MECONIUM NEWS

JANUARY 2020 | ANNUAL NEWSLETTER

EXPLORING MECHANISMS OF DISEASE TRANSMISSION IN UTERO THROUGH THE MICROBIOME

INSIDE THIS ISSUE

Icahn School of Medicine at Mount Sinai

5 Year Anniversary

Meet the MECONIUM Team

Left to Right: Sierra White, Dr. Leonid Tarassishin, Dr. Inga Peter, Paulette Magnas, Kelly Hawkins, Alexa Rendon, Dr. Anketse Debebe, Caroline Eisele
Not Pictured: Dr. Jianzhong Hu, Dr. Eunsoo Kim, Dr. Jean-Frederic Colombel, Dr. Marla Dubinsky, Dr. Joanne Stone

MECONIUM STUDY

Happy Holidays from the MECONIUM Study family to yours!

After 5 years, we would like to extend our gratitude for your continued participation. The MECONIUM families are what make research like our study possible. Since the fall of 2014, the MECONIUM study has been enrolling families like yours. We have now collected more than 5,700 samples from over 450 families!

The progress that we have made in the last 5 years would not be possible without our research team and the families that support us. Take a look inside this issue to learn more on our project updates and what to expect in 2020. We also have some adorable pictures from our favorite participants, our diaper donor babies!

Thank you for reading and enjoy!

Best Wishes,

The MECONIUM Study Team

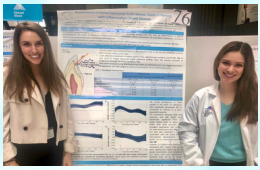
Icahn School of Medicine at Mount Sinai

RESEARCH PRESENTATIONS

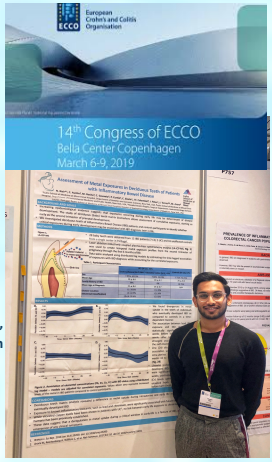
The MECONIUM Study research was presented at several conferences throughout the past year.

Leonid Tarassishin (RIGHT) – using a pipetting robot for detecting biomarkers in multiple samples from pregnant women and their babies.

Kelly Hawkins & Alexa Rendon, clinical research coordinators, presenting at the 2019 Mount Sinai Research Symposium.



Nile Nair (RIGHT), Research Associate, presenting research at the European Crohn's and Colitis Organization conference in Copenhagen.



Calprotectin

Inflammatory Bowel Disease (IBD) affects women during their reproductive years, and the effect of pregnancy on disease course is not fully understood. We aimed to profile the intestinal inflammation in IBD patients compared to controls as assessed by fecal calprotectin (FC), which is a protein biomarker found in stool that is used as a surrogate marker for inflammation. We also investigated whether maternal IBD diagnosis was associated with FC in the offspring and if there were particular bacterial taxa found in mothers' and babies' gut that correlated with FC levels in stool.

FC levels at each trimester of pregnancy and in babies throughout the first 3 years of life were measured. We also assessed microbiota composition of the maternal and baby stool.

Overall, 614 fecal samples from 341 mothers (90 IBD, 251 control) and 1,005 fecal samples from 290 infants (born to 76 mothers with and 214 without IBD) were analyzed. FC levels in pregnant women with IBD were substantially higher than in women without IBD, regardless of IBD type (Crohn's Disease vs. ulcerative colitis). In IBD mothers, FC levels showed a decline during pregnancy. Patients with flare at stool collection had the highest, while those treated with anti-tumor necrosis factor (TNF) plus thiopurine showed the lowest FC at each trimester. Babies born to mothers with IBD sustained higher FC levels than those born to control mothers at multiple time points between 2 and 36 months of age, with the highest levels recorded in babies born to mothers with active disease during pregnancy.

FC levels in IBD patients decreased throughout pregnancy, with anti-TNF plus thiopurine therapy correlated with the lowest FC levels. Maternal IBD, lower microbiome diversity and the abundance of certain microbial genera were associated with higher FC in the offspring up to 3 years of life. These findings suggest a potential favorable impact of pregnancy on IBD activity and highlight possible effect of IBD during pregnancy on the degree of mucosal inflammation in offspring, which could be mediated through altered microbiome.

THE EXPOSOME

The Exposome project consists of collecting baby teeth from Inflammatory Bowel Disease patients and healthy controls. Through tooth analysis, we can determine levels of metal exposure as far back as the second trimester of pregnancy. Our findings show that teeth from individuals who eventually develop IBD have higher levels of lead, copper, and chromium metal uptake, suggesting that metal exposure during a critical window of prenatal development can be correlated with risk of developing IBD. We just received a grant from the International Organization for the study of IBD to continue this work! Keep an eye out for tooth collection kits included in your upcoming sample kits for participants age 5 years and older.

CONTACT US

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labs.icahn.mssm.edu/peterlab/the-meconium-study/

Project Updates: What We've Been Doing

We are very excited to share the results from our most recent publication:

Gut. 2019 April 29. PMID: 31036757

"Infants born to mothers with IBD present with altered gut microbiome that transfers abnormalities of the adaptive immune system to germ-free mice"

BACKGROUND

Prenatal and early life bacterial colonization is thought to play a major role in shaping the immune system. Furthermore, accumulating evidence links early life exposures to the risk of developing IBD later in life. **We aimed to assess the effect of maternal IBD on the composition of the microbiome during pregnancy and on the offspring's microbiome.**

RESULTS

Pregnant women with IBD and their offspring presented with lower bacterial diversity and altered bacterial composition compared to control women and their babies. Maternal IBD was the main predictor of the microbiota diversity in the infant gut at 7, 14, 30, 60, and 90 days of life. Babies born to mothers with IBD demonstrated enrichment in *Gammaproteobacteria* and depletion in *Bifidobacteria*. Finally, Germ Free Mice (GFM) were exposed to third trimester IBD mother and 90-day infant stools and showed significantly reduced microbial diversity and fewer class-switched memory B-cells and T cells in the colon.

SIGNIFICANCE OF THIS STUDY

- A positive family history remains the strongest risk factor for developing IBD; however, genetic susceptibility alone explains a small proportion of disease heritability.
- IBD affects women during their reproductive years, and around 25% become pregnant after their initial diagnosis. Human studies have shown that profound changes in the microbiome occur during pregnancy and that maternal health status and maternal microbiome play a role in shaping the microbiome and immune system of the neonate.
- The role of IBD in the maternal microbiome composition during pregnancy and its impact on the offspring's microbiome remains unclear.
- Women with IBD maintain altered bacterial diversity and composition in their gut during pregnancy as compared to controls.
- Babies born to IBD mothers present with lower diversity and altered bacterial gut composition up to at least 3 months of life independent of other exposures, compared to babies born to control mothers.
- Targeting microbial imbalance in pregnant women with IBD or during early infancy could foster the development of a healthy microbiome in the offspring, thereby reducing the future risk of IBD.

Icahn School of Medicine at Mount Sinai

NEW GRANT JUST RECEIVED:

"Effect of IBD Pregnancy on placental transcriptome and the potential mediation by gut dysbiosis"

The placenta, situated at the maternal-fetal interface, is a key organ for fetal growth and development. Studies, including our own, have highlighted an integral role of placental processes involved in fetal growth.

Through this grant, we aim to explore the effect of IBD pregnancy on the placental transcriptome (the full range of genetic information expressed from an organism), and the role of maternal gut microbiome linking IBD and placental transcriptome.

*M*odulating *E*arly *L*ife Micr*O*biome through Prenatal *D*ietar*Y* Intervention in Crohn's Disease

The MECONIUM Study has added valuable data to the accumulating evidence showing that maternal health and diet as well as maternal microbiome during pregnancy have an impact on the baby's microbiome. It is already known that diet may play a role in the development and treatment of Crohn's disease by changing the gut bacterial flora.

We are enrolling for a **new clinical trial** in collaboration with the Center for Applied Nutrition at the University of Massachusetts Medical School. The trial will **assess whether a non-invasive diet intervention implemented during the third trimester of pregnancy can beneficially shift the microbiome in patients with Crohn's disease and their babies.**

Eligibility

WOMEN WHO HAVE CROHN'S DISEASE OR NO DISEASE (CONTROLS) AND ARE LESS THAN 30 WEEKS PREGNANT. WOMEN MAY CHOOSE WHETHER TO FOLLOW THE DIET INTERVENTION OR PARTICIPATE IN THE CONTROL GROUP.

IF YOU OR SOMEONE YOU KNOW IS INTERESTED IN PARTICIPATING, PLEASE EMAIL US AT: **themelodytrial@gmail.com**

https://www.umassmed.edu/nutrition/melody-trial-info/

THE MELODY TRIAL IS FUNDED BY THE HELMSLEY CHARITABLE TRUST.

		Pregnancy			Delivery	After Birth				
	Timeline	27-29 w (Baseline)	35 w	37 w		14 d	30 d	90 d	6 mo	12 mo
Crohn's disease + IBD-AID diet	Samples	Diet intervention: 30-37 weeks Stool Saliva	Stool Saliva	Stool Saliva	Umbilical cord blood	Breast milk			Stool Saliva	Stool Saliva
Crohn's disease + no diet Control + no diet	Questionnaires (Q)	24HR Basic Info Q Health history/ Reproductive Q FFQ weekly throughout		24HR	Delivery/ Postpartum Q		FFQ (diet arm only)	FFQ (diet arm only)	FFQ 24HR Follow-up Q	FFQ 24HR Follow-up Q
Babies	Samples				Meconium	Stool	Stool	Stool	Stool	Stool
	Questionnaires					IDD	IDD	IDD Rome IV	IDD 24HR	IDD 24HR

w=gestational weeks; d=days old; mo=months old
FFQ=Food Frequency Questionnaire (online) <30 minutes

24HR=24 Hour Diet Recall (by phone, three separate days) 20-30 minutes
IDD=Infant Diet and Development Questionnaire (online) 10 minutes
Rome IV=Assess functional gastrointestinal disorders in infants (by phone)


CAT
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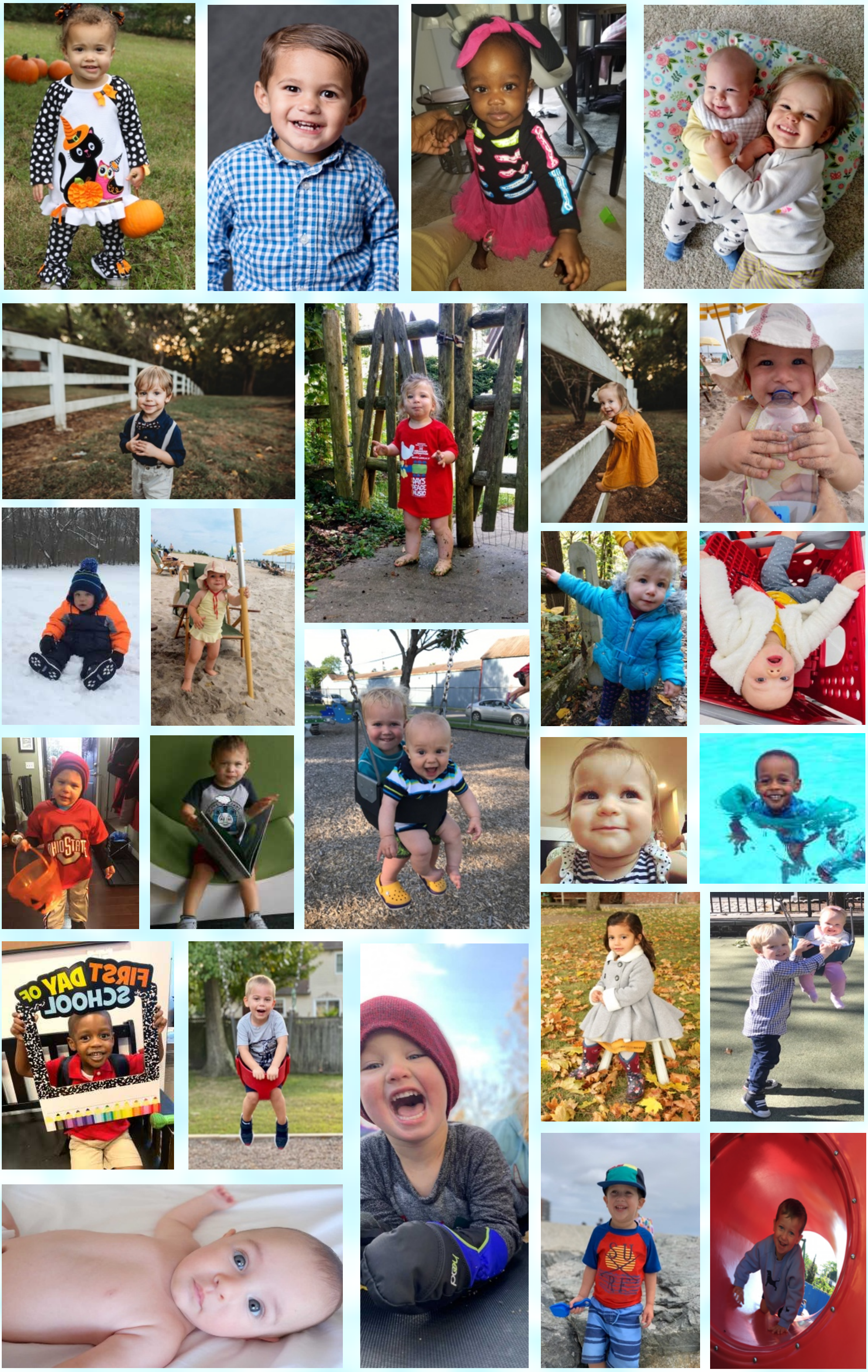
years



If you are pregnant or planning another pregnancy, you can participate in the MECONIUM Study throughout your pregnancy. Please contact the research coordinators to let us know the good news if interested!

CONTACT INFORMATION

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This study would not be possible without your participation and dedication. We are so grateful for your support of our research!