Modulating the oral microbiome to eliminate a cariogenic pathogen: a Specifically Targeted Antimicrobial Peptide against Streptococcus mutans

Pierre Kyme1, Christopher Kaplan1, Omid Sheikh1, Brian Varnum1, Xuesong He2, and Randal Eckert1

1C3 Jian, Inc., Marina del Rey, CA; 2University of California, Los Angeles, CA

Introduction to the Specifically Targeted Antimicrobial Peptide C16G2

Dental caries is a microbial infection caused primarily by Streptococcus mutans, a cariogenic bacterium that resides within the multi-species microbial flora, which is comprised mostly of benign oral bacterial species. We developed the specifically targeted antimicrobial peptide (STAMP) C16G2 (Figure 1) to have rapid and selective activity against S. mutans and not other bacteria. This selective kill is in contrast to antibiotics or other oral care products with antimicrobial effects, which have an indiscriminate impact on the oral flora. The selective removal of S. mutans could result in protective colonization by the untargeted oral streptococci leading to reduced S. mutans persistence, acid production, and caries formation.

C16G2

Figure 1 – (Left) Schematic and amino acid sequence of C16G2, including the S. mutans-targeting region; (Right) Helical wheel diagram illustrating the amphipathic nature of C16G2 that drives membrane disruption and antimicrobial activity.

In a phase 2 clinical study, subjects received C16G2 formulated in a gel for 7 days. The STAMP was administered in a custom dental tray that was worn for 30 minutes. Microbiology assessments demonstrated a ~90% reduction in salivary S. mutans (Figure 2). This reduction was maintained in the majority of subjects 7 days after the last dose (data not shown), demonstrating durability of response and suggests a possible remodelling of the subjects’ oral microbial community.

C16G2

Figure 2 – Phase 3 subject salivary S. mutans levels (% of baseline CFU/mL) after C16G2 gel (Left) or placebo gel (Right) administration in a custom dental tray (Day 7, last day of dosing).

In the current study, we utilized viable cell plating and pyrosequencing to examine the diversity of a saliva-derived multi-species planktonic culture, spiked with S. mutans JM11 (spectinomycin resistance), after outgrowth post-treatment with C16G2, vehicle (Carrier), or chlorhexidine. The treatment duration was 30 minutes.

Conclusions

C16G2 treatment resulted in selective elimination of S. mutans from a saliva-derived microbial community, followed by an enrichment of non-mutans oral streptococci during outgrowth. These findings confirm the results from a phase 2 clinical trial

Treatment with vehicle (Carrier) or chlorhexidine resulted in S. mutans overgrowth or indiscriminate killing, respectively

Reshaping of a multispecies saliva-derived oral community was achieved through targeted elimination of a cariogenic pathogen by C16G2

References

