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PERSPECTIVE

Human Pharyngeal Microbiome May Play A Protective Role in Respiratory Tract Infections

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Abstract The human pharyngeal microbiome, which resides at the juncture of digestive and respiratory tracts, may have an active role in the prevention of respiratory tract infections, similar to the actions of the intestinal microbiome against enteric infections. Recent studies have demonstrated that the pharyngeal microbiome comprises an abundance of bacterial species that interacts with the local epithelial and immune cells, and together, they form a unique micro-ecological system. Most of the microbial species in microbiomes are obligate symbionts constantly adapting to their unique surroundings. Indigenous commensal species are capable of both maintaining dominance and evoking host immune responses to eliminate invading species. Temporary damage to the pharyngeal microbiome due to the impaired local epithelia is also considered an important predisposing risk factor for infections. Therefore, reinforcement of microbiome homeostasis to prevent invasion of infection-prone species would provide a novel treatment strategy in addition to antibiotic treatment and vaccination. Hence continued research efforts on evaluating probiotic treatment and developing appropriate procedures are necessary to both prevent and treat respiratory infections.

Introduction

Respiratory tract infections (RTIs) continue to be a leading cause of morbidity and mortality worldwide, despite the emergence of antibiotics. According to a recent report by the World Health Organization (WHO), RTI-related mortality remains high, second only to that of cancers and cardiocerebrovascular diseases (World Health Statistics 2013, www.who.int). RTIs often result from new invasion and abnormal propagation of specific pathogens into airways. Apart from the number and virulence of such invasive pathogens, host defenses also govern the occurrence and severity of infection. Over the past several decades, advancements in the understanding of adaptive immunity — a major protective mechanism against pathogenic infection — have greatly influenced medical practice and are invaluable to the development of effective vaccines against infections by many lethal

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pathogens. In accordance, further elucidation of local mucosal and non-specific immunity is also important for the development of therapies to prevent pathogenic invasion [1]. Recently, increasing lines of evidence have indicated that the human microbiome (complicated bacterial communities residing in specific anatomic sites of the human body, see **Box 1**) is extensively involved in infections and other pathogen-related diseases, and has an important role in the maintenance of overall health [2]. Additionally, probiotic supplementation to restore microbiome balance may be useful as an adjuvant treatment against infections and has therefore gained much attention in current clinical research and practice especially in intestinal infections, because the overall effectiveness of antibiotics continues to decrease due to the emergence of drug-resistant pathogens [3]. We hypothesize that the pharyngeal microbiome, which resides at the juncture of the digestive and respiratory tracts, may share common features with intestinal microbiomes and could serve as a key player in the development of respiratory diseases. Here, we provide our perspective on potentially similar protective roles of the pharyngeal microbiome and discuss the strategy of using probiotics as an adjuvant therapy for treatment of RTIs based on an in-depth review of the current literature.

The pharyngeal microbiome and microecosystem

Complexity of the human pharyngeal microbiome

Hundreds of microbial species inhabit the human nasal, oral and pharyngeal cavities, including 25–40 families of bacteria, archaea, ameba and fungi, according to ample evidence from laboratory cultures [4]. The number of newly discovered species has considerably increased owing to the recent advances in metagenomic (Box 1) research techniques, especially high-throughput sequencing technology, that enable the discovery of non-culturable species [5–7]. In the pharynx, five major bacterial phyla have been identified thus far according to data released by the Human Microbiome Project (HMP): Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria and Fusobacteria (**Figure 1A**).

Box 1 Glossary

Metagenome: A composite of genomes or genes of heterogeneous taxa from a defined environment. Metagenomic analysis is directly performed on samples based on high-throughput sequencing which makes it possible to characterize all microbial compositions, including uncultivable organisms, and to analyze the collective properties of the community as a whole and its microbial interactions *in situ*.

Pangenome: A superset of genes or genomic information of all strains of a species (mainly applicable to bacteria or archaea, which have significantly variable gene contents among strains). Pangenomic analysis delivers a whole picture of species genomic properties in the context of global distribution or evolution.

Microbiome: Species surveyed at different coverages for a microbial community in a defined environment. In recent years, microbial communities within human body have been studied by using metagenomic tools and methodology.

Microecosystem: A system includes the microbial community and its defined environmental components within limited spacing and is organized in general through a network of nutrient exchanges and energy flows. In the human body, the microecosystem includes microbiome, immunity, epithelial lining and other local physiochemical factors (such as pH, temperature and nutrients).

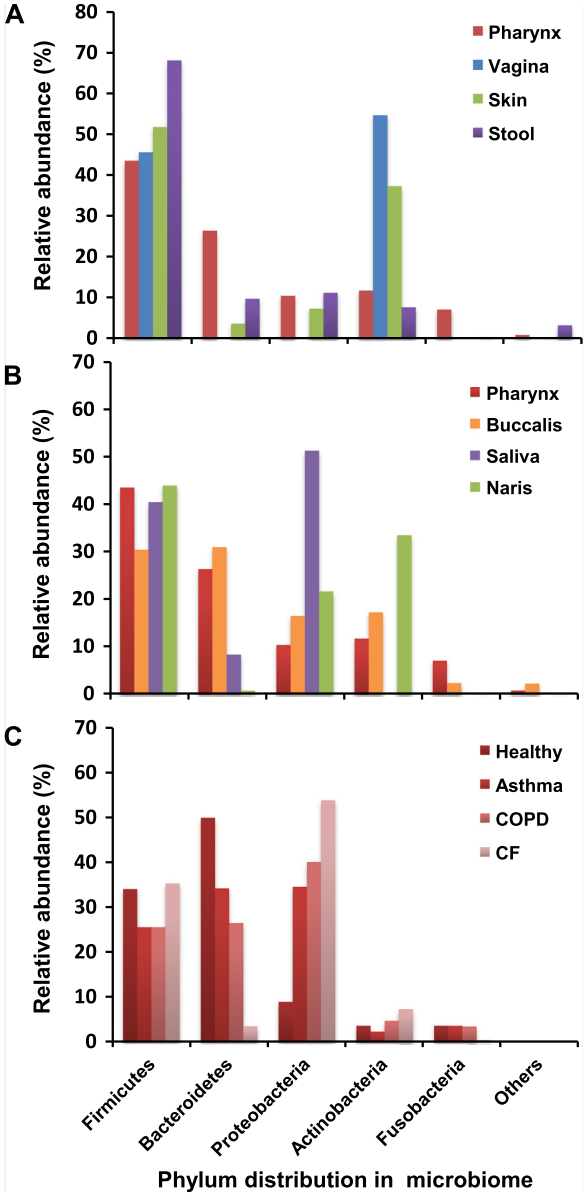

Figure 1 Relative abundance of major phyla in the microbiomes of different sites or conditions in the human body

A. Microbiomes in stool, skin, vagina and pharynx. **B.** Microbiomes in nares, saliva, buccal mucosa and pharynx. **C.** Microbiomes in the lung of healthy individuals and patients with asthma, COPD and CF. Microbial abundances (%) in panels A and B are calculated based on raw data from the Human Microbiome Project (http://hmpdacc.org/HMBSA), whereas microbial abundances (%) in panel C are calculated based on data described previously [8,9]. COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis.

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