INTIMATE STRANGERS:
MICROBIAL PARTNERS IN THE NATURAL WORLD

OLLI

SPRING 2020

LECTURE 7: VERTEBRATES AS MICROBIAL PARTNERS

VERTEBRATES AS MICROBIAL PARTNERS

MAMMALIAN MICROBIOME

METHODS FOR MICROBIOME RESEARCH

THE PITFALLS OF ENDOSYMBIOSIS

- THE CONTINUOUS PRESENCE OF A VERTICALLY TRANSMITTED SYMBIONT LEADS TO THE EVOLUTION OF DEVELOPMENTAL DEPENDENCE BEYOND THE SYMBIONT'S ORIGINAL CONTRIBUTION; THAT IS, HOSTS BECOME "ADDICTED" TO THEIR SYMBIONTS
- ADOPTION OF SYMBIONTS FOR NUTRIENT PROVISIONING IS A GATEWAY TO DEVELOPMENTAL DEPENDENCE THAT CAN ENDURE EVEN WHEN THOSE NUTRIENTS ARE NO LONGER NEEDED
- THIS "ADDICTION" CAN EVOLVE EVEN TO DELETERIOUS MICROBES, SUCH AS THE REPRODUCTIVE PARASITE *WOLBACHIA* → SYMBIONT SELFISHNESS
- IN THE HOST, ACCOMMODATION OF SYMBIONTS MAY REQUIRE THAT THEY SUPPRESS OR MODIFY IMMUNE RESPONSES, POTENTIALLY ELEVATING RISK OF PATHOGEN INVASION

VERTEBRATES AND ENDOSYMBIONTS

- TRUE ENDOSYMBIOSIS (LIKE THE CASE OF APHIDS AND *BUCHNERA*, OR INSECTS AND *WOLBACHIA*) HAS NO PARALLEL IN VERTEBRATES, FOR WHICH ALL DESCRIBED INTRACELLULAR BACTERIA ARE PATHOGENS

- THE ONLY KNOWN BENEFICIAL INTRACELLULAR MICROORGANISMS IN VERTEBRATES ARE ALGAL CELLS IN THE EMBRYOS OF THE SPOTTED SALAMANDER (*AMBYSTOMA*)

A MUTUALISTIC RELATIONSHIP

- SALAMANDERS SPEND MOST OF THEIR ADULT LIVES UNDERGROUND BUT EMERGE FOR SEMIANNUAL SPRING BREEDING IN POOLS, WHERE EGGS ARE DEPOSITED
- ALGAE LIVE IN DIRECT ASSOCIATION WITH EMBRYOS INSIDE SALAMANDER EGG CAPSULES, WHICH ARE CONTAINED IN LARGE JELLY MASSES
- ALGAE INVADE EMBRYONIC SALAMANDER TISSUES AND CELLS DURING EMBRYONIC DEVELOPMENT
- THE PRESENCE OF ALGAE CORRELATES WITH EARLIER HATCHING, DECREASED EMBRYONIC MALFORMATIONS AND LARGER SIZE
- ALGAE GET NITROGEN FROM THE EMBRYOS' BYPRODUCTS

VERTEBRATE HOSTS AND THEIR MICROBIOMES

- **FISH**: TRANSFERRING THE GUT MICROBIOTA FROM YOUNG KILLFISH INTO MIDDLE-AGED KILLIFISH SIGNIFICANTLY EXTENDS THE LIFESPANS OF THE MIDDLE-AGED KILLFISH
- **AMPHIBIANS**: IMPORTANT ON THE SKIN; PROVIDE PROTECTION TO FUNGI (MAJOR THREAT TO AMPHIBIAN BIODIVERSITY)
- **REPTILES AND BIRDS**: GUT MICROBIOMES ARE SIMILAR
- **MAMMALS**: VAST DIVERSITY IN GUT MICROBIOMES, ESPECIALLY IN HERBIVORES

VERTEBRATE HOSTS AND THEIR MICROBIOMES

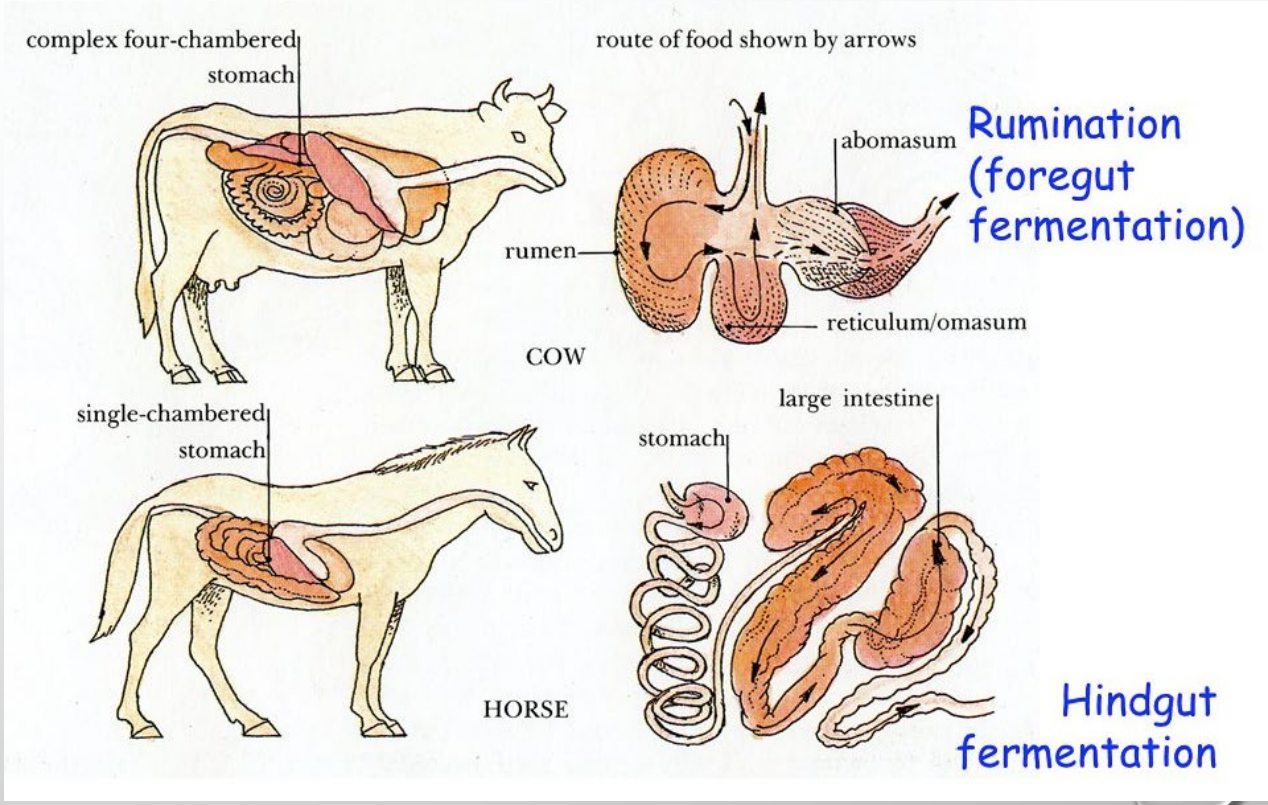
- RICHEST AND BEST STUDIED MICROBIOMES ARE THOSE IN THE GUT
- THE CHARACTER OF THE GUT MICROBIOME IS DEFINED BY THE EVOLUTIONARY HISTORY OF THE HOST AND DIET
- ALTHOUGH PLANTS ARE THE MOST ABUNDANT FORM OF FOOD, MOST NON-MAMMALIAN VERTEBRATES EAT A DIET THAT INCLUDES MOSTLY OTHER (USUALLY SMALLER) ANIMALS WITH JUST A SMATTERING OF PLANT PRODUCTS
- PLANT TISSUES CONTAIN MORE COMPLEX CARBOHYDRATES (THINK ROUGHAGE)
- VERTEBRATES DO NOT HAVE THE ENZYMATIC CAPACITY TO BREAK THEM DOWN
- TO EAT A DIET OF PLANTS (OR THAT INCLUDE A GOOD AMOUNT OF PLANTS) VERTEBRATES NEED MICROBES TO ASSIST THEM

MAMMALIAN MICROBIOMES: A CASE STUDY

- THE FIRST MAMMALS WERE CARNIVOROUS (EATING MOSTLY INSECTS AND WORMS)
- SHIFTING FROM EATING ANIMALS TO EATING PLANTS WAS AN EVOLUTIONARY BREAKTHROUGH → THE ABUNDANCE OF FOODSTUFFS ALLOWED HERBIVORES TO DIVERSIFY MUCH FASTER THAN THEIR CARNIVOROUS RELATIVES AND SPREAD INTO MANY NICHES
- TODAY, THE MAJORITY OF MAMMALS EAT PLANTS
- EVEN THE CARNIVORA (THE ORDER THAT INCLUDES CATS, DOGS, BEARS) COUNT OMNIVORES AND EVEN HERBIVORES AMONG THEM (THINK WOLVES AND FOXES FOR OMNIVORES; PANDAS FOR STRICT HERBIVORES)
- THE MORE THE DIET RELIES ON PLANTS, THE RICHER AND MORE DIVERSE THE MICROBIOME

MAMMALIAN MICROBIOME SHAPING THE HOST

- MAMMALS NEED TO HOUSE THEIR MICROBIOMES AND GIVE THEM TIME TO PERFORM THEIR ENZYMATIC ACTIVITIES
- MAMMALS EVOLVED TO ACCOMMODATE THEIR MICROBIOMES → THEY ENLARGED PARTS OF THEIR GUTS TO TURN THEM INTO FERMENTATION CHAMBERS
- TWO MODES:
  - HINDGUT FERMENTERS (AT THE END OF THE GUT): ELEPHANTS, HORSES, RHINOS, RABBITS, PIGS, ETC.
  - FOREGUT FERMENTERS (AHEAD OF THE STOMACH OR IN THE FIRST OF SEVERAL CHAMBERS): COWS, DEER, SHEEP, KANGAROOS, GIRAFFES, HIPPOS, CAMELS, ETC.
- MICROBIOMES IN FOREGUT FERMENTERS ARE MORE SIMILAR TO EACH OTHER THAN TO THOSE OF HINDGUT FERMENTERS, AND VICE VERSA



FUNCTIONS OF THE MICROBIOME

- IMPORTANT FOR DIGESTION, PRODUCING MICRONUTRIENTS (*E.G.* SOME VITAMINS, B12, K2) AND ENERGY ACQUISITION (*E.G.* CONVERTING DIETARY FIBER INTO USEFUL SHORT-CHAIN FATTY ACIDS)
- CONTRIBUTES TO DETOXIFICATION, IMMUNE SYSTEM DEVELOPMENT, BEHAVIOR, POSTEMBRYONIC DEVELOPMENT, AND A NUMBER OF OTHER FACTORS INFLUENCING HOST PHYSIOLOGY, ECOLOGY, AND EVOLUTION
- BACTERIA PROVIDE THE FIRST LINE OF DEFENSE AGAINST INSULTS FROM PATHOGENS, CARCINOGENS, AND OTHER TOXINS
- THEY CAN METABOLIZE CHEMOTHERAPEUTIC AGENTS AND MANIPULATE HOW THE HOST RESPONDS
- ADAPTIVE CAPACITY OF AN ANIMAL SPECIES IS NOT DETERMINED SOLELY BY THE HOST GENOME BUT ALSO INCLUDES THE VAST GENETIC REPERTOIRE OF THE MICROBIOME

HOW CONSTANT IS THE MICROBIOME?

- MUCH LIKE A GENETIC IMPRINT OF AN INDIVIDUAL, EACH INDIVIDUAL HAS A UNIQUE MICROBIOTA, THOUGH APPROXIMATELY ONE-THIRD OF THE MICROBIAL TYPES ARE COMMON WITHIN A HOST SPECIES
- BIOGEOGRAPHY, SEX, REPRODUCTIVE STATUS, HOST GENOTYPE, HYGIENE AND SOCIAL STRUCTURE HAVE ALL BEEN ASSOCIATED WITH ANIMAL GUT MICROBIOME DIVERSITY
- DOMINANT DRIVERS OF MICROBIOME STRUCTURE APPEAR TO BE HOST EVOLUTIONARY HISTORY AND DIET
- **DIET** CAN RAPIDLY AND REPRODUCIBLY ALTER THE MICROBIOME (SHOWN IN HUMANS AND MICE; ALSO IN ANIMALS WITH DRASTICALLY DIFFERENT PATTERNS OF FEEDING ON AN ANNUAL CYCLE, *E.G.* SOME MONKEYS)
- **HOST EVOLUTIONARY HISTORY** CAN MODULATE THE MICROBIOME. PANDAS HAVE MICROBIOMES THAT ARE MORE SIMILAR TO THEIR CARNIVOROUS COUSINS THAN TO OTHER STRICT HERBIVORES. THIS PATTERN IS ALSO EVIDENT IN NON-HUMAN PRIMATES (CLOSER RELATIONSHIP, CLOSER MICROBIOMES, INDEPENDENT OF FEEDING, BOTH IN CAPTIVITY AND IN THE WILD)

FUNCTIONAL CONVERGENCE OF MICROBIOMES: THE BIRDS AND THE BATS

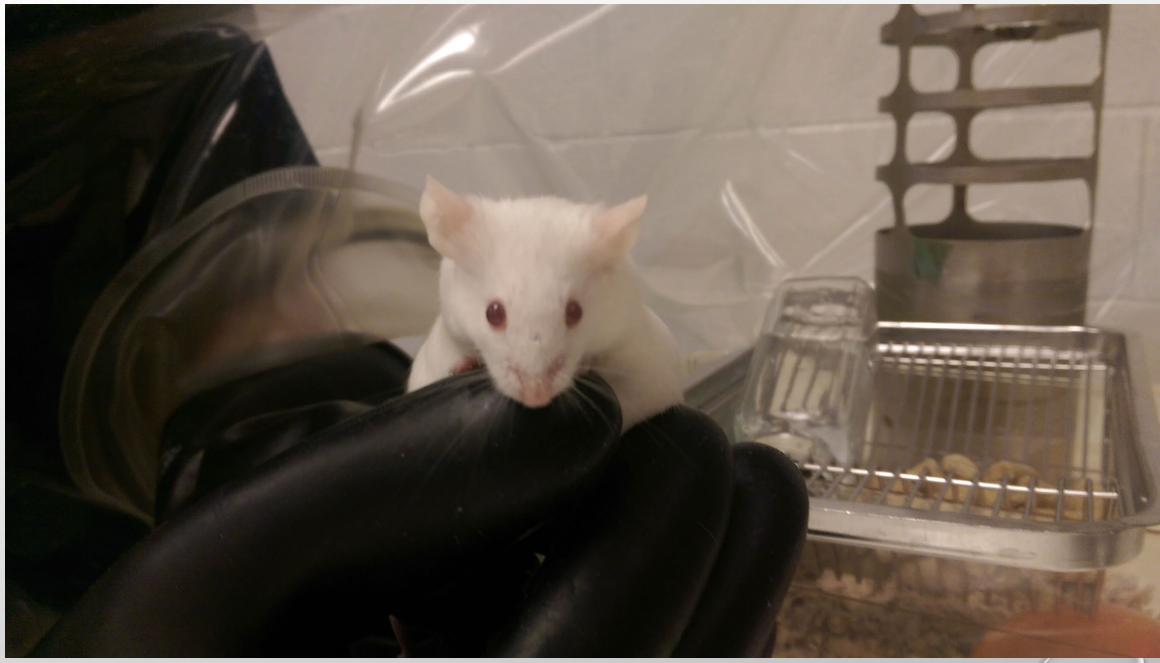
- THE STUDY LOOKED AT OVER 900 VERTEBRATE SPECIES, INCLUDING 315 MAMMALS AND 492 BIRDS
- CONTRARY TO EVOLUTIONARY HISTORY EXPECTATIONS, BIRDS AND BATS HAVE ODDLY SIMILAR MICROBIOMES
- THIS SIMILARITY HOLDS FOR ALL MEMBERS OF THE CLASS AVES (ALL BIRDS) AND ALL CHIROPODA (BATS)
- SIMILARITIES IN MICROBIOME COMPOSITION AND PATTERNS OF ASSOCIATION SUGGEST THE PRESENCE OF FLIGHT-CORRELATED HOST FACTORS EXERTING SIMILAR SELECTIVE PRESSURES ON THE ASSEMBLY OF THE GUT MICROBIOME
- BIRDS AND BATS BOTH TEND TO HAVE REDUCED INTESTINAL LENGTHS AND SHORTER INTESTINAL CONTENT RETENTION TIMES, PERHAPS AS A BY-PRODUCT OF SELECTIVE PRESSURE TO DECREASE MASS FOR MORE EFFICIENT POWERED FLIGHT
- BOTH BIRDS AND BATS ALSO HAVE GREATER RATES OF INTESTINAL PARACELLULAR ABSORPTION THAN NONFLYING VERTEBRATES, MEANING THAT A HIGHER PROPORTION OF SIMPLE NUTRIENTS ARE ABSORBED DIRECTLY BY THE HOST, POTENTIALLY DECREASING THE ROLE FOR SYMBIOTIC MICROBIAL METABOLISM

UNRAVELING SYMBIOSIS – THE MOUSE MODEL GNOTOBIOTICS AND THE GERM-FREE MOUSE

- THE AVERAGE MOUSE, LIKE THE AVERAGE HUMAN, IS HOME TO TRILLIONS OF BACTERIA
- THE AVERAGE MOUSE IN A GNOTOBIOTIC FACILITY HOSTS ZERO
- NO GERMS LIVE ON ITS SKIN, IN ITS NOSTRILS, OR IN ITS GUT
- FOOD AND WATER—EVEN ITS BEDDING—IS HEATED TO MORE THAN 100 °C TO KILL BACTERIA BEFORE BEING DELIVERED TO ITS CAGE THROUGH A STERILE, FAIL-SAFE SYSTEM OF DOUBLE DOORS

GNOTOBIOTIC MICE AS EXPERIMENTAL SUBJECTS

- GIVE RESEARCHERS THE ABILITY TO COMPARE GERM-FREE INDIVIDUALS WITH NORMALLY RAISED ONES
- GERM-FREE ANIMALS ALSO GIVE A LABORATORY THE ABILITY TO INTRODUCE ONE—OR A FEW—MICROORGANISMS AT A TIME AND LOOK AT THEM IN A SIMPLER ENVIRONMENT THAN THE BUSTLING METROPOLIS OF THE MICROBIOME
- MICE THAT ARE RAISED GERM-FREE HAVE ALTERED IMMUNE SYSTEMS, HEARTS, LUNGS, LYMPH NODES, METABOLISMS, AND IMPAIRED REPRODUCTIVE ABILITIES
- GERM-FREE MICE SHOWED ALTERED PATTERNS OF BRAIN DEVELOPMENT AND BEHAVIOR. (IF THE MICE ARE EXPOSED TO A MIXTURE OF BACTERIA, THE CHANGES REVERTE BACK TO NORMAL)



LESSONS FROM GERM-FREE MICE
I – MICROBIOTA SHAPES THE HEALTHY GUT

- GERM-FREE MICE DISPLAY ALTERATIONS IN GUT MORPHOLOGY, MOTILITY, ABSORPTION AND SECRETION
- THE CECUM OF GF MICE IS ENLARGED BY 4-8-FOLD BECAUSE OF MUCUS AND UNDIGESTED FIBER ACCUMULATION, AND THE SMALL INTESTINE IS LESS DEVELOPED, WITH REDUCED EPITHELIAL CELL TURNOVER AND IRREGULAR MICROVILLI, ALONG WITH DECREASED GUT MOTILITY PARTLY DUE TO DECREASED INNERVATION WITH SENSORY NEURONS
- GF MICE ALSO EXHIBIT DECREASED OR ABSENT EXPRESSION OF SEVERAL RECEPTORS, ESSENTIAL FOR THE RECOGNITION OF PATHOGEN-ASSOCIATED MOLECULES
- DECREASE OF INTESTINAL BARRIER INTEGRITY → BACTERIAL CONSTITUENTS CAN ENTER THE BLOODSTREAM → ONSET OF INFLAMMATION CONTRIBUTING TO INSULIN RESISTANCE

LESSONS FROM GERM-FREE MICE II – MICROBIOTA AND IMMUNITY

- GERM-FREE MICE ARE MORE SUSCEPTIBLE TO INFECTION BY BACTERIAL, VIRAL AND PARASITIC PATHOGENS
- THEY SHOW REDUCED ANTIGEN-SPECIFIC IMMUNE RESPONSES
- NUMEROUS DEFECTS IN ANTIBODY PRODUCTION
- FEWER AND SMALLER LYMPH NODES
- MICROBIOTA IS REQUIRED FOR FULL DEVELOPMENT OF ORGANS THAT MAKE AND STORE THE IMMUNITY MACHINE (THYMUS, BONE MARROW)
- IMPORTANT EARLY IN LIFE: TUNE THE IMMUNE SYSTEM TO DISTINGUISH FRIEND FROM FOE
- THE MAMMALIAN GENOME (WITHOUT MICROBES) IS NOT ENOUGH TO CREATE A MATURE IMMUNE SYSTEM

LESSONS FROM GERM-FREE MICE III – MICROBIOTA AND THE BRAIN

- GERM-FREE MICE SHOW DEFECTS IN:
- NEURONAL ACTIVITY, PLASTICITY AND SURVIVAL
- NEUROTRANSMISSION
- THE INTEGRITY OF THE BLOOD-BRAIN BARRIER
- HIGHER LEVELS OF STRESS HORMONES
- MORE SUSCEPTIBLE TO NEUROLOGICAL DISEASE-RELATED EFFECTS (*E.G.* ACCUMULATION OF B-AMYLOID LIKE IN ALZHEIMER'S DISEASE)

LESSONS FROM GERM-FREE MICE IV – MICROBIOTA AND BEHAVIOR

- SHOW ANXIETY-LIKE BEHAVIOR
- IMPAIRED LEARNING AND MEMORY
- DEFICITS IN LOCOMOTOR BEHAVIOR
- ALTERED SELF-GROOMING BEHAVIORS
- ALTERED PATTERNS OF SOCIAL COGNITION AND SOCIAL PREFERENCE
- ALTERATIONS IN SOCIABILITY, LOCOMOTOR ACTIVITY, AND REPETITIVE, STEREOTYPED BEHAVIORS IN GF MICE HAVE PARTICULAR SIGNIFICANCE FOR POSSIBLE ASSOCIATIONS WITH AUTISM SPECTRUM DISORDER (ASD)

ACQUIRING YOUR MICROBIOME

- LITTLE IS KNOWN ABOUT HOW NON-MAMMALS ACQUIRE THEIR GUT MICROBIOMES, BUT AT LEAST FOR SOME SPECIES, COPROPHAGY, EATING SOIL IN THE NEST, AND EATING REGURGITATED FOOD ARE IMPORTANT MODES OF VERTICAL TRANSMISSION
- RECENTLY IT WAS POSITED THAT OVIPAROUS VERTEBRATES MAY BE CAPABLE OF ACQUIRING PIONEER MICROBIOTA *IN OVO,* POSSIBLY THROUGH THE INOCULATION OF EGG YOLK PRIOR TO SHELLING
- THIS SUGGESTS THAT, LIKE PLACENTAL MAMMALS, THE REPRODUCTIVE TRACT OF OVIPAROUS VERTEBRATES MAY HARBOR MICROBIOTA TYPICALLY FOUND IN THE DIGESTIVE SYSTEM

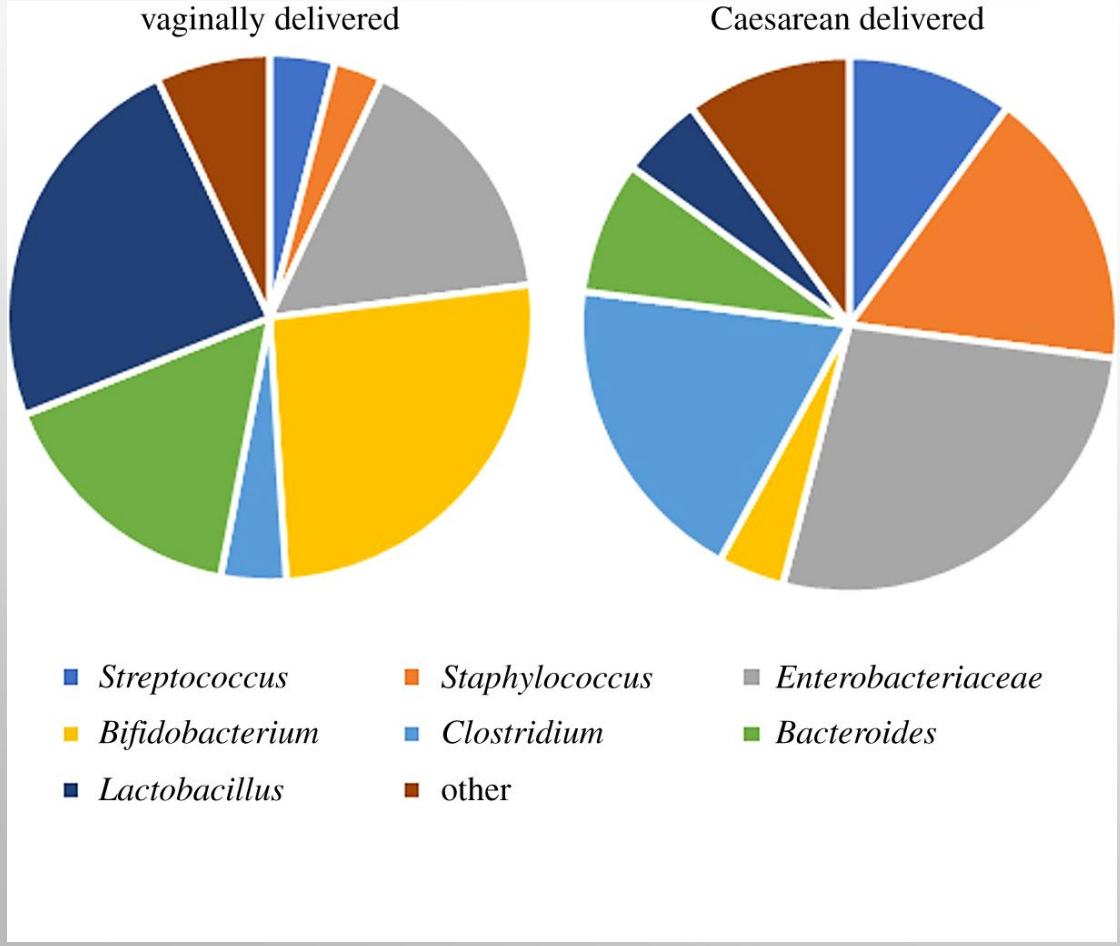
I – *IN UTERO*

- *IN UTERO* (OR THE *PRENATAL STAGE*) IS THE LEAST UNDERSTOOD PERIOD OF MICROBIAL DEVELOPMENT
- ACCEPTED DOGMA: THE WOMB IS STERILE AND, ACCORDINGLY, A NEONATE'S MICROBIOME IS FIRST SEEDED AT BIRTH
- HOWEVER, STUDIES CONSISTENTLY SUGGEST THAT MICROBIAL COMMUNITIES EXIST IN THE PLACENTA, AMNIOTIC FLUID AND MECONIUM
- FOR EXAMPLE, THE PLACENTA HARBORS A WIDE RANGE OF MICROBES, MANY OF WHICH ORIGINATE IN THE MOUTH (A PLUG FOR GOOD DENTAL HYGIENE FOR MOTHERS-TO-BE)
- THESE RESULTS ARE CONTESTED
- REGARDLESS OF POSSIBLE EXPOSURE TO MICROORGANISMS *IN UTERO*, THE FETUS IS EXPOSED TO MICROBIAL MOLECULES THAT CROSS THE PLACENTA FROM THE MOTHER

II – PARTURITION

- THE FIRST MAJOR EXPOSURE TO MICROORGANISMS HAPPENS DURING DELIVERY, AND IS HIGHLY DEPENDENT ON THE MODE OF DELIVERY
- THE MICROBIOTA OF NEONATES THAT ARE BORN VAGINALLY ARE ENRICHED IN BACTERIA THAT RESEMBLE THE MATERNAL VAGINAL MICROBIOTA
- NEONATES DELIVERED BY CAESAREAN (C-) SECTION LACK THESE SPECIES AND ARE INSTEAD ENRICHED IN SKIN COMMENSALS AND ENVIRONMENTAL MICROBES
- OVER TIME, THESE DIFFERENCES GRADUALLY REDUCE
- ASIDE: THE WHO PREDICTS THAT 10-15% OF DELIVERIES WILL REQUIRE C-SECTION; IN THE US 32% OF ALL DELIVERIES ARE BY C-SECTION

VAGINAL *VS.* C-SECTION DELIVERIES



- WHILE THERE IS NO CLEAR ANSWER TO HOW LONG AFTER BIRTH THE MODE OF DELIVERY AFFECTS THE MICROBIOTA OF THE CHILD, THE MOST SIGNIFICANT DIFFERENCES ARE FOUND UP TO 1 YEAR AFTER BIRTH
- STILL, BY THE AGE OF 6 MONTHS, THE COLONIZATION PATTERNS ARE ALMOST THE SAME BETWEEN THE TWO MODES OF DELIVERY
- ONCE THE BABY REACHES A YEAR OF AGE, SO MANY OTHER FACTORS ARE INVOLVED WITH THE DEVELOPMENT OF THE MICROBIOTA OF THE BABY THAT THE DIFFERENCES ARE MORE DIFFICULT TO ATTRIBUTE TO THE MODE OF DELIVERY

ASSOCIATED RISKS WITH C-SECTION DELIVERIES

- THE RISKS OF DEVELOPING IMMUNE-ASSOCIATED AND ALLERGIC DISEASES, AS WELL AS HARD TO TREAT INFECTIONS, ARE MUCH HIGHER FOLLOWING CS DELIVERY
- INFLAMMATORY BOWEL DISEASE , COELIAC DISEASE, CHILDHOOD ASTHMA AND OBESITY
- NOW BEING RESEARCHED: '**VAGINAL SEEDING**': ABOUT 1 H BEFORE THE CS SURGERY, A STERILE PAD SOAKED IN SALINE IS INSERTED IN THE MOTHER'S VAGINA. WITHIN MINUTES OF CAESAREAN BIRTH, THE INFANT IS INOCULATED WITH THE MOTHER'S VAGINAL FLUID THROUGH A SWAB OF GAUZE TO THE MOUTH, FACE AND BODY

III – INFANCY

- BREAST MILK *VS.* FORMULA: BREAST MILK PROVIDES PROTECTIVE MEASURES AGAINST THE RISK OF ACQUIRING INFECTIOUS DISEASES AND DEVELOPING ALLERGIC DISORDERS THROUGH ITS IMMUNOLOGICAL COMPONENTS INCLUDING IMMUNOGLOBULINS, CYTOKINES, GROWTH FACTORS AND MICROBIOLOGIC FACTORS. THESE COMPONENTS ARE ESPECIALLY IMPORTANT FOR THE GROWTH AND DEVELOPMENT OF THE YOUNG INFANT'S IMMUNE SYSTEM

immunoglobulins	prevent pathogens from entering into systemic circulationand binding to epithelial surfaces
cytokines	anti-inflammatory and immunosuppressive agents
growth factors	modulate metabolic system development (digestive, nervous, etc.)
lipids	participate in nervous system and gastrointestinal developmentprovide protection against enteric infection
proteins	nutrition, nutrient absorption, antimicrobial activity, gut and immune system development
human milk oligosaccharides (HMOs)	prebiotics, anti-adhesive, antimicrobial and antibiofilm agents
probiotics	consistent wave of commensal and symbiotic organisms

THE ROLE OF HUMAN MILK OLIGOSACCHARIDES (HMO)

- HMOS ARE THE THIRD LARGEST COMPONENT IN HUMAN MILK, AND, WHILE INFANTS ARE UNABLE TO DIGEST THEM, THEY PLAY AN IMPORTANT ROLE IN SHAPING THE MICROBIOTA OF THE DEVELOPING GUT AND BUILDING UP THE YOUNG IMMUNE SYSTEM. OVER 200 UNIQUE HMOS HAVE BEEN IDENTIFIED, RANGING FROM 3 TO 22 SUGARS PER MOLECULE
- SINCE THEY ARE RELATIVELY UNAFFECTED BY DIGESTION, HMOS ARE ABLE TO PASS THROUGH THE INFANT'S STOMACH AND SMALL INTESTINE INTACT, AND THEY ACCUMULATE IN THE COLON
- ONE OF THE PRIMARY FUNCTIONS OF HMOS IS TO ACT AS A PREBIOTIC, ALLOWING THE GROWTH OF BENEFICIAL BACTERIA., WHILE PREVENTING THE COLONIZATION OF HARMFUL PATHOGENS
- ALSO, BREAST MILK IS THE SOURCE OF THE 10^4–10^6 BACTERIAL CELLS PER DAY THAT THE INFANT CONSUMES
- WHILE THE SOURCE OF THE BACTERIA PRESENT IN HUMAN MILK IS NOT COMPLETELY CLEAR, IT IS THOUGHT TO BE A COMBINATION OF BACTERIA FROM THE INFANT'S ORAL CAVITY AND FROM THE MOTHER'S NIPPLE AND SURROUNDING SKIN

ENVIRONMENTAL FACTORS

- GENETICALLY UNRELATED PARENTS AND EVEN PETS SHARE A HIGH PROPORTION OF THEIR MICROBIOTA WITH INFANTS
- THE USE OF ANTIMICROBIALS, WHICH CAN BE ESSENTIAL, CAN IMPACT THE ECOLOGICAL SUCCESSION OF THE INFANT MICROBIOTA
- ANTIBIOTICS IMPAIR THE DIVERSITY AND STABILITY OF THE DEVELOPING MICROBIOTA IN INFANTS, WITH ABUNDANCES OF SPECIFIC TAXA REMAINING REDUCED FOR YEARS AFTER TREATMENT
- THIS CAN HAVE LONG-LASTING HEALTH IMPLICATIONS AND THEIR USE IN EARLY LIFE HAS BEEN LINKED TO AN INCREASED RISK OF SEVERAL DISEASES, INCLUDING ASTHMA, INFLAMMATORY BOWEL DISEASE AND ALLERGIES