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Oral microbiota: A new view of body health

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ABSTRACT

Oral microbiota is an important part of the human microbiota. Oral microbes can be colonized into the intestine in various ways. Oral microbiota is associated with a variety of oral diseases. Recently, increasing evidence has shown that the oral microbiota is closely related to the physical state of humans, such as diabetes, obesity, and cancer. In the future, oral microbiota will become a new target for improving the physical state of humans.

1. Introduction

About 700 kinds of microorganisms exist in the human mouth, and these microbes constitute the human oral microbiota. It is one of the most complex microbial communities in the human body [1].

In recent years, with the completion of the Human Microbiota Program [2,3], people have become increasingly aware of oral microbes [4] but have not further analyzed oral microbiota in oral diseases such as caries [5], periodontal disease [6], and oral cancer [7]. There is evidence that oral microbiota is also closely related to systemic diseases [8], including rheumatoid arthritis (RA) [9], adverse pregnancy outcomes [10], and cardiovascular disease [11]. Notably, a large number of oral microorganisms enter the downstream digestive tract from the oral cavity through saliva, and they present a particularly close relationship with digestive diseases [12].

Oral microbiota can be used as targets to treat oral and systemic diseases. This article will discuss the relationship between oral microbiota and gut microbiota.

In the future, oral microbiota may become a new target for the treatment of certain diseases.

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2. Oral microbiota

The oral cavity is a complex environment that encompasses distinct, small microbial habitats, such as teeth, buccal mucosa, soft and hard palate, and tongue, which form a species-rich heterogeneous ecological system [13] (Fig. 1A). Numerous microorganisms exist in the mouth, among which are bacteria, fungi, and viruses. Bacteria are the main inhabitants of the mouth [14]; they primarily comprise bacteria of the Firmicutes, Bacillus, Proteobacteria, and Actinomycetes [15]. Unlike gut microbiota, these types of bacteria do not change significantly. Diet and the environment have a great impact on gut microbiota [16] but exert minimal effect on the composition of oral bacteria. Healthy people from different countries have similar compositions of oral microbiota. In the human mouth, 85 species of fungi can be found. Among these fungi, the most important one is *Candida* [17]. *Candida* is neutral when the oral microbiota is normal; however, when the oral microbiota balance is broken, *Candida* will seek the opportunity to attack oral tissue. *Candida* forms a biofilm with *Streptococcus* to play a pathogenic role [18]. Viruses, mainly phages, are also part of the oral microbiota [19]. The type of phage in the mouth is constant during all stages of life [20]. Other non-original viruses may also appear in the mouth when certain diseases exist in the human body. The most common is the mumps virus [21] and HIV [22]. Oral bacteria are the main components of the oral microbiota. Common oral bacteria include *Streptococcus mutans*, *Porphyromonas gingivalis*, *Staphylococcus*, and *Lactobacillus* [23]. *S. mutans* is the main component of the oral microbiota, and it is one of the main components of dental plaque [24]. It is also the main pathogen of caries, which is a bacterial infectious disease that occurs in hard tissues of the teeth and has the highest incidence among oral diseases [25]. *P. gingivalis* is a non-glycolytic Gram-negative anaerobic bacterium that is a periodontal pathogen. Untreated *P. gingivalis*

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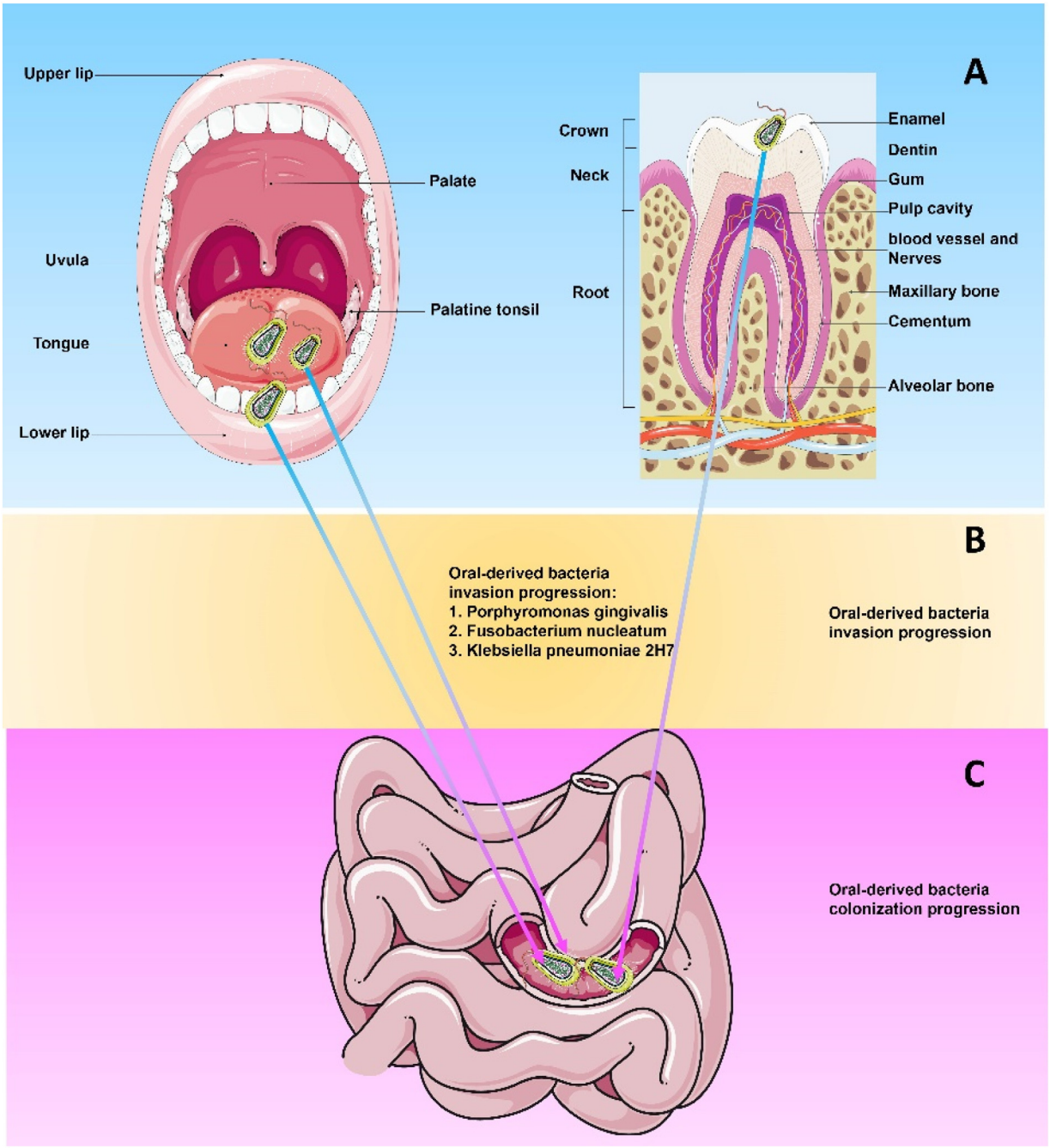

Fig. 1. Oral microbiota can invade gut microbiota directly and indirectly. (A). Basic structure of the oral cavity. (B). Progression of oral-derived bacterial invasion. (C). Progression of oral-derived bacterial colonization.

can cause gums to fall off the teeth. *Lactobacillus* refers to a bacterium that can ferment sugar to produce lactic acid. It is a group of microorganisms that live in the body and benefit the health of the host. Yogurt contains lactobacilli. *Lactobacillus* ferments sugar and produces a large amount of lactic acid, which can easily cause caries [26].

3. Interaction between oral microbiota and gut

Many experiments have shown a gathering of oral-oriented bacteria in the gut of patients with various diseases, but whether oral bacteria can induce intestinal inflammation and cause systematic diseases is unknown [27]. Recent studies have shown that oral-derived bacteria can colonize the intestines and persist there, leading to activation of the intestinal immune system and chronic inflammation [28]. Researchers transplanted saliva samples from patients with Crohn's disease into germ-free mice. This action resulted in a marked increase of T helper 1 (Th1) IFN-γ+CD4+ cells in the intestinal lamina propria. The researchers identified a bacterium that is primarily colonized in the colon, namely, *Klebsiella pneumoniae* 2H7 (Kp-2H7). This bacterium may be the main cause of TH1 cell accumulation. However, colonization of this species does not cause wild-type mice to elicit an immune response. The above experiments indicated that this strain can be colonized in the case of dysbiotic gut microbiota and act as a pathogen in susceptible hosts. A *Klebsiella* strain of bacteria can be isolated from another common intestinal disease, ulcerative colitis. Transplantation of this strain of bacteria into germ-free mice can lead to an immune

response and accumulation of TH1 cells. The results of 16 s rDNA sequencing revealed that *Klebsiella* in patients with Crohn's disease increases significantly, and Klebsiella-related genes are enriched in the gut microbiota of patients with inflammatory bowel disease (IBD) [29].

Although many studies have confirmed the close correlation between oral microbiota and digestive diseases, the physiological distance between the oral cavity and digestive system cannot be ignored. How does the oral microbiota cross this distance to the organs of the digestive system? The three ways are described as follows. 1) The oral microbiota directly invades the intestinal tract through the esophagus, causing an imbalance in the intestinal micro-ecology and affecting the digestive system [30–33]. 2) As described in a previous study on colorectal cancer, *Fusobacterium nucleatum* colonizes and functions in the colorectal tract by the blood cycling route. Oral microorganisms, especially pathogenic bacteria of periodontitis, can enter the systemic circulation through the periodontal blood, thereby acting on the whole body [34]. 3) The metabolites of oral microbiota enter the bloodstream and the systemic circulation, so that the human body is in a low-grade inflammatory state. The development of various chronic diseases of the digestive system is then promoted. Although this approach is currently not supported by direct evidence from oral microbiological studies, it has been confirmed in studies on gut microbiota imbalance leading to systemic disease. Therefore, this pathway may also be an important way for oral microbiota to act on digestive diseases [35–37] (Fig. 1).

P. gingivalis is an important bacterium that can be transferred from the mouth to gut in many diseases, including colon cancer, IBD, and diabetes. This microorganism induces dysbiosis by impairing innate host defenses while promoting inflammatory responses in phagocytic cells. This microbe can disrupt the interaction between host microbiota and mucosa by modulating the innate immune system and signaling pathway. *P. gingivalis* can target the complement C5a receptor 1 (C5aR1) [38] and Toll-like receptor 2 [39]. *P. gingivalis* can target these two receptors to activate the PI3K signaling pathway, which blocks phagocytosis and promotes inflammation.

P. gingivalis can lead to inflammation by secreting SerB in cells. SerB, a serine phosphatase, specifically dephosphorylates the p65 NF-κB homodimer, which inhibits the formation and nuclear translocation of NF-κB-p65 homodimers. Transcription of the IL8 gene is reduced, and the IL-8 neutrophil gradient is disrupted during this process. This action will contribute to the cyclical nature of periodontal tissue destruction [40] (Fig. 2).

4. Oral microbiota impacts body health by digesting food

Oral microbiota can influence body health through digesting certain types of food. Other factors include food patterns (vegetarian or not) and food extracts (like red wine). Here, we show how diet patterns and food extracts can affect body health.

4.1. Diet pattern

Diet pattern is an important factor that influences oral microbiota. Different diet patterns exist in society, such as vegetarian, western, and hunter-gatherers. Researchers have attempted to investigate the impact of different diet strategies on oral health and physiology, especially for oral microbiota. Researchers showed major differences among hunter-gatherers, traditional farmers, western diet, and vegetarians in terms of oral microbiota.

Through 16 s short-gun sequencing of salivary DNA, sufficient evidence has shown that abundance ratios of core species are significantly correlated with diet pattern. The abundance of *Neisseria* and *Haemophilus* is different between hunter-gatherers and westerners, and traditional farmers fall in between. Some oral pathogens have been found in hunter-gatherers, which show that eating too much meat carries a high risk for oral diseases. For vegetarians, the oral microbiota's composition is altered significantly at all taxonomic levels, including oral pathogens (*Neisseria* and *Haemophilus*) and respiratory tract microbes (*Campylobacter* and *Porphyromonas*) [42].

The oral microbiota's function is also changed by diet patterns. Gene function analysis demonstrated that the adaptation from hunter-gatherer to western diets may be vitamin B5 autotrophy and urease-mediated pH regulation [41,42].

4.2. Food extract

Many types of food can improve oral health, such as mushrooms and celery. However, research on how food extracts play a relevant role in improving oral flora remains limited. We selected polyphenols and catechins in food to determine how oral microbiota can improve health by digesting food. Oral microbiota can also damage oral health, such as chewing betel nut.

Many reports have shown that the consumption of green tea or purified catechins can prevent oral cancers. Researchers measured the oral microbiota of tobacco smokers before and after drinking green tea, and these smokers were at high risk for oral cancer. The sequencing results showed obvious shifts in the relative abundance of *Streptococcus* and *Staphylococcus* after green tea intake, which proved that tea can change oral microbiota and affect carcinogenesis [43].

Polyphenol is a common food extract found in grapes, cherry, red wine, and apple. Polyphenol metabolism starts in the oral cavity, but how it influences oral microbiota is unknown. Recently, alcohol polyphenols have been found to exert an antibacterial effect on oral pathogenic bacteria (such as *S. mutans*), which can inhibit the adhesion of pathogenic bacteria and biofilm formation. Some special structures can inhibit the virulence factors of *Streptococcus*. In addition, alcohol polyphenols can inhibit the host inflammatory response caused by periodontal pathogens. Thus, polyphenols are good candidates as natural therapy against oral pathogens [44].

The use of tobacco, alcohol, and areca nut is associated with oral cancer. Researchers have sequenced salivary microbiota to evaluate the influence of chewing betel nut. Bacterial diversity was found to be reduced among areca nut chewers. Betel nut chewers exhibited an increasing ratio of *Actinomyces* and *Streptococcus* and reduced relative abundance of *Parascardovia*. Thus, oral microbiota may negatively influence body health upon digesting specific food [41].

5. Oral microbiota and oral diseases

Oral microbiota can produce metabolites in the mouth, which can affect the development of a range of oral diseases.

5.1. Caries

Dental caries is the most common chronic infectious diseases in the oral cavity [45]. Bacteria are the main pathogens, and symptoms include hard tissue destruction of the teeth [46,47]. The incidence rate of dental caries is high, and the disease range is wide, occurring at any age period of humans. Dental caries has a higher incidence in children than in adults, and it is closely related to oral microbiota. A previous study found that a high frequency of eating sweets before going to bed is a risk factor for dental caries among Chinese children [48]. The latest sequencing technology determined that *Prevotella* spp., *Lactobacillus* spp., *Dialister* spp., and *Filifactor*

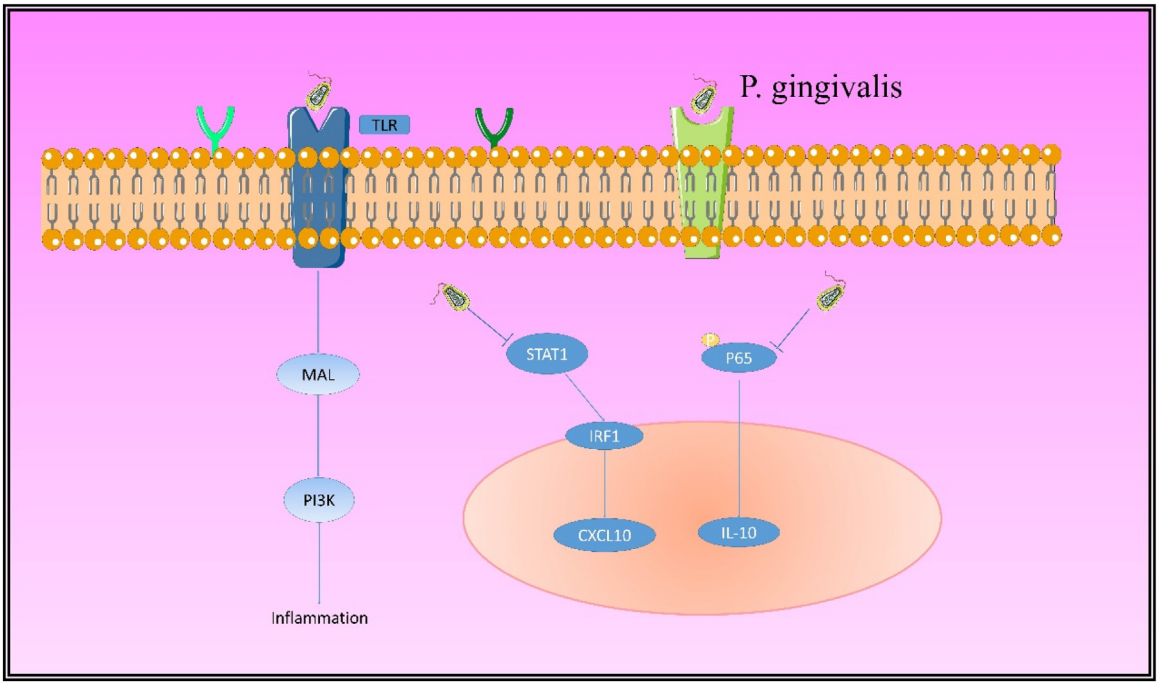

Fig. 2. Mechanism of *P. gingivalis* regulating inflammation in cells.

spp. may be involved in the pathogenesis and progression of dental caries. Compared with healthy individuals, the oral microbiota on the surface of dental caries presents increased complexity and decreased diversity, possibly due to the acidic environment. These characteristics are manifested in the salivary microbiota, which display an increase in *S. acidophilus* in dental caries. When people do not eat, the bacteria obtain nutrients from our saliva and gingival crevicular fluid, which are rich in glycoproteins [49]. These glycoproteins are broken down by bacteria into sugars and proteins. Bacteria can gain energy to survive by metabolizing these sugars and proteins. During metabolism, sugars and proteins are broken down by bacteria into acidic or basic small molecules. These acidic and basic small molecules neutralize each other when the host is not eating, leaving the mouth in a neutral state. However, when sugar or starch is ingested, acid-producing bacteria will prevail. Weak acid production will begin to corrode the teeth. In general, the speed at which teeth are corroded is comparable with the speed at which teeth are regenerated. However, if the sugar or starch in the mouth is not cleaned up in time, then the corroding rate will

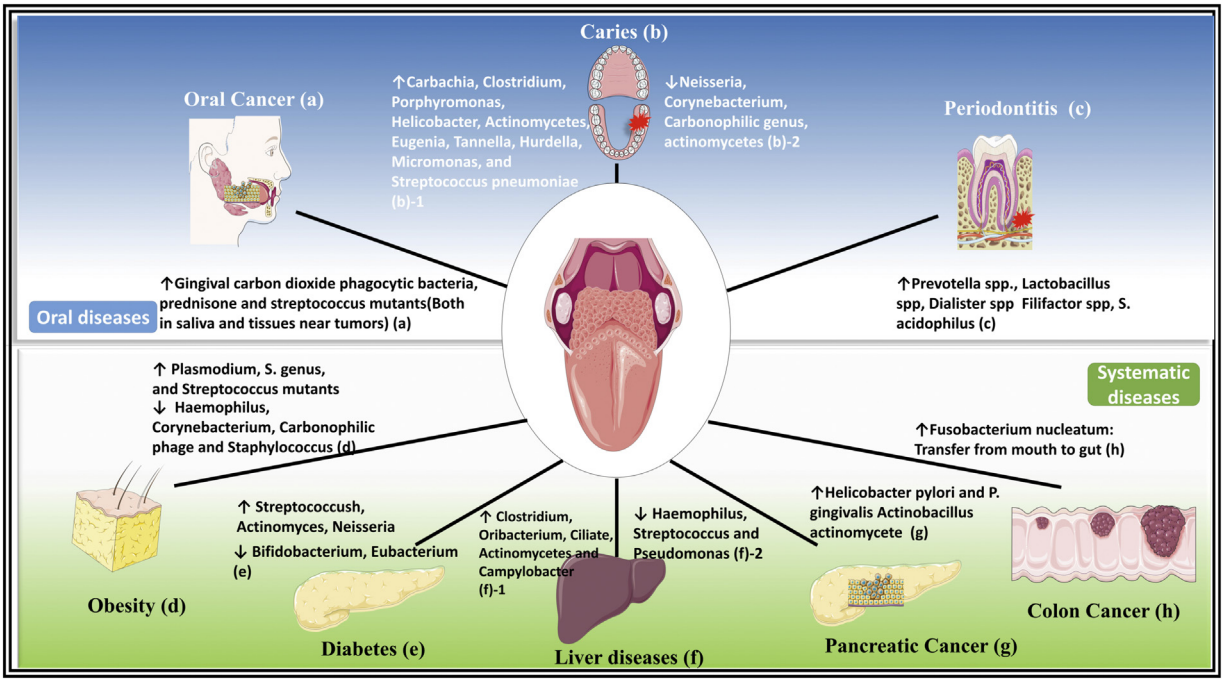

Fig. 3. Oral microbiota is related to oral and systematic diseases. Oral microbiota is altered during oral and whole body diseases. Thus, oral microbiota will be a new target for treating oral diseases and improving the body's physical state.

be higher than the speed at which the teeth repair themselves, so caries will occur.

5.2. Periodontitis

Chronic periodontitis is a common type of chronic periodontal disease with a wide age range, and it spreads from gingivitis to deep periodontal tissues. Dental plaque bacteria are the main factors of periodontal disease. Plaque includes plaque and subgingival plaque, which is a micro-ecological system with bacteria on the tooth surface or periodontal pocket. The interactions between host and microbiota determine the manner, severity, and rate of progression of the disease [50]. Therefore, the pathogen characteristics and microbiota distribution of periodontal disease are critical. Periodontal disease causes destruction of periodontal tissues (dental support tissues such as gums and alveolar bone) and constitutes a potential risk factor for certain systemic diseases. The mouth is highly suitable for microbial survival, which provides good conditions for the growth of microorganisms. The latest study found relatively high levels of *F. nucleatum* in the saliva of patients with periodontitis. The relative abundance of the genera *Carbachia*, *Clostridium*, *Porphyromonas*, *Helicobacter*, *Actinomycetes*, *Eugenia*, *Tannella*, *Hurdella*, *Micromonas*, and *Streptococcus pneumoniae* in oral microbiota of patients with periodontitis is significantly higher than that of healthy people. By contrast, *Neisseria*, *Corynebacterium*, *Carbonophilic*, and *Actinomycetes* in oral microbiota of patients with periodontitis is lower than that in healthy people. Changes in oral microbial composition in patients with periodontitis further induce alterations in community functional gene structure and gene expression lineage [51,52].

A study on the pathogenesis of periodontitis was recently conducted. Researchers found an increase in memory Th17 cells in the oral tissues near the gums of patients with periodontitis. Similarly, in the mouse model of periodontitis, Th17 cells in local inflammatory lesions also increased significantly. Unlike oral Th17 cells that are independent of IL-6 and independent of oral microbiota, the increase in periodontitis-associated Th17 cells is dependent on the imbalance of the oral microbiota and dependent on IL-6 and IL-23. Accumulation of Th17 cells and related neutrophils is essential for inflammatory tissue damage in a mouse model of periodontitis, and inhibition of Th17 cell differentiation can alleviate inflammation. Therefore, oral microbiota imbalance leads to increased local Th17 cells to promote periodontitis [53].

5.3. Oral cancer

Oral cancer is a general term for malignant tumors that occur in the mouth, and most of them belong to squamous cell carcinoma, the so-called mucosal variation. In clinical practice, oral cancer includes gingival cancer, tongue cancer, soft and hard sputum cancer, jaw cancer, oral cancer, oropharyngeal cancer, salivary gland cancer, lip cancer, maxillary sinus cancer, and cancer occurring in the facial mucosa [54]. Oral cancer is one of the most common malignant tumors of the head and neck. Genetic background, bacteria, and living habits all affect the development of oral cancer. Recent research indicated a correlation between oral microbiota and oral cancer. Specific microorganisms exist on the surface of oral cancer and in cancer tissues, and their composition is significantly different from that of normal mucosal microorganisms. Gingival carbon dioxide phagocytic bacteria, prednisone, and *S. mutans* in the saliva of patients with oral squamous cell carcinoma significantly increase. These three bacteria have potential value as diagnostic indicators for oral squamous cell carcinoma [55].

6. Regulation of oral microbiota on systematic diseases

Oral microbiota regulate oral diseases and systemic diseases such as metabolic diseases. The following sections describes how oral microbiota affects systemic diseases (Fig. 3).

6.1. Diabetes

Type 2 diabetes has become one of the most common chronic systemic diseases. It is mainly characterized by persistent hyperglycemia and disordered glucose, fat, and protein metabolism. Incidence rates around the world are constantly increasing, causing serious medical, social, and economic problems. Many studies have confirmed that the oral diseases (e.g., caries, periodontal disease, mucosa diseases) and type 2 diabetes is closely related. They play a role as mutual feedback. In the process of their interaction, oral microbiota is closely related to oral and systemic health and disease. In addition to its own symptoms, oral symptoms, such as loss of alveolar bone and loss of teeth, have become a complication of diabetes. A study has examined the relationship between diabetes and oral microbiota. Researchers conducted an in-depth study of the oral microbiota in the diabetic environment and its effects on the oral cavity by Illumina2 generation sequencing technology. The study revealed that oral microbiota is an important way for diabetes to cause complications. Oral microbiota is an important factor in the development of diabetes, and it affects oral bone development. When the oral mucosa is supplemented with antibodies of inflammatory factor IL-17, the composition of the oral microbiota of patients with diabetes will improve. Loss of alveolar bone will also greatly improve. Researchers have observed significant differences in oral microbiota between patients with type 2 diabetes and non-diabetic patients, such as TM7, *Aggregatibacter*, *Neisseria*, *Mycobacterium*, and *Eikenella*; moreover, the percentage of *Selenomonas*, *Actinomyces*, *Capnocytophaga*, *Fusobacterium*, *Veillon*, and *Streptococcus* have highly increased. Recently, researchers provided a mechanism for the improved understanding of how diabetes increases the risk and severity of tooth loss. Diabetes causes changes in oral bacterial composition, and the oral microbiota of diabetic mice is found to be more pathogenic by transplanting to germ-free mice [56,57].

6.2. Obesity

Obesity is a health problem that plagues the world. Many reports have described the relationship between gut microbiota and obesity, but whether oral microbiota and obesity are related remains unclear. Recently, 33 adult obese people and 29 healthy adults with normal weight were selected to identify the composition of oral microbiota. The study found that oral microbiota in the obese group was significantly different from that in the normal group, and the bacterial diversity and abundance of oral microbiota in the periodontal healthy obese people were significantly reduced. In the oral microbiota of obese people, the abundance of *Plasmodium*, *S. genus*, and *S. mutans* significantly increased, whereas the abundance of *Haemophilus*, *Corynebacterium*, carbonophilic phage, and *Staphylococcus* significantly decreased. The environmental adaptability of the oral microbiota of obese people and the biodegradability of exogenous substances were low, and they exhibited notable immune disease characteristics. To date, researchers have only found that the oral microbiota of obese people has changed, but the mechanism underlying such a change needs further research in the future [58].

6.3. Liver diseases

The imbalance of gut microbiota is one of the important factors that promote the development of liver disease. However, recent studies have found that both gut microbiota and the imbalance of oral microbiota are closely related to liver disease. Previous work found a significant difference in the oral (lingual) microbiota of patients with liver cancer and healthy people. The diversity of oral microbiota in patients with liver cancer was higher than that of healthy people, and the composition of the microbiota in patients with liver cancer was also significantly different from that of healthy people. Among them, *Clostridium*, *Oribacterium*, *Ciliate*, *Actinomycetes*, and *Campylobacter* have high abundance, whereas *Haemophilus*, *Streptococcus*, and *Pseudomonas* have low abundance. *Clostridium* and *Oribacterium* are biomarkers that can distinguish between patients with liver cancer and healthy people, as well as assist in the diagnosis of liver cancer without operation. Similar to patients with liver cancer, patients with cirrhosis exhibit an imbalance of oral microbiota, reduced abundance of oral symbiotic bacteria, and increased abundance of potential pathogenic bacteria (e.g., *Enterobacteriaceae* and *Enterococcus*). Researchers compared the gut microbiota of patients with cirrhosis and healthy people, and they found that the intestinal microbiota of patients with cirrhosis is enriched with a large number of oral-derived microorganisms, including *Weirong*, *Streptococcus*, and *Pasteurella genus*, *Haemophilus*, *Lactobacillus*, and *Clostridium*. These researchers speculated that oral microbes invade gut microbiota of patients with cirrhosis. Animal experiments have shown that *P. gingivalis* invades the intestinal tract, changes the gut microbiota's composition, increases intestinal mucosal permeability and insulin resistance, and causes gut's bacteria to spread to the liver, thereby causing an increase in triglyceride levels in liver tissue; these changes confirmed the ability of oral microbes to invade the gut [59,60].

6.4. Colon cancer

Previous reports have shown that gut microbiota and colorectal cancer are closely related, and the oral microbiota has been demonstrated to be closely related to colorectal cancer as well. *F. nucleatum* in the oral cavity can transfer to other parts of the body through blood cycling as the whole body's immunity declines, leading to local inflammation and indirectly promoting tumor formation.

The bacterium can be isolated from colorectal cancer tissues, and the risk of colorectal cancer is high in patients with the bacterium. *F. nucleatum* is a Gram-negative obligate anaerobic bacterium, and several studies have isolated *F. nucleatum* from colorectal cancer tissues. Patients with high abundance of *F. nucleatum* have a high risk for colorectal cancer [61]. Therefore, the number of this bacteria can be used as a potential marker for colorectal cancer. *F. nucleatum* can directly act on host cells and adhere to normal cells and E-cadherin of cancerous epithelial cells via FadA, thereby activating β-catenin-regulated transcriptional pathway and leading to increased expression of cancer marker genes. These genes then promote cancer. *F. nucleatum* can also mediate the entry of non-invasive bacteria (such as *Streptococcus* and *Campylobacter*) into cells, leading to the occurrence of local microenvironment inflammation, which indirectly promotes the occurrence and development of tumors. Studies have found that *F. nucleatum* can be transferred from the mother's mouth to fetal tissue and cause fetal death. Thus, *F. nucleatum* in the mouth can be transferred to other parts of the body. Flynn et al. found that the biofilm component of the colonic mucosa of patients with colorectal cancer is consistent with its periodontal biofilm component. However, *F. nucleatum* was not detected in the stool of patients with colorectal cancer, and the stool was only enriched in cancer and adjacent tissues. Therefore, *F. nucleatum* may not move from the oral cavity to the colorectal tumor through the digestive tract. The specific mechanism underlying its movement is unclear, but it may involve transient bacteremia in the bloodstream and then transfer to the colorectal tumor [62].

6.5. Pancreatic cancer

Pancreatic cancer is a cancer with a high mortality rate and is the fourth most common cancer to death. The etiology of pancreatic cancer is unclear. The prevalent risk factors for pancreatic cancer are genetic factors, smoking, and obesity. A close relationship exists between the imbalance of oral microbiota and the occurrence and development of pancreatic cancer. *Helicobacter pylori* and *P. gingivalis* in the oral microbiota are closely related to pancreatic cancer. A previous study compared the oral microbiota of 361 patients with pancreatic cancer and 371 patients with non-pancreatic cancer. Their results showed that the detection rate of *P. gingivalis* and *Actinobacillus actinomycete* in the oral cavity of patients with pancreatic cancer is high. Therefore, the presence of *P. gingivalis* in the patient's mouth suggests a high risk of pancreatic cancer. *P. gingivalis* can promote the occurrence and development of tumors in various ways. In animal models, *P. gingivalis* has been shown to evade host immune activation both in vivo and in vitro. *P. gingivalis* can bind to Toll-like receptors 2 and 4, activate the NF-κB pathway, induce the expression of cytokines (such as tumor necrosis factor, IL-1α, IL-6, and IL-8), and form an inflammation microenvironment, thereby promoting tumorigenesis [63]. Epidemiological investigations have found a positive association between *H. pylori* and pancreatic cancer. Patients with seropositive *H. pylori* have a high risk of pancreatic cancer (i.e., 38%), thereby suggesting that *H. pylori* may play a key role in the development of pancreatic cancer. Pancreatic cancer is positively associated with gastric ulcer. *H. pylori* can cause gastric ulcers, which can lead to lowered acid production and elevated levels of individual nitrosamines, causing increased risk of pancreatic cancer. At the same time, the low acidity caused by gastric ulcers allows the colonization of other bacteria, providing opportunities for oral bacteria to move to the digestive tract [64].

6.6. RA

RA is a systematic autoimmune disease caused by chronic inflammation. Periodontal disease and RA are similar in terms of the pathogenic mechanism, such as inflammation and bone loss. Periodontitis is observed in patients with RA. An increasing number of studies showed that periodontitis can activate RA by producing some important enzymes that enhance self-antigenicity to initiate an autoimmune response. Arthritis in mice has been found to promote alveolar bone loss. Treatment with oral antiseptics can protect against RA-induced bone loss. RA will activate the inflammatory response in the periodontium and transform into chronic systemic inflammation, which upregulates levels of inflammatory cytokines (such as IL-6, IL-1, and IL-17) in oral tissues [65,66].

RA has been found to change the oral microbiota both qualitatively and quantitatively in animal studies and clinical trials. RA exhibits high levels of *Parvimonas micra* and *Selenomonas noxia* in mice. However, in human clinical trials, the oral microbiota of patients with RA is enriched with anaerobic species such as *Lactobacillus salivarius*, *Atopobium*, *Leptotrichia*, *Prevotella*, and *Cryptobacterium curtum* but presents reduced levels of *Corynebacterium* and *Streptococcus*. Patients with RA and without periodontitis exhibit enriched levels of periodontitis-associated bacteria, such as *Prevotella* [67].

7. Conclusion and future perspective

In this review, we explored how oral microbiota affects human health. We started with the definition of oral microbiota and then explored how the oral microbiota acts on the gut microbiota. Results showed that the oral microbiota can affect oral diseases and affect the health of the whole body.

In the future, we can improve oral health by altering the oral microbiota through developing oral probiotics and enhancing body health. For example, xylitol chewing gum can reduce the load of bacteria in the oral cavity of a subject and improve oral micro-ecology homeostasis [68].

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