

Biomarker Discovery Aids in Dental Caries Risk Assessment

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“It’s difficult to believe that in this world of state-of-the-art technology that there’s still no ‘cure’ for dental caries or any definitive way to predict them,” says U.S. Air Force Capt. Jun Kyung Ko, a comprehensive dentist with the Dental Squadron in Yokota, Japan. Dr. Ko is a recent graduate of the two-year Advanced Education in General Dentistry residency at the Air Force Postgraduate Dental School at Joint Base San Antonio, Lackland, TX and a Masters of Science recipient of the Uniformed Services University (USU) Postgraduate Dental College.

Dental caries (or cavities), more commonly known as tooth decay, is one of the most prevalent chronic diseases of people worldwide. Caries can occur throughout life. More than 91% of adults have a history of dental caries.

Remarks Capt. Ko, “Oral health is essential to soldiers on the battlefield, but dental caries continues to be a major threat to warfighter health and readiness. Dental caries can lead to severe oral pain and dysfunction, and can interfere with a service member’s ability to eat, communicate, sleep, and perform assigned duties. The disease remains highly prevalent among military recruits, and it’s crucial to identify and treat it early.”

In a two-year research project collaboration with Dr. Wen Chen—a Leidos research scientist III at the Navy Medical Research Unit-San Antonio (NAMRU-SA), as well as an adjunct associate professor of the Postgraduate Dental College of USU—six peptides were discovered. They were defined as novel antimicrobial peptides and caries-associated saliva native biomarkers using peptidomics and mass spectrometric techniques. Using de novo peptide sequencing technology, Dr. Chen successfully deciphered and identified the full sequences of these six dental caries native peptide biomarkers.

Reports Dr. Chen, “They are all proline-rich antimicrobial peptides (PrAMPs), sizes 27, 21, 21, 19, 14, and 13 amino acids, respectively. None of them has been reported in the literature, and there is no documentation that these native antimicrobial peptides appear in saliva or any tissue or species. Thus, all of them are novel discoveries.”

And what exactly is a biomarker? Well, first of all, it's an abbreviated term for "biological marker," but it's also known as a molecular marker or a signature molecule. A biomarker is a biological molecule found in blood and other body fluids or tissues that is a sign of a normal or abnormal process, or a sign of a condition or disease. A biomarker can indicate that a biological process in the body has happened or is ongoing, or it may be used to identify how well the body responds to a treatment, disease, or condition.

Observes Capt. Ko, "Initially, we had no idea if we were going to find any biomarkers or not. We did wonder if there was anything out there that could be used as a biomarker to distinguish a person with caries who was high risk from a person with low risk. We already know how dental caries start and progress, but we can't really predictably and definitively measure who is more susceptible to getting them."

Capt. Ko collected samples of saliva and plaque from more than sixty caries-free and caries-active patients. The samples were treated for peptidome extraction and analyzed by Dr. Chen using state-of-the-art liquid chromatography-mass spectrometry (LC-MS) instruments housed in NAMRU-SA.

LC-MS technology with peptidomics has been used in the medical community, but not in the dental community. In the study, they first found a total of eight and then twelve biomarkers. Eight of them were in the higher expression level in caries-free saliva. The remaining four were lower expression caries-free saliva.

Of the 12 biomarkers found, Dr. Chen was able to sequence six of them with de novo peptide sequencing technology. "So now we know the exact sequences of these peptides," declares Capt. Ko. "Finding this sequence of unknown peptides takes a lot of manual labor, as well as Dr. Chen's brain. He spent many, many hours of hard work to sequence those six peptides and that's an incredible discovery!"

Their research identified that these biomarkers were actually novel, proline-rich antimicrobial peptides that had never been identified before. These peptides are an innate part of the immune response system that can be found in all classes of life. "They are really special because they can be possibly considered as broad-spectrum antibiotics," proposes Capt. Ko. "We're going to have to do a lot more research and study, but these peptides have the

potential to be therapeutic agents for inflammation, wound repair, or injury requiring angiogenesis. It's exciting stuff."

These novel and native proline-rich antimicrobial peptides have variant and complementary properties (being multicharged, highly basic or acidic, and hydrophobic or hydrophilic) of a perfect antimicrobial peptide. They could also be potential therapeutic agents against multidrug-resistant pathogenic bacteria, as well as be dental caries biomarkers.

Explains Dr. Chen, "These discovered native peptide biomarkers for dental caries have been predicted to have antibacterial properties with bioinformatic tools. We're excited with this discovery because it has key implications in preventive, diagnostic, and therapeutic application in dental caries diseases. Our current achievements provide huge potential for development of novel therapies against dental caries and multidrug resistant bacteria. We will synthesize these novel antimicrobial peptide biomarkers, test their stability in saliva, define their minimum inhibitory concentrations, study wound healing and angiogenesis functions in trauma, assay their anticancer and immunomodulatory features, and analyze their anticaries function in the *Streptococcus mutans* dental biofilm system."

So far, none of this research has appeared in scientific literature. In fact, they'll need more data in order to publish their findings. Dr. Chen and Capt. Ko hope to discover more dental caries biomarkers from ongoing research. Therefore, this study could improve caries risk assessment, preventive management, and effective/sustainable treatment for dental caries, as well as upgrade the oral health and readiness of active duty service members.

"Dr. Chen has a PhD in mass spectrometry and is a subject matter expert," offers Capt. Ko. "He takes care of the technology side of things, whereas I look at the clinical aspects of dental caries. It's a good combination of our skills, as well as a good collaboration between the Navy and the Air Force."

He adds, "I wanted to participate in this study to have some sort of impact. I wanted my efforts to count for something meaningful, and this discovery has more than fulfilled that."

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