Inhibition of oral biofilm and cell-cell communication using natural-products derivatives

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Today during the 43rd Annual Meeting & Exhibition of the American Association for Dental Research, held in conjunction with the 38th Annual Meeting of the Canadian Association for Dental Research, Steve Kasper, SUNY College of Nanoscale Science and Engineering, Albany, will present research titled "Inhibition of Oral Biofilm and Cell-cell Communication Using Natural-products Derivatives."

Many plant metabolites and structurally similar derivatives have been identified as inhibitors of bacterial biofilm formation and quorum sensing (QS). Previously, the researchers of this study demonstrated biofilm and QS inhibition using modified cysteines, similar to those produced by the tropical plant *Petiveria alliacea*. In this study the researchers expanded their compound library to examine structure-activity relationships for biofilm and QS inhibition.

Using a microplate-based screening approach, they observed the biofilm formation by three indigenous oral Gram-positive bacteria: *Streptococcus mutans* UA159, *Streptococcus sanguis* 10556, and *Actinomyces oris* MG1. Bacteria were grown in the presence of inhibitory compounds and analyzed using fluorescent staining for biomass and via confocal microscopy.

Compounds were also tested in a Vibrio harveyi QS reporter which responds to autoinducer-2 (AI-2) signaling (interspecies) but not acyl-

homoserine lactone signaling (intraspecies). Reverse transcriptase real-time PCR and global RNA sequencing (RNAseq) were used to study modified genetic expression in S. mutans UA159 in the presence of select compounds from our library.

From their 46 compound library, six were capable of inhibiting biofilm formation in all three species tested at a concentration of 1mM. All six compounds are structurally similar to S-ribosyl homocysteine, the precursor for autoinducer-2 biosynthesis. These compounds also reduced bioluminescence in V. harveyi BB170, indicating inhibition of AI-2 based QS. Gene expression analysis showed distinct down-regulation of genes previously related to quorum sensing and/or biofilm formation in S. mutans.

The use of plant-inspired cysteine derivatives to inhibit bacterial virulence may serve as a novel tool to improve oral health. The researchers of this study propose that the compounds used in this study may inhibit biofilm formation by interrupting bacterial communication pathways, particularly in AI-2 biosynthetic reactions. Since their library is derived from eukaryotic (plant) origins, this study may provide initial evidence of interkingdom signaling, which has implications for studies of the human microbiome.

More information: This is a summary of abstract #362, "Inhibition of Oral Biofilm and Cell-cell Communication Using Natural-products Derivatives," which will be presented on Thursday, March 20, 2014: 2 p.m. - 3:15 p.m. in Exhibit Hall AB of the Charlotte Convention Center.

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