Researchers’ molecule stops caries in lab rats

By Jeff Hansen, UAB News

University of Alabama at Birmingham researchers have created a small molecule that prevents or impedes tooth cavities in a preclinical model. The inhibitor blocks the function of a key virulence enzyme in an oral bacterium, a molecular sabotage that is akin to throwing a monkey wrench into machinery to jam the gears.

In the presence of the molecule, Strep- tococcus mutans — the prime bacterial cause of dental caries — is unable to make the protective and sticky biofilm that allows it to adhere to the tooth surface, where it eats away tooth enamel by producing lactic acid.

This selective inhibition of the sticky biofilm appears to act specifically against S. mutans, and the inhibitor drastically reduced dental caries in rats fed a caries-promoting diet.

“Our compound is drug-like, non-bactericidal and easy to synthesize, and it exhibits very potent efficacy in vivo,” the researchers explained in an article in Scientific Reports. It is “an excellent candidate that can be developed into therapeutic drugs that prevent and treat dental caries.”

About 2.3 billion people worldwide have dental caries in their permanent teeth, according to a 2015 Global Burden of Disease study. Current practices to prevent cavities, such as mouthwash and tooth brushing, indiscriminately remove oral bacteria through chemical and physical means and have limited success. Caries is the Latin word for rottenness.

“If we have something that can selectively take away the bacteria’s ability to form biofilms, that would be a tremendous advance,” said Sadanandan Velu, PhD., associate professor of chemistry in the UAB College of Arts and Sciences and a lead researcher in the study.

“This is particularly exciting in the broad sense of targeting microbiota using chemical probes tailored to the specific pathogen within a complex microbial community,” said Hui Wu, PhD, professor of pediatric dentistry, UAB School of Dentistry, director of UAB Microbiome Center and a lead investigator in the study.

Wu’s expertise is bacteriology and biochemistry, and Velu’s is structure-based drug design. Their interdisciplinary study also included researchers from the department of microbiology in the UAB School of Medicine.

Research details

The glucan biofilm is made by three S. mutans glucosyltransferase, or Gtf, enzymes. The crystal structure of the GtfC glucosyltransferase is known, and the UAB researchers used that structure to:

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