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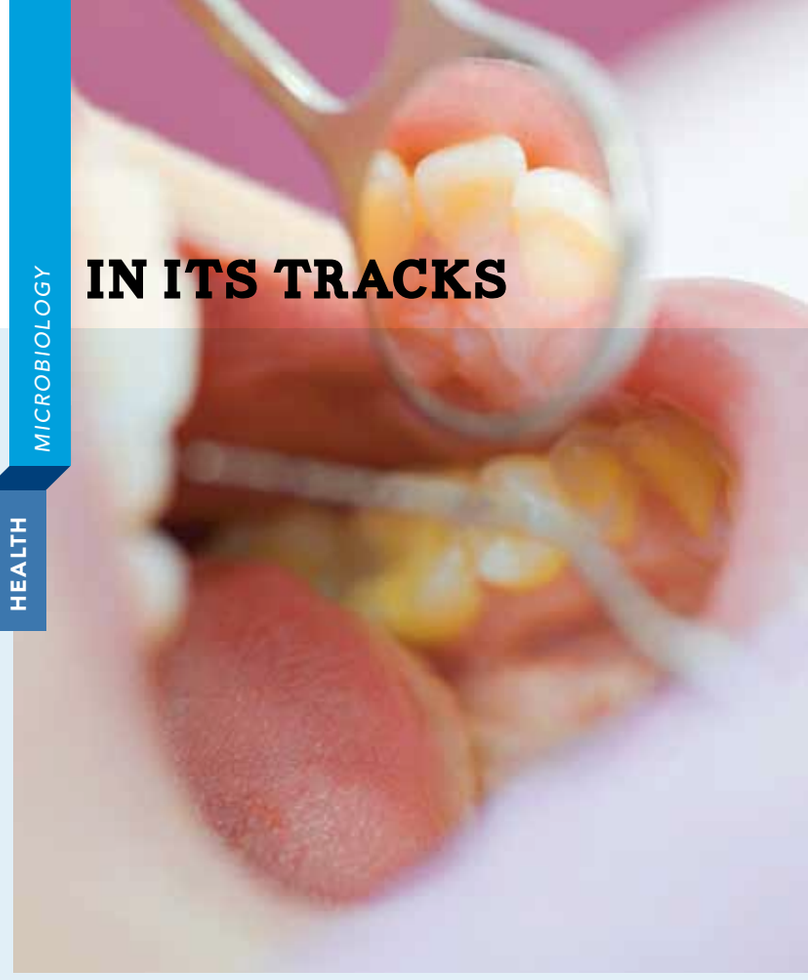
Research at Penn

STOPPING GUM DISEASE IN ITS TRACKS

HEALTH | MICROBIOLOGY



Nearly half of the U.S. adult population suffers from periodontitis, a form of chronic gum disease. Bacteria are responsible, causing inflammation and eventually bone loss, and in the worst cases, even affecting overall health.

A treatment for this prevalent disease could benefit millions of people.

With a recent finding, researchers George Hajishengallis of Penn's School of Dental Medicine and John Lambris of the Perelman School of Medicine, along with other University colleagues, have made a significant stride toward that goal. In a study published in the *Journal of Immunology,* they identified a molecular target that, if blocked, hamstrings the inflammatory activity of gum-disease-causing bacteria. The result can stave off the harmful effects of periodontitis and even reduce problems after it has taken hold of the gum tissue.

The discovery stemmed from work the researchers had previously done on the body's complement system, a component of the immune system that helps eliminate attacking pathogens. Previous investigations showed that *Porphyromonas gingivalis,* the bacterium responsible for many cases of periodontitis, takes over a complement receptor in the host to trigger inflammation and reduce the ability of immune cells to clear infections in the gums. Other lines of research indicated that Toll-like receptors, or TLRs—cellular membrane proteins that spur immune responses—may act in concert with the complement system.

The Penn study, supported by funding from the National Institutes of Health, found that mice bred to lack either a certain TLR or a complement receptor did not develop the bone loss associated with periodontitis. And mice receiving injections of one of two different molecules, designed to activate either the complement receptor or the TLR, triggered substantial inflammation. Given together, the inflammatory response soared even higher than expected.

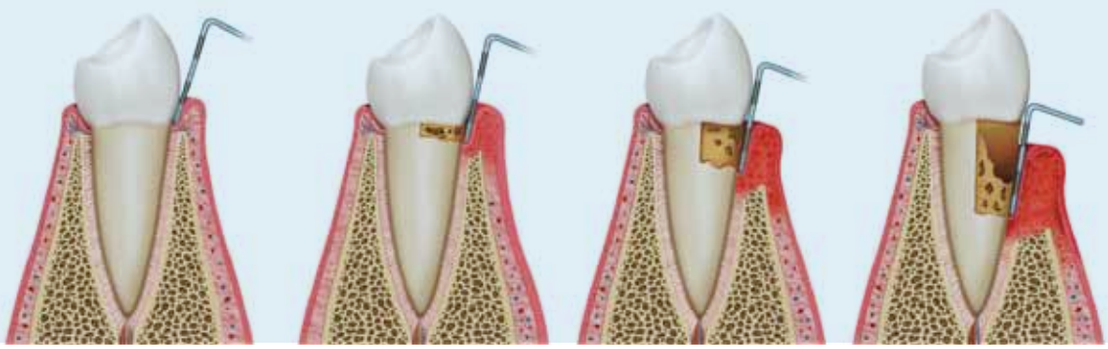
This one-two punch led Hajishengallis and Lambris to wonder whether the two receptors were acting together, and whether blocking only one of these receptors would be sufficient to tamp down the immune response upon which the bacteria capitalized.

The investigators tested a molecule that blocks only the activity of the complement receptor. Mice treated with this molecule after being exposed to *P. gingivalis* had inflammation reduced by 80 percent compared with a control group. They also had no bone loss. The molecule was even effective at reducing inflammation and inhibiting bone loss—lowering both by about 70 percent compared with a control group—when administered after the mice already had gum disease.

"Our results showed that we could inhibit the disease either in a preventive or a therapeutic mode," Hajishengallis says.

The researchers have been awarded grant funding from Penn and other sources to pursue trials of the complement inhibitor in additional model organisms.

"Our data clearly show that complement plays a very important role in periodontal diseases," Lambris says. "Our ultimate goal is to bring complement inhibitors to the clinic to treat these conditions in humans." ■



Bacterial infections in the gums can lead to chronic inflammation and even bone loss, but a drug targeted to a cellular receptor might be able to reverse this damage.