

# The gut microbiota of pregnant women with Crohn's Disease and their babies is associated with abnormalities in the adaptive immune system

- Results from the MECONIUM study -

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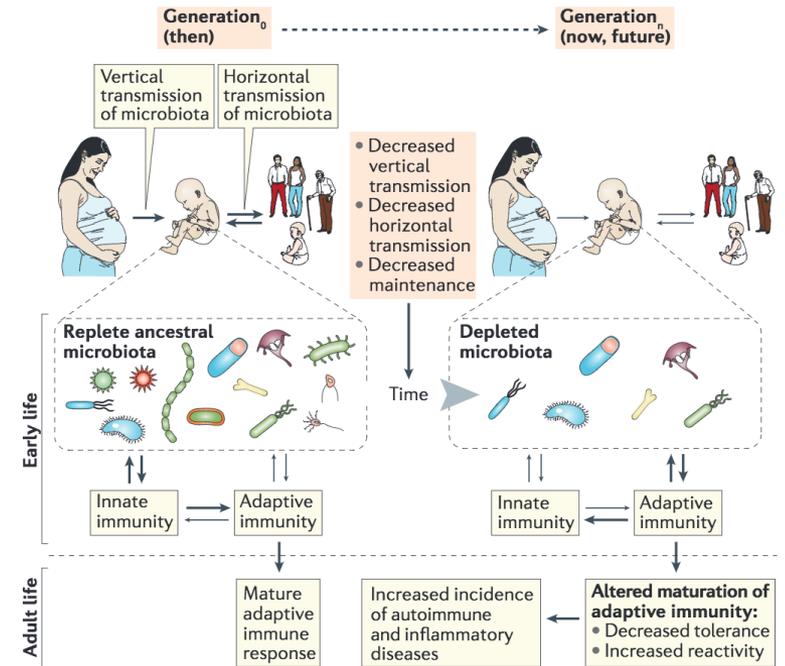
## **Disclosure of Conflicts of Interest:**

Conflict of interest :

- Consulting: Takeda and Abbvie
- Literature review: Abbvie

# Introduction

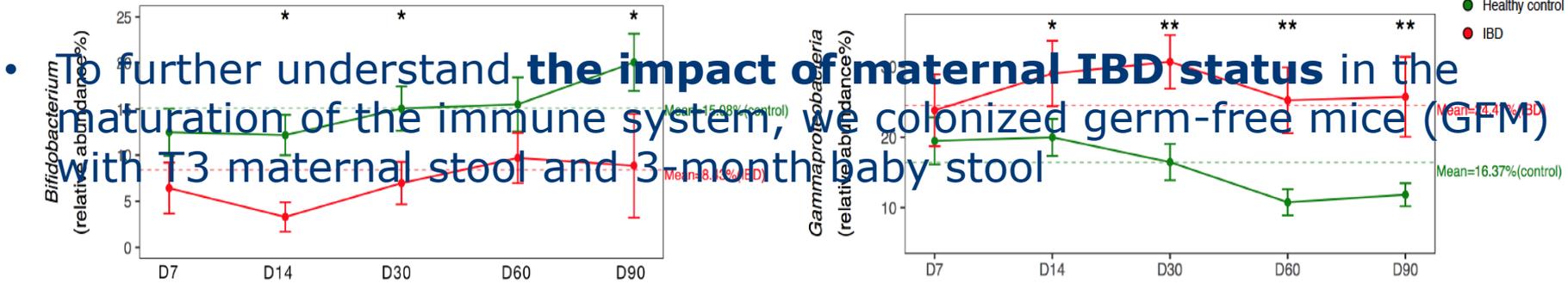
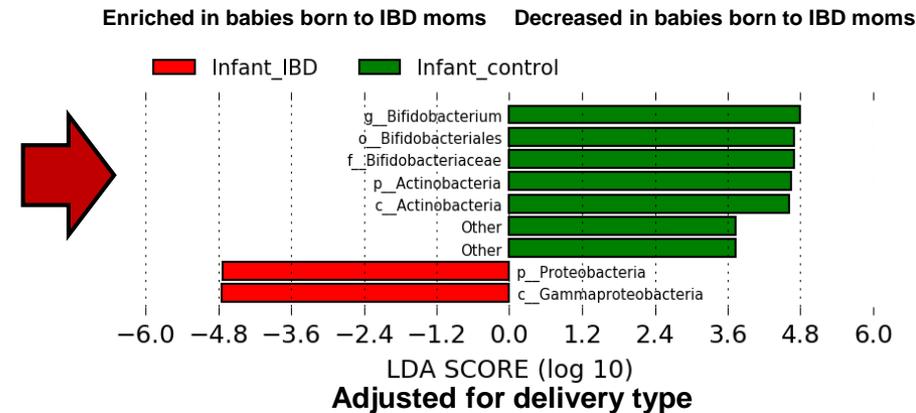
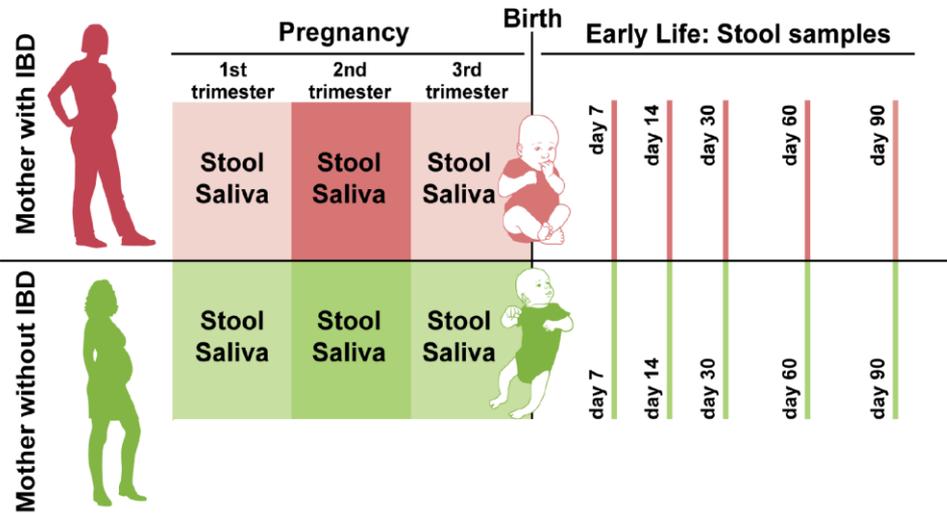
- Microbial colonization of mucosal tissues during early life plays an instrumental role in the development and education of the host mammalian immune system.
- Accumulating evidence links early life exposures (prenatal and postnatal colonization) to the risk of developing IBD later in life.



- Maternal health status has an impact on the infants' gut microbiota and immune system development.
- However, **the impact of maternal IBD on the microbiome and immune system of the infant** (at-risk population) remains unknown.

# The MECONIUM Study

- 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



# Methods

n= 8

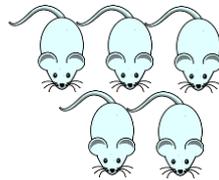


CD

*Dysbiosis*



**C57BL/6J**  
**5week old GFM**

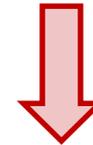


**4-5W**



Pregnancy T3  
D90

**Sacrifice**

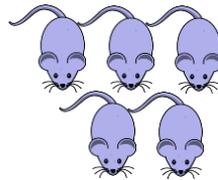


- Lamina propria cells from Large Intestine (L.I)
- Mesenteric Lymph Node (MLN) cells were isolated
- Mouse stool were collected at the time of sacrifice

*No Dysbiosis*



**C57BL/6J**  
**5week old GFM**



**4-5W**



- **Microbiome: 16rRNA analysis**
- **Immunophenotyping: flow cytometry**
  - **T cell population**
    - T regs
    - Memory T cells
    - Naïve T cells
  - **B cell population**
    - Naive B cells
    - Memory B cells

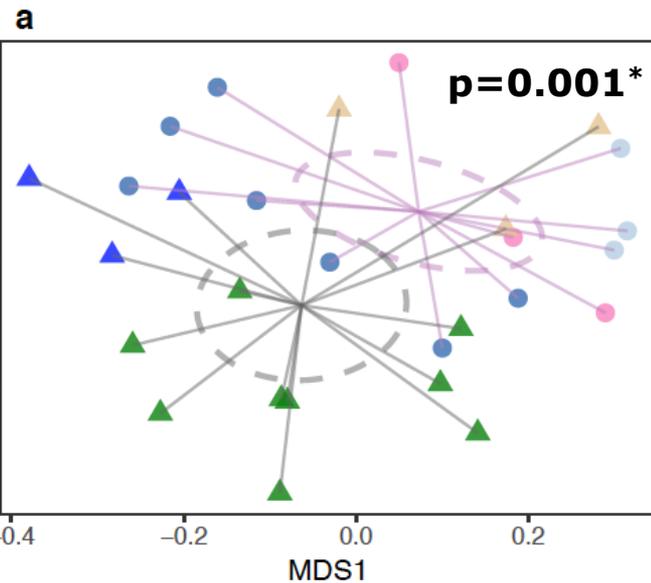
No IBD

n= 3

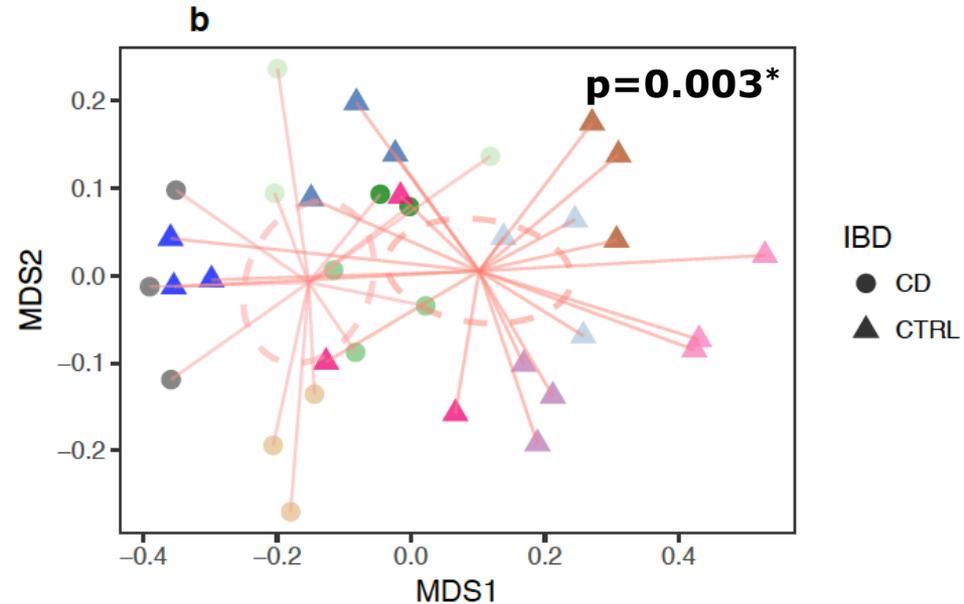
# Results - microbiome

- Colonization of GFM with stool from CD mother and their offspring resulted in different microbiome composition in mice

Gut microbiome of mice colonized with maternal stool



Gut microbiome of mice colonized with infant stool

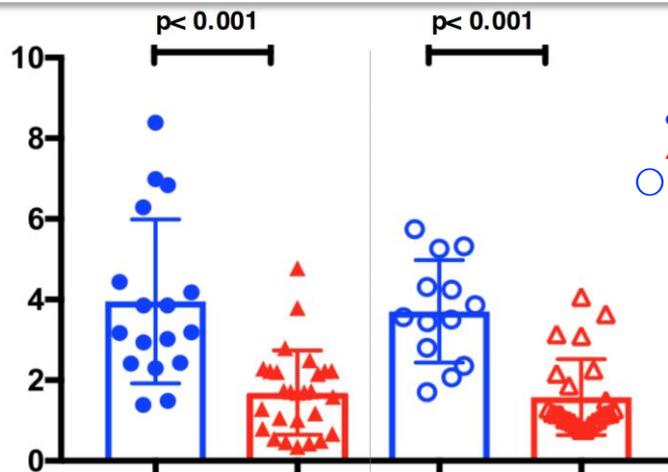
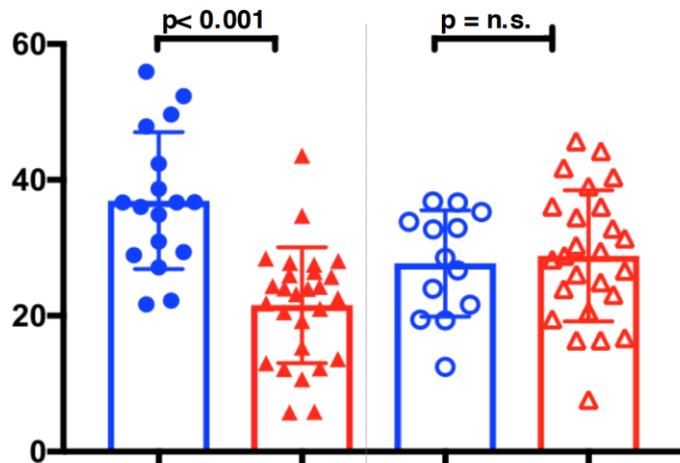


\* P values adjusted for batch and repeated sampling

## Proportion of FoxP3+ regulatory T cells (of total CD4+ cells)

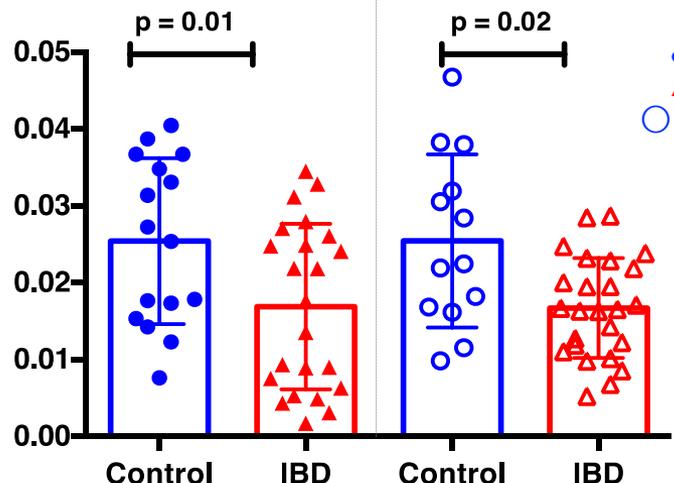
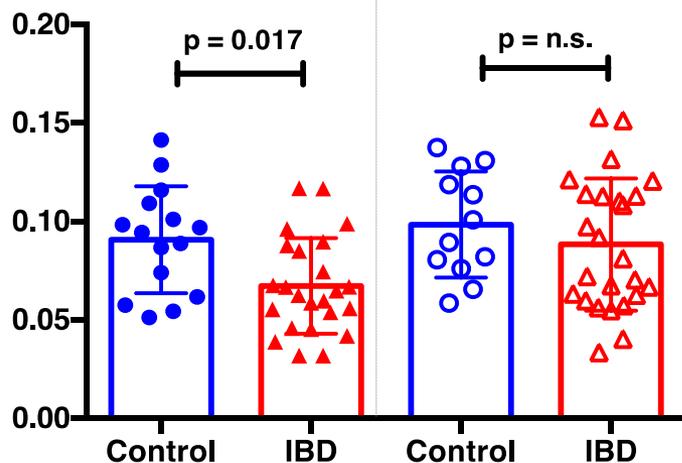
## Proportion of class switched memory B cell (of total CD19+ B cells)

Colonic lamina propria



- Control mother
- ▲ IBD mother
- Control baby
- △ IBD baby

Mesenteric lymph nodes



- Control mother
- ▲ IBD mother
- Control baby
- △ IBD baby

Mice inoculated with mother stool

Mice inoculated with infant stool

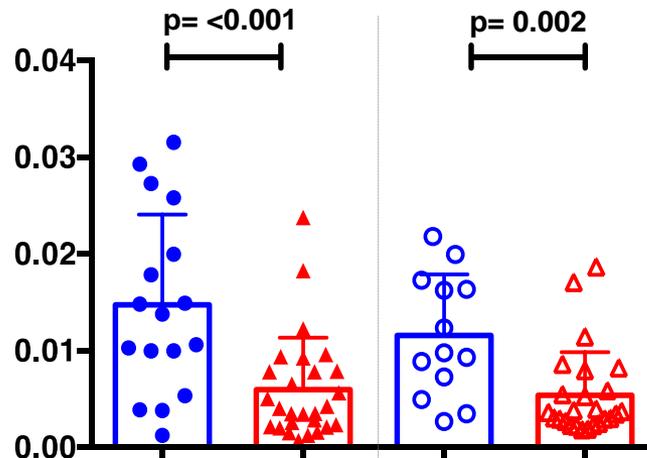
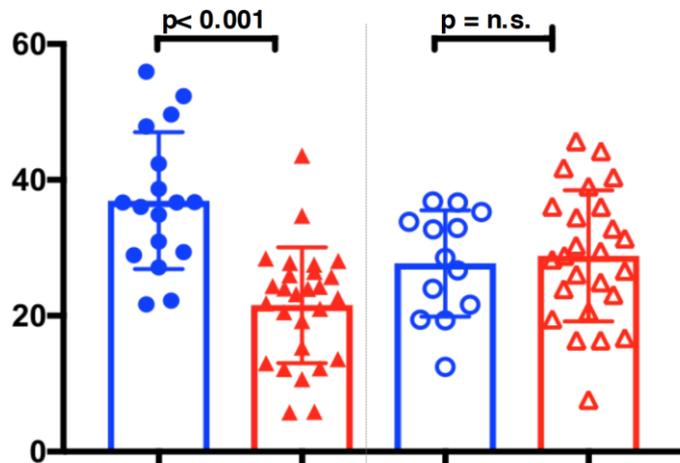
Mice inoculated with mother stool

Mice inoculated with infant stool

## Proportion of regulatory T cells

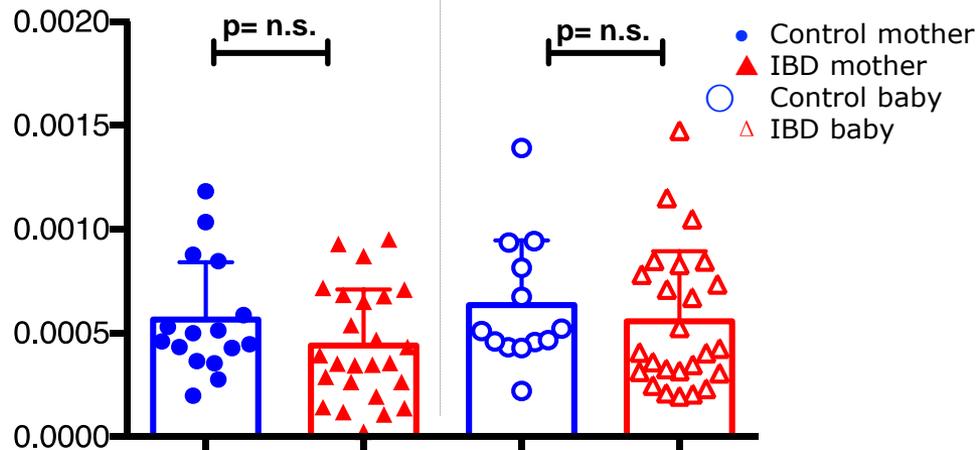
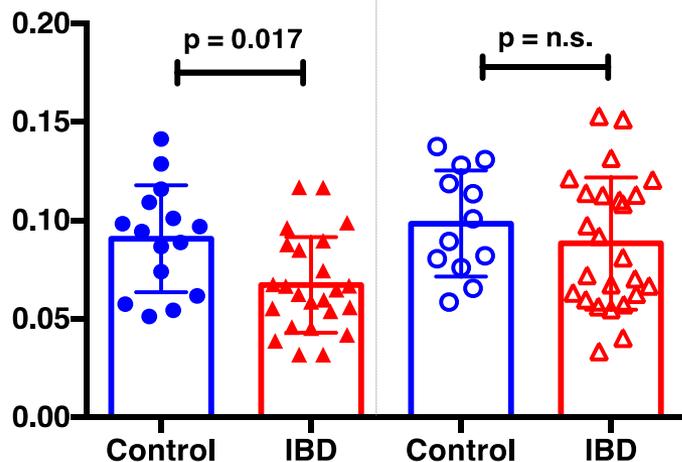
## Proportion of IgA class switched B cell

Colonic lamina propria



● Control mother  
 ▲ IBD mother  
 ○ Control baby  
 △ IBD baby

Mesenteric lymph nodes



● Control mother  
 ▲ IBD mother  
 ○ Control baby  
 △ IBD baby

Mice inoculated with mother stool

Mice inoculated with infant stool

Mice inoculated with mother stool

Mice inoculated with infant stool

## Conclusions

- The microbiome of pregnant women with IBD and their babies was associated with a weaker induction of specific cell subsets of the adaptive immune system.
- The above data suggests a functional impact of the dysbiotic microbiome resulting in impaired B cell maturation and TREG development, which may be associated with altered mucosal homeostasis
- Abnormal imprinting of the neonatal immune system in babies born from mothers with IBD could contribute to predisposition to IBD later in life.

# Acknowledgments



The MECONIUM study



**Joana Torres**



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**Ilaria Mogno**



**José Clemente**



**Jay Faith**



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**Inga Peter**

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