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The Human Gut Microbiome: A Comprehesive Guide On Its Vital Role In Human Health

[1]Aneeta Anna Galileo, [2]Mrs. Sivaranjini .S, [3]Heba Muhammed Haris , Dr . Lal Prasanth M L
[1]Student, [2]Assistant Professor,[3] Student,
[1]Deparment of Pharmacology,
[1]Dr. Moopen's college of pharmacy, Meppadi, India

Abstract: The microbial cells,including bacteria , fungi, virus and others residing within the gastrointestinal tract (GIT) are referred to as the *gut microbiome.* The number of these bacteria present ousstand the number of host cell by a factor of 10. The human gastrointestinal system is home to over 100 trillion microorganisms. The microbiome is best understood as a virtual organ of the body. This study has been undertaken to give detailed look on human gut microbiome and its role in maintaining health which is a major subject for research today. A normal and well balance gut microbiome plays important roles in drug and nutrient metabolism ,host protection , immune system development, immune modulation , maintain gut barrier , forms the gut brain axis and so on .Various maternal and environmental factors affect development of gut flora in each individuals .Also it is to be noted that the composition of gut flora may vary within individuals. Dysbiosis is the imbalance caused to normal gut flora. The dysbiosis can give rise to various disease conditions mainly metabolic disorders. Thus comprehending the gut microbiome in individuals with good health is essential for identifying its impact on several significant gastrointestinal and nutritional disorders ,as well as for making logical connections to improve human health.

Index terms –Gut microbiome, Dysbiosis, Gastrointestnal tract

I. INTODUCTION TO GUT MICROBIOME

The "gut microbiota" is the group of bacteria, archaea, and eukarya that inhabit the gastrointestinal system. Over thousands of years, they have co-evolved with the host to develop a complex and mutually beneficial interaction. One of the biggest interfaces (250–400 m2) between the host, external conditions, and internal antigens in the human body is found in the gastrointestinal (GI) tract. It is believed that there are more than 10^{14} microorganisms in the GI tract, which includes around 10 times as many bacterial cells as human cells and more than 100 times the amount of genomic content (microbiome) as the human genome. Over the course of their coevolution, the bacterial microbiota has developed a variety of strategies to retain their stable habitat and affect the eukaryotic host in a typically positive way[i].

1.1. IDENTIFICATION OF PATTERNS AND MICROBIAL SENSATIONS

The eukaryotic host must keep an eye on the microbiota and regulate its quantity and makeup in order to tolerate it and reap its benefits. Pattern recognition receptors (PRRs) are a term used to describe transmembrane or intracytoplasmic receptors that are specifically able to recognize and bind unique microbial macromolecular ligands that are known as microbial-associated molecular patterns (MAMPs) such as flagellin, lipopolysaccharide, peptidoglycans, formylated peptides, and so on. Nod-like receptors (NLRs) protect the intracellular cytoplasmic compartment, while trans-membrane Toll-like receptors (TLRs) search the external environment. PRRs implicated in viral and fungal component identification are functionally linked RIG-like helicases and C-type lectin receptors, respectively. Activation of PRRs in the gut starts regulatory pathways including the nuclear factor κB (NF-κB)/Rel and mitogen-activated protein kinase

(MAPK) pathways and caspase depending signalling cascades .These systems are examples of entangled cytoplasmic information relays that, upon activation, transduce PRR binding into transcriptional or posttranscriptional effector activities through fast posttranslational events (covalent protein modifications and controlled protein degradation)

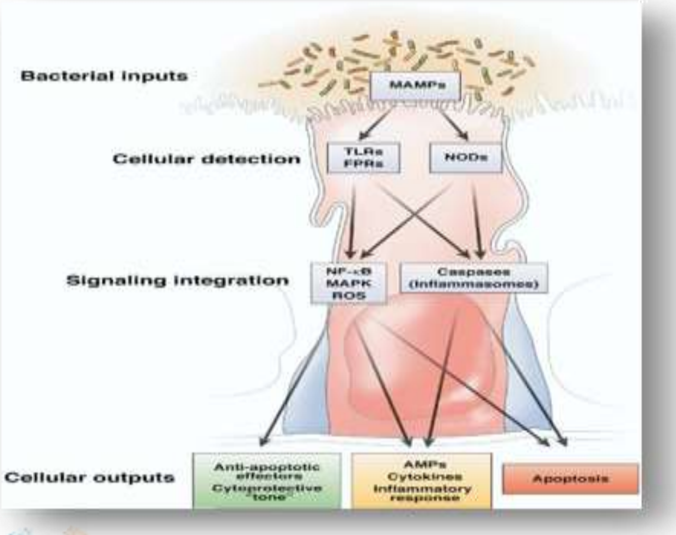

Figure 1: recognition patterns

II. COMPOSTION AND STRUCTURE

Human bodies begin to colonize with microbes as soon as they are born, and the makeup of these communities is influenced by a variety of external circumstances. The diversity and abundances of microorganisms have been examined using a variety of molecular approaches . Actinobacteria, Proteobacteria, Firmicutes, and Bacteroidetes members make up the majority of the gut microbiota in infants. On the other hand, in adults, the abundance changes to Firmicutes, then Bacteroidetes, then Actinobacteria. While adults do contain individuals of Proteobacteria, Fusobacteria, Cyanobacteria, and Verrucomicrobia, their numbers are quite low[ii].

2.1. HUMAN BACTERIOME

2.1.1. STOMACH

Most microbes cannot thrive in the stomach because of its extreme acidity. Firmicutes, Bacteroidetes, Actinobacteria, Fusobacteriota, and Proteobacteria are the five major phyla that comprise the majority of the gastric microbiota's bacteria. Prevotella, Streptococcus, Veillonella, Rothia, and Haemophilus are the most common genera.[iii]

2.1.2. INTESTINE

Rod-shaped bacteria and gram-positive cocci are the most common microorganisms in the small intestine. Gram-negative Enterobacteriaceae bacteria are supported by alkaline conditions in the distal section of the small intestine. the human body's greatest bacterial ecology is found in the large intestine.Obligate anaerobes like Bacteroides and Bifidobacterium make up around 99% of the flora found in the large intestine and excrement. The intestinal microbiota is dominated by five phyla: Actinomycetota, Bacteroidota, Bacillota (Firmicutes), Pseudomonadota, and Verrucomicrobiota. Of these, Bacteroidota and Bacillota make up 90% of the composition[iv].

2.2. HUMAN VIROME

The term "virome" describes a group of viruses. Nine organ systems—the colon, liver, lung, heart, brain, kidney, skin, blood, and hair—have been used to define the human virome. The viruses that make up the gut virome are classified as eukaryotic (mostly those that infect human cells), bacteriophages (also known as phages), archaeal (found in food and the environment), and plant (found in food) viruses. As a person ages, their gut virome becomes less dynamic until it eventually stabilizes in maturity[v].

2.3. HUMAN MYCOBIOME

In most parts of the body including gastro intestinal tract the abundance of fungi is very low. The fungi normally makes only up to 0.001-0.1% of total microbial community. Changes in the human mycobiome have been linked to a number of illnesses in humans, such as hepatitis, cystic fibrosis, obesity, and inflammatory bowel disease. It has been suggested that any fungal colonization of the GI tract is a symptom of illness .The mutualism between fungi and human is not understood completely ,there are about 50 genera of fungi in GI tract of human.[vi]

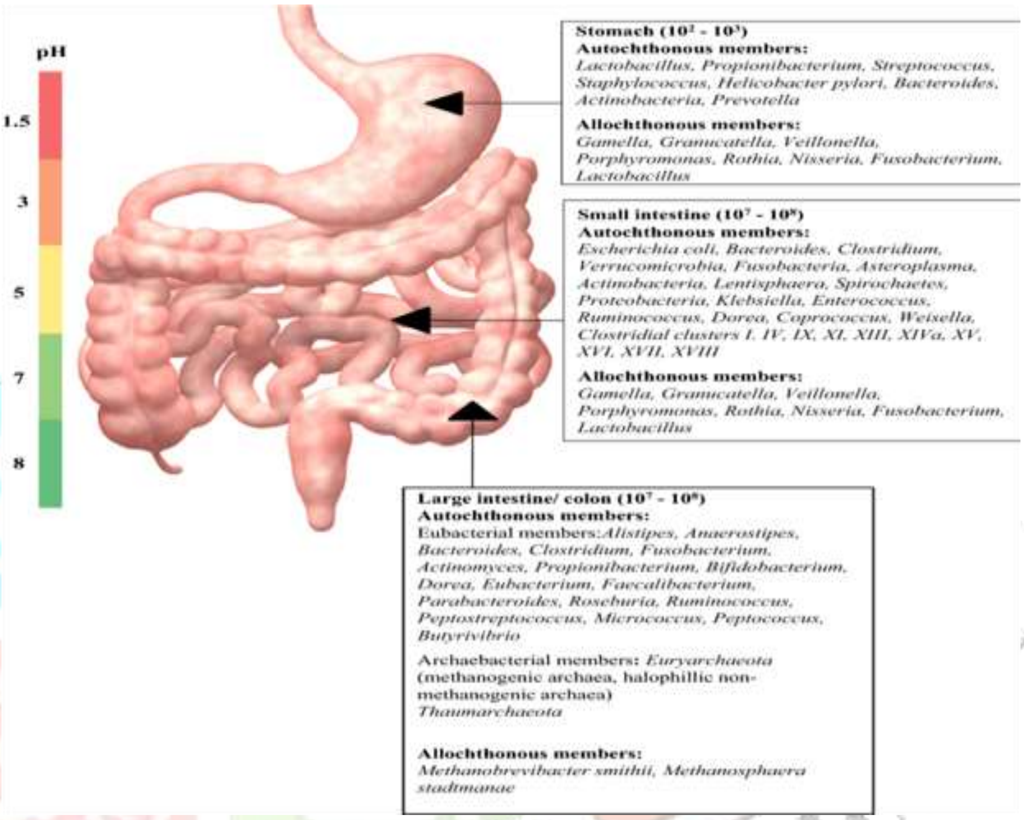

Figure 2:composition and structure of human gut flora.

III. DEVELOPMENT AND BIOGEOGRAPHY

3.1. DEVELOPMENT OF INFANT GUT MICROBIOTA

A child's first 1000 days are a crucial time for the immune system's development and the formation of the gut microbiota. The fetus's growth and development are greatly impacted by the environment it is in while it is inside the mother and by interactions between it and her. It was discovered that pregnant women's microbiota composition varies throughout pregnancy and differs from that of non-pregnant women in numerous ways . When compared to the first trimester, the gut microbiota in late pregnancy is smaller, with an increase in Proteobacteria, Actinobacteria, and Streptococcus and a decrease in Firmicutes.When it comes to the infant's gut microbiota's early colonization, delivery is quite important. One of the most prevalent microbes of the mother vaginal flora, Lactobacillus, is found in the skin, mouth, and intestines of neonates delivered vaginally . The mother's microbiota, which is present in the breast milk, mouth, skin, vaginal area, feces , and surrounding environment are the first microbes of infant's body. Enterobacteriaceae and Staphylococcus overpopulate the newborn's gut microbiota immediately after birth , but Bifidobacterium and some lactic acid bacteria eventually replace them . The relative quantity of Bacteroides steadily rises as the baby gets closer to being weaned, which causes Bifidobacterium to be competitively excluded from the gut microbiota. Following weaning, adult-type microorganisms take the place of the Bifidus flora; they primarily consist of bacteria including Bacteroides, Prevotella, Ruminococcus, Clostridium, and Veillonella. By the age of three, a child's gut microbiota resembles that of an adult[vii].

3.2. FACTORS AFFECTING DEVELOPMENT OF INFANT GUT MICROBIOTA

Table 1.: factors affecting development of infant gut flora.[viii]

CATEGORY	FACTORS	DESCRIPTION
Maternal	Gestational age	Compared to preterm newborns, whose gut microbio diversity is lower, full-term infants develop microbiota mo quickly.
Maternal	Mode of delivery	While a caesarian section reduces this exposure, vagin delivery exposes infants to mother vaginal and perian microorganisms.
Maternal	Maternal vaginal microbiota	Pregnancy reduces the variety of microbes in the vagin microbiota, which may have an effect on the microbiome the unborn child . Premature birth risk may rise wi dysbiosis.
Maternal	Maternal health status	Obesity, gestational diabetes, and inflammation can impa the infant’s intestinal microbiota and increase the risk of g dysbiosis.
Maternal	Maternal diet	Whether or not the mother is obese, a high-fat diet can affe the first colonization of germs in kids
Maternal	Exposure to antibiotics during pregnancy	Pregnancy-related antibiotic use can change the makeup the infant's gut microbiome and lower the microbial loa They may also affect the bacteria in breast milk.
Environmental	Gestational age	The gut microbiota development of premature infan exposed to large doses of antibiotics and prolonged hospit stays is changed.
Environmental	Method of feeding	Breastfeeding has a major effect on the development of th gut microbiota and encourages Bifidobacterium growth Formula feeding alters the composition of the g microbiota, although new developments try to promote th growth of Bifidobacterium.
Environmental	Soild food introduction	When solid foods with indigestible carbohydrates a introduced to an infant, their gut flora is impacted, resultin in a functional gene pool that is comparable to an adult's.

3.3. BIOGEOGRAPHY

The spatial distribution and variety of microbial communities within the gastrointestinal system are referred to as the biogeography of the human gut microbiome.

The gastrointestinal tract of humans is a large biological region that is home to multiple unique ecosystems. Distinct environmental factors impact microbial populations differently in every ecosystem. Based on their habitat and degree of Helicobacter pylori infection, bacterial communities in the human gastrointestinal tract can be classified into four main classes: the healthy upper gastrointestinal tract, the H pylori-positive upper gastrointestinal tract, the lower gastrointestinal tract, and excrement. Prevotella is one of the genera that is relatively abundant in the oral microbiome[ix]. The authors found that the stomach's microbial composition—which includes a clearly distinguishable gastric microbiome—is significantly influenced by the existence or absence of a H pylori infection. Because H pylori sequences were not found in the lower gastrointestinal tract or in feces, it should be emphasized that H pylori does not colonize the lower digestive system and does not change the microbial makeup of the colon. The lower gastrointestinal tract is made up of distinct communities than the upper gastrointestinal tract. Higher amounts of Actinobacteria, mainly Bifidobacterium, were found in the feces. Numerous research have shown the potential importance of this genus for gut health. Members of the genus Bifidobacterium can form microbial "reservoirs" in the lumen that sustain.[x]

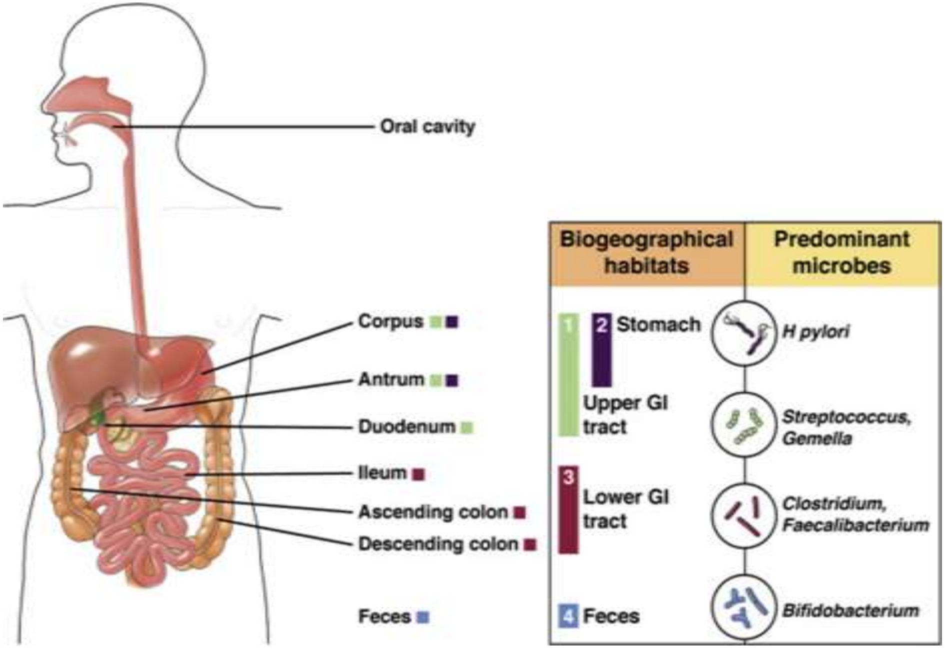

Figure 3: biogeographic distribution of gut microflora[xi]

IV. OVERVIEW OF DIFFERENT GUT MICROBES

Bacteria are the major inhabitants of the gut. Owing to their profusion in the colon, bacteria also account for up to 60% of the dry mass of excrement. The gut flora also includes viruses, protists, fungi, and archaea, albeit little is known about their functions. Since many gut species cannot be cultivated, research on them outside of their hosts has been limited. Microbe populations can differ greatly, yet most people share a modest number of core microbial species. The goal of the Human Microbiome Project is to provide a more thorough description of the microbiota found in the human gut and other body parts.

4.1. COMMOM BACTERIAL GENERA

In the human gut, Bacillota (Firmicutes), Bacteroidota, Actinomycetota, and Pseudomonadota are the four predominant bacterial phyla.

4.1.1. BACTERIODS

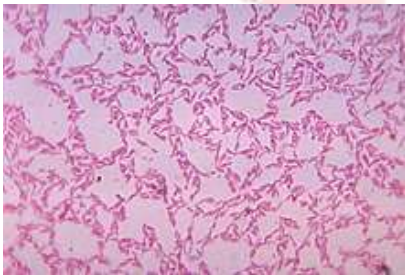

Figure 4 : bacterioids

Gram-negative, obligatory anaerobic bacteria belong to the genus Bacteroides. Depending on the species, Bacteroides species are either motile or nonmotile bacilli that do not create endospores. Membranes from Bacteroides contain sphingolipids. In addition, their peptidoglycan layer contains meso-diaminopimelic acid. The majority of the gastrointestinal microbiota in mammals is composed of mutualistic Bacteroides species, which are essential to the host intestine's capacity to degrade complicated substances into simpler ones. Simple sugars can be used by Bacteroides species in the stomach when they are present, but their main energy sources are complex glycans acquired from plants and hosts. Research indicates that an individual's long-term diet has a major impact on the composition of their gut microbiome; people who eat a lot of animal fats and protein have a higher concentration of Bacteroides bacteria[xii].

4.1.2. CLOSTRIDIUM

Figure 5: clostridium

A genus of anaerobic, Gram-positive bacteria is called Clostridium. Animals, including humans, and soils are home to several Clostridium species. This genus contains a number of important human pathogens, such as the tetanus and botulism causal agents. Additionally, a healthy female's lower reproductive system is home to Clostridium species. In 1891, William H. Welch discovered gas bubbles inside infected blood vessels during the autopsy of a 38-year-old man, which led to the first isolation and identification of the bacteria as a unique one. During the first month of life, they begin to colonize the intestine of breastfed newborns and settle in close proximity to intestinal cells in a particular area of the intestinal mucosa. In addition to interacting with other resident microbe populations, this location enables them to play a critical role in regulating immunological, metabolic, and physiologic processes in the gut throughout an individual's lifecycle. Because of their unique position in the mucosa, Clostridium spp. have an effect on normal intestinal physiology and structure. They also continuously interact with gut cells to participate in the pathways leading to these functions. Specifically, commensal Clostridia release butyrate as a fermentation byproduct, which is crucial for the metabolic health of colonocytes[xiii].

4.1.3. FAECALIBACTERIUM

Faecalibacterium is the name of one genus of bacteria. Among the species that comprise the genus are Faecalibacterium prausnitzii, Faecalibacterium butyricigenerans, Faecalibacterium longum, Faecalibacterium duncaniae, Faecalibacterium hattorii, and Faecalibacterium gallinarum. As one of the most common and important commensal bacteria in the human gut microbiota, Faecalibacterium prausnitzii (now called Faecalibacterium duncaniae) is the first species to be identified. It is rod-shaped, anaerobic, mesophilic, and gram-positive. About 5% of the entire fecal microbiota in healthy humans is made up of Faecalibacterium prausnitzii, while this can occasionally reach 15%. Because of its anti-inflammatory properties, it might aid in the dysbiosis brought on by an imbalance in the gut flora. It is one of the main producers of butyrate in the intestine. The reason butyrate acts as an anti-inflammatory gut bacterium is that it stops NF-kB and IFN-y from being synthesized[xiv].

4.1.4. EUBACTERIA

A genus of Gram-positive bacteria belonging to the Eubacteriaceae family is called Eubacterium. These bacteria can be identified by their inflexible cell walls. They could move or not move at all. They have a flagellum if they can move.This anaerobic bacteria is a member of the Lachnospiraceae family, which includes significant butyrate makers that live in the intestinal microbiota. Butyrate and other SCFAs preserve the intestinal barrier, reduce intestinal inflammation, and alter gut motility via several processes . The production of GLP-1 and GLP-2 supports the endocrine function by preserving insulin sensitivity and glucose tolerance. Insulin sensitivity and energy metabolism were enhanced when Eubacterium halli was given to obese and diabetic db/db mice; body weight and food intake were unaffected.

4.1.5. RUMINOCOCCUS

One genus of bacteria in the Clostridia class is Ruminococcus. These are Gram-positive, anaerobic gut microorganisms. Significant populations of one or more species from this genus are present in the gut microbiome of humans. The first of multiple species to be discovered was reportedly Ruminococcus bromii, which was discovered in the human intestine in 1972.They might contribute to the breakdown of plant cell wall in the colon.R. albus, R. callidus, and R. bromii are less common in individuals with inflammatory bowel disease, according to one study.Patients with amyotrophic lateral sclerosis and Parkinson's disease also have lower Ruminococcus abundance. Crohn's disease is linked to R. gnavus. The correlation between R. gnavus strains and disorders have been discovered, such as the ability to modify host metabolism, secondary bile acids, tryptophan metabolic pathways, and induce an anti- or pro-inflammatory host response[xv].

4.1.6. PEPTOCOCCUS

Within the Peptococcaceae family of bacteria lies the genus Peptococcus, which is Gram-positive. The genus contains species that are found in the human microbiome, particularly in the bacteria that make up the gut flora. They are a component of the oral, upper respiratory, and large intestinal flora.[xvi]

4.1.7. PEPTOSTREPTOCOCCUS

A genus of anaerobic, Gram-positive, non-spore-forming bacteria is called Peptostreptococcus. The tiny, spherical cells can be found singly, in pairs, or in short chains. Usually, cilia are used to propel them. These Slow-growing bacteria are a natural resident of a healthy woman's lower reproductive tract . These belong to the intestinal microbiota. Both pathogenic and septicemic forms of these organisms can occur in immunocompromised or traumatized hosts, endangering them. Infections with Peptostreptococcus can result in necrotizing soft tissue infections and abscesses in the breast, lung, liver, and brain. They take part in infections that are mixed anaerobic. they produce acetic, formic, propionic, caproic, iso-butyric, butyric, iso-valeric, and iso-caproic acids by the metabolism of peptone and amino acids. It is also possible to create other alcohols and volatile amines

4.1.8. BIFIDOBACTERIUM

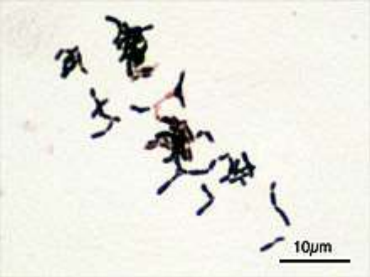

Figure 6 : bifidobacterium

Bifidobacterium is the name of a genus of gram-positive, nonmotile , anaerobic bacteria that are usually branched. These are the typical inhabitants of the gastrointestinal system. They are probiotics that are extensively utilized. A few of the many beneficial health effects that different species and/or strains of bifidobacteria may exert include the regulation of intestinal microbial homeostasis, inhibition of pathogens and harmful bacteria colonizing and/or infecting the gut mucosa, modulation of local and systemic immune responses, repression of procarcinogenic enzymatic activities within the microbiota, production of vitamins, and the bioconversion of various dietary compounds into bioactive molecules .Bifidobacteria fortify the gut mucosal barrier and lower the amount of lipopolysaccharides in the colon. Although conclusive research results are still awaited, bifidobacteria may be beneficial to those with IBS[xvii].

4.1.9. ESCHERICHIA

A genus of rod-shaped, facultatively anaerobic, Gram-negative, non-spore-forming bacteria belonging to the Enterobacteriaceae family is called Escherichia. Escherichia species provide their hosts some of the vitamin K that is produced by microbes in their digestive systems when they live in warm-blooded animal digestive tracts. There are several pathogenic Escherichia species.They are members of gut for abut 90% of individuals.one of the first organism to colonize neonatal gut. E. coli is a facultative anaerobe that may contribute to the depletion of oxygen along the mucosal surface of the gastrointestinal tract (GI), hence facilitating the colonization and dominance of stringent anaerobes . Human-associated E. coli is by definition a mutualist due to its function in the developing baby's gut, its ability to manufacture vitamin K , and its propensity to provide colonization resistance (protection against infections) .When pathogenic they may cause infections like UTI, simple diarrhoea to dysentery[xviii].

4.1.10. LACTOBACILLUS

A genus of rod-shaped, microaerophilic, gram-positive, aerotolerant anaerobes that do not generate spores is called Lactobacillus. Species of Lactobacillus are important members of the microbiota found in both humans and animals in several bodily regions, including the female reproductive system and the digestive system The human body and Lactobacillus have a mutualistic relationship in which the host supplies nutrition to the bacteria while also providing defense against disease invasion. One of the most prevalent probiotics in food, such as yogurt, is lactobacilli. It has a wide range of uses in promoting human health, including the treatment of dermatitis, diarrhea, and vaginal infections.

Functions:

- Vaginal health: The vaginal flora of healthy women is dominated by one of the four Lactobacillus species: Lactobacillus crispatus, Lactobacillus gasseri, Lactobacillus jensenii, and Lactobacillus iners.
- Against pathogens: The hydrogen peroxide that the Lactobacilli produces inhibit the growth and pathogencity of Candida albicans invitro and invivo. Limosilactobacillus reuteri may be able to stop the growth of a range of bacterial species by using glycerol to make antibacterial chemical reuterin.
- As probiotics : IBD, urogenital and viginal infections are treated using probiotics.
- Maintain oral health: Avoiding dental carries[xix].

Numerous fungal species, such as Candida, Saccharomyces, Aspergillus, Penicillium, Rhodotorula, Trametes, Pleospora, Sclerotinia, Bullera, and Galactomyces, have been found in the gut[xx].

V. ANIMAL MODELS USED FOR MICROBIOTA STUDIES

Studies have demonstrated that the gut microbiota creates an impenetrable barrier against invaders, triggers the host defense mechanism, controls inflammation, and plays a role in energy production. In order to evaluate the roles of host-microbe interactions and disease-associated changes in the composition of the gut microbiota in illnesses, certain species, such as rodents and some nonhuman primates, have been employed in experimental models of perturbations in the gut microbiota. Numerous additional species have also been employed in biomedical research, including the ferret, marmoset, woodchuck, micro pig, and tree shrew.On the other hand, little is known about their gut microbiomes.

5.1. MOUSE MODELS

The vast majority of currently in use murine strains, that is, strains of the species Mus musculus, share a common ancestor that dates back more than a century and originates from Asian or European fancy mice, which are typically yellow, white, or some other eye-catching color, and were domesticated as pets in China as early as 1200 BC. From then till now, many scientists have been drawn to the benefits of utilizing mice as models for human diseases due to their small size, ease of care when kept in high numbers, and ability to be genetically changed or inbred. According to estimates, mice currently make up more than 90% of the rodents utilized in pharmaceutical research. Despite the over 90 million years of evolution separating the human and mouse lineages, over 85% of their genetic sequences remain the same.

5.1.1. COMPARISON BETWEEN HUMAN GUT & MOUSE GUT

These days, M. musculus mice are frequently used to methodically investigate the effects of pathogens, nutrition, and/or host genotype on microbial diversity in the gastrointestinal tract and to connect these findings to human conditions.

Table 2 : comparison of human gut and mouse gut.

MOUSE	HUMAN
Stomach :Glandular PH 1	Stomach : Non glandular , PH 3-4
Small intestine : 10 cm per kg	Small intestine:1500 cm per kg
Cecum :hardly separated from colon, separate appendix	Cecum :large fermentation bag , appendix hardly separated
Large intestine: 1.5 cm per kg	Large intestine : 700 cm per kg
Colon : segmented	Colon : pellet formation

The two primary bacterial phyla in the murine digestive tract are the Firmicutes and the Bacteroidetes, and the phylogenetic composition of the bacterial communities in both humans and mice appears to be similar at the phylum level. The phylum Deferribacteres, which humans only find in trace amounts in the stomach, was shown to be present in high quantities in the murine intestinal tract . The primary species of this phylum, Mucispirillum schaedleri , is known to populate the mucus layer in mice. Furthermore, mice are home to a unique morphological member of the Firmicutes called segmented filamentous bacteria (SFB), also known as "Candidatus arthromitus." The microbiota of 16 human patients and three commonly used mouse lines was shown to have a similar appearance but a highly distinct quantitative difference in a recent comparative investigation of their phylogenetic composition . There are allegedly over 80 microbial gut genera that humans and mice share. However the strains of the same species in mice and humans can differ significantly, as demonstrated by the strains of L. reuteri .[xxi]

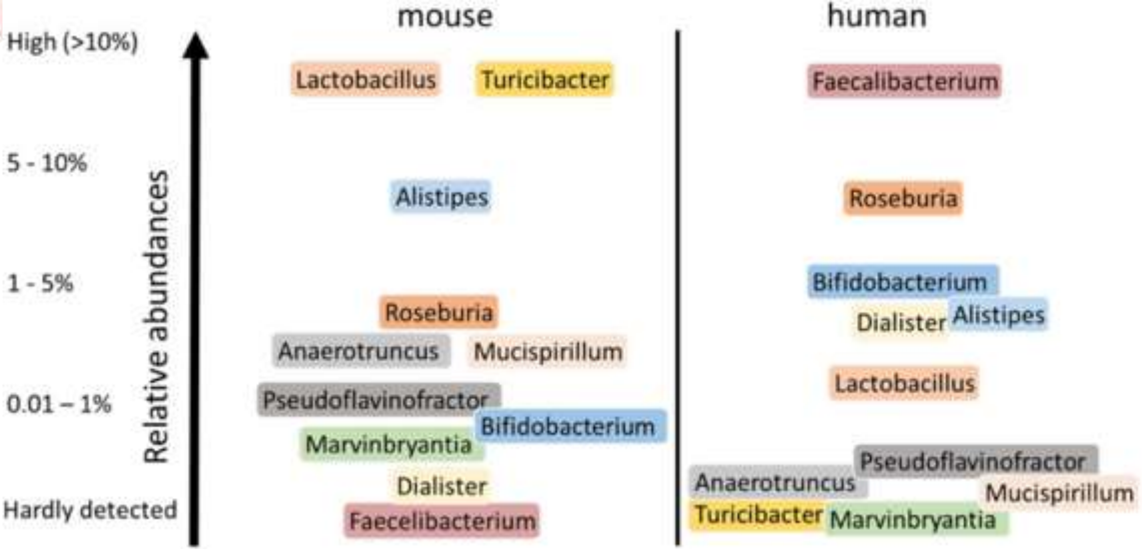

Figure 7. abundance of microbial species in mouse and human gut

5.1.2. CURRENTLY USED MOUSE STRAINS

There are a lot of distinct mouse strains out there, specifically when you take into account the quantity of genetically altered mice. The genealogies of more than 400 inbred strains have been identified and characterized. The genetic closeness of the inbred strains is advantageous as it enhances the reproducibility of the experimental methods. The majority of inbred strains exhibit significant genetic and phenotypic similarities and are derived from either Mus musculus domesticus or M. musculus musculus .But the microbiota of wild wood mice differs greatly from that of inbred strains, which are descended from wild mice. There have been demonstrated to be significant seasonal variations in the gut microbial community structure of Apodemus sylvaticus .

5.2. FERRET

At the phylum level, the proportion of Firmicutes in the gut microbiota of humans and ferrets was similar (63.37% vs. 62.19%, respectively). The ferret's gut microbiota contained more Proteobacteria (17.36% vs 5.61%, respectively, test, $P < 0.05$) and Fusobacteria (11.22% vs 0.14%, respectively, t test, $P < 0.05$) than the human's. Actinobacteria (1.32% vs 8.24%, respectively, t test, $P < 0.001$), Bacteroidetes (1.90% vs 21.37%, respectively, t test, $P < 0.001$), and Verrucomicrobia (0.05% vs 0.81%, respectively, t test, $P < 0.05$) were present in lower amounts.

5.3. MARMOSET MONKEY

In the gut microbiota of the marmoset, there were more Actinobacteria and Tenericutes than in the human microbiota, and fewer Firmicutes Compared to the human gut microbiota, the marmoset gut microbiota contained more Bifidobacterium, Libanicoccus, Fusobacterium, Enterococcus, Phascolarctobacterium, and unidentified Prevotellaceae and Enterobacteriaceae, but fewer unidentified Erysipelotrichaceae, Fusicatenibacter, Blautia, Faecalibacterium, and some unidentified Ruminococcaceae and Lachnospiraceae .

5.4. MINI PIG

In the gut microbiota of the mini pig, there were more Bacteroidetes and Spirochaetes than there were Firmicutes , Actinobacteria , and Proteobacteria . Less Bifidobacterium, Bacteroides, Fusicatenibacter, Blautia, Faecalibacterium, and some unidentified Erysipelotrichaceae and Lachnospiraceae were found in the mini pig gut microbiota at the genus level, but more Lactobacillus, Terrisporobacter, Turicibacter, and some unidentified Clostridiales and Spirochaetaceae.

5.5. WOOD CHUCK

In the gut microbiota of the woodchuck, there were more Bacteroidetes and Fusobacteria (7.05% vs 0.14%, respectively, t test, $P < 0.05$) than there were Firmicutes (44.43% vs 62.19%, respectively, t test, $P < 0.05$) and Actinobacteria (3.02% vs 8.24%, respectively, t test, $P < 0.001$). Less Bifidobacterium, Fusicatenibacter, Blautia, Faecalibacterium, and some unidentified Erysipelotrichaceae, Lachnospiraceae, and Ruminococcaceae were found in the woodchuck gut microbiota at the genus level, but more Porphyromonas, Ezakiella, Fusobacterium, Peptoniphilus, and Campylobacter were found.

5.6. TREE SHREW

In the gut microbiota of the tree shrew, there were more Bacteroidetes (38.89% vs 21.37%, respectively, t test, $P < 0.05$) and Fusobacteria (9.99% vs 0.14%, respectively, t test, $P < 0.05$) than in the human microbiota, and fewer Firmicutes (40.68% vs 62.19%, respectively). Less Bifidobacterium, Fusicatenibacter, Blautia, Faecalibacterium, and some unidentified Lachnospiraceae and Ruminococcaceae were found in the gut microbiota of tree shrews, but higher levels of Bacteroides, Peptoclostridium, Fusobacterium, Erysipelatoclostridium, and Parabacteroides were found.[xxii]

6. IMPORTANCE OF GUT MICROFLORA IN HUMAN HEALTH

The gut microbiota and the gut mucosa have a symbiotic interaction that supports important immunological, metabolic, and gut-protective processes in healthy individuals.

6.1. NUTRIENT METABOLISM

One of the main sources of nourishment for the gut flora is dietary carbohydrates. Colonic organisms such as Bacteroides, Roseburia, Bifidobacterium, Fecalibacterium, and Enterobacteria create short chain fatty acids (SCFA) such as butyrate, propionate, and acetate by fermenting the carbohydrates that elude proximal digestion and indigestible oligosaccharides. The host can obtain abundant energy from these SCFA. Most species in the genus Bacteroides are involved in the metabolism of carbohydrates; they do this by expressing enzymes such as glycoside hydrolases, polysaccharide lyases, and glycosyl transferases. The best example of them is the organism Bacteroides thetaiotaomicron, whose genome codes for a substantial amount more hydrolases than the human genome—roughly 260. organisms include Lactobacillus species, Bifidobacterium species, and Oxalobacter formigenes. Furthermore, microbial proteinases and peptidases act in tandem with human proteinases to form a productive machinery for protein metabolism that improves the gut microbiota. Many transporters on the bacterial cell wall help to ease the entry of amino acids into the bacterium from the intestinal lumen. The amino acids are subsequently transformed into small signaling molecules and antimicrobial peptides (bacteriocins) via a variety of gene products. Important examples include the bacterial enzyme histamine decarboxylase, which produces histamine from L-histidine and is encoded by the hdcA genes of bacteria. The synthesis of vitamin K and various components of vitamin B is one of the gut microbiota's other significant metabolic functions. Conjugated linoleic acid (CLA), which has immunomodulatory, antiobesogenic, antiatherogenic, and hypolipidemic properties, has been shown to be produced by Bacteroides species. To a certain degree, the primary bile acids in the human colon can also be dehydrated and deconjugated by Bacteroides fragilis and E. coli, resulting in the secondary bile acids deoxycholic and lithocolic acids. Recent studies have shown that the breakdown of various phenolic compounds, or polyphenols, that are absorbed through diet is influenced by the human gut flora.

6.2. XENOBIOTICS AND DRUG METABOLISM

It has been known for more than 40 years that the gut microbiota can degrade various substances, including drugs. Thanks to a growing body of research, the effect of the gut microbiota on xenobiotic metabolism is now sufficiently known, and this knowledge may have a major influence on future treatments for a range of illnesses. The competitive inhibition of hepatic sulfotransferases by the gut microbial metabolite p-cresol can reduce the metabolism of acetaminophen in the liver. Furthermore, it has recently been shown that digoxin and other cardiac glycosides inactivate digoxin by upregulating an operon in the common Actinobacteria bacteria Eggerthella lenta that includes cytochrome.

6.3. IMMUNE SYSTEM DEVELOPMENT AND MODULATION

The dynamic and ongoing interactions between the gut microbiota and its metabolites impact how a host's immune system develops. By engaging with the innate immune system via particular receptors that identify and bind to particular compounds linked to bacteria, intestinal epithelial cells neutralize pathogen threats. This procedure results in the release of cytokines, white blood cells, and protective peptides. It also triggers an immune response in the host. The outcome could be an inflammatory reaction to harmful species, a protective reaction to commensal bacteria, or a catalyst for the host's cell death.The gut microbiota heps in gut immunomodulation when combined with the innate and adaptive immune systems. Numerous immune system components and cells, including effector and regulatory T cells, resident macrophages and dendritic cells in the lamina propria, Group 3 innate lymphoid cells, and B (plasma) cells that produce intracellular antibodies, participate the immunomodulatory process. This shows that the gut microbiota may play a part in the development of a robust GALT. The proliferation and function of Foxp3+ T regulatory (Treg) cells are reliant on the gut microbiota. Innate lymphoid cell (ILC) differentiation is reliant on gut microorganisms. It is thought that gut microbes may either directly or indirectly regulate ILCs. Evidence for the former comes from the discovery that the bacterial metabolite indole-3-aldehyde activates ILC by activating the aryl hydrocarbon receptor, which results in the production of IL22.[xxiii]

6.4. MAINTENANCE OF GUT BARRIER INTEGRITY

It has been observed that Bacteroides thetaiotaomicron induces the production of short proline-rich protein 2A (sprr2A), which is necessary for desmosome maintenance at the epithelial villus . The peptidoglycan in microbial cell walls stimulates TLR2-mediated signaling, which is another mechanism that keeps tight junctions intact. Additionally, the Lactobacillus rhamnosus GG strain generates two soluble proteins, p40 and p75, which can inhibit the cytokine-induced programmed cell death of intestinal epithelial cells in a manner dependent on the EGFR and protein kinase C (PKC) pathways. Another pathway that controls gut microbiota-mediated preservation of the gut barrier function is the endocannabinoid system. For example, by lowering metabolic processes, the Gram-negative bacteria Akkermansia muciniphilia can raise the amounts of endocannabinoids that regulate gut barrier functions.

6.5. HOST PROTECTION

By an action called Barrier or Competitive – exclusion effect , In the gut lining, numerous bacteria compete with pathogens for nutrition and attachment sites while also producing antimicrobial chemicals. This keeps pathogens from colonizing the gut lining. It has been observed that nonpathogenic bacteria struggle with one another for these attachment sites on the border of intestinal epithelial cells, obstructing the attachment of pathogenic, enteroinvasive bacteria and their subsequent penetration into the epithelial cells.Furthermore, the intestinal microbiota can outcompete pathogenic bacteria for resources simply by virtue of their vast numbers because bacteria fight for nutrients in their immediate environs and maintain their collective habitat by allocating and consuming all resources. Additionally, by generating antimicrobial compounds called bacteriocins, bacteria can stop the growth of their rivals[xxiv]**.**

6.6. GUT BRAIN AXIS

The intestinal microbiota and its metabolites may be able to reach the brain through the gut–brain axis, a communication pathway that combines immunological, hormonal, and neuronal signals between the gut and the brain .Because of the bidirectional nature of this communication pathway, the brain can control immunological and gastrointestinal processes, including peristalsis and mucin formation. Enteric microbiota appears to have a significant role in GBA, as shown by both experimental and clinical data. It interacts directly with the central nervous system (CNS) via neuroendocrine and metabolic pathways, in addition to local interactions with intestinal cells and the ENS. More than 20 years ago, the administration of oral antibiotics to patients suffering from hepatic encephalopathy resulted in a frequently dramatic improvement. This finding provided the most persuasive evidence of a gut microbe-brain relationship in humans . Meanwhile, new research indicates that anxiety and depressive-like behaviors are influenced by microbiota and more recently, dysbiosis in autism. In actuality, the microbiome of autistic persons varies depending on how severe their condition is. The growth and maturation of the CNS and ENS depend on bacterial colonization of the gut . The lack of microbial colonization is linked to changes in gastrointestinal sensory-motor processes as well as altered neurotransmitter turnover and expression in both neural systems . Research conducted on GF animals has also shown that the microbiota controls the set point for HPA activity and affects stress reactivity and anxiety-like behaviour . The presence of the microbiota also leads in modification of the serotoninergic system. The presence of neurotransmitter receptors on bacteria is necessary for communication between CNS effectors and bacteria.

7. CONCLUSION

The study of the gut microbiome underscores its pivotal role in human health, revealing that this complex community of microorganisms is integral to maintaining overall well-being. A diverse and balanced microbiome supports essential physiological functions, including digestion, metabolism, and immune system regulation, and is linked to a reduced risk of various health issues. Dysbiosis, or microbial imbalance, has been associated with conditions ranging from gastrointestinal disorders to systemic diseases such as obesity and diabetes. The interplay between diet, lifestyle, and microbiome composition highlights the potential for personalized approaches to enhance health through targeted dietary and therapeutic interventions. Ongoing research continues to illuminate the intricate relationships between the gut microbiome and health, promising advancements in preventive and personalized medicine.

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