

A Research on the Relationship between Intestinal Flora and Human Longevity

Muzi Cui¹ Jianhua Wu² Yin Zhang² Sixing Liu³ Shifeng Shuai⁴ Liyi Dan¹ PingPing Yan^{5*}

1. Second Clinical College of Hainan Medical University, Haikou, Hainan, 570100, China
2. First Clinical College of Hainan Medical University, Haikou, Hainan, 570100, China
3. School of International Nursing, Hainan Medical University, Haikou, Hainan, 570100, China
4. School of Clinical, Hainan Medical University, Haikou, Hainan, 570100, China
5. Clinical Skills Center of Hainan Medical University, Haikou, Hainan, 570100, China

ARTICLE INFO

Article history

Received: 11 October 2021

Revised: 18 October 2021

Accepted: 24 January 2022

Published Online: 31 January 2022

Keywords:

Intestinal flora

A long life

Life and health

ABSTRACT

The exploration of human life and health is advancing with the changes of the times. With the growth of age, the occurrence of chronic diseases of human immunity and organ system is frequent, which has a serious impact on human health. Genes, environment and other random factors determine the outcome of longevity, and intestinal flora is considered to be a decisive factor affecting human health and longevity, mainly because of its huge impact on human immunity, growth and development. The study of the relationship between intestinal flora and longevity is beneficial to improve the health status of the elderly and improve the overall life level of human beings, which has great scientific research value. This review will review the role of intestinal flora in longevity.

1. The Necessity of Intestinal Microbiota Studies in Longevity Studies

1.1 The Intestinal Flora of Normal People

Abundant microorganisms grow in the intestinal tract of the organism, especially bacteria, whose number varies from 500 to 1000 and reaches 10¹² to 10¹⁴. Among them, the number of genes existing in human body is only one hundredth of the number of genes owned by microorganisms, and the number is more than 9.87 million according to relevant data^[1,2]. Intestinal flora is interdependent and interacts with each other to maintain

the ecological balance in the intestinal tract. It plays an important role in intestinal immunity, digestion and absorption, growth and development, and biological antagonism, etc., and constitutes an essential part of life^[3]. Intestinal flora can be roughly divided into three categories: 1) Dominant flora: mainly obligate anaerobic bacteria, including Bacteroides, bifidobacterium, Eubacter, lactobacillus, etc., which can be colonized in the deep surface of intestinal mucosa and are beneficial to the health of the host, with low immunogenicity; 2) Opportunistic pathogens: most of them are facultative anaerobic bacteria, including enterococcus and enterobacter, which are not the dominant flora of the

*Corresponding Author:

PingPing Yan,

Clinical Skills Center of Hainan Medical University, Haikou, Hainan, 570100, China;

Email: 1289762133@qq.com

intestinal tract. They are symbiotic with the host and generally not infectious. When the human immune system is low or the intestinal flora is disturbed, it will cause harm to human health. 3) Pathogenic bacteria: they can swim on the surface of the intestinal lumen, and are less likely to colonize in the intestinal lumen for a long time. Most of them are passing bacteria, which will cause damage to human body only when the number reaches a certain level^[4].

1.2 Intestinal Flora and Longevity

Longevity refers to people have a healthy constitution, to ensure the quality of life, and to get a longer life. Factors affecting human longevity are numerous and complex. In general, in addition to natural disasters, human-made disasters, disease, plague and other factors, there are genetic genes, nature, social, family, gender, disease, diet, lifestyle, psychological state and other factors^[5]. Back in 1908, a scientist from Russia won the Nobel of “probiotics in the gut” and systematically expounded the association between “beneficial bacteria” and the secret of longevity^[6]. They found that the human gut contains 10¹³-10¹⁴ microorganisms, which are mainly bacteria, and their total number is about 10 times that of human cells. The human gut flora is a complex system, mainly in Firmicutes, Bacteroides, proteobacteria, Actinobacteria and Wartinobacteria. However, with the development of science and technology, people gradually realize that the relationship between intestinal flora and human body is not only simple parasitic and parasitism, but also its complex relationship needs to be constantly explored^[7,8]. The intestinal flora indirectly affects human health by affecting the immune system, causing related diseases, and affecting growth and metabolism, thus acting as a factor affecting human longevity^[9].

2. The Effect of Intestinal Flora on Longevity

2.1 Intestinal Flora and the Immune System

Intestinal flora contributes to antigen exposure in early life and is one of the richest sources of early immune stimulation and adaptation^[10]. The continuation of life and health is closely related to the normal functioning of the body’s immune system. The diversity and sufficiency of intestinal flora in normal individuals play an indispensable role in the normal activation of the immune system, so as to ensure the normal progress of the body’s life activities^[11,12]. Innate lymphoid cells (ILCs) and T lymphocytes are widely distributed in the gastrointestinal mucosa, which play an important role in the regulation of intestinal flora and the function of the immune system.

At the same time, intestinal flora can also directly or indirectly regulate the growth and development of ILCs^[13,14]. Nikolaeva by normal human and animal physiology such as gastrointestinal tract flora of live microorganisms extracted by drug made of probiotics applied in 60 days weaned 60 newborn calf and 45 days weaned 60 found on big white piglets injected extracted by gastrointestinal flora probiotics drug research object innate immune factors have along with the age and the characteristics of the activated^[15]. Intestinal flora plays an important role in T lymphocyte polarization and function regulation. Studies have shown that TLR can be expressed in gastrointestinal epithelial cells to regulate intestinal flora, activate TLR2-4 and NF- κ B signaling pathways, secrete regulatory T cell polarizing cytokines, and specifically bind to B cell κ -light chain, thereby ensuring bacterial tolerance and maintaining normal immune function^[16,17]. Intestinal flora is an important factor in the immune system of the body, which plays a crucial role in the homeostasis of the internal environment, life health and longevity.

2.2 Intestinal Flora and Chronic Diseases

The harm of chronic diseases is a major obstacle to ensuring the longevity and health of individuals. Intestinal flora is interdependent with the body and plays an indispensable role in maintaining the homeostasis of the body’s internal environment and resisting the invasion of foreign pathogens^[18]. Abstract: Intestinal flora plays an important role in the regulation of obesity in typical chronic diseases by promoting the production of short-chain fatty acids, reducing the content of fast-induced Adipose Factor (FIAP), and resisting chronic mild inflammatory response. To improve obesity and inflammation. However, long-term high-fat diet can still inhibit the improvement of intestinal microflora structure^[19,20]. At the same time, the increase of gastrointestinal flora promotes the generation of short-chain fatty acid bacteria and plays a certain role in the hypoglycemic effect in the treatment of diabetes^[21,22]. Studies have shown differences in gastrointestinal flora such as Bacteroides and actinomycetes between diabetic patients and healthy subjects, and complex changes were observed during the treatment of low-fat diet through the 6-month follow-up of subjects. Butyrate producing bacteria *Anarunrotruncus* showed a slight increase, while *Roseburia* significantly increased at T1 stage, but at later stage gradually decrease^[23]. Changes in the structure of gastrointestinal flora and other physical and chemical properties can lead to the destruction of pancreatic β cells and increase the incidence of diabetes. Therefore, the normal diversity and abundance of intestinal flora are important factors affecting the

occurrence and development of chronic diseases, and thus play an important role in individual health and longevity.

2.3 Intestinal Flora and Growth Metabolism

Intestinal flora is a complex microbial community in human body, which plays a very important role in cell growth and development, nutrient uptake and other aspects^[24]. Gill's team used large-scale shotgun sequencing and 16S rRNA-based full-length gene technology to comprehensively understand functional genes of intestinal flora and found that they play a significant role in human metabolic pathways and processes^[25,26]. In addition, there is also a research by used at the same time based on nuclear magnetic resonance (NMR) and mass spectrometry (GC - MS) metabolomics technology, dynamic detection and monitoring of family member's overall metabolic spectrum (urine metabolism of 1 H NMR spectrum) characteristics change, first discovered the human microbiome can affect human body metabolic phenotype, and found that affect the function of human body metabolic phenotype bacteria such as *B.thetaiotaomicron*, *Pseudobutyrvibrio* main sequence Similar to *Clostridium* and *Bacteroidetes*, and related human metabolites were found^[24]. In addition, the study of Thaiss CA et al. on intestinal G- showed that the activation of il-23-IL-22 pathway in myeloid cells inhibited the transcriptional activity of rhythm gene *Nr1d1*, thus activating *NFIL3* and further regulating *CD36* and other molecules to promote lipid metabolism in vivo^[27]. At the same time, Watad A et al., through their studies on the occurrence and development of diseases in different seasons, showed that intestinal flora can monitor the normal expression of rhythmic lipid metabolic procedures in the body by regulating the transcription of *NFIL3* gene in intestinal epithelial cells and some internal clocks^[28], thus further affecting metabolism in the body.

3. Summary and Outlook

With the rapid development of sequencing and genome technology in the scientific field, it has become possible to explore the composition and function of intestinal microbes^[29], and the study on intestinal flora and longevity has also become hot. At present, some existing research from basic research "intestinal flora and regulating mechanism of aging" "gut bacteria to improve the mechanism of different diseases" and "bacteria biological rhythm biorythm of relations" with the host and so on, at the same time, also have to centenarians intestinal flora and its way of life, environmental factors such as the relevance of research^[30-32]. However, intestinal

flora is in a complex relationship with the human body to achieve ecological balance in vivo, and can interact with the host through metabolism and genetic inheritance^[33]. Therefore, it is very important to reveal the dynamic relationship between intestinal flora and longevity and one of the important directions of future research on intestinal flora and longevity is to carry out personalized regulation of intestinal flora on the basis of understanding the characteristics of intestinal flora. In addition, the study on the intestinal flora of the families of long-lived people can also further explore the influence of genetic factors on the intestinal flora.

References

- [1] Qin, J., Li, R., Raes, J., et al., 2010. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature*. 464(7285), 59-65.
- [2] Li, J., Jia, H., Cai, X., et al., 2014. An integrated catalog of reference genes in the human gut microbiome. *Nat Biotechnol*. 32(8), 834-841.
- [3] Zhe Luan, Bin Yan, Gang Sun, 2018. Research progress on longevity and intestinal microecology. *Chinese Journal of Gerontology*. 3(13), 3321-3323.
- [4] Wangjing Tang, Xiangdong Zhu, Rui Shen, et al., 2018. Research progress of ulcerative colitis and intestinal microflora. *Journal of Shaanxi University of Traditional Chinese Medicine*. 109-114.
- [5] Haiyan Cen, Yuqi Zhang, 2018. Research progress on influencing factors related to longevity. *Guangxi Medical*. 40(12), 1351-1353.
- [6] Podolsky, S.H., 2012. Metchnikoff and the microbiome. *Lancet*. 380(9856), 1810-1811.
- [7] Kim, K.A., Jeong, J.J., Yoo, S.Y., et al., 2016. Gut microbiota lipopolysaccharide accelerates inflamm-aging in mice. *BMC Microbiol*. 16, 9.
- [8] Heintz, C., Mair, W., 2014. You are what you host: microbiome modulation of the aging process. *Cell*. 156(3), 408-411.
- [9] Biagi, E., Franceschi, C., Rampelli, S., et al., 2016. Gut microbiota and extreme longevity. *Curr Biol*. 26(11), 1480-1485.
- [10] Öner Özdemir, 2013. Mechanisms of preventative and therapeutic role of probiotics in different allergic and autoimmune disorders. *Journal of Immunology*. (3), 103-118.
- [11] Yang, R.Y., Zhang, F., Jin, J.X., et al., 2020. Research progress on the relationship between diet and intestinal microflora. *Chinese Journal of Microecology*. 32(9), 113-1117.
- [12] Qinm, Q.Q., Miao, J.J., Wang, Sh.Y., et al., 2017. Association between intestinal flora and immunity in

- middle-aged and aged people by PCR-DGGE. *Journal of Hygiene Research*. 46(1), 40-45.
- [13] Pan, D.D., Qin, H.L., 2018. Advances in the study of innate lymphocytes in intestinal homeostasis and disease. *Chinese journal of Microbiology and Immunology*. 38(6), 464-467.
- [14] Zhang, H., Wang, Y., Chen, H.Y., 2020. Research progress on the role and mechanism of intestinal flora in host immune response. *Microbiologica Sinica*. 60(4), 629-640.
- [15] Nikolaeva, O., Andreeva, A., Altynbekov, et al., 2020. Probiotic drugs impact on the innate immunity factors. *Journal of Global Pharma Technology*. 12(1), 38-45.
- [16] Yang, X.Zh., 2018. Research progress on the relationship between TLR2 and gastrointestinal diseases. Chongqing Medical University.
- [17] Wang, Y., 2018. To explore the therapeutic mechanism of Gegenqinlian Decoction in treating T2DM metabolic endotoxemia based on intestinal flora and LPS/TLR-4/NF- κ B signaling pathway. Gansu University of Traditional Chinese Medicine.
- [18] Wang, D., Wu, H., Liang, X.Y., et al., 2019. Advances in the Application of Intestinal Flora in Anti-Tumor Therapy. *Journal of Nutritional Oncology*. (2), 59-66.
- [19] Zhou, Y.M., Zhao, Sh., Jiang, Y., et al., 2019. Regulatory Function of Buckwheat-Resistant Starch Supplementation on Lipid Profile and Gut Microbiota in Mice Fed with a High-Fat Diet. *Journal of Food Science*. 84(9).
- [20] Li, X.X., Yu, M.L., Lu, Sh.F., et al., 2017. The role and significance of intestinal microflora and intestinal epithelial cells in type 2 diabetes induced by high fat and high sugar. *Chinese Journal of Diabetes*. 25(9), 842-846.
- [21] Fei, J., Luo, J.T., Zhang, X.Y., et al., 2018. Role of short-chain fatty acids in regulating human energy metabolism by intestinal flora. *Chinese Journal of Diabetes*. 10(5), 370-373.
- [22] Sun, Y., Huang, Y.Ch., Ye, F.H., et al., 2020. Effects of probiotics on glycemic control and intestinal dominant flora in patients with type 2 diabetes mellitus: A protocol for systematic review and meta-analysis. *Medicine*. 99(46), e23039.
- [23] Liu, Ch.G., Shao, W., Gao, M., et al., 2020. Changes in intestinal flora in patients with type 2 diabetes on a low-fat diet during 6 months of follow-up. *Experimental and therapeutic medicine*. 20(5), 40.
- [24] Wang, B.H., 2007. Study on intestinal microbial diversity and its correlation with human metabolism. Zhejiang university.
- [25] Gill, S.R., Pop, M., Deboy, R.T., et al., 2006. Metagenomic analysis of the human distal gut microbiome. *Science*. 312, 1355-1359.
- [26] Schloss, P.D., Llarger, B.R., Handelsman, J., 2004. Integration of microbial ecology and statistics: a test to compare gene libraries. *Appl Environ Microbiol*. 70(9), 5485-5492.
- [27] Thaiss, C.A., Nobs, S.P., Elinav, E., 2017. NFIL-training the host circadian rhythm-microbes fine-tune the epithelial clock. *Cell Metab*. 26(5), 699-700.
- [28] Watad, A., Azrielant, S., Bragazzi, N.L., et al., 2017. Seasonality and autoimmune diseases: the contribution the four seasons to the mosaic of autoimmunity. *J Autoimmun*. 82(6), 13-30.
- [29] Heping Zhang, 2019. Probiotics, Gut microbiota and health. *Chinese Science Bulletin*. 7.
- [30] None, 2020. Improving gut flora may prolong life. *Hyology*. 128.
- [31] Shirong Wang, Zhen Tian, Zhuoming Qin, 2014. Discussion on the correlation between intestinal health and longevity. *Chinese Journal of Microecology*. 26(08), 991-993.
- [32] Tiancheng Xu, Lixia Pei, Lu Chen, et al., 2019. Bio-rhythm phenomenon of bacterial flora and its clinical significance. *Medical Schools of Thought Contend*. 10(5), 4-7.
- [33] Collino, S., Montoliu, I., Martin, F.P., et al., 2013. Metabolic signatures of extreme longevity in northern Italian centenarians reveal a complex remodeling of lipids, amino acids, and gut microbiota metabolism. *PLoS One*. 8(3), e56564.