Cytomegalovirus proteins, maternal pregnancy cytokines, and their impact on neonatal immune cytokine profiles and acute lymphoblastic leukemogenesis in children

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Supplemental Tables to accompany the manuscript:

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Supplemental Table 1: Characteristics of 130 cases with childhood acute lymphoblastic leukemia and 460 healthy controls

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Supplemental Table 1: Characteristics of 130 cases with childhood acute lymphoblastic leukemia and 460 healthy controls.

Characteristic	ALL group (n = 130)		Control Group (n = 460)		P value
	No. of Participants	%	No. of Participants	%	
Sex					0.8
Female	57	43.8	196	42.6	
Male	73	56.2	264	57.4	
Race/ethnicity					0.83
Non-Latino White	40	30.8	131	28.5	
Latino all races	69	53.1	258	56.1	
Non-Latino Other	21	16.2	71	15.4	
Year of birth					0.54
2000-2002	49	37.7	162	35.2	
2003-2005	57	43.8	192	41.7	
2006-2009	24	18.5	106	23.0	
Birth weight, g					0.56
<2,500	54	41.5	181	39.3	
2,500-2,999	3	2.3	17	3.7	
3,000-3,499	22	16.9	67	14.6	
3,500-3,999	42	32.3	143	31.1	
>=4,000	9	6.9	52	11.3	
Length of gestation, weeks					0.69
26-36	108	83.1	371	80.7	
37-41	10	7.7	42	9.1	
42-44	9	6.9	24	5.2	
Unknown	3	2.3	23	5.0	
Plurality					0.25
Singleton	124	95.4	448	97.4	
Multiples	6	4.6	12	2.6	
Birth order					0.75
First	52	40.0	171	37.2	
Second	44	33.8	154	33.5	
Third or later	34	26.2	135	29.3	
Delivery mode					0.04
Vaginal	81	62.3	330	71.7	
Cesarean section	49	37.7	130	28.3	
Maternal age, years					0.23
<25	29	22.3	138	30.0	
25-34	79	60.8	252	54.8	
≤35	22	16.9	70	15.2	
Mother's place of birth					0.51
United States	74	56.9	247	53.7	
Foreign	56	43.1	213	46.3	

Supplemental Table 2: Relationship of cytokines and CMV proteins at birth to risk of childhood acute lymphoblastic leukemia

Marker	Tertile	Case n (%)	Control n (%)	Adjusted [a] OR (95% CI)	p	Mutually adjusted [b] OR (95% CI)	p	Continuous [c] OR (95% CI)	p
IL-1β	1st (low)	55(42.3)	154(33.5)	1.00		1.00		0.81(0.52-1.25)	0.34
	2nd	27(20.8)	153(33.3)	0.50(0.29-0.84)	<.01	0.43(0.22-0.87)	0.02		
	3rd (high)	48(36.9)	153(33.3)	0.89(0.56-1.42)	0.63	0.70(0.30-1.62)	0.40		
IL-2	1st	26(20.0)	154(33.5)	1.00		1.00		1.21(0.94-1.56)	0.15
	2nd	55(42.3)	153(33.3)	1.97(1.16-3.35)	0.01	1.90(1.03-3.49)	0.04		
	3rd	49(37.7)	153(33.3)	1.86(1.08-3.19)	0.02	1.82(0.93-3.54)	0.08		
IL-4	1st	38(29.2)	154(33.5)	1.00		1.00		1.04(0.79-1.36)	0.79
	2nd	46(35.4)	153(33.3)	1.18(0.72-1.94)	0.52	1.47(0.78-2.78)	0.23		
	3rd	46(35.4)	153(33.3)	1.24(0.75-2.04)	0.41	1.59(0.78-3.25)	0.20		
IL-5	1st	45(34.6)	154(33.5)	1.00		1.00		1.03(0.81-1.32)	0.80
	2nd	35(26.9)	153(33.3)	0.79(0.48-1.32)	0.37	1.03(0.56-1.92)	0.92		
	3rd	50(38.5)	153(33.3)	1.17(0.73-1.88)	0.52	0.96(0.52-1.79)	0.90		
IL-6	1st	42(32.3)	154(33.5)	1.00		1.00		1.11(0.86-1.44)	0.41
	2nd	43(33.1)	153(33.3)	1.01(0.61-1.65)	0.98	1.25(0.68-2.29)	0.47		
	3rd	45(34.6)	153(33.3)	1.20(0.73-1.99)	0.47	1.68(0.86-3.30)	0.13		
IL-8	1st	57(43.8)	154(33.5)	1.00		1.00		0.90(0.59-1.35)	0.60
	2nd	34(26.2)	153(33.3)	0.60(0.36-0.98)	0.04	0.52(0.26-1.03)	0.06		
	3rd	39(30.0)	153(33.3)	0.75(0.46-1.22)	0.25	0.51(0.23-1.16)	0.11		
IL-10	1st	41(31.5)	154(33.5)	1.00		1.00		0.91(0.70-1.18)	0.46
	2nd	47(36.2)	153(33.3)	1.14(0.69-1.86)	0.61	0.84(0.47-1.50)	0.55		
	3rd	42(32.3)	153(33.3)	1.00(0.60-1.66)	0.99	0.66(0.34-1.27)	0.21		
IL-12-p70	1st	37(28.5)	154(33.5)	1.00		1.00		1.19(0.94-1.51)	0.14
	2nd	35(26.9)	153(33.3)	1.03(0.61-1.75)	0.90	1.32(0.70-2.49)	0.39		
	3rd	58(44.6)	153(33.3)	1.59(0.98-2.57)	0.06	1.62(0.88-2.97)	0.12		
TNF–α	1st	45(34.6)	154(33.5)	1.00		1.00		1.09(0.77-1.53)	0.64
	2nd	43(33.1)	153(33.3)	0.91(0.56-1.48)	0.70	1.18(0.58-2.39)	0.64		
	3rd	42(32.3)	153(33.3)	0.90(0.55-1.48)	0.67	1.32(0.58-3.00)	0.51		
VEGF	1st	48(36.9)	154(33.5)	1.00		1.00		1.02(0.81-1.28)	0.86
	2nd	41(31.5)	153(33.3)	0.81(0.50-1.32)	0.40	0.83(0.45-1.54)	0.56		
	3rd	41(31.5)	153(33.3)	0.79(0.48-1.31)	0.36	0.80(0.44-1.46)	0.47		
GM-CSF	1st	29(22.3)	154(33.5)	1.00		1.00		1.27(0.96-1.69)	0.10
	2nd	43(33.1)	153(33.3)	1.44(0.84-2.46)	0.19	1.55(0.79-3.04)	0.21		
	3rd	58(44.6)	153(33.3)	1.94(1.15-3.29)	0.01	2.38(1.11-5.13)	0.03		
INF-γ	1st	48(36.9)	154(33.5)	1.00		1.00		1.11(0.83-1.49)	0.49
	2nd	41(31.5)	153(33.3)	0.89(0.55-1.47)	0.66	0.91(0.50-1.67)	0.77		
	3rd	41(31.5)	153(33.3)	0.92(0.56-1.53)	0.76	1.00(0.50-2.00)	1.00		
ARG-2	1st	39(30.0)	154(33.5)	1.00		1.00		1.16(0.88-1.52)	0.28
	2nd	50(38.5)	153(33.3)	1.33(0.82-2.18)	0.25	1.63(0.88-3.01)	0.12		
	3rd	41(31.5)	153(33.3)	0.95(0.57-1.60)	0.85	1.15(0.58-2.29)	0.69		
TGF-β1	1st	38(29.2)	154(33.5)	1.00		1.00		1.01(0.81-1.26)	0.95
	2nd	54(41.5)	153(33.3)	1.44(0.89-2.35)	0.14	1.48(0.84-2.61)	0.18		
	3rd	38(29.2)	153(33.3)	0.93(0.56-1.57)	0.80	1.00(0.56-1.78)	0.99		
CMV-IL10	1st	41(31.5)	154(33.5)	1.00		1.00		1.27(1.01-1.59)	0.04
	2nd	40(30.8)	153(33.3)	1.01(0.61-1.68)	0.95	0.96(0.56-1.66)	0.89		
	3rd	49(37.7)	153(33.3)	1.26(0.77-2.07)	0.35	1.47(0.85-2.54)	0.17		
CMV-PP65	1st	48(36.9)	154(33.5)	1.00		1.00		1.05(0.85-1.29)	0.68
	2nd	36(27.7)	153(33.3)	0.73(0.44-1.20)	0.22	0.78(0.45-1.35)	0.37		
	3rd	46(35.4)	153(33.3)	0.93(0.57-1.50)	0.76	1.13(0.67-1.93)	0.64		
CMV-vCXC	1st	49(37.7)	154(33.5)	1.00		1.00		0.98(0.79-1.21)	0.82

2nd	34(26.2)	153(33.3)	0.67(0.40-1.12)	0.13	0.75(0.42-1.33)	0.33		
3rd	47(36.2)	153(33.3)	0.92(0.57-1.48)	0.73	1.00(0.58-1.73)	0.99		

[a] All models adjusted for age at collection, year of birth (2000-2002, 2003-2005, 2006-2009), sex, race/ethnicity, birth weight (<2500, 2500-2999,3000-3499, ≥3500 grams), gestational age (26-26, 27-41, 42-44 weeks, unknown), plurality (single vs multiple), birth order, mode of delivery (vaginal vs cesarean), mother's age at delivery (≤24, 25-34, ≥35 years), and mother's birthplace (United States vs other).

[b] Mutually adjusted: All cytokines were simultaneously included in one model, along with birth characteristics lised in [a].

[c] OR per unit increase in marker level, adjusting for all markers and birth characteristics listed in [a].

Supplemental Table 3: Relationship of cytokine/CMV protein derived principal components to risk of childhood acute lymphoblastic leukemia

Prin.	Tertile	Case n (%)	Control n (%)	Adjusted [a] OR (95% CI)	p	Mutually adjusted [b] OR (95% CI)	p	Continuous [c] OR (95% CI)	p
PC1	1st (low)	26(20.0)	154(33.5)	1.00		1.00		1.25(1.02-1.54)	0.04
	2nd	48(36.9)	153(33.3)	2.01(1.16-3.47)	0.01	2.03(1.15-3.58)	0.02		
	3rd (high)	56(43.1)	153(33.3)	2.12(1.25-3.61)	<.01	2.29(1.32-3.96)	<.01		
PC2	1st	44(33.8)	154(33.5)	1.00		1.00		0.96(0.77-1.18)	0.68
	2nd	46(35.4)	153(33.3)	1.06(0.65-1.73)	0.82	1.06(0.62-1.80)	0.84		
	3rd	40(30.8)	153(33.3)	0.98(0.59-1.64)	0.94	1.03(0.58-1.80)	0.93		
PC3	1st	42(32.3)	154(33.5)	1.00		1.00		1.01(0.82-1.24)	0.96
	2nd	41(31.5)	153(33.3)	1.00(0.61-1.64)	0.99	1.13(0.65-1.94)	0.67		
	3rd	47(36.2)	153(33.3)	1.03(0.63-1.69)	0.91	1.07(0.63-1.83)	0.80		
PC4	1st	48(36.9)	154(33.5)	1.00		1.00		0.94(0.76-1.16)	0.58
	2nd	38(29.2)	153(33.3)	0.81(0.50-1.33)	0.41	0.80(0.48-1.34)	0.39		
	3rd	44(33.8)	153(33.3)	0.98(0.60-1.60)	0.93	1.00(0.60-1.67)	0.99		
PC5	1st	37(28.5)	154(33.5)	1.00		1.00		1.04(0.85-1.28)	0.69
	2nd	53(40.8)	153(33.3)	1.48(0.91-2.42)	0.12	1.68(1.00-2.85)	0.05		
	3rd	40(30.8)	153(33.3)	0.99(0.59-1.67)	0.98	1.05(0.61-1.80)	0.86		
PC6	1st	48(36.9)	154(33.5)	1.00		1.00		0.99(0.81-1.20)	0.89
	2nd	46(35.4)	153(33.3)	0.94(0.59-1.51)	0.81	1.09(0.65-1.84)	0.74		
	3rd	36(27.7)	153(33.3)	0.70(0.42-1.16)	0.16	0.73(0.43-1.23)	0.24		
PC7	1st	40(30.8)	154(33.5)	1.00		1.00		0.99(0.80-1.23)	0.95
	2nd	45(34.6)	153(33.3)	1.10(0.67-1.82)	0.70	1.26(0.74-2.13)	0.40		
	3rd	45(34.6)	153(33.3)	1.08(0.65-1.78)	0.78	1.09(0.64-1.87)	0.74		
PC8	1st	46(35.4)	154(33.5)	1.00		1.00		1.00(0.82-1.22)	0.97
	2nd	40(30.8)	153(33.3)	0.86(0.52-1.40)	0.54	0.86(0.51-1.45)	0.57		
	3rd	44(33.8)	153(33.3)	0.95(0.58-1.54)	0.83	0.94(0.57-1.55)	0.80		
PC9	1st	39(30.0)	154(33.5)	1.00		1.00		1.24(1.01-1.53)	0.04
	2nd	39(30.0)	153(33.3)	1.01(0.61-1.68)	0.97	0.98(0.57-1.66)	0.93		
	3rd	52(40.0)	153(33.3)	1.40(0.86-2.29)	0.18	1.53(0.92-2.54)	0.10		
PC10	1st	40(30.8)	154(33.5)	1.00		1.00		1.14(0.92-1.40)	0.23
	2nd	38(29.2)	153(33.3)	0.88(0.53-1.48)	0.64	0.90(0.52-1.55)	0.71		
	3rd	52(40.0)	153(33.3)	1.17(0.72-1.91)	0.52	1.21(0.72-2.01)	0.00		

[a] All models adjusted for age at collection, year of birth (2000-2002, 2003-2005, 2006-2009), sex, race/ethnicity, birth weight (<2500, 2500-2999,3000-3499, ≥3500 grams), gestational age (26-26, 27-41, 42-44 weeks, unknown), plurality (single vs multiple), birth order, mode of delivery (vaginal vs cesarean), mother's age at delivery (≤24, 25-34, ≥35 years), and mother's birthplace (United States vs other).

[b] Mutually adjusted: All PCs were simultaneously included in one model, along with birth characteristics listed in [a].

[c] OR per unit increase in PC, adjusting for all PCs and birth characteristics listed in [a].