Targeting specific bacteria in the oral microbiome

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A lack of tools that kill selected members of the oral microbiome has hampered the ability to study specific roles of bacteria within bacterial communities. Work by Guo et al. shows the potential of antimicrobial peptides as a tool to assess the role of individual species in the microbial community.

The oral microbiome is an extremely complex system harboring over 700 species of bacteria representing at least 13 different phyla [1]. In health, the oral ecosystem maintains microbial homeostasis. However, if homeostasis breaks down due to a substantial change in a parameter that is critical to maintaining ecological stability at a certain site, it may result in the outgrowth of previously minor components of the community, leading to disease [2]. Despite the current wealth of knowledge about the composition of the oral microbiome under different environmental conditions, the nature of the microbial interactions leading to homeostasis or dysbiosis is largely unknown. One of the major challenges to understanding the role of individual organisms in the oral biofilm is the lack of tools that directly target one organism, without also targeting other members in the biofilm. Moreover, conventional treatment of infectious diseases using antibiotics results in the killing of most members of the community, both pathogens and commensal bacteria. The human body contains commensal microflora as an integral part of complex mucosal surfaces, which offers protection against pathogenic organisms. Given the importance of maintaining a healthy microbiome, there is new interest in developing targeted antimicrobial therapies that eliminate a certain pathogen while maintaining the rest of the commensal community intact [3]. Furthermore, overuse of antibiotics has led to the emergence of multidrug resistant microorganisms, and the subsequent and constant demand for new strategies to overcome this problem. Recently, antimicrobial peptides have emerged as an attractive new avenue to treat infectious diseases [4].

A recent study published in the Proceedings of the National Academy of Sciences by Guo et al. [5] is a powerful demonstration of how it is possible to target specific members of the community to manipulate the oral microbiome using newly developed methodologies based on antimicrobial peptides. The same group had previously developed a synthetic peptide (C16G2) that specifically targets Streptococcus mutans [6], a major pathogen in dental caries. In the case of caries, reducing the total bacterial load through the use of broad-spectrum antibacterial agents would reduce caries incidence; however, broad killing of the bacteria alone allows for equal competition between cariogenic bacteria and non-pathogenic organisms to re-establish the biofilms, thus resulting in a lack of long-term protection due to the persistence of cariogenic bacteria within the dental plaque [7]. In this proof of concept manuscript, Guo et al. demonstrated, using an in vitro oral multispecies biofilm, that C16G2 has the potential to be used as a therapeutic agent, selectively killing S. mutans in a short period of time [5].

The targeted antimicrobial peptide consists of two moieties joined together: a nonspecific antimicrobial peptide that acts as the killing moiety and a species-specific binding peptide that binds to a selected organism, facilitating the delivery of the killing moiety to the cell [6]. Thus, by just changing the species-specific binding peptide, we could select for the species we would like to remove from the oral biofilm. The possibility of killing only individual species opens the door to understanding the ecological function of different members of the microbial community. In order to develop novel ways to control plaque composition, there is a critical need to identify the elements that regulate microbial homeostasis present in plaque during health. When perturbed, these elements drive the enrichment of putative oral pathogens, and thus open up novel ways to control plaque composition.

The authors explore not only the potential for clinical application but also the possibility of using peptides in microbial ecology to study microbial homeostasis in the oral microbiome. Guo et al. used a saliva-derived multispecies planktonic cultured microbial community, spiked with S. mutans, to assess the effect of C16G2. The treated communities were allowed to recover for 24 hours at 37°C in anaerobic conditions. What they observed was a community-level impact on composition and abundance by simply removing S. mutans from the community. Other Streptococcus species, including Streptococcus mitis, Streptococcus cristatus, Streptococcus oralis and Streptococcus sanguinis, occupied the opening created by the removal of S. mutans. C16G2 treatment also had a negative effect on the growth of Veillonella spp. [5]; these organisms require lactic acid produced by S. mutans to grow.

The long-term effects of this kind of manipulation are yet unknown, but all the species of streptococci that increased in number after killing S. mutans have been associated with healthy oral microbial communities [8], which suggest that this targeted approach may be more
efficient in shifting the community back to health than using more generic antibiotics.

Building upon Guo et al.’s developments, it is logical to apply this approach to assess the ecological role of other known members of the oral microbiome. It is well established that oral dysbiosis leads to another important inflammatory disease: periodontitis [9]. Its etiology is more complex than caries because periodontitis involves the combined action of the community in the development of disease rather than a single pathogen, making it more difficult to identify the culprits of dysbiosis. Recently, a series of papers proposed the idea of the ‘keystone’ pathogen, showing that Porphyromonas gingivalis, an important periodontopathogen, can modulate the behavior of the dental biofilm even at low-abundance numbers [10]. The use of targeted peptides against P. gingivalis will shed light on its role as ‘keystone’ pathogen once removed from the oral biofilm. Moreover, selective removal of other species will open up the possibility of manipulating the microbiome to our advantage, targeting species whose removal might lead to a healthier community.

References