

Review

A biological hypothesis: is it possible that human symbiotic microbiota coding hunger genes for human beings?

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The increasing number of literatures focus on the correction between symbiotic microbiota and noncommunicable diseases (NCDs) bring new light for prevention to NCDs. It is well known that the microbiota could be largely influenced by different foods, different foods will conversely influence human health. However, there still is no clue bridging the link between hunger sensation and microbiota. Based on recent research progresses between microbiota and obesity and diabetes, together with our studies, we proposed a biological hypothesis that the human symbiotic microbiota might code hunger genes for human beings. This hypothesis was supported with clinical evidences by using the flexible fasting (FF) technology. When we used the FF technology to feed the gut flora with plant polysaccharides and dietary fibers, the candidates can survive normally by using internal glycogen and fat with low or even no hunger sensation. The theory of "gut flora-centric theory (GFCT)" was then developed to explain this phenomenon. When the gut flora begins to reproduce their own offsprings in human gastrointestinal tract, they will digest and destroy the gastrointestinal mucosa to obtain the carbon sources. This signal will be transferred from gut to human brain as hunger sensation. Further efforts should focus on the mechanism underlying how and why did the symbiotic microbiota trigger and transfer the hunger sensation by activating the hunger genes. Taken together, the conjecture linking between human symbiotic microbiota and hunger sensation will probably improve prevention and control on NCDs.

Key Words: noncommunicable disease; microbiota; hunger sensation; hunger gene; gut flora-centric theory; flexible fasting; operating system

Introduction

For thousands of years we are told that we must eat food every day. It seemed to be an unalterable principle in human society, because if we did not eat food, then the formidable and uncontrolled hunger sensation will cause us die. Many diabetes patients have the experience of desperate and terrible hypoglycemia which is rather dangerous to the body. However, the Chinese old and famous proverb that "chronic diseases come from eating five kinds of grains" faintly and dimly indicated that if we did not have correct eating patterns, then we will be suffered from a large number of noncommunicable disease (NCDs). Therefore the facts "we have to eat" and "we must eat food" have been the golden laws and precious rules in our life almost from the beginning of the human history. Few people think about the origin of hunger sensation because it is one of the unalterable principles. However, when we began to ask the question that "where did the hunger sensation come from", we found that it is actually not a quite common question on the "origin of hunger sensation" and

finally hypothesized that the human symbiotic microbiota probably coding the hunger genes for our human beings.

Did the hunger sensation come from gut flora?

It is well known in classical and modern genetics that "a gene

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coding for an enzyme". Almost all of the biological processes were coded by genes following the central dogmas¹. This has been the law of the life science and occupying a dominant position in biological and medical science studies. When the human genome project (HGP) was successfully completed in 2000, many scientists celebrated this great success²⁻⁴. However even after a decade, the occurrence of NCDs such as obesity and diabetes is still growing up⁵⁻⁷. In case of necessity, the USA government proposed the precision medicine project⁸⁻¹⁰. However several papers published recently pointed out that there is a long to go for the precision medicine because NCDs were still out of control¹¹⁻¹³.

During our studies, we also asked the question why there are so many NCDs in China. When a large number of literatures focused on the importance of human symbiotic microbiota with NCDs such as obesity, diabetes, hypertension, stroke, cancer, autism, depression¹⁴⁻²⁴, we were also attracted by this interesting research field. Following the interesting and valuable studies of Dr. Gordon Ji²⁵⁻²⁸ and Dr. Liping Zhao²⁹⁻³³ on the close relationship between microbiota with obesity, we began to test whether we can control the fat of our own body by controlling the gut flora. Luckily and interestingly, we finally demonstrated that when using the plant polysaccharides and dietary fibers to feed the gut flora, together with significantly reducing food intake, then the body weight can physiologically and normally reduce. These clinical studies have been published recently to support this new hypothesis³⁴⁻³⁷. This is also an important evidence to support the interesting findings of Dr. Gordon and Liping Zhao that low calorie intake and polysaccharide and dietary fiber is beneficial for health, together with the elicitation of fasting studies by Dr. Longo³⁸⁻⁴³. Based on these studies, we asked the question, is it possible that the human symbiotic microbiota coding hunger genes for human beings?

In other words, we found that although we human beings indeed did need foods to eat every day, however it seemed the hunger sensation comes from gut flora but not from the human brain itself. When the gut flora needs carbon sources and nitrogen sources to reproduce their offsprings in human gastrointestinal tract, they will digest and destroy gut mucosa and transmit the hunger sensation signals to the body, which will be transferred and transduced to our brain by vagus and neuroendocrine system⁴⁴. Then the human brain will control the body to eat food to meet the food needs by gut flora. When the food was intaken after feeding, then most of the nutrients will be absorbed by the small intestine and some others will be used by gut flora. In other words, each of us need to eat, but the hunger sensation and food-eating signals were probably originated from the gut flora other than from human brain⁴⁵⁻⁴⁹.

Development of the gut flora-centric theory (GFCT)

Regarding the clinical evidences to support this hypothesis that "human symbiotic microbiota coding hunger genes for human beings", we have demonstrated that when we control the hunger sensation and food-eating signals by using the flexible fasting (FF) technology by feeding the gut flora with plant polysaccharides and dietary fibers but no food for human body, then the human body will have a special status similar like the camel living in desert. The human body can physiologically decompose the internal glycogen and fat to provide energy for the body. The candidates can then normally and healthily live for 7-14 days by

only feeding the gut flora and drinking enough water everyday but without food for human body. The clinical evidences were obtained from several hospitals to provide direct support on the hypothesis that "hunger sensation comes from gut flora" and have been published in recent years^{34-37, 45-53}. Only when based on these important facts, can we realize that the hunger genes of the human beings seemed to not be coded by human genomic DNA systems, but by the genes of the human symbiotic microbiota especially the symbiotic microbiota (gut flora). Therefore, this new hypothesis will probably contribute on the updates of current knowledge on eating behavior from fundamental and essential level, which means that the current textbook will probably need to be updated in near future. As a large number of NCDs were caused by unhealthy eating patterns, most of the NCDs will then be improved by precisely targeting the abnormal gut flora based on the gut flora-centric theory (GFCT).

Frankly speaking, before our GFCT studies, almost all of the efforts looking for the hunger genes are focusing on human genes such as leptin and ghrelin⁵⁴⁻⁵⁶. It is really not easy and rather difficult for people to pay attention on the possibility that symbiotic microbiota coding hunger genes for human beings. It is also of great interests to ask why the nature place the hunger genes in microbiota other than the human genomic DNA systems. We suggested it is probably a law of the nature because the gastrointestinal tracts of the human beings are best place for the symbiotic microbiota to reproduce their offsprings. This phenomenon could also be recognized with the meaning of animal evolution as we recently reported⁵⁷. It might probably be another central dogmas of life science that the symbiotic microbiota driving the evolution of animals and human beings by coding the hunger genes to "teach" the animals and human being to eat food for living⁵⁷. We will discuss this perspective in further works.

Future works beyond the GFCT theory

As described in Dickens' famous and classic literary of "A tale of Two Cities", although this is the worst of times because of the out of control of NCDs worldwide, however, our current hypothesis that "human symbiotic microbiota coding hunger genes for human beings" might bring new light on the prevention and control of NCDs. Future works should focus on the identification of the spirit-needing genes (if existed) that was coded by the OS/3 (the 3rd operating system, also named as human language and consciousness system), where the symbols, abstraction, logic, and reasoning are the basic coding processing similar as the "A, C, G, and T" bases in the OS/1 (the 1st DNA-OS as the human genomics) and OS/2 (the 2nd DNA-OS as human symbiotic microbiota), while the reasoning, thinking and judgment constitute the world of consciousness, mental, mind and spirit. Based on these new explanations of human body as well as the consciousness coding systems (OS/3), we will probably have a new understanding of the nature and the world to enjoy the forthcoming human life in the future.

Conclusion

To find the genes coding for hunger sensation is of great importance for human beings. In this short review, we briefly introduced the new hypothesis that the human symbiotic microbiota coding hunger genes for human beings with clinical

evidences coupled with logical reasoning analysis. As a new hypothesis, further works are needed to address the underlying molecular mechanisms. We expected as a new begin by focusing on the symbiotic microbiota coding hunger genes for human beings, the NCDs will probably have a new chance by precisely targeting the mysterious and amazing symbiotic microbiota in human gut.

Declarations

List of abbreviations

FF: flexible fasting; GFCT: gut flora-centric theory; NCD: noncommunicable disease; OS: operating system

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Authors' contributions

CZ proposed the hypothesis and finalized the manuscript. WG, ZL, DG and YG provided valuable suggestion on the manuscript.

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Competing interests

The authors declare that they have no competing interests.

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