



# Dysbiotic Gut Microbiome of Infants Born to Mothers with Inflammatory Bowel Disease (IBD) is Mitigated by Early Life Environmental Factors

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## Background and goals

- The MECONIUM Study (Exploring MEchanisms Of IBD traNsmission In Utero through the Microbiome) is a prospective study that recruits pregnant women with and without IBD and their offspring. **The overall goal of the MECONIUM study is to explore the role that IBD plays in the composition of the maternal and infant microbiome.**
- Previous study results showed that children born to mothers with IBD present with gut microbiota dysbiosis from birth up to 3 months, particularly in the *Bifidobacterium* and *Gammaproteobacteria* genus.
- Here, we investigated the effect of environmental factors known to impact the microbiome, including mode of delivery (C-section versus vaginal delivery), exposure to antibiotics in early life, and feeding behavior (exclusively breast-feeding, exclusively formula-fed, or mixed feeding) on infants' bacterial profiles in the context of mother's IBD status.
- We hypothesized that the dysbiotic microbiome seen in infants born to mothers with IBD can be improved when environmental factors known to have a negative effect on the microbiome are absent in early life.

## Methods

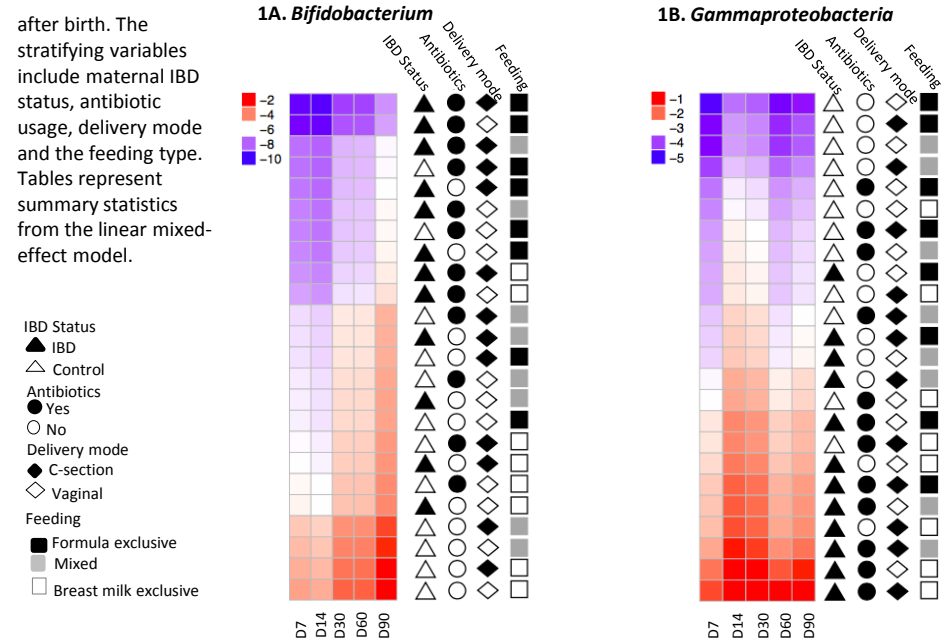
- 306 stool samples obtained during the first 3 months after birth, at 7 (D7), 14 (D14), 30 (D30), 60 (D60) and 90 (D90) days from 79 babies (26 born to IBD mothers) were sequenced for 16S rRNA.
- LefSe analysis was conducted across all time-points, adjusting for delivery mode.
- A multivariate linear mixed model was used to determine associations between microbiota and mother's IBD status, delivery mode, infant antibiotic exposure, and feeding behavior (breastfed, formula-fed, or mixed-feeding), obtained prospectively.

## Results

Table 1. Participant characteristics and exposures.

Participant Type	Infants born to IBD mothers	Infants born to control mothers	P value
<b>n</b>	26	53	-
<b>Male gender</b>	69.2%	39.6%	0.013
<b>Mean gestational age at delivery (weeks)</b>	39.5±1.08	39.3±1.67	0.36
<b>C-section</b>	46.2%	30.2%	0.16
<b>Preterm birth</b>	5.70%	0%	0.55
<b>Birth weight, kg</b>	3.41±0.38	3.29±0.52	0.82
<b>Low birth weight</b>	0%	3.8%	0.31
<b>Exclusive breastfeeding</b>	50%	39.6%	
<b>Exclusive formula</b>	15.4%	4%	0.073
<b>Mixed feeding</b>	35.6%	50%	
<b>Exposure to antibiotics</b>	3.8%	9.4%	0.66
<b>Exposure to probiotics</b>	11.5%	13.2%	0.83

**Figure 1. The trajectories of *Bifidobacterium* and *Gammaproteobacteria* in babies' microbiome and their associations to key exposure variables.** Heat maps represent the relative abundances of (a) *Bifidobacterium* and (b) *Gammaproteobacteria* by different exposures, at D7, D14, D30, D60, and D90



<i>Log2(Bifidobacteria)</i>	Estimate ± SE	t value	P-value	<i>Log2(Gammaproteobacteria)</i>	Estimate ± SE	t value	P-value
Intercept	-4.8±0.35	-14.0	2.1 <sup>-32</sup>	Intercept	-3.5±0.22	-16.3	4.7 <sup>-40</sup>
Maternal IBD	-1.3±0.49	-2.63	0.01	Maternal IBD	1.0±0.29	3.6	0.00056
C-section Delivery	-0.24±0.49	-0.49	0.62	C-section Delivery	0.16±0.29	0.57	0.57
Antibiotics_Yes	-1.3±0.92	-1.46	0.15	Antibiotics_Yes	0.73±0.57	1.28	0.20
Formula_Exclusive	-1.5±0.85	-1.79	0.07	Formula_Exclusive	-0.53±0.53	-1.01	0.31

## Conclusions

- Sub-optimal microbiome features previously observed in babies born to IBD mothers were mitigated in early life when baby was born vaginally, was not exposed to antibiotics, and was exclusively or even partially breastfed.
- The early-life microbiome may play a role in the development of the infant's immune system, so manipulation of a dysbiotic infant microbiome in early life through environmental exposures can possibly intervene in disease risk later in life.