

## Gut Microbiome: A Guide through 'The Nuts and Bolts' for Early Researchers

## Ousman Bajinka<sup>1\*</sup>, Yurong Tan<sup>1</sup>, Lucette Simbilyabo<sup>2</sup>

<sup>1</sup>Department of Microbiology, Central South University Changsha, Hunan Provinces, China;<sup>2</sup>Department of Neurosurgery, Central South University Changsha, Hunan Provinces, China

## ABSTRACT

**Introduction:** The popular definition is the collection of trillions of microbes that inhabit the human gut and these are called microbiota or microbiome. A paradigm shift is emerging since biomedical researchers are considering the power of intestinal microbes into human health care interventions. Hence there is a need to demystify the new born research cohort to the early scientists and researchers. This review dwelled on the intimate connections existing between microbiota and the body metabolisms, the immune system and the central nervous system that is given the name gut brain axis.

**Results:** From the recollection of the emerging studies, the roles of microbes as fundamental to human health are winning an upper hand and this new born field is shifting the attention of researchers to functional medicinal approach.

**Discussion:** However, scientists are still faced with more questions than answers as to what is a normal gut microbiome, are the variation in diversity is a result of metabolic disorders and autoimmune diseases or causative factors? The consensus is that, the greater the diversity in the microbial composition, the healthier the individual and vice-verse.

**Conclusion:** With Probiotics and Prebiotics, the intervention of personalized diet, fecal transplanting and a scientific study of nutrition, there is a big hope that how the microbes shaped our gut, will shape human health in the near future.

Keywords: Microbiome; Microbiota; Intestinal flora; Metabolism; Diversity

#### INTRODUCTION

Science has been fascinating enough throughout human history, wholly due to the discovering of what, for a very long time has been mysteries. What sciences have to offer is beyond human imaginations and human species will continue to discover what has been covered for millenniums and the journey to the city of knowing the unknown is through research and the interconnection between science and research is the only power that lies within the reach of scientists.

The discipline of research in a bid to establish facts and proofs or to disproof hypothesis is not a mere sprint but a marathon undertaking. It all started with the understanding of the existence of some living creatures that cannot be seen with human naked eyes. At first, no one took the 'microbial world' on serious note as human were only obliged to encounter the macro world. The 'animalcule' as first seen on simple microscope in the 1680s has indeed thrilled the scientists into wondering what lies beneath what the eye cannot see and mind could not imagine [1]. There is another force of power beyond our limits, our 'coast guards', the 'cousins' who lived before us and will live even after us are making us a 'superhuman'.

Until then, it is understood that microbes found in the oral cavity are not exactly the same species found on the skin, in the gut and in the vagina [2]. This uniform diversity in human microbiota composition is prominent among individuals of different age and also between healthy and diseased individuals [2]. More questions will submerge and even more than the

Correspondence to: Yurong Tan, Department of Microbiology, Central South University Changsha, Hunan Provinces, China, E-mail: yurongtan@mail.csu.edu.cn.

Received: February 10, 2020; Accepted: February 24, 2020; Published: March 2, 2020

Citation: Bajinka O, Tan Y, Simbilyabo L (2020) Gut Microbiome: A Guide through 'The Nuts and Bolts' for Early Researchers. Appli Microbiol Open Access 6:170. Doi: 10.35248/2471-9315.20.6.170

**Copyright:** © 2020 Bajinka O, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

answers as to the reasons why we are not alone. In fact, we the humans will continue to wonder because 'what we do not know is more than what we know' or perhaps what we thought we know. What is microbiota, their composition and the stability is still a question left not answered despite the definition of Operational Taxonomic Units (OUT). According to Human Microbiome Project, TOU is hoping to make up a defined microbiota and the diversity of microbes found in an individual. Until, today lots of progresses have been encountered in studies regarding microbiome and its association to the host.

In essences, this review deals with the integral study of gut microbiota and its relation to diet, health and the understanding microbial influence on metabolisms. There is a need for better understanding of inter-individual variations, the impact of gut microbiome on body immunity, the diversity of microbial communities in and on gastrointestinal tract, diseases occurrences like; obesity, diabetes, neurogenic disorders, cardiovascular diseases, cancers and liver diseases among individuals with distorted microbiome otherwise called 'dysbiosis'. We are yet to ascertain if the dysbiosis is the causes or the consequences of the metabolic disorders that lead to disease stages in human population.

We found this virgin ecosystem, very stable and rich in diversity with natural fauna and flora. Bacteria and other single-cell organisms were living on this earth for billions of years. Then evolution enables multi-cellular organisms like plants and animals to surface [3]. Natural selection was optimal. Despite the survival of the fittest, animals would only feed on green grass when its greener and on dry grasses in periods when rains are not falling. The carnivores will only hunt to eat, and that is to say only when they are hungry. 'Exploitation' was not a word found in the English Dictionary. We the human at a species level, found microbes in this biosphere and they never go away. This is due to the fact that they were here before us, outnumbered us and are even more adaptable to the climate changes than the human population. In order to live while fitting into the system, the human species have to adapt to the bacteria as they were here before us and now living on and inside us. In fact numerous studies have found that bacterial communities in human gut microbes generally do not bear resemblance to bugs found in the environment and this is an indication of successful co evolution between human as host. Please note that is not human and the host microbes. Considering the view of the evolution, it its microbes hosting human [4,5].

Human gut microbiota entails the total genome constitutions of the microbes living inside the intestine. The opinion of seeing them as a distinct organ is a point in the right direction. The champion league interactions between the environmental factors, the host (human) and the antigens in the human body all takes place in the human gastrointestinal (GI) tract. The quality and quantity of food type and the microbes from the environment to our gut determine the integrity of the microbiota of 'super organism' [6]. The relationship between these microbes and their host is being increasingly recognized and playing a pivotal role in human health. Two terminologies will be used throughout this review and should not bring any atom of confusion. While microbiome is the collective genomes of microorganisms found in a specific territory, microbiota is the community, the species of microorganism themselves.

When the word 'microbe' is mentioned, diseases causing agents come to mind. Apparently, microbes produce toxins, cause food poisoning, series of respiratory diseases, cardiovascular diseases, genital infections, when bacteria gets into the blood stream, it cause inflammation and sepsis and have been devastating humans for centuries. Animals and plants are not exceptional to these devastating stories of the microbes. Again, not all microbes are bad for human existences.

Fermentation industries cannot go without yeast, fungi are used for antibiotics and food, *Bifidobacterium longman* in breast milk and even some bacteria in the intestine are associated with the regulation of some autoimmune disorders. Obesity, asthma, diabetes, food allergies and inflammatory conditions of our gut and brain are all studied using the microbial diversity. In fact an imbalance in the normal gut microbiota has been link with some gastrointestinal conditions like irritable bowel syndrome, and inflammatory bowel disease.

Diseases are experimentally diagnosed, vaccines are developed, antibiotics are administered and the technologies on the rise and so do the genome sequencing that gave birth to a trending discipline of sciences called the human gut microbiome. What goes in the mouth must reach the stomach and the living ecosystem of intestine are probably even more democratic than what the modern politicians would read from the books. Microbes are very specific to their task and they never intended to make us feel sick. Their purpose of living on and in us is practically to seek shelter and feeding. In fact, in a normal immune functioning, we have lived with them for times and time again. Feel the excitement that arise when dad and mummy says today you will spend the weekend with your favorite cousins. Human microbiota is the cousin to the human cells and these two are interpedently and interrelated through time and space. Babies born through genital track, first say hello to their commensal during the labor while the C-section born babies will get it through the first meal or Probiotics supplement [7,8]. Although emerging researches are coming up with diverging views, we hold on to the theory of being born sterile.

#### COMPOSITION AND FUNCTIONS OF GUT MICROBIOME

From more than 1000 species of bacteria in our gut, we already lost a vast majority of our microbiome. This is evidently based on a research that was conducted to compare our microbiome and that of the apes. A genus Bacteriodes was found to be 5 times more abundant in human population than the apes and this is attributed to our love for eating more meat-based diet than plant based-diet. Despite the fact that we are just 2% differences in our genome to that of the chimpanzees, this trend does not follow on the gut microbiome which shows even more differences. However, in human the patterns of human gut microbiome is temporal perhaps patients seen under intensive care units, lose their home gut microbiota and this is can be called a 'completely ecologically collapse'.

#### What make gut microbiome?

To some, when the term gut microbiota or intestinal flora is mentioned, bacteria come to mind. However, human gut microbiota entails with the total population of microorganisms that live and colonize our gut. These organisms, other than bacteria includes; archaea, viruses, phages, fungi and protozoan [9,10]. The most common phyla of bacteria detected by the up to date technologies are Bacteriodetes and Firmicutes [10]. Your microbiota is not the same with any other individual. Twin study correlates this theory. Generally, people living in the same communities are likely to be feeding on similar food and in effect show similarities in their gut microbiome however, scientists are yet to confirm among the benign microbes, what bacteria is good or bad against other bacteria. We would need a coherent baseline for this and it might not be too soon perhaps Meta analysis requires tangible data and through effective time period. The genetic factors that should be seen as another major cofounding factor should be considered and this is independent of the environmental and ecological factors.

#### Development of gut microbiome

We were all born haphazard and tried to resemble adult flora just after 3 years although this is still in the debate [8-31], the distribution and territorial immigrant status is not based on capitalism instead natural selection as to what phyla or species will get settled in the esophagus, small intestine and the large intestine and our individual ecosystem changes during the growth stages in life [9,10]. The populations of microorganisms living in our gut at a given time are not consistence, that is to say they are temporary when it comes to dominating and different bacterial species colonize different parts of our bodies. Bacteria reproduce every 20 min and the shift in population depends on what nutrient is available in the gut at a point in time. Babies' microbial population resemble adult-like as they grow and the population found in old age group too is distinct of the middle age group, however other factors come in play that may include the environment and the diet type [7]. We generally inherit our microbes from our mothers, the food we eat, and from the people we spend our daily lives with and from our house, buildings including offices and shops.

#### Characterization of gut microbiome

Due to the limitations on culture dependent population of microbes, we now devised culture independent that give birth to the use of polymerase chain reactions (PCR) for DNA amplifications and sequencing to identify the gene sequence and hence knowing what microbes are present [11,12]. Novel molecular technologies are promising as they will shed more lights to the signatures of the microbes. In another words, the sequencing of the genes of these microbes will bring us closer to microbiota health intervention [13,14]. To add more reliable and sensitive identification of gut microbiota that will save both time and energy input, molecular methods of microbial

OPEN O ACCESS Freely available online

identifications like the high throughput gene sequencing technology through 16S rRNA based sequencing of the genes and the analysis using bioinformatics enable a genome based characterization [15]. Based on these genome sequencing approaches, we are able to establish the presence of fungi for up to 1% as of today. This concept might change as more sophisticated machines will be used for microbial characterizations. Presences in the human gut are virus and parasites and these are yet are to be studied at length, however numbers of studies are underway [15] and based on the Illumina MiSeq platform, highthroughput sequencing analysis of the 16S rRNA gene enable even more characterization of bacterial phyla. The analysis of microbial community data depends on the following but not limited to; w.A.T.E.R.S, the RDP pyrosequencing tools, mother and QIIME.

#### Gut host symbiosis

'Find the germs and kill the germs'. These are the words of Louis Pasteur to his assistant during the early stages of disease outbreak intervention, and also the time in the history when the microbiologists were refuting the spontaneous generation theory and replacing it with the germ theory of disease. Instead of killing the bugs, we can understand the mechanisms and in fact, the majority of the gut bacteria are non-pathogenic to the host cell and these benign have already signed the biological MOU with the gut and some have co-habited with the enteroorganisms in a relationship called 'symbiosis' [15,16]. The symbiotic relationship between microbes and bacteria at the time being (although fascinating results are emerging from fungal host relationship studies) will fall under the immunological response of the gut microbiome.

#### Factors influencing gut microbiome

Apart from the food we feed on and feeding habits, our intermediate environment also influence our microbial load. Temperature is one of the external factors as well. The internal factors like microbial interactions, intestinal pH, physiological factors like, host secretions, bile acids, and immune therapy, bacterial mucosal receptors, immune responses and drug therapy greatly influence the composition and diversity of our gut microbiota [17]. These changes in the gut ecosystem does not happen in years but in matter of minutes, hours and days depending on the influence of the external factors like diet, drugs and toxic substances like smokes. Also sedatives and drugs used to attenuate the pain contribute a lot in the dysbiosis. Furthermore, even the bugs that we ascertain pathogenic might be useful in for vaccine production. In essence we the humans should be very considerable when it comes to eliminating what nature has put in place. A schematic diagram extracting from Zheng et al. shows factors contributing to the alteration of gut microbiome and the diseases mechanism of diabetes type 1(Figure 1).



Gradually the intestine will not withstand all these factors, leading intestinal permeability and this is studied to be associated with a decreased in gut microbiome diversity. In effect, islet  $\beta$  cells will be destroyed through excessive activation of innate immunity, adaptive immunity and the molecular mimicry.

#### Gut and antibiotics

Due to the shortage of thorough diagnostic approaches, doctors are left with the only option to prescribe broad spectrum antibiotics. Broad spectrum antibiotics will not only eliminate the bad bugs (pathogens), but also benign or good bacteria will be washing away [18,19]. Viral infections should not be treated using antibiotics; a case scenario will be a poor boy sneeze and got into a pharmacy only to be administering antibiotics. One, antibiotic resistances will be a persisting case and an imbalance of normal gut microbiota may come as a result due to the interference with the epithelial lining. In fact our antibiotics when administered on broad spectrum are believed to wipe out even the good bugs. They eliminate useful molecules that help in the integrity of the epithelial lining of the intestine. The response to chemotherapy and immunotherapy also influenced the composition of microbiota [20-33].

# GUT MICROBIOTA IN HEALTH, DISEASES AND RELATED MECHANISMS

One of the catalytic factors attracting interests to study in depth regarding human gut microbiota is its association with large number of diseases. From sexually transmitted infections to neurogenic disorders, neurotoxicity, psychopharmacology and psychiatry, epilepsy, mental health, spondylo arthritis and luminal diseases such as inflammatory bowel disease [21] and irritable bowel syndrome and the metabolic diseases like diabetes, obesity [34-36], and allergic disease are trending physicochemical conditions that require a marathon research to make it to the finishing point [22].

The study of gut and neurodevelopmental illness, although the establishing of scientific facts is still at the virgin stage, has attracted lots of scientific attentions [10]. Apparently, gut

microbes when get into blood stream causes infections, they can cause some neurological disorders and interfere with metabolism. These are also studied in parallel with other cofounding factors.

Moreover, the second phase of the NIH Human Microbiome Project is concentrating on three models of microbiomeassociated human conditions, inflammatory bowel diseases, the dynamics of preterm birth and diabetes type 2. The longitudinal studies of disease-specific cohorts by analyzing microbiome and their host activities while creating integrated data sets of microbiome and their host functional properties. One of the successes was on the pathogenesis of Crohn's disease (CD) where its mechanisms, and its clinical application are linked to the adverse reactions of gut microbiota and this gave rooms for a new therapeutic interventions on enteric disease [37]. Cardiovascular diseases like atherosclerosis, heart failure, atrial fibrillation, myocardial fibrosis and hypertension have been studied to be linked with the gut microbiota. The mechanisms of these diseases and gut microbiota metabolic pathways mainly trimethylamine-N-oxide plays a big role in the pathogenesis of disease mentioned above [34].

The bridge that link gut microbiome and the liver is the portal vein and this has a bidirectional interaction. Any changes in the gut microbiota composition influences the pathogenesis and the onset of the some liver diseases like, viral hepatitis, cholestatic disorders, Alcohol Related Liver Diseases (ALD) and nonalcoholic fatty liver disease (NAFLD). Much work is done on liver cirrhosis and its diseases mechanism is thoroughly understood and the association with the alteration of gut microbiome however, the good news is that microbiome-based treatment approaches are more promising [38].

#### Role of gut in health

A typical co-evolution is what you will be confronted with when visited gastrointestinal tract (GI) tract. For example, the division of labor force in the large intestine is enabling bacteria to be very specific with their functions in digesting the food that we eat by producing diet depended chemical that the cells of our body cannot produce. Complex molecules such as polysaccharide non digestible by humans and in order to make do with these nutrients, bacteria will help to break down these molecules into very significant short chain fatty acids like butyrate, acetate, and propionate [15]. Butyrate is crucial for maintaining the integrity of epithelial cell lining and also has an anti-inflammatory effect. Only if we know that these microbes never meant to make us sick; in fact if we appropriately feed them with the diet that they prefer, they will help in maintaining our health. Microbes protect us from germs, they enable easy digestion of the food we eat, boost our immune system and the new research that shows that microbes influence our moods. And the bottom line is, these microbes are already homed, they are not leaving so long you are living and it is better for them to be fed otherwise they will feed on our epithelial lining and made us vulnerable to other factors.

#### THE PROMISING INTERVENTIONS

#### Microbiome projects

Powerful projects like the US Human Microbiome Project (HMP) that is aimed at understanding the role of residential microbes in human health [4] and European Metagenomics of the Human Intestinal Tract (MetaHIT) with supporting evidence backed by quality data has proven that; attaining a normal gut flora confers health benefits up to the genetic level [23,24]. While the entire human genome has 22,000 genes [25], the gut microbiome alone is found to be reported with a gene catalog of 3.3 million by the MetaHIT [26].

With the availability of baseline genome, number of interesting researches is underway. One of these interesting studies is HMO-related gene cluster 1. It is identified as a factor responsible for human milk oligosaccharide digestions [10]. This and similar experiments being tried or still on the trial will shed more light into the gut microbiome human relationship and thorough biochemical and metabolic reaction mechanisms we will be compared and contrasted to establish the scientific grounds.

#### Fecal transplanting

Bank my stool is an approach that scientists are using and it leads to a therapy called 'fecal transplanting', administering a stool of a health individual into dysbiosis microbiota. It might sound wired but someone's feces can be your life saving therapy and in fact this is effective in treating Clostridium dificile. In sense, fecal transplanting is the transfer of the stool of healthy individuals to save lives. However, it is still 'too morning' to bring this approach into clinics since we do not know the long term consequences, we could not characterized what other viable particles are in the stool apart from the benign microbes and also since the future consequences in this intervention are not certain, we need to buy some time in order not to anticipate the downstream effects. A study that involves twin whose feces were transplanted into germ free mice and the mice developed obesity and lean, based on the feces receive from the obese and lean twin respectively is creating more follow up studies. Apparently, with the increasing burden of clostridium infections in the hospitals, the healthcare system will definitely ensure that fecal microbial transfer is available in hospitals. Based on the Meta analysis, stool banking is a reliable, guaranteed, timely and accessible for transplanting depending on the demand of the patients and due to its user-friendly workflow, its safety and quality of procedures is easily traceable.

## Personalized food or medicine

The promising technologies that will drive us to this wealthy nation of microbes will provide more insights as to the 'totality of species'. Powerful tools are still emerging and the wholegenome sequencing on the illumine platform has a lot to offer. Furthermore, the feasibilities of transplanting inter-species microbial communities (human to mice) will raise the prospects in the personalized therapy approaches [27]. The occurrence of malnutrition or under nutrition in under developed countries can be reduced with the introducing of individualized gut microbiome that can enhance effective absorptions of nutrients. Mediterranean diet is studied to be effective on the fight against cardiovascular disorders. Although the newly born trend of study on the influence of microbes on the choice of food, more supporting evidence is still required before leaping into conclusions.

#### Food as the best medicine

Food is the best medicine and food has been the medicine during pre-antimicrobial and these words are clearly written on the wall for us to see. Achieving better health is related to the intake of foods rich in dietary fiber and this influence the gut microbiota and the glucose response to food. With this basis and the hope in the future results associating diets and health, personalized diet are not far reaching. One individual will soon be programmed on specific diets and based on the 'gut power,' normal human health is assured. Moreover, the patient's genetic data will be used to inform the healthcare decisions, and this is hoped to be soon in the clinics [28].

### Probiotics and prebiotics

Until now, there is a scientific consensus that Probiotics supplementation has numerous benefits on human health. Probiotics are live microorganisms, when administered in adequate amounts; confer health benefits to the host [29]. The balance of energy in human system is determined at certain extent by the microbes in our gut and the gut microbiota is strongly influence by the medication and diet we depend on. Probiotics are studied to confer changes on digestive tract by producing metabolites that modulate the activities of the intestinal microbes and also they stimulate intestinal epithelium directly. Prebiotics are substrates that are selectively utilized by host microorganisms conferring health benefits [19].

Polyphenols as antioxidants that protect body tissue against oxidative stress, inflammations, cancers and coronary heart disease also is found to be enhancing the growth of beneficial bacteria while inhibiting the growth of pathogens and in this regard are exhibiting Prebiotics effects. The issue of junk foods and food rich in high carbohydrates with the dysbiosis is indeed debatable. Dysbiosis is the term refers to as the imbalance ecosystem of gut microbiota and the lesser the diversity of the microbes in the gut, the poorer the health of an individual [30].

#### Gut brain connection

The gut microbiome brain axis is another trending area of research arising from the gut power to determine the influence of microbes on some neurotransmitters and studies concluded that microbes are crucial in maintaining our moods especially happy mood. Quiet number of ideas and suggestions are paving ways for studies that will create links between gut microbiota and human emotional health [21]. The enteric nervous system is still regarded as the second brain and most of these brain cells are residing in our gut. Animal based neuroscience study on mice reveals that the neurotransmitters serotonin and dopamine, which are responsible for the human mood and emotional response, are regulated by the gut microbes. Emerging studies are revealing that the bidirectional pathway between gut microbiota and the central nervous system (CNS) influence the onset of some neural development, behavior and cognition. The mediators of psychopathology are now recognized as direct representatives of gut microbiota [35].



**Figure 2:** Communication pathways linking the gut microbiome with brain function [Rogers et al.].

According the recent studies, myelination of nerves found in the prefrontal cortex region of the brain is totally regulated by the microbes in our gut. And myelin sheaths are composed of fatty tissue that confers protection to the neurons or nerve cells [35]. Microbiome in some specific psychiatric conditions are schematically drawn explains how the 'second brain'

bidirectional communicate with the first brain as shown in Figure 2.

In this review, we were able to devise the schematic scheme of the promising interventions that scientists and healthcare givers hope to bring a giant leap in the science of gut microbiome and human health. Below are the promising interventions as shown in Figure 3.



Human microbiome projects emerged purely to study the symbiosis relationship between human and their host microbes [8]. Although we grow to develop a normal gut microbiota, we are faced with both external and internal factors that brought the imbalance in the diversity of species composition, interventions like Probiotics and Prebiotics supplement have falling on the line of health protocol and the study of gut, health and metabolic disorders are at large. With the personalized diet that is hoped to be in the clinics in the near future, the understanding of gut brain connection and the success of the clinical trials that will future fecal transplanting, gut as an alternative diseases therapy will ensure effective healthcare approach.

#### DISCUSSION

Although, human microbiome is really coming to the forefront among the recent biomedical and medicinal approach, questions still arise as whether humans inhabit microbes or microbes inhabit human. Apparently what is crucial is how human species can live with the microbes successfully. Until the time of this review, scientists although still working keenly on human gut microbiome, we still have doubts in some uncertainties.

We are trying to link microbes to someone's choice of food and appetite, natural Probiotics in food and Probiotics supplementation while taking positive directions to serving as vaccine. The effect of pesticides in food on the gut microbiome is still in the debate and the influence of organic food on the

#### Bajinka O, et al.

microbiome is still at the virgin stage of research. Is human health affected by even that low dose of antibiotics in food and shall this be replaced with drugs and chemical like foods based on profound studies of our gut microbiota?

We need a complete new course on how we view our health. What we still don't know overweighed what we know and perhaps we assumed to know. Human species are the only group who has the ability to reason and involve in the intervention of technology. This is what we are told in schools. This is what books and journals will talk on and these are the universal concepts. However, is this complete reality? We haven't taken time to study completely what we cannot see with our eyes, our magnifying objects; DNA sequencing and genetic markers have lots of limitations.

We still cannot win the battle of antibiotic resistance; bacteria are engineering ways to resist our chemically synthesized drugs that has undergone rigorous clinical trials, the quorum sensing is still a mystery. This trend is seeing with fungi and viral against antifungal and antiviral drugs respectively. Microbes are no longer afraid of us despite our last generation technologies, our drugs with static or cidal effects, our vast knowledge in understanding of human anatomy, physiology and our being human to sum it all. Perhaps these microbes have over centuries been working on their own technologies, to develop resistance mechanisms, learning how to live successfully on human and even contribute on our metabolism. An old African man said, 'an enemy inside is more dangerous than enemy outside' and in fact, it is high time we stopped believing that germs and microbes are enemies and look upon them as beneficent workers.

If we are to fight a 'no win battle', we need to find ways of buying more time. Perhaps there is a future in human medicine; Understanding the fighting tactics of your opponents is a step towards succeeding or perhaps winning for this time period. We live with microbes although some are pathogenic, only when one condition or the other is changed. All the other factors remaining constant; normal immunity, regular exercise and eating healthy food, microbes will only help in the metabolic activities in the body, strengthening our immunity, and provides structural integrity to the intestine. Hence, it is imperative to adjust to the external factors in attaining a friendly ecosystem with our intestinal flora.

Forward are the interventions that scientists should embark on to convince the physicians that gut microbiota can be used in treating some disorders seen among patients? As of now, if human healthcare intervention is like a pizza, only a slice is known to us and this implies to the study of human gut microbiome to the healing of metabolic disorders. We need to understand the molecular functions, the DNA, RNA; the metabolites of the microbes and these, when combined with the gastroenterology approaches, with a clear understanding of human nutrition while eliminating commercially low fiber-dietbased in the system, and feeding on fresh vegetables and plantbased diet, we will definitely get rid of chronic diseases. To be clearer, animal protein and dairy products are also healthy to feed on. One of the ways forward is to manifest Koch's postulate in the study of microbiome as an interventions. And this is a challenge that scientists will face regarding recruiting volunteers that will come forward in to ascertain gut microbial composition and diseases.

Fecal transplantation is still in the factory, not enough grounds are assembled yet in respect to who will be a donor and to who will be transplanting. In a bid to avoid running into similar incompatible issues in blood transfusions, the in depth understanding of human microbiota as to the role they play in human health is what we need to explore at length before anything. In fact, despite the widespread found in fecal microbiota transplantation in the treatment of recurrent Clostridiodes dificile infection, some limitations like lack of the unavailability of dedicated centers, the complexities related to regulation and safety monitoring and also the donor recruitment are major obstacles. However, consensus are meet related to the stool banking processing ranging from selecting and screening of donors, collection, preparation and storage of feces (this includes services and clients), ethical issues, registries, monitoring of outcomes and the role in the clinical practices.

A handsome number of projects, publications and cutting-edge sciences in gut microbiology are shedding more light into this trending discipline of health research. However, due to the diverging conclusions and speculations, we still need to do more work to establish much complex analysis.

A great deal of attention should be paid on to the microbiome modulators. These are the diet we feed on, the Prebiotics and Probiotics and the antimicrobials administered. These obviously affect the gut microbial community, again is dysbiosis a cause or a consequence of the diseases sought to be scientifically established while making basis on specific diseases. The science behind Probiotics and Prebiotics is really getting kicked started and they are prepared to modulate the functions of human gut microbiota. Personalized medicinal approaches will be fascinating however; it is still rather early morning to wake up with this therapy at large.

Overall, we need a holistic approach and views into human intestinal genome in relations to human health and breakthroughs should be convincing enough to the medical frontiers. As of now we have gone some miles into the study of human and host microbes but we can only complete the holistic approach if we turn our attentions on the interaction between the microbes themselves found in the intestine.

One swab at a time exploring world human microbiome seems crazy but it is an amazing sample collection around the globe to create a library of human microbiome. Once this project reaches the finishing point, scientists will have clues in relating individual microbes not only to the diet they feed on but also to what gut microbial diversity their natural environment can pull in. The distribution of microbes will also no doubt shed more lights on the lost microbiota and perhaps new species will be identified. We can restore our microbes that are at the brink of extinction.

#### CONCLUSION

You are what you eat, so eat well and healthy. The era of preantibiotics, food was serving as the therapeutic interventions. With one of the most talk about study where germ free mice were seen obese after being injected with the genes of already obese mice, lots speculated that gut microbiota bear a significant functional role in maintaining the normal and balanced health of a human.

Improving on the gut microbes requires a great deal of understanding the intestinal ecosystem and the interaction of humans and microbes in this biosphere. In a nutshell, normal ecosystem diversity or biodiversity is the key and this applies to our gut microbiome. Imbalance in these microbes lead to dysbiosis and this has been studied to be directly influencing the physiology of the microbes and affecting human health.

One fascinating study that requires a gentlemen attention is the influence of immune response to vaccine by the microbes. Cancer and other inflammations are hoped to be much looked under microscope.

The bottom line in the study of human microbiota is to profoundly understand the vast communities of microorganisms inhabiting the gastrointestinal tracts. An inside knowledge regarding the understanding of the initial development, factors affecting or contributing to their fluctuation in composition, what can enhance their stability for a period of time and their response to transient perturbations. Although gut microbiome is not far from poorly understood, in order to move this intervention to the clinics for therapeutics, gaining the basic insights is imperative.

#### REFERENCES

- Dobell C. The discovery of intestinal protozoa in man. Proc R Soc Med. 1920; 13(Sect Hist Med): 1–15.
- 2. Lederberg J, McCray A. Ome sweet 'omics: A genealogical treasury of words. The Scientist. 2001;15:8.
- Lozupone CA, Stombaugh JI, Gordon JI, Jansson JK, Knight R. Diversity, stability and resilience of the human gut microbiota. Nature. 2012; 489 7415: 220–230.
- Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The human microbiome project. Nature. 2007; 449 7164: 804–810.
- Schloss PD, Handelsman J. Status of the microbial census. Microbiol Mol Biol Rev. 2004;68 4:686-691.
- 6. Elizabeth Thursby and NathlieJuge. Introduction to the human microbiota. Biochem J. 2017; 474 11: 1823–1836.
- Mackie RI, Sghir A, Gaskins HR. Developmental microbial ecology of the neonatal gastrointestinal tract. Am J Clin Nutr. 1999;69 5:1035S-1045S.
- 8. Sekirov I, Russell SL, Antunes LC, Finlay BB. Gut microbiota in health and disease. Physiol Rev. 2010;90 3:859-904.
- 9. Marchesi JR. Prokaryotic and Eukaryotic Diversity of the Human Gut. Adv Appl Microbiol. 2010;72:43-62.
- 10. Sai ManasaJandhyala, RupjyotiTalukdar. Role of the normal gut microbiota. World J Gastroenterol. 2015; 21 29 : 8787-8803.
- 11. Gensollen T, Iyer SS, Kasper DL, Blumberg RS. How colonization by microbiota in early life shapes the immune system. Science. 2016;352 6285:539-544.

- Kim M, Yu Z. Variations in 16S rRNA-based microbiome profiling between pyrosequencing runs and between pyrosequencing facilities. J Microbiol. 2014; 52:355–365.
- Liu L, Li Y, Li S, Hu N, He Y, Pong R, et al. Comparison of nextgeneration sequencing systems. J Biomed Biotechnol. 2012; 251-364.
- Lagier JC, Hugon P, Khelaifia S, Fournier PE, La Scola B, Raoult D. The rebirth of culture in microbiology through the example of culturomics to study human gut microbiota. Clin Microbiol Rev. 2015;28 1:237-264.
- 15. den Besten G, van Eunen K, Groen AK, Venema K, Reijngoud DJ, Bakker BM. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. J Lipid Res. 2013;54 9:2325-2340.
- 16. Le Chatelier E, Nielsen T, Qin J, Prifti E, Hildebrand F, Falony G, et al. Richness of human gut microbiome correlates with metabolic markers. Nature. 2013;500 7464:541-546.
- Ley RE, Lozupone CA, Hamady M, Knight R, Gordon JI. Worlds within worlds: evolution of the vertebrate gut microbiota. Nat Rev Microbiol. 2008;6 10:776-788.
- Dethlefsen L, Huse S, Sogin ML, Relman DA. The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. PLoS Biol. 2008;6 11:e280.
- Hemarajata P, Versalovic J. Effects of Probiotics on gut microbiota: Mechanisms of intestinal immunomodulation and neuromodulation. Therap Adv Gastroenterol. 2013;6 1:39-51.
- Dethlefsen L, Relman DA. Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation. Proc Natl Acad Sci U S A. 2011;108 Suppl 1:4554-4561.
- Kennedy PJ, Cryan JF, Dinan TG, Clarke G. Irritable bowel syndrome: A microbiome-gut-brain axis disorder? World J Gastroenterol. 2014; 20 39: 14105–14125.
- 22. Ferreira CM, Vieira AT, Vinolo MA, Oliveira FA, Curi R, Martins Fdos S. The central role of the gut microbiota in chronic inflammatory diseases. J Immunol Res. 2014;2014:689492.
- 23. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, et al. A human gut microbial gene catalogue established by metagenomic sequencing. Nature. 2010; 464 7285: 59–65.
- Lagier JC, Hugon P, Khelaifia S, Fournier PE, La Scola B, Raoult D. The rebirth of culture in microbiology through the example of culturomics to study human gut microbiota. Clin Microbiol Rev. 2015;28 1:237-264.
- 25. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, et al. A human gut microbial gene catalogue established by metagenomic sequencing. Nature. 2010; 464 7285: 59–65.
- 26. Consortium IHGS. Finishing the euchromatic sequence of the human genome. Nature. 2004;431 7011:931-945.
- 27. Turnbaugh PJ, Ridaura VK, Faith JJ, Rey FE, Knight R, Gordon JI. The effect of diet on the human gut microbiome: A metagenomic analysis in humanized gnotobiotic mice. Sci Transl Med. 2009;1 6:6ra14.
- 28. Turnbaugh PJ, Hamady M, Yatsunenko T, Cantarel BL, Duncan A, Ley RE, et al. A core guts microbiome in obese and lean twins. Nature. 2009;457 7228:480-484.
- Binns N. Probiotics, Prebiotics and the gut microbiota. In: Gibson GR, Sanders ME (eds) Health effects of Prebiotics and Probiotics, Intestinal Life Science Institute (ILSI). Belgium: ILSI 2013; PP. 16– 20.
- Chang, C, Lin, H. Dysbiosis in gastrointestinal disorders. Best Pract Res Clin Gastroenterol. 2016;30 1:3-15.
- 31. Dominguez-Bello MG, Costello EK, Contreras M, Magris M, Hidalgo G, Fierer N, et al. Delivery mode shapes the acquisition

and structure of the initial microbiota across multiple body habitats in newborns. Proc Natl Acad Sci USA. 2010;107 26:11971-11975.

- 32. Ng KM, Ferreyra JA, Higginbottom SK, Lynch JB, Kashyap PC, Gopinath S, et al. Microbiota-liberated host sugars facilitate postantibiotic expansion of enteric pathogens. Nature. 2013;502 7469:96-99.
- 33. Claesson MJ, Cusack S, O'Sullivan O, Greene-Diniz R, de Weerd H, Flannery E, et al. Composition, variability, and temporal stability of the intestinal microbiota of the elderly. Proc Natl Acad Sci USA. 2011;108 Suppl 1:4586-4591.
- 34. Peng J, Xiao X, Hu M2. Interaction between gut microbiome and cardiovascular disease. Life Sci. 2018;214:153-157.

- 35. GB Rogers. Gut dysbiosis, altered brain function, and mental illness. Mol Psychiatry. 2016;21 6:738-748.
- Peilin Zheng, Zhixia Li, Zhiguang Zhou. Gut microbiome in type 1 diabetes: A comprehensive review. Diabetes Metab Res Rev. 2018;34 7:e3043.
- 37. Z Shen. Intestinal microbiota in Crohn's disease. J Gastroenterol Hepatol.2017;32 1804–1812.
- 38. Zhou R, Fan X, Schnabl B. Role of the intestinal microbiome in liver fibrosis development and new treatment. Transl Res. 2019;209:22-38.