 0.02 | 6.0×10 ⁻⁴ | -3.6×10 ⁻⁵ | 2.5×10 ⁻⁶ | 2.0×10 ⁻⁸ | 1.0×10 ⁻⁹ |
| C2 | -0.10 | 4.4×10 ⁻³ | 2.0×10 ⁻³ | 1.1×10 ⁻⁴ | -1.2×10 ⁻⁵ | 8.5×10 ⁻⁷ |
| C3 | 0.06 | 5.6×10 ⁻³ | N/A | N/A | N/A | N/A |
| C4 | -0.20 | 0.03 | N/A | N/A | N/A | N/A |
| C5 | -9.29 | 0.26 | -6.93 | 0.78 | 6.81 | 0.43 |
| C5:1 | -3.89 | 0.56 | N/A | N/A | N/A | N/A |
| C5-OH | -0.36 | 0.08 | N/A | N/A | N/A | N/A |
| C3-DC | 0.91 | 0.1 | N/A | N/A | N/A | N/A |
| C4-DC | 18.56 | 0.41 | -50.43 | 1.67 | 40.19 | 1.92 |
| C5-DC | -25.06 | 0.92 | 85.79 | 8.6 | -118.09 | 23.9 |
| C6 | 10.16 | 0.31 | -2.24 | 0.42 | N/A | N/A |
| C8 | -1.47 | 0.2 | 0.11 | 0.02 | -2.0×10 ⁻³ | 3.0×10 ⁻⁴ |
| C8:1 | 13.29 | 0.5 | -52.96 | 2.51 | 55.61 | 3.64 |
| C10 | 4.99 | 0.32 | -10.87 | 0.91 | 3.97 | 0.52 |
| C10:1 | -2.33 | 0.27 | N/A | N/A | N/A | N/A |
| C12 | 2.47 | 0.19 | -4.00 | 0.37 | 2.1 | 0.22 |
| C12:1 | 5.17 | 0.3 | -13.00 | 0.85 | 9.71 | 0.72 |
| C6-DC | -4.20 | 0.36 | 9.65 | 2.13 | N/A | N/A |

| | | | | | | |
|----------|-------|------|--------------------|-------|----------------------|----------------------|
| C14 | -3.03 | 0.32 | 1.94 | 0.48 | N/A | N/A |
| C16 | 2.99 | 0.07 | -0.58 | 0.02 | 0.04 | 1.5×10 ⁻³ |
| C16:1 | -9.73 | 0.55 | 18.06 | 1.63 | -10.40 | 1.59 |
| C18 | -7.96 | 0.23 | 4.96 | 0.2 | -1.02 | 0.05 |
| C18:1 | 4.09 | 0.18 | -1.70 | 0.11 | 0.24 | 0.02 |
| C18:2 | -4.22 | 0.19 | 3.01 | 0.35 | -1.22 | 0.17 |
| C14-OH | 27.02 | 1.83 | -287.34 | 35.03 | N/A | N/A |
| C16-OH | 10.91 | 2.58 | -239.18 | 62.78 | 1585.56 ^a | 460.58 |
| C16:1-OH | 7.32 | 1.09 | 18.72 ^b | 8.87 | N/A | N/A |
| C18:1-OH | 3.84 | 0.82 | N/A | N/A | N/A | N/A |
| Constant | 36.72 | 0.11 | N/A | N/A | N/A | N/A |

GALT, galactose-1-phosphate uridyl transferase; N/A, not available; 17-OHP, 17-hydroxyprogesterone TSH, thyroid-stimulating hormone.

All terms are significant at P < 0.001 unless otherwise noted.

^aP<0.01 ^b0.01≤P<0.05.

Ryckman. Metabolic predictors of gestational age. Am J Obstet Gynecol 2016.

Supplemental Table S2. Univariable analyses of clinical characteristics in infants born term and preterm with cord blood spots collected.

| | Cord | | | P-value |
|--|----------------|----------------|----------------|----------|
| | Total | Term | Preterm | |
| | n = 641 | n = 604 | n = 36 | |
| Gestational Age* (weeks) mean (SD) | 39.2 (1.7) | 39.4 (1.2) | 34.4 (2.0) | <0.0001 |
| Gestational Age Category* (completed weeks), n (%) | | | | |
| ≥37 weeks | 604 (94.4) | 604 (94.4) | 0 (0.0) | <0.0001 |
| 32-36 weeks | 33 (5.2) | 0 (0.0) | 33 (91.7) | |
| <32 weeks | 3 (0.5) | 0 (0.0) | 3 (8.3) | |
| Birthweight (grams), mean (SD) | 3045.1 (456.5) | 3093.8 (402.7) | 2229.7 (534.1) | <0.0001 |
| Birthweight category (grams), n (%) | | | | <0.0001 |
| ≥4000g | 12 (1.9) | 12 (2.0) | 0 (0.0) | |
| 3500-3999g | 95 (14.8) | 95 (15.7) | 0 (0.0) | |
| 3000-3499g | 256 (40.0) | 254 (42.1) | 2 (5.6) | |
| 2500-2999g | 221 (34.5) | 210 (34.8) | 11 (30.6) | |
| 2000-2499g | 41 (6.4) | 30 (5.0) | 11 (30.6) | |
| 1500-1999g | 12 (1.9) | 3 (0.5) | 9 (25.0) | |
| 1000-1499g | 3 (0.5) | 0 (0.0) | 3 (8.3) | |
| <1000g | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| Age at Collection (hours), mean (SD) | NA | NA | NA | NA |
| Sex n (%) | | | | 0.5814 |
| Male | 313 (48.9) | 297 (49.2) | 16 (44.4) | |
| Female | 327 (51.1) | 307 (50.8) | 20 (55.6) | |
| Multiple gestation | 25 (3.9) | 17 (2.8) | 8 (22.2) | <0.0001 |
| SGA n (%) | | | | |
| Intergrowth | 106 (16.6) | 101 (16.7) | 5 (13.9) | 0.657 |
| Busia specific | 76 (12.6) | 76 (12.6) | 8 (22.2) | 0.096 |
| Treatment arm | | | | 0.0761** |
| DP | 323 (50.5) | 310 (51.3) | 13 (36.1) | |
| SP | 317 (49.5) | 294 (48.7) | 23 (63.9) | |

*As measured by ultrasound between 12-20 weeks. **Each infant counted even if part of a multiple gestation. Continuous variables described using mean and standard deviation and categorical variables using frequencies and proportions. T-tests and Chi-squared tests for continuous and categorical variables respectively were used to compare cases and controls

Supplemental Table S3. Univariable analyses of mean levels of metabolic makers in infants born term and preterm from cord blood spots.

| Variable | Cord | | | |
|----------------------------------|-----------------------|-----------------------|-------------------------|-----------------------|
| | <u>Term (n = 627)</u> | | <u>Preterm (n = 39)</u> | |
| | Mean (sd) | 95% CI | Mean (sd) | 95% CI |
| Acylcarnitines | | | | |
| Free Carnitine | 2.84 (0.31) | 2.81 to 2.86 | 2.99 (0.36) | 2.87 to 3.11 |
| C-2 | 2.86 (0.34) | 2.83 to 2.88 | 2.98 (0.4) | 2.84 to 3.11 |
| C-3 | -0.14 (0.35) | -0.17 to -0.11 | -0.11 (0.31) | -0.22 to -0.01 |
| C-4 | -1.79 (0.32) | -1.81 to -1.76 | -1.41 (0.55) | -1.6 to -1.23 |
| C-4DC | -1.91 (0.39) | -1.94 to -1.88 | -2.15 (0.4) | -2.28 to -2.01 |
| C-4OH | -2.83 (0.43) | -2.86 to -2.79 | -2.41 (0.69) | -2.64 to -2.17 |
| C-5 | -2.44 (0.39) | -2.47 to -2.41 | -2.09 (0.51) | -2.26 to -1.92 |
| C-5OH | -2.59 (0.34) | -2.62 to -2.56 | -2.56 (0.41) | -2.7 to -2.42 |
| C-6 | -3.13 (0.32) | -3.16 to -3.11 | -2.91 (0.44) | -3.06 to -2.76 |
| C-8 | -3.56 (0.38) | -3.59 to -3.53 | -3.39 (0.35) | -3.51 to -3.27 |
| C-10 | -3.4 (0.42) | -3.43 to -3.36 | -3.31 (0.4) | -3.45 to -3.18 |
| C-12 | -2.61 (0.63) | -2.66 to -2.56 | -2.7 (0.41) | -2.84 to -2.56 |
| C-12:1 | -3.59 (0.43) | -3.63 to -3.56 | -3.52 (0.38) | -3.65 to -3.39 |
| C-14 | -2.08 (0.37) | -2.11 to -2.05 | -2.02 (0.3) | -2.13 to -1.92 |
| C-14:1 | -2.97 (0.52) | -3.02 to -2.93 | -2.89 (0.38) | -3.01 to -2.76 |
| C-16 | 0.67 (0.33) | 0.64 to 0.7 | 0.63 (0.29) | 0.53 to 0.73 |
| C-16:1 | -2.39 (0.35) | -2.42 to -2.36 | -2.31 (0.36) | -2.43 to -2.19 |
| C-16:1OH | -3.18 (0.33) | -3.21 to -3.16 | -3.35 (0.28) | -3.44 to -3.26 |
| C-18 | -0.24 (0.34) | -0.26 to -0.21 | -0.32 (0.3) | -0.42 to -0.22 |
| C-18:1 | -0.36 (0.33) | -0.39 to -0.33 | -0.31 (0.31) | -0.42 to -0.21 |
| C-18:2 | -1.88 (0.34) | -1.91 to -1.85 | -1.88 (0.27) | -1.97 to -1.79 |
| Amino Acids/Intermediates | | | | |
| Alanine | 5.51 (0.24) | 5.49 to 5.53 | 5.51 (0.29) | 5.41 to 5.61 |
| Arginine | 2.25 (0.51) | 2.21 to 2.29 | 2.35 (0.54) | 2.17 to 2.54 |
| Citrulline | 2.32 (0.26) | 2.3 to 2.34 | 2.23 (0.28) | 2.14 to 2.33 |
| Glutamate | 5.04 (0.26) | 5.02 to 5.06 | 5.08 (0.33) | 4.97 to 5.19 |
| Leucine | 4.7 (0.21) | 4.68 to 4.72 | 4.83 (0.28) | 4.73 to 4.92 |
| Methionine | 2.99 (0.18) | 2.97 to 3 | 3.02 (0.28) | 2.93 to 3.11 |
| Ornithine | 2.95 (0.3) | 2.92 to 2.97 | 2.86 (0.34) | 2.75 to 2.98 |
| Phenylalanine | 4.18 (0.2) | 4.17 to 4.2 | 4.32 (0.25) | 4.24 to 4.41 |
| Succinylacetone | -0.7 (0.22) | -0.72 to -0.69 | -0.72 (0.25) | -0.81 to -0.64 |
| Tyrosine | 3.79 (0.21) | 3.78 to 3.81 | 3.9 (0.23) | 3.82 to 3.98 |
| Valine | 4.73 (0.17) | 4.71 to 4.74 | 4.79 (0.2) | 4.72 to 4.85 |
| Hormones | | | | |
| 17-Hydroxyprogesterone | 4.97 (1.1) | 4.88 to 5.06 | 4.9 (1.4) | 4.43 to 5.37 |
| Thyroid Stimulating Hormone | 1.78 (0.74) | 1.72 to 1.84 | 1.75 (0.75) | 1.5 to 2.01 |

All variables are natural log transformed

Supplemental Table S4. Cross validated multivariable logistic cord model built within the Busia cohort.

Cord

AUC: 0.935 95% CI: 0.894-0.977

| Variable | Parameter Estimate | OR (95% CI) |
|------------------------|--------------------|--------------------|
| Intercept | 8.63 | NA |
| Birthweight (per 100g) | -0.55 | 0.62 (0.54-0.73) |
| Alanine | -0.72 | 0.08 (0.01-0.57) |
| C4 | -2.53 | 0.18 (0.03-0.94) |
| C4-DC | -0.94 | 16.78 (2.85-98.78) |
| C4-OH | -2.13 | 0.13 (0.03-0.56) |
| C16:1-OH | -1.95 | 3.45 (1.09-10.94) |

Supplemental Table S5. Classification statistics of cord models used to determine preterm birth

Cord

| | Ryckman | Busia |
|---------------------------|---------|-------|
| Sensitivity | 64.1 | 52.8 |
| Specificity | 83.6 | 99.2 |
| Positive Predictive Value | 52.1 | 79.2 |
| Negative Predictive Value | 84.8 | 97.2 |
| Accuracy | 82.4 | 96.5 |

Supplemental Table S6. Weeks of difference between cord model determined gestational ages and ultrasound determined gestational ages.

| | <u>Ryckman Cord</u> | | <u>Busia Cord</u> | |
|---------------|----------------------------|--------------------------|--------------------------|--------------------------|
| | Frequency (%) | Cumulative Frequency (%) | Frequency (%) | Cumulative Frequency (%) |
| Perfect Match | 23 (3.6) | 23 (3.6) | 37 (5.8) | 37 (5.8) |
| ≤1 Week | 210 (32.8) | 233 (36.4) | 353 (55.2) | 390 (60.9) |
| ≤2 Weeks | 203 (31.7) | 436 (68.1) | 181 (28.3) | 571 (89.2) |
| ≤3 Weeks | 128 (20.0) | 564 (88.1) | 51 (8.0) | 622 (97.2) |
| ≤4 Weeks | 52 (8.1) | 616 (96.3) | 11 (1.7) | 633 (98.9) |
| ≤5 Weeks | 17 (2.7) | 633 (98.9) | 6 (0.9) | 639 (99.8) |
| 5+ Weeks | 7 (1.1) | 640 (100.0) | 1 (0.2) | 640 (100.0) |

*Perfect Match is $\pm 1/2$ day.

Supplemental Table S7. Weeks of difference between cord model determined gestational ages and ultrasound determined gestational ages in infants born SGA.

| | Ryckman Cord | | | | Busia Cord | | | |
|----------------|------------------------|------------------|---------------------------|-----------------|------------------------|------------------|---------------------------|-----------------|
| | <u>Intergrowth SGA</u> | | <u>Busia Specific SGA</u> | | <u>Intergrowth SGA</u> | | <u>Busia Specific SGA</u> | |
| | No SGA (n = 534) | SGA (n = 106) | No SGA (n = 556) | SGA (n = 84) | No SGA (n = 534) | SGA (n = 106) | No SGA (n = 556) | SGA (n = 84) |
| Perfect Match* | 23 (4.3) | 0 (0.0) | 23 (4.1) | 0 (0.0) | 33 (6.2) | 4 (3.8) | 36 (6.5) | 1 (1.2) |
| 0-1 Week | 206 (38.6) | 4 (3.8) | 204 (36.7) | 6 (7.1) | 313 (58.6) | 40 (37.7) | 327 (58.8) | 26 (31.0) |
| 1-2 Weeks | 181 (33.9) | 22 (20.8) | 188 (33.8) | 15 (17.9) | 147 (27.5) | 34 (32.1) | 154 (27.7) | 27 (32.1) |
| 2-3 Weeks | 96 (18.0) | 32 (30.2) | 110 (19.8) | 18 (21.4) | 29 (5.4) | 22 (20.8) | 28 (5.0) | 23 (27.4) |
| 3-4 Weeks | 21 (3.9) | 31 (29.3) | 24 (4.3) | 28 (33.3) | 7 (1.3) | 4 (3.8) | 6 (1.1) | 5 (6.0) |
| 4-5 Weeks | 6 (1.1) | 11 (10.4) | 6 (1.1) | 11 (13.1) | 4 (0.8) | 2 (1.9) | 4 (0.7) | 2 (2.4) |
| 5+ Weeks | 1 (0.2) | 6 (5.7) | 1 (0.2) | 6 (7.1) | 1 (0.2) | 0 (0.0) | 1 (0.2) | 0 (0.0) |

Values are frequency (column %). Busia specific SGA determined using WHO calculator

*Perfect Match is $\pm 1/2$ day.