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The Gut Microbiota of Pregnant Women with Crohn's Disease and their Babies Transfers Abnormalities of the Adaptive Immune System to Gnotobiotic Mice
- Results from the MECONIUM study -

Seki, Akihiro[1,3]; Torres, Joana[1, 2]; Tarassishin, Leonid[4]; Hu, Jianzhong[4]; Eisele, Caroline[4]; Nair, Nilendra[4]; Britton, Graham J.[3, 5]; Mao, Qixing[4, 7]; Clemente, José C.[6, 5]; Faith, Jeremiah[6, 5]; Colombel, Jean Frederic[1]; Peter, Inga[4]; Mehandru, Saurabh [1,3,6]

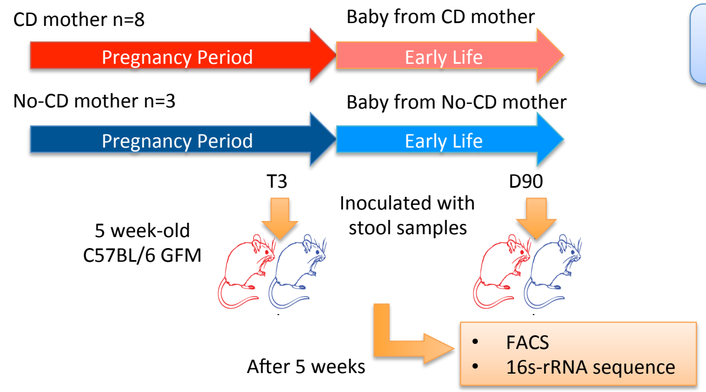
1. Department of Medicine, Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY, United States. 2. Gastroenterology, Hospital Beatriz Ângelo, Loures, Portugal. 3. Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, NY, United States. 4. Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, United States. 5. Institute for Genomics and Multiscale Biology, Icahn School of Medicine at Mount Sinai, New York, NY, United States. 6. Precision Medicine Institute, Department of Medicine, New York, NY, United States. 7. Department of Thoracic Surgery, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research and Nanjing Medical University Affiliated Cancer Hospital, Nanjing, China.

Icahn School of Medicine at Mount Sinai

Introduction

- ✓ The **MECONIUM study** is a prospective study set to understand the role of IBD in the composition of maternal microbiome during pregnancy and their offspring´s microbiome.
- ✓ Inflammatory bowel disease (IBD) is characterized by an aberrant immune response against intestinal microbiome in genetically-predisposed individuals.
- ✓ We hypothesized that maternal IBD-associated dysbiosis may impact early life microbiota and the priming of the immune system.
- ✓ We characterized the immune response to the gut microbiome in pregnant women with and without Crohn's Disease (CD) and their newborns by inoculating their stool against germ free mice (GFM).

Methods



- ✓ Stool from 3rd trimester (T3) of 11 pregnant women (8 with CD, 3 healthy control) and their 90 day-old babies (D90) were corrected.
- ✓ These stools were analyzed by 16s sequencing and transplanted into 5 week-old C57BL/6 germ free mice (GFM) and sacrificed 5 weeks later.
- ✓ Mononuclear cells harvested from the colon lamina propria and the mesenteric lymph node (MLN) from the mice inoculated with stool were collected for flow cytometry analyses (FACS) and immune profiling.
- ✓ Mouse feces collected at sacrifice were sequenced for 16S-rRNA.

Results

Table 1. Participant Characteristics

No	IBD Status	Delivery type	Age	BMI	Family history of IBD	Age at Diagnosis	CD Location	Harvey-Bradshaw index	Medication	Pro-biotics
1	Control	Vaginal	38	27.1	Unknown	NA	NA	NA	NA	No
2	Control	Vaginal	39	31.5	No	NA	NA	NA	NA	No
3	Control	Vaginal	33	29.7	Unknown	NA	NA	NA	NA	No
4	CD	C-section	28	22.5	Yes	A1 (< 17y)	L2 (colonic)	Remission: <5	Remicade	No
5	CD	C-section	26	26.7	Yes	A1 (< 17y)	L1 (ileal)	Remission: <5	None	No
6	CD	Vaginal	32	31.6	Yes	A2 (17 - 40 y)	L2 (colonic)	Remission: <5	Humira	No
7	CD	Vaginal	36	24.5	No	A1 (< 17y)	L3 (ileocolonic)	Remission: <5	None (past:Remicade)	No
8	CD	Vaginal	32	29.5	Yes	A2 (17 - 40 y)	L1 (ileal)	Remission: <5	None (past:Remicade)	No
9	CD	Vaginal	35	27.4	No	A2 (17 - 40 y)	L3 (ileocolonic)	Remission: <5	Ustekinumab, Lialda	No
10	CD	C-section	39	28.9	Yes	A2 (17 - 40 y)	L2 (colonic)	Remission: <5	Remicade, Asacol	No
11	CD	Vaginal	34	25.4	Yes	A2 (17 - 40 y)	L2 (colonic)	Remission: <5	Pentasa, Remicade	No

Figure 1. β-diversity between human stool samples grouped by IBD Status.

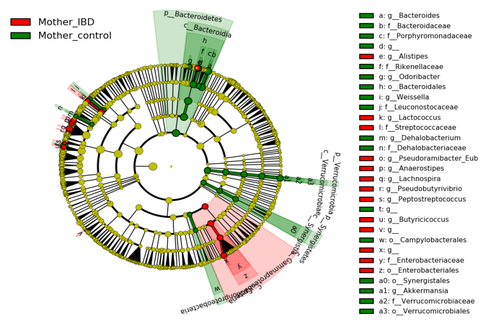


Figure 2. The gut microbiome of GFM colonized with maternal stool (a) and baby stool (b) has significant difference in overall microbiota by maternal IBD status.

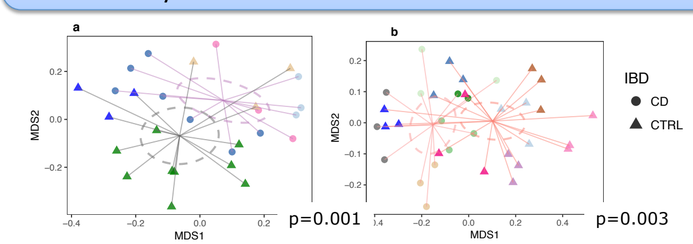
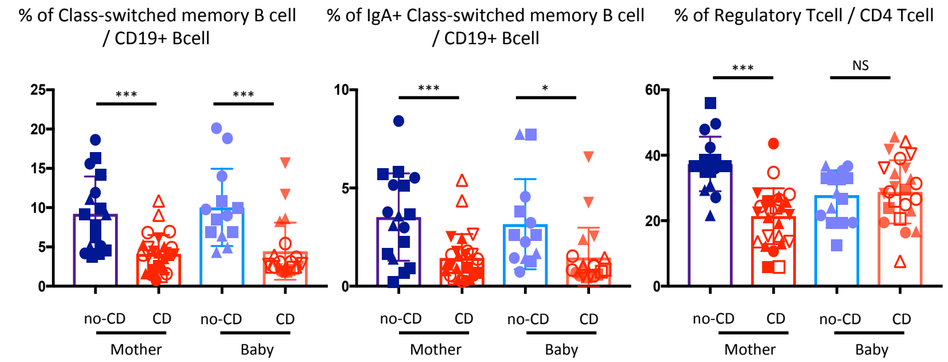
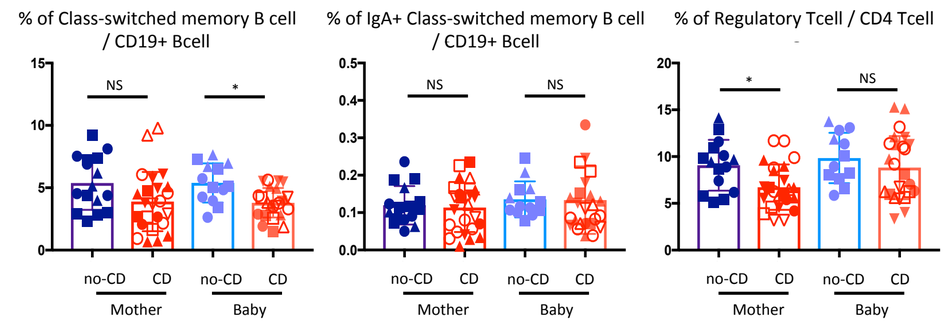


Figure 3. Germ-free mice inoculated with the stool of mothers with CD and their 90 day-old babies have significant abnormalities in the adaptive immune cells compared to mice inoculated with stool from non-CD controls.

Colonic lamina propria



Mesenteric lymph node



* P<0.05, ***p<0.005, NS not significant

Conclusion

- ✓ The microbiome of pregnant women with Crohn's Disease and their babies was associated with a weaker induction of specific cell subsets of the adaptive immune system.
- ✓ These results suggest a functional impact of the dysbiotic stool resulting in impaired B cell maturation and TREG development, which may alter mucosal homeostasis and culminate in inflammation following noxious environmental triggers.

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