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Research progress on the relationship between oral saliva flora and liver cirrhosis

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Abstract: *Oral microecology is an extremely complex ecosystem. The oral microbiome is also closely related to oral diseases and even systemic diseases. With the development of molecular biology technology, people have a deeper understanding of the correlation between oral microbiome and various diseases. This article will review the relationship and interaction between oral saliva flora, oral-gut-liver axis, and liver cirrhosis based on the current research progress of the oral microbiome.*

Keywords: *Oral salivary flora; liver cirrhosis; high-throughput sequencing technology; oral-gut-liver axis*

1. Introduction

The number of human oral microorganisms is huge and diverse, and the microorganisms colonized in the oral cavity together constitute the oral microbiome [1]. At present, there are about 700 kinds of microorganisms in the human oral cavity, and the oral microbiome is the second largest complex microbial community after the gut microbiome [2].

The inherent structure of the oral cavity provides conditions for the attachment, colonization and survival of microorganisms. The interaction between microorganisms, the host and the environment jointly maintains the dynamic balance of the oral micro-ecosystem, which is very important for maintaining the health of the host [3]. However, under certain conditions, this dynamic balance is disrupted, and bacteria that were originally non-pathogenic or weakly virulent become opportunistic pathogens causing caries, periodontal disease, periapical disease, oral mucosal lesions, etc. A variety of oral diseases [4-5], and even closely related to systemic diseases [6-8]. With the development of genomics, people have a deeper understanding and understanding of microorganisms. This article will review the relationship between oral salivary flora and liver cirrhosis.

2. Oral micro-ecology

The oral micro-ecosystem is extremely complex, and the inherent anatomical structure and its physicochemical properties in the oral cavity provide a suitable environment for the survival of oral microorganisms. The dynamic balance of microecology is significant to our health. Due to the phenomenon of colonization resistance, the presence of symbiotic flora in the oral cavity can prevent the invasion of pathogens and maintain the immune function of the body, thereby protecting the health of the body [9]. However, the defense capacity of the oral microbial barrier is limited. When some physicochemical factors, bacterial factors or host factors change, the oral homeostasis is destroyed, and some opportunistic pathogens dominate. These microorganisms can be directly transferred, enter the blood or stimulate inflammation. Reactions and other ways act on the body, leading to the progression or occurrence of the disease [10].

The balance and stability of the oral microecology is closely related to the health of the whole body. In recent years, studies on oral flora and other systemic diseases have emerged in an endless stream, such as Alzheimer's disease [11], esophageal cancer [12], pancreatic cancer [13], Crohn’s disease [14], and liver disease (such as hepatitis [15], nonalcoholic liver disease [16], liver cirrhosis [17]). These studies not only promote a comprehensive understanding of the oral flora, but also deepen the understanding of

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the close relationship between oral health and general health.

3. Oral saliva flora

Saliva is one of the important components of oral microecology. It has the functions of swallowing, lubrication, buffering, digestion, metabolism, antibacterial, immunity, protection, etc. It is of great significance for the maintenance of oral homeostasis and the prevention of diseases. At the same time, saliva is the basis for the survival of microorganisms in the oral cavity, and the biofilm formed on the surface of teeth and mucous membranes is conducive to the early colonization and adhesion of microorganisms.

The genetic information of a large number of oral microorganisms is stored in saliva, and 1 ml of saliva of healthy adults contains about 100 million bacterial cells [18]; salivary flora includes bacteria floating in saliva and other anatomical structures in the oral cavity of exfoliated cells, representing almost the entire oral microbiome [19]. Saliva DNA is of high quality and can be used as an important carrier for detecting microbiological information. Secondly, saliva collection is convenient, safe and cost-effective, and has certain advantages in the diagnosis and monitoring of oral diseases and systemic diseases.

3.1. Research methods of salivary flora

Compared with traditional microbial culture methods, the booming high-throughput sequencing technology in recent years has made it possible to analyze and study microorganisms that were difficult to cultivate in the past, and greatly promoted the in-depth study of the oral microbiome. At present, about 65% of the oral flora can be cultured in vitro, and the gene sequences of its representative strains can be sequenced and analyzed by high-throughput sequencing technology.

(1) PCR technology, commonly used including nested PCR, multiplex PCR, real-time fluorescence quantitative PCR and digital PCR. For example, Lu analyzed the oral salivary flora of patients with recurrent aphthous ulcers by applying real-time fluorescence quantitative PCR technology and found that the number of Streptococcus, Veillonella and Neisseria in oral microorganisms was significantly lower than that of healthy people [20].

(2) Terminal restriction fragment length polymorphism (T-RFLP). This DNA fingerprinting method can be used to compare the composition of microbial communities in a large number of samples. This technique has high repeatability and precision, and can be used to study the structural differences and succession of oral microbial communities.

(3) Denatured gradient gel electrophoresis (DGGE). This technology has good convenience and reliability. According to different sequences, DNA fragments undergo denaturation and melting at different concentrations, so as to stay in different gel band positions, and a band on its fingerprint is Represents a microbial group to identify different biological groups.

(4) High-throughput sequencing technology, which can sequence hundreds of thousands to millions of DNA molecules in parallel [21]. This technology has the advantages of high throughput, short read length, high accuracy and cost-effectiveness, low cost, and greatly shortened sequencing cycle[22-24].The application of high-throughput sequencing technology to study the oral microbiome enables us to study the structure and diversity of oral microbiota at the cluster level of OUT (Operational Taxonomic Units), giving people a new and full understanding and thinking about the oral microbiome At the same time, it also provides strong technical support for the study of oral flora and related diseases.

4. Liver cirrhosis and the oral-gut-liver axis

Liver cirrhosis is a chronic, progressive and destructive disease of the liver, a pathological stage characterized by diffuse liver fibrosis, pseudolobular formation, and vascular proliferation inside and outside the liver one of the chronic liver diseases [25]. The intestinal mucosal barrier is damaged in patients with liver cirrhosis, the bile acid metabolism is disordered, the defense function is decreased, and intestinal flora disorder is prone to occur. However, the intestinal flora imbalance leads to bacterial translocation, and a large amount of endotoxin is produced to form gut-derived endotoxemia, and accelerated the development of liver cirrhosis [26].

The oral cavity is the beginning of the digestive tract, and the oral flora can be swallowed into the

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digestive tract with saliva. At present, there are three main ways for the oral flora to cause digestive tract diseases: (1) The oral flora invades the intestinal tract, leading to the intestinal flora Disorders; (2) local inflammation in the mouth or bacteria acting on other organs with blood circulation during dental operations; (3) the metabolites of oral flora enter the blood, causing endotoxemia, stimulating systemic inflammation, and promoting the occurrence of digestive tract diseases [27]. High abundance of oral flora can be detected in tissues of inflammatory bowel disease, appendicitis, and colorectal tumors [17]. Qin applied metagenomic methods to analyze the gut microbes of patients with liver cirrhosis. Compared with the human oral microbiome database (HOMD), they found that the genus Streptococcus, Veillonella, Lactobacillus, Fusobacterium is of oral origin [28]. Aberg found that periodontal disease and chronic liver disease are closely related, suggesting that periodontitis may promote the development of liver cirrhosis [29]. Studies by Bajaj have shown that the relationship between the oral cavity and the gut microbiota can be regulated by improving the oral environment. Periodontal therapy can reduce endotoxemia and systemic inflammatory response in patients with liver cirrhosis, which is beneficial to the regulation of the oral gut-liver-axis [30].

In the study of the oral-gut-liver axis, there are many studies on the intestinal flora and liver cirrhosis, and the regulation of the gut-liver axis has a positive significance for the treatment of liver cirrhosis [31].However, the microbial dynamics of oral flora and intestinal flora are consistent [27], and the two influence each other, but there are few studies on the relationship between oral flora and liver cirrhosis, and there are still relatively large theoretical and practical gaps.

5. Conclusion

Patients with liver cirrhosis are prone to oral problems such as bad breath, dental caries, periodontitis, oral mucosa ecchymosis, and candida infection, and are accompanied by the disturbance of oral flora [18]. Treatment is helpful for the control of endotoxemia and systemic inflammation in patients with liver cirrhosis. Therefore, it is of great significance to provide active oral hygiene guidance to patients with liver cirrhosis and to control and treat intraoral infectious diseases.

The development of high-throughput sequencing technology has provided strong technical support for people to study oral microbiome. The existing microbiome research evidence also shows that the imbalance of oral microecology is closely related to systemic diseases. The relationship between oral flora and liver cirrhosis and the specific mechanism of action of the oral-gut-liver axis have not been elucidated, and more comprehensive and accurate research evidence is needed in the future. In view of the individual-specificity and relative stability of oral saliva, rich in oral microbial gene information, and easy to collect, economical, safe and effective, it has certain advantages in the diagnosis and monitoring of oral diseases and systemic diseases, and can be used as a health screening tool in the future. An important carrier for screening and disease screening.

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