

of atopy. Of the 37 participating children, 22 (59.5%) were born by vaginal delivery. Of the 15 women who had a cesarean section, (66.7%) had an elective cesarean. Only one study participant used probiotics during pregnancy. Maternal infection and/or use of antibiotics were not exclusion criteria in our study. The mean neonatal gestational age was within normal limits. One neonate had an Apgar score of 1 at 5 minutes, was intubated, and admitted to the neonatal intensive care unit (NICU); this neonate was delivered by non-elective cesarean at 37 weeks of gestation. Of note, exclusion of this child did not appreciably change the results of our analyses; thus, results are presented for all subjects. There were no significant differences in race/ethnicity, maternal age, maternal history of atopy, maternal smoking during pregnancy, neonatal gender, gestational age, birth length, or Apgar score between children born by cesarean section and those born by vaginal delivery. Children born by cesarean section were more likely to weigh more at birth than those born by vaginal delivery.

Cytokine secretion by mode of delivery

In Figure 1, we show the distributions of cytokines (IL-13, IL-10, and IFN- γ) produced by neonatal CBMCs at baseline and after stimulation with antigens (*Fel d 1*, *Der f 1*, PHA, and LPS), which were mostly single-tailed. Whereas IFN- γ had the highest rate of detection by ELISA, IL-10 had

the lowest rate of detection, particularly at baseline and after allergen stimulation (Table 2).

In bivariate analyses (Table 2), secretion of IL-13 by CBMCs in response to *Fel d 1* and *Der f 1* was significantly higher in neonates born by cesarean section than in those born by vaginal delivery. Secretion of IL-13 by CBMCs (at baseline and after stimulation with PHA and LPS) and IFN- γ (at baseline and after stimulation with antigens and PHA) was also higher in neonates born by cesarean section than in those born by vaginal delivery, but such differences were not statistically significant. There was a non-significant trend for reduced secretion of IL-10 by CBMCs at baseline in neonates born by cesarean section.

After adjustment for potential confounders in multivariate linear regression analyses (Table 3), birth by cesarean section was significantly associated with increased secretion of IL-13 by CBMCs after stimulation with allergens, PHA, and LPS. In this multivariate analysis, cesarean section was also associated with increased secretion of IFN- γ by CBMCs at baseline and after stimulation with *Fel d 1* and PHA. In contrast, cesarean section was associated with reduced secretion of IL-10 by CBMCs at baseline ($p = 0.08$). In these multivariate models, maternal atopy was independently associated with IL-13 secretion by CBMCs at baseline and after stimulation with allergens and PHA,

Table 2: Association between Cytokine Secretion by CBMCs and Mode of Delivery

Cytokine Levels (pg/ml)								
		Vaginal Delivery (n = 22)			Cesarean Section (n = 15)			
	median	ranges	% with Detectable Value±	median	ranges	% with Detectable Value±	wilcoxon p-value†	
IL-13								
Media	0.01*	0.01–47.58	40.9	3.77	0.01–32.96	57.1	0.25	
Fel d I	0.01	0.01–66.27	33.3	10.40	0.01–126.38	71.4	0.04	
Der f I	0.01	0.01–75.65	40.9	26.14	0.01–65.61	85.7	0.01	
PHA	25.18	0.01–223.54	63.6	39.31	7.50–246.04	100.0	0.22	
LPS	5.46	0.01–565.55	50.0	20.19	0.01–44.65	78.6	0.39	
IFN-γ								
Media	3.69	0.01–53.02	50.0	6.32	0.01–39.75	85.7	0.24	
Fel d I	1.24	0.01–52.00	50.0	9.22	0.01–34.18	85.7	0.41	
Der f I	8.10	0.01–58.93	59.1	16.52	0.01–54.95	85.7	0.43	
PHA	11.10	0.01–173.58	63.6	23.23	0.01–866.65	85.7	0.38	
LPS	20.03	0.01–218.70	68.2	15.21	0.01–85.27	85.7	0.97	
IL-10								
Media	0.01	0.01–49.96	18.2	0.01	0.01–0.01	0	0.10	
Fel d I	0.01	0.01–355.80	27.3	0.01	0.01–78.57	14.3	0.37	
Der f I	0.01	0.01–399.46	36.4	0.01	0.01–175.30	28.6	0.44	
PHA	21.50	0.01–759.45	59.1	0.01	0.01–367.98	42.9	0.23	
LPS	181.91	0.01–787.56	95.5	259.11	0.01–863.05	78.6	0.65	

*Low value of 0.01 was assigned to undetectable cytokine level.

± Percentage of cord blood samples in which cytokine measured by ELISA have detectable values within each category of mode of delivery.

† For comparison of cord blood cytokines between neonates born by vaginal delivery and those born by cesarean section.