

Periodontitis: Researchers search for a new active substance

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Targeted, efficient and with few side effects: A new method for combating periodontitis could render the use of broad-spectrum antibiotics superfluous. It was developed and tested for the first time by

a team from Martin Luther University Halle-Wittenberg (MLU), the Fraunhofer Institute for Cell Therapy and Immunology IZI and Periotrap Pharmaceuticals GmbH. The aim is to neutralize only bacteria that cause periodontitis while sparing harmless bacteria. The study appeared in the *Journal of Biological Chemistry*.

Periodontitis is a common bacterial inflammation of the gums. According to the World Health Organization WHO Oral Health Study, almost 10 percent of the [global population](#) is affected with a severe form of the disease, which can lead to tooth loss as well as increasing the risk of other diseases, such as Alzheimer's and cardiovascular disease. Until now, treatment has mainly involved the use of broad-spectrum antibiotics that attack all [bacteria](#) in the mouth. However, this has some disadvantages: "One side effect of the treatment is that it also destroys all the harmless or beneficial bacteria in the oral cavity. In addition, the bacteria can ultimately develop resistance to the antibiotics," explains Dr. Mirko Buchholz from Periotrap Pharmaceuticals, who led the new study alongside Professor Milton T. Stubbs, a biotechnologist at MLU.

The researchers therefore looked for a way to eradicate only the harmful bacteria in the mouth. A team from Fraunhofer IZI's Department of Drug Design and Target Validation in Halle developed a test substance that attacks glutaminyl cyclase, a specific [enzyme](#) in the bacteria that plays a special role in metabolism. Inactivation of this enzyme harms the bacteria and, ideally, no periodontitis can develop. To test its effectiveness, the researchers joined forces with the Clinics for Dental Medicine at the University of Bern, Jagiellonian University in Krakow and the University of Louisville in Kentucky (USA). They found that the new substance successfully suppresses the growth of pathogenic bacteria.

The new test substance has a special feature: It only works on the harmful bacteria. "Our target, glutaminyl cyclase, comes in two different variants. Normally, plants and bacteria have one variant of the enzyme

and mammals another. The two variants work in a similar fashion, but they differ significantly in their structure. It's a bit like flat-tip versus Phillips screwdrivers," explains Stubbs. Surprisingly, the bacteria that trigger periodontitis have the mammalian variant of the enzyme. "This is crucial for our approach because it gives us a possible target so we only kill the pathogenic bacteria and leave the harmless ones intact," says Mirko Buchholz. To minimize possible side effects in advance, the team compared the bacterial enzyme with the human variant. "There are small but significant differences between the enzymes," says Stubbs. These differences are probably sufficient for the new substance to not affect the human enzymes. Therefore, only minor [side effects](#) are to be expected.

The researchers' study provides initial evidence that the approach essentially works. It must now be fine-tuned in further studies and tested in subsequent clinical trials. It may therefore take some years before the research from Halle becomes a marketable drug.

More information: Nadine Taudte et al, Mammalian-like type II glutaminyl cyclases in *Porphyromonas gingivalis* and other oral pathogenic bacteria as targets for treatment of periodontitis, *Journal of Biological Chemistry* (2021). [DOI: 10.1016/j.jbc.2021.100263](https://doi.org/10.1016/j.jbc.2021.100263)

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