THE MICROBIAL MATERNAL HERITAGE:
THE JOURNEY OF BACTERIA IN EARLY LIFE AND INFLUENCE ON MASTITIS AND ALLERGY
THE HUMAN MICROBIOME

★ An average adult has ~1.5 kilograms of gut bacteria
★ \(10^{13}\) cells per gram of colonic content
★ Microorganisms are an integrated part of our physiology
HUMAN GUT MICROBIOTA DIVERSITY

Unborn  Baby  Toddler  Adult  Elderly

Ottman et al. (2012) Front Cell Infect Microbiol. 2:104
BACTERIA AND HOST INTERACTIONS AT THE GUT EPITHELIAL BARRIER

The gut epithelium covers over 250 square meters. Enough to cover a tennis court!

The gut epithelium separates us from the microbiota but also interacts with it and thus affects host immune status and physiology.

- Barrier function
- Adsorption
- Innate defense
- Mucus production
- Hormone secretion
CROSS TALK BETWEEN MICROBIOTA AND IMMUNE SYSTEM

The lamina propria is connective tissue constituted by stromal cells, blood vessels, nerves, and immune cells.

Macrophages and dendritic cells are strategically located next to the epithelial layer.

Sampling luminal antigens and orchestrating the innate and adaptive immune response

Tolerance mechanisms prevent reactions against the microbiota and food antigens
A FRONTIER FOR PHARMACEUTICAL & NUTRITIONAL DISCOVERY

Therapeutics
Probiotics
Prebiotics
Antibiotics

Gut Microbiota

Effectors
Metabolites
Antigens
Toxins
Proteins
Ecological interactions

Diagnostics
Personalized
Patient stratification
Prediction/prevention

Diseases & disorders
Obesity
Atopic asthma
Autism
IBD
Type I diabetes
Colon cancer

Roeselers et al., 2012 Pharmacological Research
SOME ECOLOGICAL QUESTIONS

★ How is the gut microbiota assembled?

★ Is microbiota assembly a deterministic or stochastic process?

★ What are the effects of host genotype, physiology, and environment?

★ How can we tell what aspects of this tremendous biodiversity matters?

★ How much is our microbiota/microbiome evolving as a reflection of our changing lifestyles/biosphere?

★ What is therapeutic potential of the microbiota/microbiome?

★ How and when can/should we intentionally manipulate this system?
WHERE DOES THE MICROBIOTA COME FROM?

- We are born sterile!
- Colonization of the mammalian gut with microbes begins immediately at birth.
- Upon passage through the birth canal, infants are exposed to a complex microbial population (Redondo-Lopez et al., 1990 Rev Infect Dis 12: 856–872)
- Infants delivered through c-section have different microbiota compared with vaginally delivered infants (Huurre et al., 2008 Neonatology 93: 236–240).
Acquisition of the microbiome in early life by vertical transmission, and factors modifying mother-to-child microbial transmission.
CESAREAN SECTION

odds ratio (OR) for asthma at 8 years

Roduit C et al. Thorax 2009;64:107-113
HUMAN GENETICS

Monozygotic twins have similar microbiota

Zoetendal et al., Microbial Ecology in Health & Disease 2001
Dicksved et al., ISME Journal 2008
Breast-fed babies develop a microbiota often dominated by *Bifidobacteria*.

Formula-fed babies develop a more “adult-like” microbiota.

DEVELOPMENT OF THE INTESTINAL MICROBIOTA

- **Prepartal**: Sterile?
- **Birth**: Inoculation with maternal/environmental microbiota
- **4 days**: Genetics
- **20 days**: Mode of delivery
- **4-6 months**: Antibiotics

**Dietary influence**
- Human milk
- Formula
- Weaning transition to adult
GALACTO- AND FRUCTO-OLIGOSACCHARIDES AND GUT HEALTH

Nutricia developed an innovative concept of adding prebiotics oligosaccharides to infant milks, in order to mimic the composition of oligosaccharides in breast milk.

★ Stimulation of specific *Bifidobacterium* and *Lactobacillus* species;
★ Reduction in pathogenic bacteria.
★ Relief of gastrointestinal symptoms
★ Reduction of digestive problems
FORMULA WITH GOS/FOS: MORE LIKE BREAST-FED INFANTS

Dose-dependent bifidogenic effect after feeding a scGOS/LcFOS supplemented infant formula

Supplementation levels of a unique mixture of Prebiotics [g/100ml]

SCGOS/LCFOS & MICROBIOTA METABOLISM

SCFA patterns similar to that of breast milk

![Acetate](chart1)
![Propionate](chart2)
![Butyrate](chart3)
HIGHER FAECAL SC-IGA SECRETION IN INFANTS FED ON PREBIOTIC INFANT FORMULA

The origin of the bacteria present in breast milk has become a controversial issue in the last years.

A possible route may include the establishment of the mothers' skin microbiota and infants' oral microbiota into the mammary gland.

Also Bacteria are postulated to translocate from the mothers' intestine to the mammary gland via the mesenteric lymph nodes.
**WHAT IS MASTITIS?**

- Mastitis is an inflammation (infectious or non-infectious) of the breast tissue.

- *Staphylococcus aureus* is the most common etiological organism responsible, but *S. epidermidis* and streptococci are occasionally isolated as well.

- Early stages of mastitis can present with local pain, redness, swelling, and warmth, later stages also present with systemic symptoms like fever and flu-like symptoms and in rare cases an abscess can develop.
TREATMENT OF INFECTIOUS MASTITIS DURING LACTATION: ANTIBIOTICS VERSUS PROBIOTICS

Significant reduction of bacterial taxa counts in breast milk after the probiotic treatment

352 women with mild infectious mastitis

A) daily 9 log10 *L. fermentum* CECT 5716 (n=127)
B) daily 9 log10 *L. salivarius* CECT 5713 (n=124)
C) Prescribed antibiotics (n=101)

TREATMENT OF INFECTIOUS MASTITIS DURING LACTATION: ANTIBIOTICS VERSUS PROBIOTICS

...with a significant reduction in pain score

Antibiotic group
At day 21, 27 women reported an intense pain (score 0–4), 45 women improved but still reported discomfort for breastfeeding (5–7), and only 29 women recovered completely (8–10)

Breast pain score from 0 (most painful) to 10 (no pain)

A) *L. fermentum* CECT 5716 (n=127)
B) *L. salivarius* CECT 5713 (n=124)
C) Antibiotics (n=101)

IN SUMMARY

★ Microbial colonization in the first 1000 days of life may have a big influence on metabolic, immune, and gut health

★ Following birth, the human intestine is rapidly colonized

★ Colonization is influenced by gestational age, mode of delivery (vaginal birth vs. c-section), diet (breast milk vs. formula), sanitation, and antibiotics

★ Breastfed infants typically have a microbiota dominated by Bifidobacterium sp

★ Formula-fed infants may benefit from infant formulas containing prebiotic oligosacharides

★ Recent studies have shown that breastmilk represents a continuous supply of bacteria to the infant gut

★ Mammary dysbiosis may lead to mastitis, a condition that represents the first medical cause for undesired weaning

★ The use of probiotic L. fermentum CECT5716 or L. salivarius CECT5713 appears an efficient alternative to antibiotics for the treatment of infectious mastitis during lactation.