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Research progress of gut flora in improving human wellness

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ABSTRACT

Human wellness is the ultimate goal of our efforts in improving the human life. Special foods are undoubtedly important in achieving human wellness. However, overeating significantly leads to obesity and diabetes. These chronic diseases will in turn affect the human wellness. Therefore, "dietary restriction and proper exercise" were introduced in the human daily life. Different foods cause various effects on the human health. The diversification of diet is a priority for nutritionists to keep our body healthy. To avoid diabetes mellitus, special foods for ketogenic diet, low-carbon diet, and low-calorie intake are also gradually attracting attention. In addition, the hypothesis that "hunger sensation comes from gut flora" brings new light to the research on the biological motivation for humans to eat food. This hypothesis has been gradually demonstrated using the flexible fasting technology by providing special foods, such as plant polysaccharides and dietary fibers. The response to food-needing signals from the gut flora to these foods demonstrates the importance of the gut flora in improving human wellness. The gut flora is probably an essential factor for translating the food-eating signals and converting the nutrition to our body. Therefore, "gut flora priority principle" is developed to guarantee human wellness. The 16S rRNA sequencing and mass spectrometric techniques can be used to identify the gut flora, which may guide us to a new era of human wellness based on gut flora wellness.

1. Introduction

Food-eating behavior is important in our daily life. Usually, the eating behavior of humans includes breakfast, lunch, and dinner in a day in most countries. Different countries exhibit varying tendencies for food styles and various cooking cultures. As one of the ancient countries, China features about 5000 years of cooking cultures. Compared with the fast-food cultures, for example, in America, the Chinese foods are welcome in most countries. However, in recent years, the urgently increasing chronic diseases indicate the problems in unhealthy eating behaviors or unsafe foods. The relationships between foods and health are extremely important in the prevention and control of chronic diseases as documented in a large number of literature [1–9]. For a long time, our laboratory focused on the study of molecular mechanisms underlying the chronic diseases, such as stroke and ischemia injuries, in recent years; however, finding the etiology of chronic diseases poses difficulty [10–12]. Given the rapid progresses in the field of gut flora study and chronic diseases, we queried whether a direct and hidden link to the gut flora probably exists between special foods and the human health. Different foods correspond to various gut flora, whereas different gut flora correspond to distinct diseases, as indicated in an increasing number of literature [13–16]. Therefore, a new model named "gut flora-centric theory (GFCT)" was then developed based on these studies and our own research. The GFCT model will probably provide a new understanding and explanation to bridge the special foods and human wellness.

2. Brief introduction to the "gut flora-centric theory (GFCT)"

At first, we will briefly introduce the concept of "GFCT". The GFCT is a new hypothesis focusing on the biological motivation of why humans need to eat food every day. Almost from the beginning of the human society, humans were told to eat food. Of course, if food is unavailable, then the uncontrollable hunger sensation and accompanying hypoglycemia will result in unexpected body

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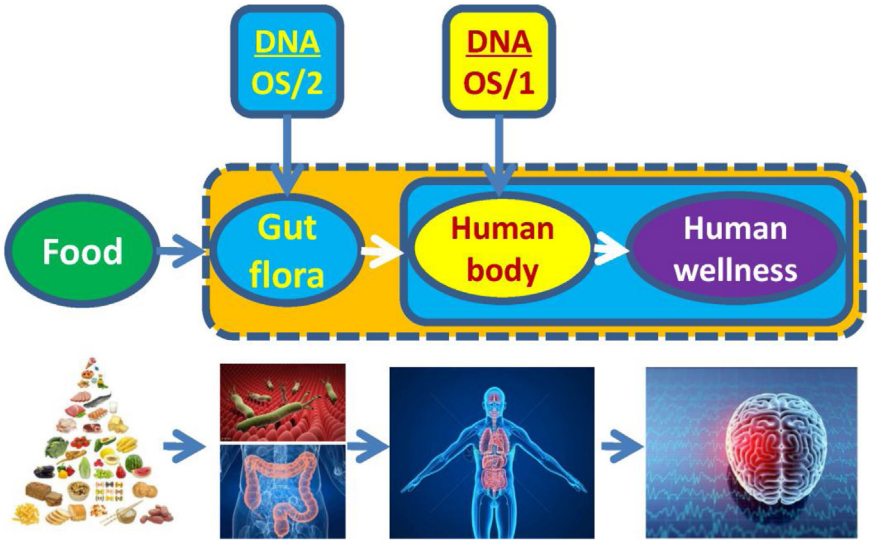

Fig. 1. Gut flora is the bridge for translating the food-eating signals into human wellness. A healthy gut flora creates good health and human wellness.

injuries. Therefore, as an important matter regarding the human eating behavior, a few people ask this question: what are the biological basis and motivation for humans to eat foods? Starting from 2013, as an obese man myself with a body mass index higher than 34, I used my own body to test how to control the body weight following the suggestions by Dr. Liping Zhao in Science [17–23] and the related studies on obesity and the gut flora by Dr. Gordon JI [24–31]. Immediately afterward, I gradually discovered that my hunger sensation seemed to originate from the gut flora, because when I ingest special foods, such as plant polysaccharides and dietary fibers, to feed the gut flora but provided no food for my own body through three meals a day, my hunger sensation gradually diminished and disappeared. Not only my body weight but also my diabetes mellitus and severe fatty liver were significantly improved. Shortly thereafter, the related clinical trials based on the flexible fasting (FF) technology were initiated and have been successfully completed [32–38]. By carefully analyzing and examining the important clinical results, we finally proposed the new finding that "hunger sensation comes from gut flora" because of the "universal reproducing power of the microbiota" living in the gastrointestinal tract after birth [39]. Therefore, we unexpectedly discovered that the food-eating signals originate from the gut flora but not from the cerebral feeding center with neural circuits of motivation to control food intake, which is current knowledge [40]. When we used the FF technology to control the hunger sensation, the volunteers can normally live for 7–14 days without human food but only food for the gut flora and 3–5 L of water every day, similar to camels living in the desert [33,34,41–43]. This kind of lifestyle can directly benefit obese people because the human body can then automatically burn the internal fat to provide energy [33]. In short, the gut flora controls the hunger sensation of human beings. Detailed introductions on the GFCT theory have been reported recently [38,39].

3. Understanding the relationships between special foods and health with gut flora

After the GFCT theory was proposed and developed in recent years [33,38,39], we pondered on the relationship between the gut flora and human beings. The human body is now widely accepted as a symbiotic structure working together with the microbiota within our body [44,45], with more than 90% of the microorganisms living in our gut (mostly in the large intestine) [46,47]. The human genomic DNA is the 1st genomic DNA (termed as operating system 1, OS/1), whereas the symbiotic microorganism genomic DNA is the 2nd genomic DNA system (termed as operating system 2, OS/2) [39,45]. Therefore, the human body could be regarded as a two-genomic-DNA-driven system, with the OS/1 as host and the OS/2 including the symbiotic microorganisms (mostly in the gut flora). Animals are carnivores, omnivores, or herbivores [48]. Different gut flora structures exist in animals with specific food preferences [49,50]. Similarly, in humans, food preference is also frequently observed. Some people opt for a vegetarian lifestyle for their beliefs, whereas others show no specific preference for different kinds of food [51]. Considerably extreme food preference will result in allotriophagia [52]. Fortunately, the 16S rRNA sequencing technology could be used to identify the metagenomics information on the gut flora and determine whether the gut flora is normal or abnormal [53–55]. Together with the viewpoint of the GFCT theory, the food preference information is probably recorded and memorized by the gut flora. If such is the case, then the gut flora functions as the interpreter for transmitting the food preference signals to the human brain via the vagus [56–58]. Theoretically, when the gut flora needs a carbon source for energy to reproduce in the human gut under the control of "universal reproducing power of the microbiota," then the hunger sensation signals will be sent from the gut to the brain. Therefore, for biological reasons, the food-eating behavior primarily aims to meet the food-needing signals of the gut flora. Different gut floras memorize various types of foods [39]. If suitable foods are available to match the memories of the gut flora, then the gut flora will help the human body to digest the food to produce nutrition not only for themselves but also for the human body.

4. Gut flora is essential to bridge the best foods for human wellness

Human wellness is the first-of-all pursuit for everybody. However, what are the best foods for achieving human wellness? According to the above discussion, based on the GFCT theory, the human wellness should include three parts: (1) wellness of the human body; (2) wellness of the gut flora; (3) maximum matching of the best foods and healthy gut flora (Fig. 1). Therefore, we prefer the "gut flora priority principle (GFPP)" in our daily lives when considering food preferences and eating behaviors [38,59]. In detail, as the biological motivation of human beings to eat food originates from the gut flora, then feeding the gut flora is a prior-

ity. Therefore, we should provide special foods, such as prebiotics, to first meet the need of the gut flora and food for our body next [60–62]. Adequate food should at least be available for the gut flora to guarantee its wellness. Otherwise, the gut flora will malfunction and fail to correctly transmit the food-eating signals toward the brain. In short, satisfying the gut flora is the first priority, and satisfying the human body comes second. The human wellness needs the gut flora wellness as the gut flora is the key point for hunger sensation and food-eating behavior.

5. Best foods are measurable based on changes in the gut flora

The best gut flora is critically important to bridge the direct link between the best foods and human wellness. Fortunately, the large-scale rRNA sequencing technology and mass spectrometry technique provide scientific and convenient approaches for this purpose. To identify whether a kind of food is suitable for human health, one of the best ways is to compare the differences in the gut flora in volunteers before and after using special foods. Usually, the 16S rRNA sequencing technology is sufficient to determine whether the gut flora improves or worsens [54]. The commercial companies can provide biological sample preparations from the feces and use the 16S rRNA sequencing and the following bioinformatic data analysis and interpretation for identification. On this basis, the use of any antibiotics will destroy the gut flora and directly result in body injuries [63–65].

Dividing foods into two types (one for the gut flora and the type for the human body) is important in daily life. Notably, all the foods for the human body can also be used by the gut flora. However, not all foods for the gut flora can be utilized by the human body. In this field, a large number of prebiotics, such as plant polysaccharides and dietary fibers, serve as food for the gut flora but could not be utilized by the human body [66–68]. The gut flora can decompose dietary fibers into short-chain fatty acids to provide nutrition for the intestinal epithelial cells, which will in turn support the wellness of the gut flora [69–71]. We have used the text mining approach to identify the novel prebiotics for further studies [72]. Normally, both the nutrition for the human body and gut flora, such as starch, rice, noodles, fruits, vegetables, fish, shrimps, meat, eggs, and milk, are combined together. The increased diversity of the nutrition indicates the increased diversity of the gut flora [73–75]. A gut flora with more diversity will provide the body with more abilities and capacities for digesting food and avoiding excessive food preference. Therefore, the foods with increased diversities must be ingested to keep the diversity of the gut flora to guarantee the wellness of human beings.

6. Conclusions

In this paper, we briefly introduced the GFCT theory and its potential application in food science to maintain the human wellness. Irregular eating behaviors and abnormal life styles will directly or indirectly injure the gut flora health and in turn influence the translation of foods into nutrition by the gut flora. Therefore, maintaining the gut flora health is critically important for digesting foods according to current studies. In addition, the suggestions of “dietary restriction and proper exercise” should be the golden rule and precept for human wellness, where the gut flora is the hidden factor for maintaining the human health. Altogether, we will probably enter a new era to enjoy human wellness based on the gut flora wellness and on the basis of the “GFPP” to develop and utilize special foods as specific nutrition sources for human wellness.

Competing interests

The authors declare that they have no competing interests.

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