Role of microbiome in health and disease - A review

ABSTRACT

The study researches into the microbiome about the indigenous microbial communities (microbiota) and the host environment that they inhabit and how it has changed clinicians’ ideas about microbes in human health and diseases. Microbiomes’ role in health is inevitable but also somehow relates to the cause diseases in humans. Based on this study, we realized that most of the microbes that inhabit our body supply crucial ecosystem services that benefit the entire host-microbe system. These services include, the production of important resources, bioconversion of nutrients, and protection against pathogenic microbes. On the other hand, diseases can result from a loss of beneficial functions due to disruption of already existing microbial ecosystem in our body or the introduction of maladaptive functions by invading microbes. It is quite understandable how the dynamics and function of the indigenous microbiota has altered our view of microbes in maintaining homeostasis and causing disease. This study discusses how disruption of the beneficial functions of the microbiota can lead to diseases. The human gut, which is the major microbial ecosystem found in our body, contains various microbes which helps us maintain our health and how even a slight disruption to this ecosystem might cause crucial diseases such as obesity, inflammatory bowel diseases and atherosclerosis.

Key words: Microbiome, Commensal bacteria, Mutualistic relationship, atherosclerosis

INTRODUCTION

The term “microbiome” was originally used to refer to a collection of the genomes of the microbes in a particular ecosystem, whereas “microbiota” was used to refer to the actual organisms. Microbiome is being used with the emphasis on BIOME (as in community) and not OME (as in genomics). Currently, microbiome has been defined as the ecological community of commensal, symbiotic, pathogenic microorganisms as well as their genomes that literally colonize the internal and external surfaces of our bodies. A healthy adult harbors approximately 100 trillion bacteria in the gut alone, which are roughly about 10x the number of human cells one possesses. A human possesses about 23,000 genes where microbiome contributes to 3,300,000 genes approximately. In other words, we can say that we are more bacteria than human. Although it is often stated that the number of microbial cells is approximately 10 times the number of human cells, recent studies have estimated we harbour 37 trillion human cells as well as at least 100 trillion microbial cells and a quadrillion viruses in and on our bodies. Given these calculations, the ratio microbial-to-human cell is around 3-fold. It is reasonable enough to view microbiome as an organ as it weighs roughly 1 kg even without a distinct structure. Since the inception of the Human Microbiome Project (HMP) in 2007, the fundamental understanding of the human microbiome has grown at an ever-accelerating pace. In 2013, HMP healthy cohort study, and the many associated studies,
which provided more details on methodology, bioinformatics analyses, and additional cohorts, has led to over 350 publications (Cani P D, 2018).

Culture-independent high-throughput sequencing has now resulted in large expansion of the repertoire of microbiota and microbiome. This has allowed for measurement of the structure and dynamics of microbial communities, the relationships between their members, what substances are produced and consumed, the interaction with the host, and differences between healthy hosts and those with disease. It is hypothesized that the composition of the microbiome may influence the host’s health by contributing to its metabolic and immune functions (Zhang and Heng, 2017). We all know that every species here undergoes evolutionary processes, but we never knew that these microbiomes have also come a long way and have co-revolutionize with the host. Host and microbiome have evolutionary aligned interests and interplay with neither wishing harm on the other. Lack of some genes in bacterial symbionts are critical to other bacteria, but some genes that bacteria retain benefits the host only. Microbiome provides critical biosynthetic pathways that significantly extends the host metabolic and physiologic capacity (Liang et al., 2018).

ROLE OF MICROBIOME IN HEALTH AND ITS BENEFITS

The (healthy) human gut harbors a highly complex and abundant microbial community (representing bacteria, viruses, and protozoa), also known as the gut microbiota, which exists in an equilibrium with its host. The composition of such a microbiota is markedly influenced by the environment and diet, as well as host’s genetics and health status (Willis and Gabaldón, 2020). Since many of the microorganisms harbored by the gastrointestinal tract of animals are considered symbiotic, it indicates that their presence is beneficial for both host and microbe, shifts in microbiota composition can exert a substantial impact on the host’s physiology. The body is colonized by many organisms (the normal flora) which can be positively beneficial (assist in digestion, play a role in toxin degradation). They live on or within the body without causing diseases, and play an important role in protecting the host from pathogenic microbes. Figure 1 shows examples of normal flora present on different sites of human body.

Commensal bacteria provide various benefit to the host. Some of it includes protective, metabolic and structural functions. In protective functions, commensal bacteria cause pathogen displacement by competing with pathogens for nutrients and receptor site. These bacteria also produce anti-microbial factors. Metabolic functions include control of epithelial cell differentiation and proliferation, metabolism of dietary carcinogens, synthesis of vitamins, fermentation of non-digestible dietary residue (inulin, pectin, etc.) and epithelial-derived mucus, ion absorption and salvage of energy. One of the main metabolic function is the expansion of host metabolic capacity. Bacteria express glycoside hydrolase, an enzyme used to convert glycans into useable sugars. No enzyme encoded in human genome is capable of digesting glycans like bacterial enzymes. Most carbohydrates can only be digested by bacteria and produce short chain fatty acids (SCFA), which are the primary fuel for colonocytes. 10-15% of adult energy might either be generated by SCFA production or stored as fat (Ogunrinola...
Besides, there are a few other functions of commensal bacteria structurally such as barrier fortification, induction of IgA, apical tightening of tight junctions and immune system development. Mutualistic relationship between host and microbes are widely evident. Mutualism means that the relationship will benefit both parties, the host as well as the microbes. The microbiota in our body also helps in specific functions such as, it helps seal body spaces, mitigate intestinal pathogens, maintain tissue homeostasis and facilitate fermentation of dietary fibres as described earlier. Besides, it produces a critical energy yield, much needed for our body. It helps in producing metabolic end products along with therapeutic drug processing (Falony et al., 2019). Finally, the microbiomes help in providing signals among cells and organ systems. For example, butyrate produced with the help of microbiota are used as the source of energy for gut epithelial cells whereas acetate and propionate help in lipogenesis and gluconeogenesis. Lipogenesis is the process which leads to triglyceride formation, while, gluconeogenesis is the process of making glucose molecules. Symbiosis (balance) with microbiome is the reason for good health whereas dysbiosis of microbiome results in diseases. In other words, microbiome may cause disease, directly or indirectly, when delicate balance between host in microbes is perturbed(Rui-xue Ding et al,2019).

**ROLE OF MICROBIOMES IN DISEASES AND ITS EFFECTS**

The mindset that bacteria causing infection is well known, well accepted and have known treatments is what has possibly “blinded” the richness of our microbial medical community ecosystems to health and diseases(Liang et al, 2018). The possible microbiome-associated diseases are, acne, antibiotic-associated diarrhoea, asthma/allergies, autism, autoimmune diseases, cancer, dental cavities, depression and anxiety, diabetes, eczema, gastric ulcers, hardening of the arteries, inflammatory bowel diseases, malnutrition and obesity( Willis and Gabaldón, 2020).

**OBESITY**

Most studies conducted on obesity are from stools and not lumens. There were few controlled 'feed studies'. Switching between animal and plant based diets immediately changes microbiome. Obesity is associated with less diverse ‘rich’ microbiota, where there will be changes in enterotype ratios or low gene count which is the best marker in pathology. Most changes due to macronutrients are best shown with gnotobiotic mice but many specific areas of discovery are emerging. The relationship between diet intake, gastrointestinal microbiota and obesity can be clearly seen in Figure 2 below. Diet is the major determinant of gut microbiota composition. Gastrointestinal microbiota which produces short chain fatty acids will stimulate satiety hormones which will lead to reduced diet intake. At the same time, energy intake also affects the host weight. Hunger/satiety hormones will affect the host’s appetite. Microbiota alter colonic energy harvest, host gene expression and increase host inflammation. This proves that obesity and weight loss are well associated with altered microbiota (Joossens and Vandeputte, 2020).Gut microbiota induced obesity is explained by 4 main mechanistic pathways which are,changes in energy harvesting, changes in metabolic pathways, the role of induced inflammatory responses, and possible changes in brain and behavior. Intestinal microbiota causes enterocyte glucose and lipid absorption, production of lipopolysaccharides, produces short chain fatty acids and influences body adiposity. Lipopolysaccharides will influence intestinal permeability and toll-like receptors (TLR) signaling. TLR signaling is also activated by taste receptors. This signaling will cause inflammation and immune activation. Short chain fatty acids will influence liver gluconeogenesis and lipogenesis. It will also activate...
G-protein receptor 41/43 signaling which will eventually activate immune system and cause inflammation. Body adiposity causes adipokine signaling which will finally lead to inflammation and immune activation also. Although there is limited understanding on the symbiotic relationship between us and our gut microbiome, and how disturbances of this relationship affects our health, there is compelling evidence for an important role of the gut microbiota in the development and perpetuation of obesity (Bresalier and Chapkin, 2020).

INFLAMMATORY BOWEL DISEASE

Host–microbiota interactions shape local and systemic inflammatory diseases. Dysbiosis of gut microbiota, aberrant function of the intestinal epithelial barrier and innate and acquired immune system predispose to development of inflammatory bowel diseases (IBDs). IBDs can be caused by extrinsic (environment) and intrinsic (genetic background) factors. One of the factors are infections usually caused by Shigella sp. Salmonella sp. and others. Reduction in Dysbiosis, Bacteroidetes and Clostridia and increase in Enterobacteriaceae can lead to IBD as well. Epithelial barrier breach, aberrant negative immune response and dysregulated immune response are other factors contributing to IBD. There are few evidences for the role of microbiota in IBD. Recent increase incidence in IBD is too rapid to be attributed to genetic factors alone. Westernized diet of increased fat and red meat is associated with increased incidence of IBD. Increased fiber and fruit decrease the risk of Crohn’s disease and increased vegetable intake decreases the risk of ulcerative colitis. Firmicutes sp. are decreased in Crohn’s diseases, specifically Faecalbacteriumprausnitzii. Decreased F.prausnitzii is associated with risk of post-recurrence of ileal Crohn’s disease. Vitro and animal studies demonstrate anti-inflammatory properties of F.prausnitzii and increase in IL-10 and short chain fatty acids.

ATHEROSCLEROSIS

There are few roles of gut microbiome in non-gastrointestinal diseases. Production of specific metabolites by gut microbiota has the power to affect distant organs. This is the evidence that gut microbiota contributes to atherosclerosis through metabolism of dietary lipid phosphatidylcholine. Food rich in phosphatidylcholine are major source of choline. Choline broken down by intestinal microbiota forms trimethylamine that is metabolized by the liver to trimethylamine oxide, which promotes development of atherosclerosis. However, the underlying mechanism on how trimethylamine oxide causes atherosclerosis is still unclear. Consumption of choline correlates positively with Bacteroidesenterotype that is associated with a Westernized diet.

CONCLUSION

Based on the above, it can be clearly seen that microbes in our body play various important roles and at the same time causes diseases in humans. Even a slight change of imbalance between microbes and host can result in detrimental effects on our body. Microbes have been established in our body since birth and is highly influenced by many external and internal factors such as food intake, environment, genetic factors and many others. One of the few roles that microbes play in a person’s body is, the protective function. Microbes provides protection by competing for space and nutrients with incoming pathogens. Pathogens are microorganisms which invade our body and immune system and causes diseases in a host. Besides that, it also secretes antimicrobial substances which will help in getting rid of pathogens. Microbes also has many metabolic functions which includes, control of epithelial cell differentiation and proliferation, metabolism of dietary carcinogens, synthesis of vitamins, fermentation of non-digestible dietary residue (inulin, pectin, etc.) and epithelial-derived mucus, ion absorption and salvage of energy. One of the main metabolic function is the expansion of host metabolic capacity. Moreover, it has structural functions such as, barrier fortification, induction of IgA, apical tightening of tight junctions and immune system development.

Declaration and competing interest

The authors declare that there are no conflicts of interest.

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