# Breastfeeding and the Microbiome

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## Objectives

- At the conclusion of this session, participants will be able to:
  - Identify ways the microbiota is passed from mother to baby
  - Identify roles the microbiome plays in the development of the baby
  - Identify ways the microbiome contributes to the health of the breast

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# What is the microbiome?

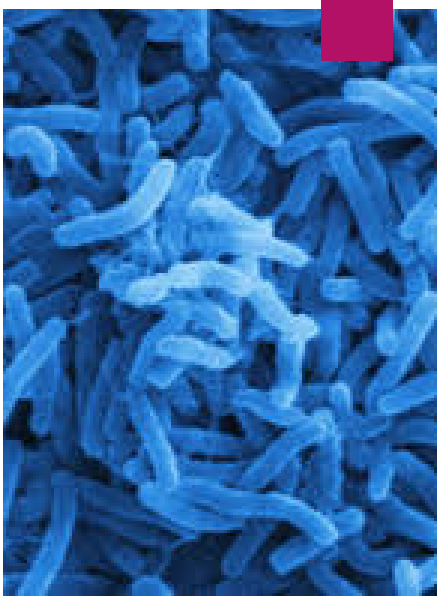
# The microbiome

- The ecological community of commensal, symbiotic, and pathogenic microorganisms that share our body
- The human body has an estimated $3.9 \times 10^{13}$ colonizing microorganisms (greater than the number of cells in the body)
  - Its influence is so broad it is recognized as another organ
  - 1-3% of an individual's mass
- The largest concentrations of microbes occupy the gut, skin, and oral cavity
- Co-evolve with the immune system so they are well tolerated

# Role of the microbiome

- Interacts dynamically with the host and the environment
- Shapes the immune system via the development of the capability to discern self from non-self, invasive pathogens from commensal microbes (tolerance)
- Responsible for the synthesis of vitamins, isoprenoids and other nutrients
  - An individual's metabolism is part human, part microbial
- Enhanced natural mucosal barrier function by reducing pathogen colonization- growth of a protective biofilm, competition for binding sites and nutrients, alteration of pH
- Promotes enzymatic activity
- Influenced by diet, age, exercise, health status, culture, ethnicity, location

- The maternal microbiome alters during gestation, particularly that of the vagina, intestines, and the breast- make a healthy baby
- Influence the brain and behavior- gut-brain axis
  - Communication mechanisms still being elucidated- includes immunological, endocrine, metabolic, and neural pathways
  - Biochemical complexity of the gut is greater than that of the brain
  - Gut microbiota hormones also act as neurotransmitters within the CNS

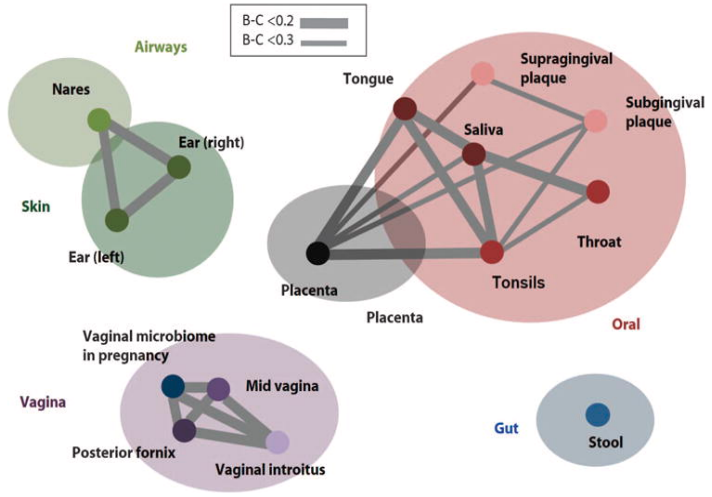


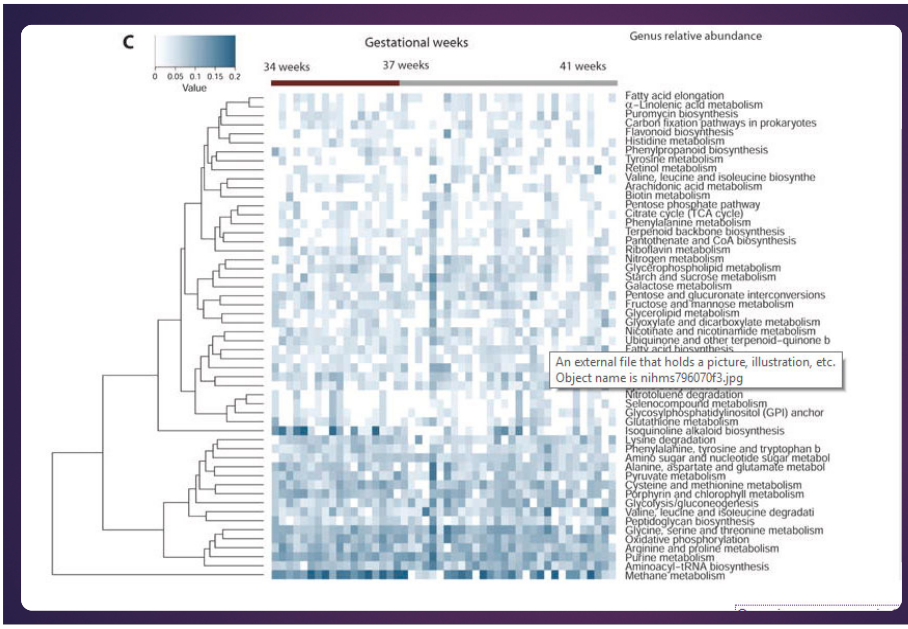
# Establishment of the infant microbiome

## Prenatal Exchange

- The placental microbiome is distinct from that of other parts of the body
- A low-abundance/biomass but metabolically rich microbiome
- Largely composed of nonpathogenic commensal microbiota from the Firmicutes, Tenericutes, Proteobacteria, Bacteroidetes, and Fusobacteria phyla
- Most similar to that of the **oral cavity**
  - Link between maternal periodontal disease and preterm birth

Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J.The placenta harbors a unique microbiome.Sci Transl Med. 2014 May 21;6(237):237ra6

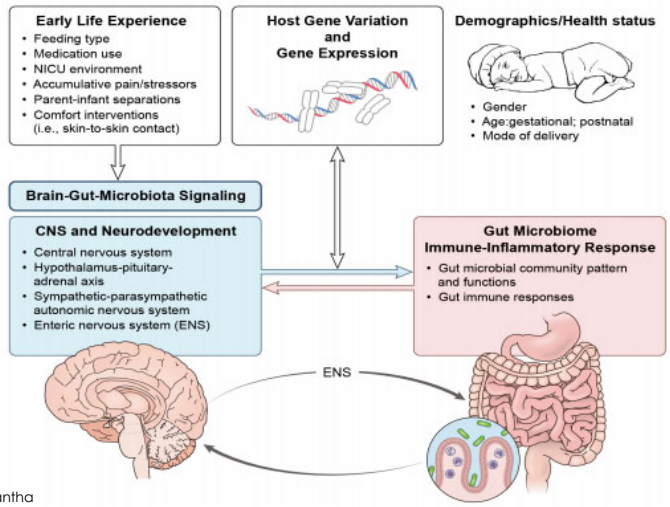



Heat mapping of metabolic activity of the placental microbiome

# Peripartum and the first week of life

- The neonatal microbiome is largely determined by maternal offspring exchange
- Birth represents the infant's first major microbial inoculation
- Intense colonization begins immediately following birth, increases in diversity as the individual ages, and converges toward an adult microbial community by 3 years of age
  - Cessation of breastfeeding most significant driving factor towards adult microbial profile
- In the first week of life, the full-term neonatal gut microbiome is largely colonized by the Actinobacteria (including Bifidobacterium), Proteobacteria, Bacteroides, and Firmicutes (including the Lactobacillus spp., which dominate the vaginal flora)




Xiaomei Cong, Wanli Xu, Rachael Romisher, Samantha Poveda, Shaina Forte, Angela Starkweather, Wendy A. Henderson. Gut **Microbiome** and **Infant** Health: Brain-Gut-**Microbiota** Axis and Host Genetic Factors. Yale J Biol Med. 2016 Sep; 89(3): 299–308.

# Causes of durable disruptions

- Mode of delivery
- Antibiotics
- Feeding modality
- Prematurity
- Hospitalization

- **Practices that compromise the colonization of the newborn should be used prudently and followed by measures to restore the natural composition of the microbiome**

# Mode of delivery

- Vaginal delivery results in microbiota typically encountered in the female reproductive tract
- Cesarean delivery results in a microbiota of organisms predominantly associated with skin bacteria and the hospital environment
  - Increased risk of asthma, inflammatory bowel disease, immune deficiencies, leukemia, Crohn's disease, systematic connective tissue disorders, juvenile arthritis, type 1 diabetes, obesity
  - Higher levels of *Clostridium difficile* and at increased risk of MRSA
- Differences introduced by mode of delivery persist long term and can be noted for years

# Feeding Modality

- Breastmilk introduces new microbes into the neonate
- The breastmilk microbiota varies by stage of lactation, gestational age, maternal health status, mode of delivery
- Dominated by *Staphylococcus, Streptococcus, Serratia, Pseudomonas, Corynebacterium, Ralstonia, Propionibacterium, Sphingomonas*, Bradyrhizobiaceae), *Bifidobacterium* and *Lactobacillus* spp.
- Breastfed infants have lower fecal pH
  - Favors proliferation of acid-tolerant *Lactobacilli* and *Bifidobacteria*
  - Restricts the growth of Enterobacteria, Clostridia, and Bacteroides

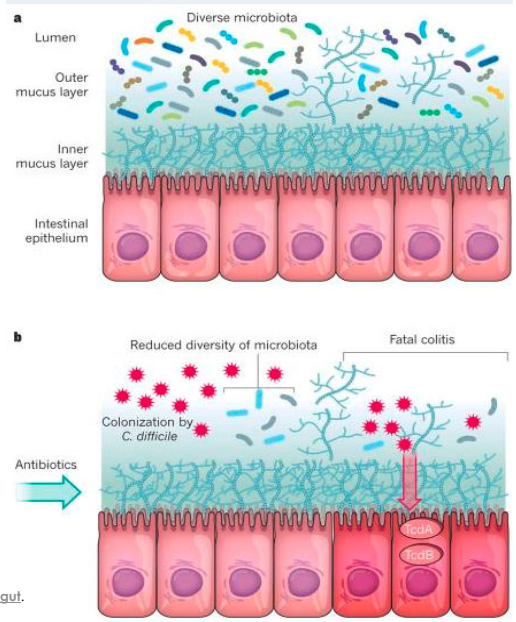
- Provides bioactive components important to optimizing gut microbial colonization
- Over 200 unique human milk oligosaccharides (prebiotics) have been identified to date
  - A major nutrient source for *Bifidobacteria*, especially *Bifidobacterium longum infantis*
  - High levels of *Bifidobacteria* are correlated with lower incidence of potentially pathogenic microbes

# Formula

- Introduction of formula or early solids (>4 months of age) alters colonization patterns in the intestines
- Even in small amounts can alter the structure and relative abundances of the microbiota normally found in the breastfed infant gut
- May reduce the benefits of exclusive breastmilk feeding

# Antibiotics

- Antibiotic use selects for resistant and resilient microbial strains
- May drive gut dysbiosis
- Restricts gut microbiota diversity
- Increased susceptibility to aggressive bacterial infections (*C. difficile*, vancomycin-resistant *Enterococcus*)



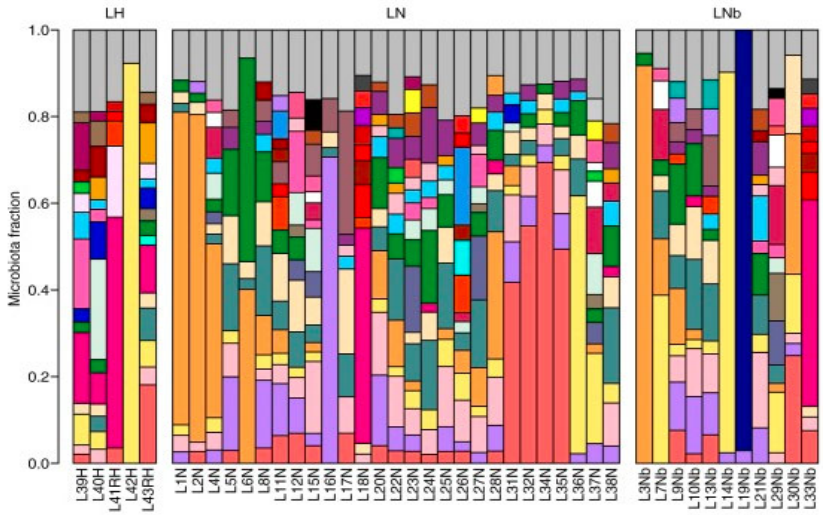

Andreas J. Bäumler, Vanessa Sperandio. Interactions between the microbiota and pathogenic bacteria in the gut. Nature. 2016 Jul 6; 535(7610): 85–93.

# Prematurity/Hospitalization

- Infants born prematurely demonstrate an altered colonization pattern
  - Gut microbiota of preterm infants is less diverse at birth than that of full-term infants
- Immune immaturity and physical stress
- Fortification of feedings, receipt of motility agents, diuretics, corticosteroids can all affect the microbiota
- The hospital environment is a reservoir for infectious agents
- Both term and preterm infants hospitalized in early life are at increased risk for nosocomial infection

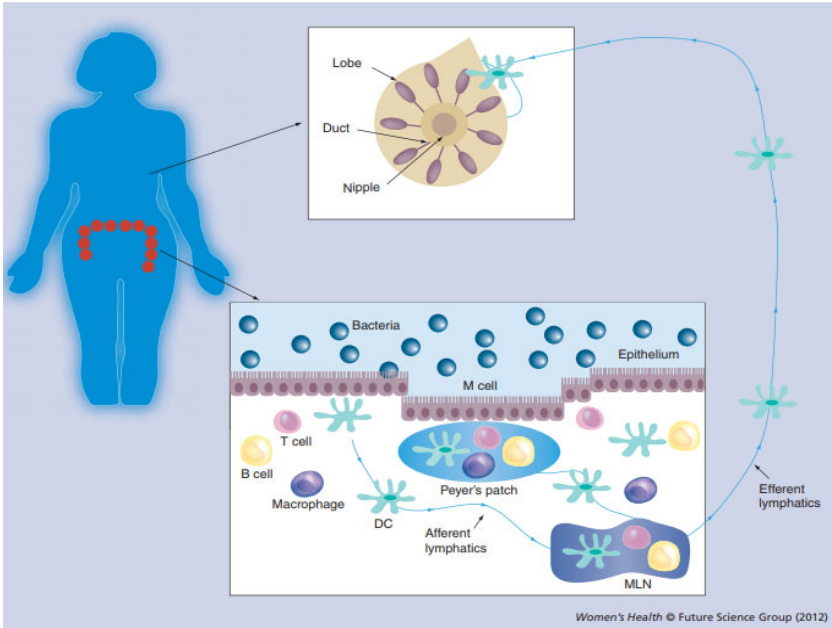
# Microbiota of the human breast

- Breast tissue is not sterile
- The breast microbiome contributes to the health of the breast tissue
- Bacteria in the milk ducts begins to appear in the 3rd trimester
- In addition to the milk, bacteria have been located on the skin, in the lobules, and in the lactiferous ducts (absent from the fatty tissue in studies to date)
- Multiple species of bacteria have been identified in the breast/milk
  - *Proteobacteria* and *Firmicutes* predominate




Urbaniak C1, Cummins J, Brackstone M, Macklaim JM, Gloor GB, Baban CK, Scott L, O'Hanlon DM, Burton JP, Francis KP, Tangney M, Reid G. Microbiota of human breast tissue. Appl Environ Microbiol. 2014 May;80(10):3007-14.

- Maternal intestinal bacteria are transmitted to the breast
  - Proposed modes of transfer
    - Via the skin of the nipple and areola
    - translocation across the mucosal membranes of the mouth, intestine, urogenital tract and skin
    - Bacteria captured and carried by the dendritic cells via the bloodstream and mesenteric lymph nodes




# Molding the microbial consortia

# Prevention and restoration strategies

- Initiate and sustain breastfeeding!
- Antibiotic stewardship
- Avoidance of medically unnecessary c-sections
- Pre and Probiotics
  - Maternal use of oral probiotics during pregnancy is thought to modulate expression of TLR-related genes in the placenta and the fetal gut- Rautava S, et al. 2012
  - Further research needed on strain, dose, timing
  - Being added to some infant formulas

- Seeding of infants born via c-section with vaginal swabs
  - Immediately after birth infants swabbed with vaginal fluid over their entire bodies and mouth
- Enhance maternal microbiota and diet
  - Maternal fatty acid provide restructures infant gut microbiota- Robertson et al, 2018