BASECLEAR

EXPERTS MEETING

Infant and Pregnancy Microbiome

Thursday May 14th, 2020

AGENDA

All times are Central European Time (CET)

AGENDA

SESSION 1: EXPLORING INFANT MICROBIOME

10.50 **Welcome & Opening expert meeting**
Dr. Radhika Bongoni – Business Developer, BaseClear

11.00 **The Nature and Nurture of our Microbiome**
Dr. Clara Belzer – Associate Professor, Wageningen University

11.15 **Mother-infant microbiome interface: Early determinants and long-term health implications**
Dr. Anne Salonen – Principal Investigator Human Microbiome Research Program, University of Helsinki

11.30 **Does the gut microbiome affect immune changes in the pregnant mouse?**
Dr. Marijke Faas – Associate Professor, UMCG

11.45 **Less is more: infant gut microbiome analysis by shallow shotgun sequencing captures near-complete taxonomic and functional microbial profiles**
Dr. Ali May – Product manager bioinformatics, BaseClear

12.00 **Panel Discussion**

SESSION 2 : MODULATING INFANT MICROBIOME

15.00 **Symbiotics in Early life nutrition for C-section born infants**
Dr. Kaouther Ben Amor – Senior Team Leader Probiotics, Danone

15:15 **Human Milk Oligosaccharides as a Novel Functional Food Ingredient**
Dr. Katja Parschat – Deputy Head of research and development, Jennewein Biotechnologie

15:30 **Characterising the young infant gut mycobiome**
Dr. Steve James – Researcher, Quadram Institute Bioscience

15:45 **How to translate microbiome diversity in infants?**
Dr. Maciej Chichlowski – Mead Johnson Nutrition / Reckitt Benckiser

16.00 **Panel Discussion 2**

16:40 **Pub Quiz with Virtual Toast**

BaseClear hosts

Radhika Bongoni

Radhika is Business Developer at BaseClear, with focus on markets for application of microbial genomics in food, feed and pharma industries. Radhika received her Ph.D. in Food technology (2014) from Wageningen University & Research (the Netherlands) and an MBA (2015) from Tias School for Business & Society (the Netherlands). With techno-commercial expertise, she is involved in business growth and market penetration by fostering relationships with partners. Prior to BaseClear, Radhika was responsible for establishing dietary supplements market in western Europe, India, South Africa and Russia.

RADHIKA BONGONI, PHD
Business Developer

Derek Butler

Derek is the commercial director of BaseClear. Derek completed a bachelor's degree in Biotechnology at Dublin City University in 1995, specialising in Genetics and Immunology. He continued his studies at University College Cork and in 2001 received his PhD degree for work on the genetic regulation of lactic acid bacteria. In the same year he took up a post-doctoral position at the University of Groningen where his work focused on the identification of novel enzymatic activities from thermophilic bacteria. In 2004 Derek joined Lactrys where he worked on vaccine development in probiotic bacteria before joining BaseClear in 2006. He has now more than 15 years' experience working on microbial genomics research projects together with industrial partners.

DEREK BUTLER, PHD
Commercial director

The Nature and Nurture of our Microbiome

Dr. Clara Belzer
Associate Professor, Wageningen University

ABSTRACT

The microbiota has a pervasive impact on immune and metabolic health. Changes in birth mode and infant feeding, antibiotic use and overall nutrition over the last decades have impacted microbiota acquisition and the establishment of host microbial symbioses which is hypothesized to be associated with the dramatic global rise of immune related disorders. Human produced glycans (human milk and mucus) play an important role in the way microbial species in the gastrointestinal tract function and contribute to health. The ability of the microbiome to ferment host-produced glycans makes them keystone species within the intestinal microbiota, crucial for immune, metabolic and neurologic imprinting. Interaction between microbes mucus and milk leads to dependencies shaping the overall intestinal microbiome structure in early and later life, and microbial roles in maintaining host health. Additionally, this leads to applicability of glycans for nutritional strategies, such as innovative nutritional and microbial intervention strategies by which the structure and function of the microbiome can be modulated to prevent or treat disease.

BIO

Dr. C. Belzer is associate professor at the Laboratory of Microbiology of Wageningen University. The Belzer group resaerch is focussed on microbiome in reation to mucus and milk. After obtaining her Phd at the Erasmus Medical Center dr. Belzer did a posdoc at Harvard medical school. By now dr. Belzer has years of experience on gut microbiome studies on anaerobes, including synthetic communities and probiotics.
The group of dr. Belzer works on several microbiome HMO related topics some also in collaboration medical centers and industry. Dr. Belzer has the lead in several projects such as; H2020_eat2bnice, JPI_earlymicrohealth, TTW_PPS-earlyfit, TKI_Inside, TKI_Ansynto.

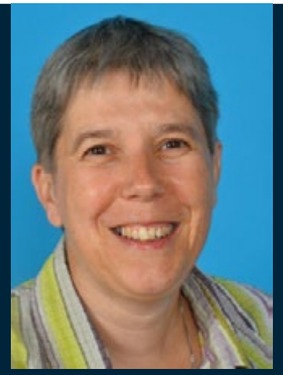
Mother-infant microbiome interface:
Early determinants and long-term health implications

Dr. Anne Salonen
Principal Investigator Human Microbiome Research Program,
University of Helsinki

ABSTRACT:
Early life microbiota is an important factor for long-term human health and development. The first bacteria populating the gut of naturally born infant come primarily from the mother. Many factors in modern life, such as birth by ceasarean section and antibiotic use can however jeopardize the evolutionally conserved mother-infant microbiota transfer and subsequent colonization process. Disturbed early colonization is believed to contribute to the increased risk of immune-mediated and metabolic diseases related to caesarean section birth and early antibiotic use. However, the assertion of causality between gut microbiota alterations and negative health outcomes is difficult in humans. I will highlight recent results and successful research strategies on this important topic.

BIO
Dr. Anne Salonen is a principal investigator and adjunct professor at University of Helsinki, Finland. She is also a deputy director of the Human Microbiome Research Program at the Medical Faculty, University of Helsinki. Dr. Salonen has multidisciplinary training in biosciences and PhD in microbiology. Since 2007 she has been studying human microbiomes and her current research is focused on the composition and activity of the intestinal and vaginal microbiota in health and disease. She is a co-principal investigator of the Finnish Health and Early Life Microbiota (HELMI) birth cohort which consists of ca. 1000 infants and focuses on studying environmental, lifestyle and genetic factors that modify early gut microbiota development, and their relation to child health and well-being.

Does the gut microbiome affect immune changes in the pregnant mouse?



Dr. Marijke Faas
Associate Professor, UMCG

ABSTRACT

Pregnancy is associated with adaptations of the maternal immune response and with changes in the gut microbiota. We hypothesized the gut microbiota are involved in inducing (part of) the maternal immunological adaptations during pregnancy. To test the role of the microbiome on maternal immune response, we sacrificed pregnant (day 18) and non-pregnant conventional and germfree mice. Splenic (various Th cell populations) and blood immune cells (monocyte subsets) were measured by flow cytometry. Feces were collected from the conventional mice before and during pregnancy (days 7, 14, and 18) and microbiota were measured using 16S RNA sequencing. In pregnant conventional mice, the percentage of Th1 cells was decreased, while the percentages of Treg cells and Th2 cells were or tended to be increased vs. non-pregnant mice. In germfree mice, only the percentage of Th1 cells was decreased in pregnant vs. non-pregnant mice, with no effect of pregnancy on Treg and Th2 cells. The percentages of monocyte subsets were affected by pregnancy similarly in conventional and germfree mice. However, the activation status of monocytes (expression of CD80 and MHCII) was affected by pregnancy mainly in conventional mice, and not in germfree mice. The microbiota of conventional mice were significantly different at the end of pregnancy (day 18) as compared with pre-pregnancy (Permanova, $p < 0.05$). Correlation (Spearman's coefficient) of pregnancy affected microbiota with pregnancy affected immune cells, showed 4 clusters of bacteria and 4 clusters of immune cells, some of these clusters were correlated with each other.

The different immunological adaptations to pregnancy between conventional and germfree mice, such as the increase in Treg and tendency to an increase in Th2 cells in conventional pregnant mice only, may suggest that the microbiota may play a role in adapting the maternal immune response to pregnancy.

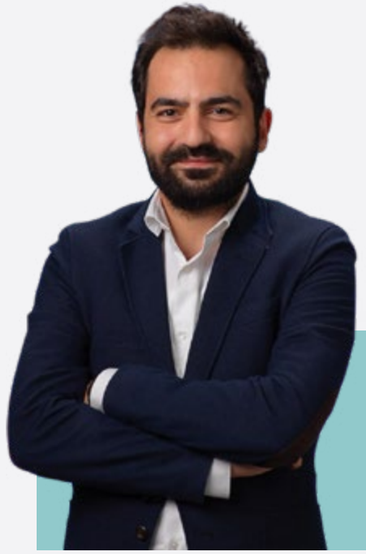
BIO

Marijke Faas studied Medical Biology at the University of Groningen and is now Associate Professor at the University Medical Centre Groningen, heading the research group "Immunoendocrinology". She started her research line on reproductive immunology during her PhD studies. Since then she focussed on how immune responses are affected by the female reproductive condition and which factors are involved in affecting this response. Having started with mainly studying peripheral immune responses, the research line has been extended throughout the years with placental immune responses and, more recently, intestinal immune responses. Throughout the years, it has become clear that immune responses are very different in pregnancy and that the placenta and factors produced by the placenta into the maternal circulation are important for inducing these changes. With the recent knowledge of the health effects of the microbiome (gut and other bodily sites), especially the effects on immune responses, she has become interested in the role of the microbiome in the adaptations of the immune responses to pregnancy. We are now also studying the role of the microbiome in the adaptations of the immune responses to pregnancy, using for instance germfree mice. We have shown that maternal microbiome changes correlate with changes in the maternal and fetal immune responses in mice and that immunological adaptations to pregnancy are different in germfree mice compared with conventional mice. Future experiments focus on finding bacterial species and microbiome modulatory treatments that are able to affect maternal or fetal immune responses, which may potentially be used for treatment of pregnancy complications.

Less is more:
infant gut microbiome analysis by shallow shotgun sequencing captures near-complete taxonomic and functional microbial profiles

ABSTRACT

Shallow shotgun metagenome sequencing is a cost-effective approach for analysing the human microbiome. With a good study design and appropriate bioinformatics, as few as 1 million short NGS reads per sample are enough to get a near-complete picture of the taxonomic and functional microbial profiles. To test the applicability of the shallow shotgun approach on infant gut microbiome projects, we have analysed two recently published infant microbiome datasets and compared the results we obtained from the deep sequencing of the samples to those generated by shallow sequencing. In addition, to assess the added value of an integrated infant gut microbiome gene catalogue, we generated a gene catalogue from each study and compared how well the microbial functional profiles calculated by using either catalogue, and their combination, correspond to each other. In this meeting, we will share our results and experience with these two datasets which strongly indicate the feasibility of the shallow shotgun method and the added value of an infant microbiome gene catalogue.



BIO

Ali May studied Biological Sciences and Bioengineering at Sabanci University, Istanbul. He then moved to the Netherlands where he obtained his master's degree in Bioinformatics (cum laude) in 2012 from Vrije Universiteit (VU) Amsterdam. During his PhD work that followed, joint between the departments of Bioinformatics and Preventive Dentistry, he developed data analysis methods for studying the compositional and functional differences in the human oral microbiome in health and disease. After obtaining his degree he joined BaseClear in 2016, where he creates DNA data analysis services and products for microbial genomics where applications of genome characterisation and microbiome research play key roles.

Symbiotics in Early life nutrition for C-section born infants

Dr. Kaouther Ben Amor
Senior Team Leader Probiotics, Danone

ABSTRACT

Infants born by C-section miss the exposure to the maternal vaginal microbiota and this absence of microbial inoculation has been associated with a delayed colonization of commensal bacterial members such as Bifidobacterium. This compromised microbial inoculation may impact the health of the new-born and epidemiological data from cohort studies indicate associations between C-section and, immune and metabolic disorders such as asthma and obesity. The objective of this study was to determine the effect of a specific mixture of short-chain galactooligosaccharides and long-chain fructooligosaccharides (scGOS/lcFOS, ratio 9:1) and the probiotic strain Bifidobacterium breve M-16V in restoring the delayed colonization of Bifidobacterium observed in term C-section delivered infants.

In a multi-country, randomised, double-blinded, controlled study, we determined the effect of short-chain galacto-oligosaccharides (scGOS), long-chain fructo-oligosaccharides (lcFOS) and Bifidobacterium breve M-16V on the gut microbiota of cesarean-born infants. Infants were randomized to receive a standard formula (control), the same formula with scGOS/lcFOS (ratio 9:1) and B. breve M-16V (synbiotic), or with only prebiotics (scGOS/lcFOS, Ratio 9:1) (prebiotic) from birth until week 16. Synbiotic supplementation resulted in a higher level of bifidobacteria from the first days of life until and a lower level of Enterobacteriaceae from the first days of life until the end on the intervention compared to controls. This was accompanied with a lower fecal pH and higher acetate. In the synbiotic group, B. breve M-16V was detected 6 weeks post-intervention in 38.7% of the infants indicating a good persistence of the probiotic to colonize the infant gut. Interestingly, a lower percentage of subjects with AEs of skin disorders were reported in the synbiotic group compared to the control group and specifically of eczema/atopic dermatitis which was significantly lower in the synbiotic.

This synbiotic concept supported the early modulation of Bifidobacterium in C-section born infants that was associated with the emulation of the gut physiological environment observed in vaginally delivered infants. Our data suggest a potential positive effect on skin related disorders, this observation Potential health benefits need to be investigated in future studies.

BIO

Kaouther Ben Amor holds a PhD degree from Wageningen University in Microbial Eco-physiology of the Human Intestinal Tract. Since 2006, she is working at Danone Nutricia Research with focus on the role of the early life development of the gut microbiota in health and disease. In her current position as senior team leader probiotics, her responsibility is to advance science-based solutions for early life and specialised adult nutrition. Probiotics, prebiotics, postbiotics and synbiotics are her main area of focus as microbiome modulators and as tailored nutrition solutions.

Human Milk Oligosaccharides
as a Novel Functional Food Ingredient

Dr. Katja Parschat
Deputy Head of research and development,
Jennewein Biotechnologie

ABSTRACT

Human milk oligosaccharides (HMOs) comprise a large group of carbohydrates unique in their high concentration and structural complexity to human breast milk. Accumulating evidence demonstrates that HMOs provide a variety of potential benefits to the breast fed infant. HMOs are prebiotic serving as substrate for specific potentially beneficial bacteria, they act directly antimicrobial and have been shown to reduce the risk of bacterial or viral infections by inhibiting the adhesion of pathogens to cell surfaces, thus, HMOs are involved in shaping the gut microbiome in infants that are breast fed or receiving HMOs by infant formula. HMOs reach the circulation and can be detected in the blood and urine of HMO fed infants so also systemic effects such as immunomodulatory effects and anti-inflammatory effects are attributed to HMOs. Additionally, specific HMOs are assumed to improve neuronal development and positively improve cognition in the first years of life. While sialic acid deriving from sialylated HMOs directly serve as building blocks for brain tissues, other effects on memory and cognition might be due to metabolites of bacterial HMO degradation.

HMOs are synthesized in the mammary gland; however, exposure may already begin long before birth. HMOs have been detected in amniotic fluid and recently evidence of HMOs in the blood cord was provided suggesting HMO transfer from the maternal to the infant circuit. Detection of bacterial DNA in meconium raises the question if HMOs already in utero effect the infant's microbiome development.

Only since a few years HMOs are approved as Novel Food and commercially available in large amounts but more and more infant formula is already on the market containing HMOs as functional ingredient.

BIO

- Diploma in general biology 1998 at the Carl von Ossietzky Universität, Oldenburg, Germany
- PhD 2004 from the Carl von Ossietzky Universität in Oldenburg with the thesis:
- Genes of Arthrobacter ilicis Rü61a involved in quinaldine degradation: characterization and functional expression of the quinaldine 4-oxidase genes.
- 2004-2010 post-doc at the Westfählische-Wilhelms-Universität in Münster (Institute for molecular biology and biotechnology), Germany. Further work on the gene regulation of genes involves in bacterial degradation of aromatic pollutants.
- 2010 to now: senior scientist at Jennewein Biotechnologie GmbH, responsible for strain development for the fermentative production of human milk oligosaccharides and functional monosaccharides
- Since 2017 responsible for the first clinical trial of Jennewein Biotechnologie assessing the influence of a 5 HMO blend on the development of neonates and their gut microbiome.
- Since 2017 deputy head of the research and development department at Jennewein.

Characterising the young infant gut mycobiome

Dr. Steve James
Researcher, Quadram Institute Bioscience

ABSTRACT
The human gastrointestinal (GI) tract contains a large and extremely diverse array of microbes from all three domains of cellular life (Archaea, Bacteria and Eukarya) along with viruses. In the case of the Eukarya, fungi are typically the principle representatives, but are often overlooked due to their lower abundance when compared to their bacterial counterparts. Despite this, there is growing evidence to show that the fungal micro-biota (mycobiome) is an important component of the human microbiome, and which can have a significant impact on human health. In this short talk, I will present and discuss results from a recent study which focused on defining the early life gut mycobiome in a small cohort of young infants, all of whom were less than 2 years of age and born preterm.

BIO
I am a molecular microbiologist currently working at the Quadram Institute Bioscience, Norwich, UK. I am a member of Prof. Simon Carding's research group, which in turn is part of the Institute's Gut Microbes and Health programme. My research focuses on studying and defining the fungal component (mycobiome) of the human gut microbiota. One area of particular interest to me is the early life gut mycobiome, and the questions relating to how its first establis hed, how it subsequently develops over time and how it influences human health and disease.

How to translate microbiome diversity in infants?

Dr. Maciej Chichlowski
Mead Johnson Nutrition / Reckitt Benckiser

ABSTRACT

Diversity is a key measure in microbiome analysis, with more diverse gut microbiome considered stable and healthy. While diversity measures usually capture useful information relating to microbiome structure, there are other key factors such as cross-feeding, species composition and microbial products which may impact health and development. For example, the gut microbiome of formula-fed infants is more diverse but less stable compared to breast-fed infants. Higher bacterial diversity in formula-fed infants leads to a shift towards an adult-like microbiome at a quicker rate. Lower diversity in infants receiving human milk is likely due to the dominance of Bifidobacterium, which preferentially utilize human milk oligosaccharides. In this talk, I will discuss several factors impacting microbiome diversity in early life.

BIO

Dr. Maciej Chichlowski is a Principal Scientist in the Global Nutrition Science team in RB. In his role, he identifies beneficial ingredients and assesses their biological relevance and potential efficacy for use in a range of infant formula and pediatric nutritional products. Maciej has over seventeen years of experience in the field of gastrointestinal physiology, prebiotics and probiotics. He has published numerous peer reviewed journal articles and patent applications.
Born and raised in Poznan, Poland, Dr. Chichlowski earned a PhD in Physiology from North Carolina State University. His first postdoctoral appointment was at Duke University Medical Center where he focused on bacterial-mucosal interactions in the pathogenesis of inflammation-associated colon cancer. During his second postdoctoral appointment at the University of California, Davis, he received funding from National Institutes of Health to analyze the effects of human milk oligosaccharides on the function of select bifidobacteria in the GI tract.

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MORE INFORMATION?
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