

Interrelation Between Oral Microbiota & Oral Pathology

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Abstract

The human microbiome plays a significant role in oral health. Oral health is result of mutualistic interaction between different inter and intra species in host. The microbiota plays an important role in human health from entraining immune system development and maintaining homeostasis to influencing autoimmune diseases and allergies.

Key-words: Microbiota; Oral diseases; Dysbiosis; Candidate Phyla Radiation.

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Introduction

Over the last decade, our understanding of the composition and functions of the human microbiota has increased exponentially¹. Moreover, there is good evidence that humans have evolved to coordinate to ensure its survival in a microbially dominated world. Humans are biological units that include numerous microbial symbionts and their genomes, together with our symbiotic microbial residents, humans form holobiont²⁻⁴. The collective microbial genome in human body encodes 500 times more genes than the human genome. Human oral cavity harbour immensely diverse active microbial communities. The oral microbiome can be seen as a group of diverse microbial biofilms⁵. The microbiota plays an important role in human health from entraining immune system development and maintaining homeostasis to influencing autoimmune diseases and allergies. Microbiome and host relationship is dynamic, influenced by lifestyle, diet, tobacco consumption and stress. To address this divergence and maintain a harmonious state to protect health and prevent disease, we must not focus on the host and its residents as separate units, but instead consider the holobiont as one. Oral cavity not only harbours enormously diverse bacterial species, but also is home to a multitude of bacteria as well as fungi, viruses and newly discovered candidate phyla radiation^{6,7}. Throughout human evolution during industrial revolution and modern era, environment has continuously shaped the composition of our microbiome. Alteration in harmonious state of oral microbiota (dysbiosis) leads to various diseases including caries, periodontitis, endodontic infections, alveolar osteitis, tonsillitis and oral cancer². Influence of oral microbiota on health requires holistic view. Oral community interactions need to be studied to understand the mechanism of ecology of holobiont.

Bacteria

The bacterial community of oral cavity is dominated by the phyla Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, Spirochaetes and Fusobacteria which account

for 96% of species detected and less frequently Prevotella, Veillonella, Neisseria, and Haemophilus^{8,9}. Dental plaque exists in a relatively stable microbial homeostasis. Microbial dysbiosis is triggered by environmental or host factors, such as excessive sugar intake in the case of caries, or the inflammatory response to oral plaque¹⁰. Subsequently, the bacterial population within dental plaque shifts toward a more pathological community. For example *S. mutans*, lactobacilli, members of the genera Bifido bacterium, Propioni bacterium and Scardovia are fundamental players in caries and periodontitis oral pathologies. On contrary, however, there is evidence that oral streptococci play important roles in protecting against dental caries and periodontitis^{11,12}. Studies have shown that many streptococci including *S. sanguinis*, *S. oralis*, *S. gordonii*, and *S. mitis* produce hydrogen peroxide (H₂O₂) which inhibits the growth of other oral bacteria including pathological mutant streptococci. Oral bacterial abundance and variants varies with the oral health and environment. In oral cancer patients, phylum Fusobacteria increases dramatically and Actinobacteria genera is found to be less abundant. Change in oral microbiota not only causes oral cancer but can influence the internal organs as well. Granulicatella adiacens and *S. mitis* have significant variation between chronic pancreatitis patients. Microbial dysbiosis has been implicated in some cancers due to unequal ratio of beneficial symbionts to pathogens. The *J. ignava* has been shown to have strong association with infection of oral squamous cell carcinoma, esophageal cancer with *Treponema denticola*, *Streptococcus mitis*, *Streptococcus anginosus* and *Fusobacterium nucleatum*, another component of the oral microbiome, has been associated with colorectal cancer. The levels of *Streptococcus* and *Rothia* has been reported to be increased oral cavity cancer¹³⁻¹⁶.

Viruses

Although viruses and phages (virome) are the most abundant biological entities, has been understudied compared to the bacterial element. It is now known that healthy humans carry a large diversity of both eukaryotic viruses and

prokaryotic phages⁵. Herpesviridae, Papillomaviridae, and Anelloviridae are among the most common eukaryotic virus families present and are asymptomatic in healthy individuals. Several studies have examined the association of Herpes viruses, such as herpes simplex virus, human cytomegalovirus, and Epstein-Barr virus, with periodontal disease. As in many other microbial communities, phages are thought to play a significant role in shaping the oral microbiome. The lysogenic viruses like, Siphoviridae establishes a dynamic equilibrium associated with host species and also provides a huge opportunity for the transfer of genetic information. Horizontal gene transfer is thought to be responsible for massive diversity of organisms. Recent work has shown that phage-mediated/mobile genetic elements are critical for the spread of antibiotic resistance in the oral cavity¹⁷. Estimation is that 60–70% of known bacterial genomes contain prophages, number of that is likely to increase. These prophages actively participate in shaping the microbiota of human host and its immune system. Lytic viruses, like Myoviridae and Podoviridae rapidly eliminate their bacterial hosts that pass a particular population threshold, preventing outgrowth and dysbiosis. Viruses and Phages shape human oral microbiota by maintaining the proper ratio of good and bad bacteria. There is a high correlation between host health and abundance of lytic or lysogenic viruses⁶.

Fungi

Healthy oral cavity is home to more than 75 genera of fungi. Fungal component of the oral microbiome is not limited to a few species, principally *Candida*; rather it is represented by a large number of diverse fungi, *Cladosporium*, *Aureobasidium*, *Aspergillus* and *Malassezia* spp. are a frequent member of the healthy oral mycobiome. Deciphering the interconnections among fungal species and their relation with other oral flora will give an insight to novel treatments for the prevention of oral pathologies.

Candidate Phyla Radiation

We now know that the oral cavity not only harbours enormously diverse bacterial species, but also is home to a multitude of yet-to-be

cultured ultra-small bacteria belonging to the newly classified 'candidate phyla radiation' (CPR) group. All CPR genomes are small and most lack numerous biosynthetic pathways⁶. The CPR group of bacterial organisms was discovered only recently and changed our perception of the diversity of life in oral microbiota. TM7x was recently isolated from the human oral cavity as an obligate epibiont that lives on the surface of its bacterial host, *Actinomyces odontolyticus* actinosynbacter XH001, representing thus far the only in vitro cultivated and stably maintained member of the CPR group. CPRs mutually with their hosts have considerable impact on oral microbial ecology^{6,19}.

Conclusion

Human oral microbiota comprises not only in of bacteria, but it is the mutualistic interaction between bacteria, viruses, fungi and newly discovered CPRs. Their inter and intra relations defines the hygiene and local immunity of oral cavity.

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