Supplementary Material

Title: Prediction and associations of preterm birth and its subtypes with eicosanoid enzymatic pathways and inflammatory markers

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Plasma Lipid Parent Compounds

α-linolenic acid	[αLA]
Arachidonic acid	[AA]
Docosahexaenoic acid	[DHA]
Eicosapentaenoic acid	[EPA]
Linoleic acid	[LA]

Plasma Inflammation Markers

C-reactive protein	[CRP]
Interleukin-1β	[IL1β]
Interleukin-6	[IL6]
Interleukin-10	[IL10]
Tumor necrosis factor α	[TNF]

Plasma Eicosanoids: Cyclooxygenase Pathway

13,14-dihydro-15-keto-prostaglandin D2	[3,14DHK-PGD2]
13,14-dihydro-15-keto-prostaglandin F2α	[13,14DHK-PGF2α]
15-deoxy-12,14-prostaglandin J2	[15DO12,14-PGJ2]
9-oxooctadeca-dienoic acid	[9-oxoODE]
Bicyclo-prostaglandin E1	[BCPGE1]
Bicycle-prostaglandin E2	[BCPGE2]
Prostaglandin A2	[PGA2]
Prostaglandin B2	[PGB2]
Prostaglandin D2	[PGD2]
Prostaglandin D3	[PGD3]
Prostaglandin E1	[PGE1]
Prostaglandin E2	[PGE2]
Prostaglandin E3	[PGE3]
Prostaglandin J2	[PGJ2]
Thromboxane B2	[TXB2]

Plasma Eicosanoids: Lipoxygenase Pathway

Resolvin D1	[RVD1]
Resolvin D2	[RVD2]
Leukotriene B4	[LTB4]
Leukotriene C4 methyl-ester	[LTC4-ME]
Leukotriene D4	[LTD4]
Leukotriene E4	[LTE4]
13S-hydroxy-octadecadienoic acid	[13S-HODE]
5-hydroxy-eicosatetraenoic acid	[5-HETE]
8-hydroxy-eicosatetraenoic acid	[8-HETE]
12-hydroxy-eicosatetraenoic acid	[12-HETE]
15-hydroxy-eicosatetraenoic acid	[15-HETE]
13-oxooctadeca-dienoic acid	[13-oxoODE]
5-oxoeicosatetraenoic acid	[5-oxoETE]
12-oxoeicosatetraenoic acid	[12-oxoETE]
15-oxoeicosatetraenoic acid	[15-oxoETE]

Plasma Eicosanoids: Cytochrome P450 Pathway

12,13-dihydroxy-octadecenoic acid	[12,13-DiHOME]
9,10-dihydroxy-octadecenoic acid	[9,10-DiHOME]
5,6-dihydroxy-eicosatrienoic acid	[5,6-DHET]
8,9-dihydroxy-eicosatrienoic acid	[8,9-DHET]
11,12-dihydroxy-eicosatrienoic acid	[11,12-DHET]
5,6-epoxy-eicosatrienoic acid	[5(6)-EET]
8,9-epoxy-eicosatrienoic acid	[8(9)-EET]
14,15-epoxy-eicosatrienoic acid	[14(15)-EET]
11,12-epoxy-eicosatrienoic acid	[11(12)-EET]
9,10-epoxy-octadecenoic acid	[9(10)-EpoME]
12,13-epoxy-octadecenoic acid	[12(13)-EpoME]
20-carboxy arachidonic acid	[CAA]
11-hydroxy-eicosatetraenoic acid	[11-HETE]
16-hydroxy-eicosatetraenoic acid	[16-HETE]
17-hydroxy-eicosatetraenoic acid	[17-HETE]
18-hydroxy-eicosatetraenoic acid	[18-HETE]
20-hydroxy-eicosatetraenoic acid	[20-HETE]
9S-hydroxy-octadecadienoic acid	[9S-HODE]

Plasma Protein Damage Markers

3-nitrotyrosine	[NY]
o,o'-dityrosine	[DY]
3-chlorotyrosine	[CY]

Plasma Angiogenic Markers

Placental growth factor	[PGF]
Soluble fms-like tyrosine kinase-1	[sFlt-1]

Urinary Oxidative Stress Markers

8-hydroxydeoxyguanosine	[8-OHdG]
8-isoprostane	[8-IP]

Supplemental Figure 1. Schematic representation of individual biomarkers according to the media in which they were measured and the group they belong to.
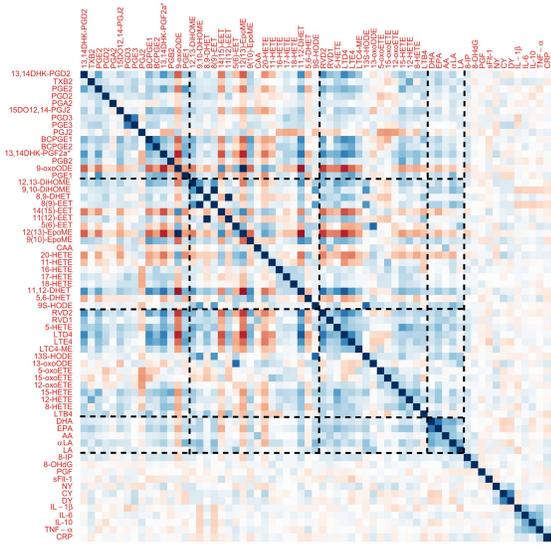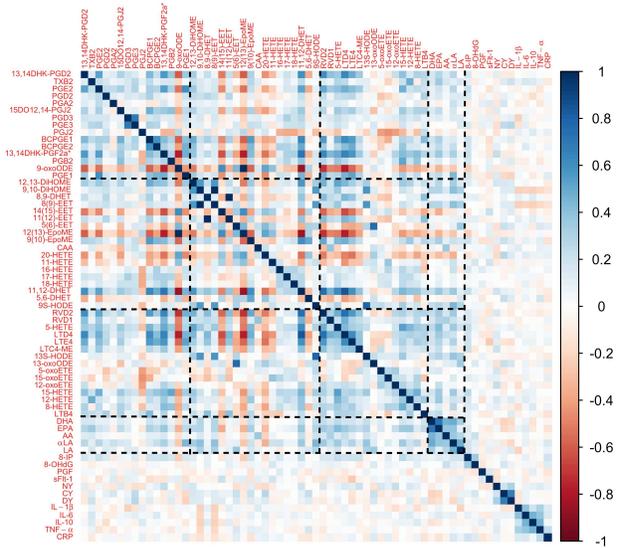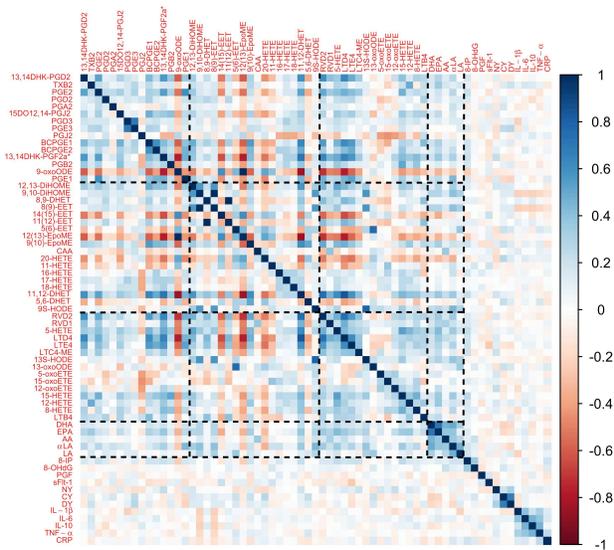
Supplemental Figure 2. Weighted correlations among biomarkers. Correlations were calculated using inverse probability weighting for all preterm (A), spontaneous preterm (B), and placental preterm (C) to account for case-control sampling.

Supplemental Table 1. Log odds ratios (95% confidence interval) of preterm birth estimated using logistic regression and adaptive elastic-net

Biomarkers	All Preterm Birth		Spontaneous Preterm Birth		Placental Preterm Birth	
	Logistic Regression[*]	Adaptive Elastic-Net[†]	Logistic Regression[*]	Adaptive Elastic-Net[†]	Logistic Regression[*]	Adaptive Elastic-Net[†]
CRP	-0.18 (-0.54, 0.18)	NA	-0.25 (-0.69, 0.19)	NA	-0.02 (-0.57, 0.53)	NA
TNF-α	0.14 (-0.20, 0.48)	NA	-0.06 (-0.46, 0.34)	NA	0.42 (-0.10, 0.94)	NA
IL-10	0.44 (0.09, 0.79)	NA	0.20 (-0.20, 0.60)	NA	0.71 (0.22, 1.20)	NA
IL-6	0.36 (-0.001, 0.72)	NA	0.32 (-0.12, 0.75)	NA	0.26 (-0.25, 0.76)	NA
IL-1β	0.14 (-0.21, 0.48)	NA	0.15 (-0.27, 0.58)	NA	0.19 (-0.34, 0.71)	NA
DY	-0.07 (-0.42, 0.27)	NA	-0.01 (-0.45, 0.42)	NA	0.02 (-0.48, 0.52)	NA
CY	0.15 (-0.19, 0.50)	NA	0.21 (-0.22, 0.64)	NA	0.15 (-0.36, 0.67)	NA
NY	0.26 (-0.12, 0.64)	NA	0.20 (-0.27, 0.67)	NA	0.07 (-0.44, 0.58)	NA
sFlt-1	0.17 (-0.18, 0.52)	NA	0.18 (-0.26, 0.62)	NA	0.05 (-0.46, 0.55)	NA
PGF	-0.52 (-0.90, -0.14)	-0.24	-0.28 (-0.73, 0.16)	NA	-1.23 (-1.92, -0.54)	-0.15
8-OHdG	-0.23 (-0.60, 0.13)	NA	-0.48 (-0.96, 0.002)	NA	-0.11 (-0.59, 0.36)	NA
8-isoprostane	0.02 (-0.40, 0.43)	NA	0.47 (-0.27, 1.22)	NA	-0.25 (-0.78, 0.28)	NA
13,14DHK-PGD2	0.54 (0.14, 0.94)	NA	1.01 (0.49, 1.53)	NA	-0.15 (-0.63, 0.33)	NA
TXB2	0.16 (-0.18, 0.50)	NA	0.13 (-0.29, 0.54)	NA	0.18 (-0.32, 0.68)	NA
PGE2	0.28 (-0.09, 0.64)	NA	0.56 (0.05, 1.06)	NA	-0.09 (-0.59, 0.41)	NA
PGD2	0.21 (-0.14, 0.57)	NA	0.24 (-0.20, 0.67)	NA	0.22 (-0.31, 0.74)	NA
PGA2	0.25 (-0.10, 0.61)	NA	0.41 (-0.05, 0.87)	NA	0.12 (-0.37, 0.61)	NA
15DO12,14-PGJ2	0.41 (0.06, 0.77)	0.23	0.76 (0.27, 1.26)	0.11	-0.12 (-0.60, 0.36)	NA
PGD3	0.19 (-0.17, 0.55)	NA	0.42 (-0.04, 0.89)	NA	-0.04 (-0.54, 0.46)	NA
PGE3	0.01 (-0.34, 0.37)	NA	0.07 (-0.38, 0.52)	NA	-0.02 (-0.53, 0.50)	NA
PGJ2	-0.15 (-0.51, 0.20)	NA	-0.48 (-0.93, -0.02)	NA	0.23 (-0.37, 0.83)	NA
BCPGE1	0 (-0.34, 0.34)	NA	0.23 (-0.18, 0.64)	NA	-0.62 (-1.23, -0.01)	NA
BCPGE2	0.06 (-0.28, 0.40)	NA	0.23 (-0.18, 0.65)	NA	-0.55 (-1.12, 0.03)	NA
13,14DHK-PGF2a*	0.19 (-0.15, 0.54)	NA	0.61 (0.18, 1.05)	NA	-0.49 (-1.07, 0.09)	NA
PGB2	0.30 (-0.13, 0.72)	NA	0.65 (0.07, 1.23)	NA	-0.10 (-0.56, 0.36)	NA
9-oxoODE	-0.36 (-0.70, -0.02)	NA	-0.65 (-1.06, -0.25)	NA	0.30 (-0.33, 0.93)	NA
PGE1	0.16 (-0.19, 0.51)	NA	0.34 (-0.11, 0.79)	NA	-0.23 (-0.71, 0.26)	NA
12,13-DiHOME	0.32 (-0.02, 0.66)	NA	0.46 (0.05, 0.87)	NA	0.14 (-0.35, 0.64)	NA
9,10-DiHOME	0.37 (-0.01, 0.74)	NA	0.65 (0.15, 1.16)	NA	-0.06 (-0.58, 0.45)	NA
8,9-DHET	0.49 (0.06, 0.91)	NA	0.78 (0.18, 1.37)	NA	-0.001 (-0.51, 0.51)	NA
8(9)-EET	0.37 (-0.01, 0.74)	NA	0.65 (0.15, 1.16)	NA	-0.06 (-0.58, 0.45)	NA
14(15)-EET	-0.09 (-0.43, 0.25)	NA	-0.26 (-0.65, 0.13)	NA	0.49 (-0.18, 1.16)	NA

11(12)-EET	0.48 (0.06, 0.90)	NA	0.77 (0.18, .135)	NA	-0.002 (-0.51, 0.50)	NA
5(6)-EET	-0.37 (-0.72, -0.01)	-0.10	-0.63 (-1.08, -0.18)	-0.16	0.30 (-0.26, 0.86)	NA
12(13)-EpoME	-0.36 (-0.70, -0.02)	NA	-0.65 (-1.06, -0.25)	NA	0.30 (-0.33, 0.93)	NA
9(10)-EpoME	0.42 (0.04, 0.79)	NA	0.91 (0.37, 1.46)	NA	-0.20 (-0.70, 0.31)	NA
CAA	0.09 (-0.25, 0.43)	NA	0.25 (-0.19, 0.69)	NA	-0.09 (-0.57, 0.39)	NA
20-HETE	-0.13 (-0.47, 0.22)	NA	-0.35 (-0.77, 0.07)	NA	0.49 (-0.13, 1.11)	NA
11-HETE	-0.07 (-0.41, 0.27)	NA	-0.36 (-0.78, 0.05)	NA	0.52 (-0.06, 1.10)	NA
16-HETE	0.04 (-0.31, 0.39)	NA	0.10 (-0.35, 0.55)	NA	0.01 (-0.50, 0.51)	NA
17-HETE	-0.02 (-0.36, 0.32)	NA	0.19 (-0.24, 0.62)	NA	-0.29 (-0.81, 0.23)	NA
18-HETE	-0.002 (-0.34, 0.34)	NA	0.33 (-0.11, 0.76)	NA	-0.30 (-0.82, 0.23)	NA
11,12-DHET	0.5 (0.15, 0.86)	NA	0.96 (0.52, 1.39)	NA	-0.78 (-1.58, 0.03)	NA
5,6-DHET	-0.10 (-0.44, 0.25)	NA	-0.31 (-0.74, 0.12)	NA	0.29 (-0.24, 0.81)	NA
9S-HODE	0.14 (-0.20, 0.48)	NA	0.27 (-0.16, 0.70)	NA	0.03 (-0.48, 0.55)	NA
RVD2	0.21 (-0.12, 0.55)	NA	0.46 (0.05, 0.87)	NA	-0.39 (-0.96, 0.17)	NA
RVD1	0.65 (0.25, 1.05)	NA	0.98 (0.47, 1.49)	0.02	0.14 (-0.44, 0.73)	NA
5-HETE	0.34 (-0.002 ,0.69)	NA	0.69 (0.25, 1.13)	NA	-0.16 (-0.66, 0.34)	NA
LTD4	0.38 (0.03, 0.72)	NA	0.88 (0.44, 1.32)	NA	-0.80 (-1.57, -0.03)	NA
LTE4	0.38 (-0.02, 0.89)	NA	0.67 (0.17, 1.17)	NA	-0.18 (-0.86, 0.50)	NA
LTC4-ME	0.30 (-0.07, 0.66)	NA	0.53 (0.04, 1.03)	NA	-0.10 (-0.56, 0.36)	NA
13S-HODE	0.28 (-0.08, 0.64)	NA	0.45 (-0.01, 0.91)	NA	0.33 (-0.22, 0.88)	NA
13-oxoODE	-0.25 (-0.61, 0.10)	NA	-0.39 (-0.83, 0.05)	NA	0.21 (-0.34, 0.76)	NA
5-oxoETE	0.28 (-0.08, 0.64)	NA	0.57 (0.10, 1.05)	0.16	-0.16 (-0.68, 0.37)	NA
15-oxoETE	0.17 (-0.19, 0.52)	NA	0.12 (-0.33, 0.57)	NA	0.26 (-0.27, 0.79)	NA
12-oxoETE	0.27 (-0.09, 0.63)	NA	0.53 (0.06, 1.00)	NA	-0.20 (-0.72, 0.32)	NA
15-HETE	0.39 (0.02, 0.77)	NA	0.67 (0.19, 1.15)	NA	-0.002 (-0.51, 0.50)	NA
12-HETE	0.37 (0.01, 0.74)	NA	0.51 (0.04, 0.98)	NA	0.12 (-0.37, 0.62)	NA
8-HETE	0.29 (-0.09, 0.66)	NA	0.49 (-0.04, 1.01)	NA	-0.01 (-0.49, 0.47)	NA
LTB4	-0.31 (-0.67, 0.04)	-0.13	0.05 (-0.37, 0.47)	NA	-0.83 (-1.42, -0.23)	-0.10
DHA	0.36 (0, 0.73)	NA	0.84 (0.35, 1.34)	NA	-0.44 (-1.04, 0.16)	NA
EPA	0.43 (0.06, 0.79)	NA	0.87 (0.37, 1.37)	NA	-0.29 (-0.84, 0.25)	NA
AA	0.29 (-0.06, 0.64)	NA	0.56 (0.10, 1.02)	NA	-0.08 (-0.59, 0.42)	NA
αLA	0.50 (0.11, 0.88)	NA	0.89 (0.33, 1.44)	NA	0.07 (-0.47, 0.61)	NA
LA	0.36 (-0.003, 0.72)	0.26	0.54 (0.07, 1.00)	NA	0.20 (-0.34, 0.74)	NA

[*]Log odds ratios were estimated by fitting logistic regression on covariates and individual biomarkers (*Model 1*)

[†]Only point estimates are reported for the log odds ratios estimated by adaptive elastic-net. Zero coefficients are recorded as NA.