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Review Article

Nature of Human Gut Microbiome: How do they play in Cardiovascular Disease?

Abstract

Cardiovascular disease is the number one killer of death around the world. Most of the cardiovascular diseases are caused by sedentary life style, bad eating habit, tobacco smoking, high alcohol intake, dyslipidemia and genetic factors .Recently the idea of human microbiome science has emerged in diseases pathogenesis .The human gut is a house of trillions of microbial floral. Since a couple of decades ago, there has been interesting insights into the human gut microbiota and have highlighted its increasingly association to cardiovascular (CV) and metabolic diseases. Trimethylamine N-oxide (TMAO), which is a metabolic product from gut microbiota plays a central role in cardiovascular disease pathogenesis. Nature of microbial inhabitants within the host has been noticed by the numbers of scientists and researchers to understand more about the hidden mechanism of diseases pathogenesis including cardiovascular disease, metabolic and autoimmune diseases and it has become a good hope to develop new drug designs to prevent metabolic and cardiovascular disease in near future.

Introduction and Nature of Microbiome

Microbiome is the collection of all the microorganisms living in association with the human body. Different numbers of microorganisms including three domains of life and viruses are involved in the communities of microbiome [1]. These microbes are generally not harmful to us, and in fact they are essential for playing of important role for health. For example, they produce some vitamins that we do not have the genes to make, break down our food to extract nutrients we need to survive, teach our immune systems how to recognize dangerous invaders and even produce helpful anti-inflammatory compounds that fight off other disease-causing microbes [2]. There are a number of studies have shown that changes in the composition of our microbiomes relates to numerous disease states [3]. The human body is the host of trillion of microbial flora representing thousands of microbial species from Archaea, Bacteria, and Eukarya [4]. Healthy immune system and microbial plays a key role for human health. Any alterations in gut microbiota (dysbiosis) can cause different health problems including metabolic and neuronal diseases, coronary heart disease, inflammatory bowel disease, colorectal cancer, malnourishment, rheumatoid arthritis, autoimmune and psychiatric disorders etc [5]. This brief article discusses the potential role of the gut microbiome in cardiovascular disease.

Microbiome and cardiovascular disease

In the setting of cardiovascular disease, substantial hemodynamic changes, such as, alteration in vascular permeability, hypoperfusion and intestinal wall congestion, can change gut morphology, function, and possibly the growth and composition of gut microbiota. Such changes can disrupt the barrier function of the intestines and exacerbate systemic inflammation via microbial or endotoxin translocation into systemic circulation [6]. Recently, the concept in trimethylamine N-oxide (TMAO) has emerged as a key mediator that provides a mechanistic link between gut microbiota and multiple cardiovascular diseases [6,7]. Researchers reported findings from several studies involving people and animals, that the gut microbiome directly changes the function of blood platelets, influencing the risk for heart attack and stroke.

Basically, when certain nutrients, such as choline (abundant in red meat, egg yolks, and dairy products) and L-carnitine (found in red meat as well as some energy drinks and supplements) are ingested, the gut bacteria that break it down produce a compound called trimethylamine (TMA). This in turn, is converted into the compound, trimethylene N-oxide (TMAO) in the liver [8]. In mice model, gut microbiomes generate TMAO that promotes impaired glucose tolerance, inhibits hepatic insulin signaling, and exacerbates adipose tissue inflammation in mice that are maintained on a high-fat high-sugar diet 8. Similarly, number of studies has emerged on animals and humans show that TMAO has also been suggested as a key player molecule mediating the development of type-2 diabetes mellitus and cardiovascular disease [9]. In

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addition, a group of three phospholipid-associated molecules choline, betaine, and TMAO are associated with atherosclerosis according to a metabolomics concept. After several number of reports about gut microflora affecting the metabolism of amines and aromatic metabolites have emerged, researchers and microbome scientists have been focusing on wide range of studies that has suggested a role for the gut microbiom in a diverse range of diseases such as obesity, type 2 diabetes and aspects of the metabolic syndrome, drug metabolism, autism spectral disorder, autoimmune disease, colitis and Chron's disease [10]. Nevertheless, the implication of microbioms in number diseases is not only complex but also divergence interactions between the huge quantities and diverse range of microbes found in the gut and the human.

How TMAO plays in cardiovascular disease

TMAO is commonly seen in a variety of marine microbiota, where it serves as an important substrate in the anaerobic metabolism of a number of bacteria. Some studies in gnotobiotic mice have shown that TMAO harbors in the serum of animals colonized with TMA-producing bacteria [11]. Increase intake of phosphatidylcholine leads to a higher production of TMAO, was significantly associated with an increased risk of all-cause and CVD-specific mortality. Dietary choline and l-carnitine are metabolized by intestinal bacteria to produce TMA, which is, in turn, absorbed into the bloodstream and oxidized to TMAO by enzyme flavin monooxygenase 3 in the liver. Flavin monooxygenase 3 is reported to be a main integrator of hepatic cholesterol, lipid metabolism and inflammation [9,12]. Recently it is demonstrated that the metabolic pathway of complex phosphatidylcholine–choline involving gut microbiota in contributing to the pathogenesis of atherosclerotic coronary artery disease in animal models [12]. Some studies show that the platelet activity through the potentiation of cytoplasmic calcium release may be increased by TMAO, by which it may predispose to a hyper-coagulating status and increased thrombotic events [13]. The prolongation of angiotensin effects, which is also likely to worsen cardiac remodeling, may be related by regulation of TMAO and leads to detrimental outcome in heart failure [14]. TMAO also plays a role in the metabolic networks mechanism of type 2 diabetes that has impacted to increase the risk of cardiovascular disease. A Meta-analysis done by Yoriko Heianza et al states that increase circulation levels of gut microbiota metabolites, including TMAO and its precursors, are associated with an increased risk of major adverse cardiac events and all-cause mortality [15].

Future therapeutic perceptive by targeting gut microbes

After several studies focused on gut microbes relation to cardiovascular disease has been done over a course decade, the researcher and scientist are trying to develop to target gut microbion to reduce and prevent cardiovascular disease. Recently Cleveland Clinic researchers have designed a potential new class of drugs that may reduce cardiovascular risk by targeting a specific microbial pathway in the gut. Dr. Hazen's team from Cleveland Clinic has developed a new series of inhibitors, called mechanism-based inhibitors; that were designed to not kill the bacterial cells and, therefore, likely do not contribute to antibiotic resistance and it helps potently to interrupt the gut microbial pathway that produces TMAO [16]. All the way, a large number of drug developers and scientists in other different centers are also trying to designate to target the gut microbion in cardiovascular disease prevention and metabolic problem. The gut microbiome is an important key player in several kinds of disease process and it has wide spread aspects to human health.

Conclusion

Gut microbial is an important part of metabolic mediator in cardiovascular disease. It has many hidden potential effects to alter human metabolism and immune changes that may lead to diseases. Since cardiovascular disease is a major cause of death around the world, we are focusing to prevent the burden of dangerous heart disease by numerous ways including the concept and implications of microbome that has come to be a part of new hope to combat metabolic disorders and heart disease.

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