

Dental Research Yields Powerful Product In The Fight Against Periodontal Disease

SUNY Stony Brook



A therapeutic use for a well-known family of antibiotic drugs is the basis of a revolutionary treatment. An ingenious series of experiments by dental researchers at SUNY Stony Brook leads to Periostat, which works by inhibiting the human host response to dental plaque.

“ Certain organs in our body — the heart and lungs for example — seem to receive more attention than others when it comes to health and maintenance. Teeth on the other hand, are something that many of us take for granted. It usually isn't until later in life when teeth may become susceptible to chronic problems, and require painful and costly procedures to save them.

Considered a silent condition with few symptoms in its early phases, periodontal disease can sneak up on adults. In too many cases, by the time periodontal disease is diagnosed, it is quite advanced. In the U.S. alone, more than 65 million adults—one out of every three—suffer from periodontal disease, and its escalating incidence makes it the second largest health-care problem after the common cold.

There is no cure for periodontal disease, but a product called Periostat® has proven to be revolutionary in the management and control of this disease. The discovery of Periostat® was the result of a fruitful collaboration that began 30 years ago in a dental research laboratory. At that time, Lorne Golub, D.M.D., M.D. (honorary), Nungavarum Ramamurthy, D.V.M., Ph.D., and Thomas McNamara, Ph.D., of the Department of Oral Biology and Pathology in SUNY Stony Brook's School of Dental Medicine were investigating a specific family of enzymes known to break down collagen, a connective tissue that is a primary component of our bones, skin and teeth.

Bacterial Infection Isn't the Culprit

Before the line of experimentation spearheaded by Golub and colleagues, efforts to combat periodontal disease focused on the bacteria that build up around teeth known as dental plaque. Researchers understood that the body's natural immune response helped fight the plaque-causing bacteria, but a big breakthrough in the field was the discovery that enzymes produced by these immune cells and other human host cells—rather than the bacterial infection—were in fact responsible for the actual breakdown of the gums and bone that support teeth. In other words, it was the body's own host response to the bacteria that was causing the most damage and initiating the destruction of soft tissue and bone in the mouth.

Golub and colleagues began experimenting with ways to inhibit the host derived tissue-destructive enzymes such as collagenase using an already well-known compound: tetracycline. Though tetracycline works as a powerful antibiotic when used at certain doses, the molecule exerts a completely different mode of action when used at lower non-antibiotic levels. The investigators focused on a type of tetracycline called doxycycline and found that it effectively inhibited the activity of the enzymes, classified as matrix metalloproteinases, that break down collagen and gum tissue.

Perhaps most critical was their demonstration that this property of doxycycline occurred at low, non-antibiotic doses and therefore would not create drug-resistant strains of bacteria. They also chemically modified the tetracycline molecule to eliminate the antibiotic activity of the drug and created new compounds called chemically modified tetracyclines, or CMTs, some of which showed enhanced anti-enzyme properties.

The Research Foundation of SUNY went on to file several patents for these discoveries, which represented a new therapeutic use for an old family of drugs. The first product was named Periostat®, and a startup company was launched in 1992 after it purchased the exclusive license for the technology. Under the guidance of its first chief executive officer, Brian Gallagher, CollaGenex Pharmaceuticals Inc., located in Newtown, Pennsylvania, committed itself to developing innovative medical therapies in the dental and dermatology markets.

Gallagher continued to lead the company, taking it public in 1996, and Periostat® received approval from the U.S. Food and Drug Administration approved in October 1998. Today the product remains the only FDA-approved matrix metalloproteinase inhibitor drug and systemic treatment for periodontal disease. "Periostat® is the most successful chronic prescription product ever launched in the dental market," says David Pfeiffer, CollaGenex's senior vice president of sales and marketing. "Before Periostat®, the only prescriptions written by dentists were for short-term analgesics and antibiotics."

Millions Rely on Periostat® for Improved Oral Health

The acceptance of this therapy is reflected in its widespread use by dental clinicians worldwide. To date, more than 4 million prescriptions have been filled for Periostat®. One of the most important features of Periostat® is that it works systemically in patients. Whereas other periodontal therapies are effective only at specific tooth sites, Periostat® is

delivered to all tissues supporting the teeth simultaneously, offering a whole-mouth approach to the treatment of periodontal disease. The product is highly regarded as an adjunct therapy to the conventional, non-surgical standard of periodontal care, mechanical scaling and root planing, which is designed to physically remove bacteria and deposits from tooth surfaces.

The enzyme-suppressing technology behind Periostat® and its systemic effects have led the Stony Brook investigators and others to explore and identify its therapeutic potential in a wide range of medical diseases that share a similar etiology with periodontal disease. Inflammatory diseases characterized by destruction of the body's connective tissues, cardiovascular disease, cancer metastases and diabetes-related complications are some examples where Periostat®-related technology holds the promise of delivering powerful therapies.

Clinicians who prescribe Periostat® say it has changed the way they practice. Maria Emanuel Ryan, D.D.S., Ph.D., professor and director of clinical research in the Department of Oral Biology and Pathology at SUNY Stony Brook, can attest to the change that this technology has meant to her practice. "As a clinician, I now have a new way to manage my patients. By administering Periostat® as a pill twice a day, it amplifies or gives a boost to the response that I can achieve by mechanical scaling and root planning alone," says Ryan. "For a lot of people who may not have responded well to traditional periodontal therapy, we now can achieve a positive response with Periostat® and can better manage their disease, in some cases without any surgery. I find that all modes of therapy, both non-surgical and surgical, have been improved in patients who are taking this medication."

Ryan also has witnessed firsthand the improved quality of life that patients enjoy thanks to Periostat®. "To a lot of patients who didn't have much hope, this treatment gives them the hope that they can better manage this disease and maintain their teeth," she says.

Though periodontal disease has not been considered life-threatening, it recently has been linked to an increased risk for a number of systemic conditions such as heart and respiratory diseases, diabetes and adverse pregnancy outcomes. "There is no known cure for periodontitis — it requires a lot of work to control the disease — and many patients become despondent over this," says Ryan.

"But Periostat® really provides us with another tool to better manage this disease and has spared many patients from needing dentures or implants. In the end, patients always prefer to keep their own teeth."

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