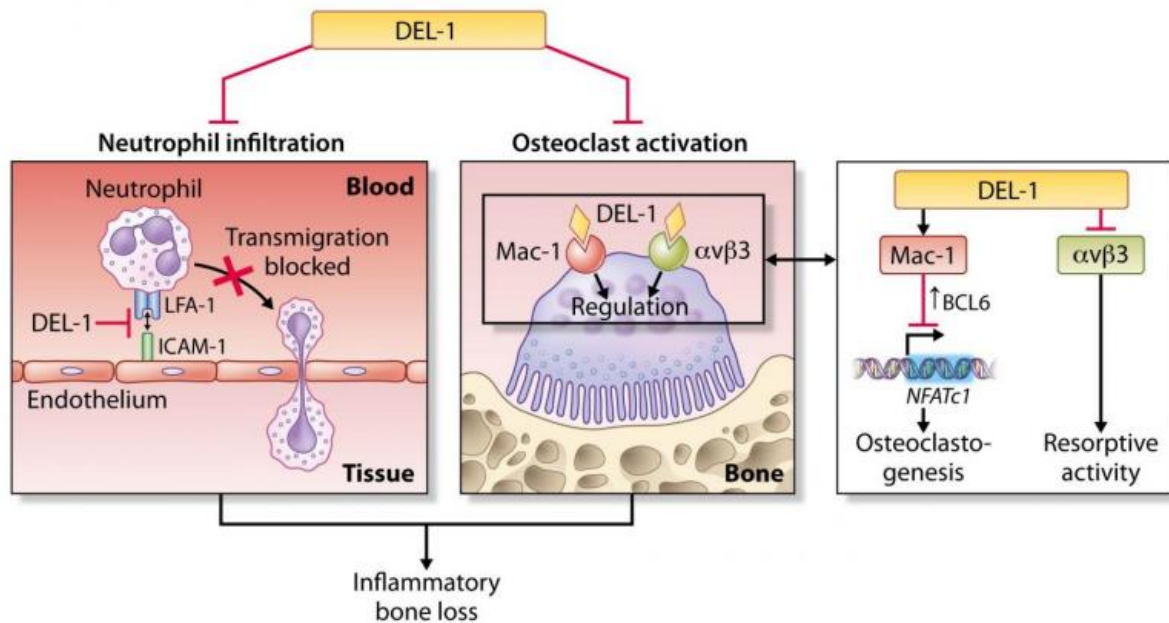


Study blocks inflammatory bone loss in gum disease

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An illustration depicts how the protein Del-1 inhibits both neutrophil movement and osteoclast activity to prevent bone loss in periodontitis, a severe gum disease. Credit: University of Pennsylvania

Periodontitis, a severe form of gum disease, doesn't just cause soft-tissue inflammation and bleeding. It also destroys the bone that supports the teeth. If it progresses unchecked, it can lead to tooth loss and is even associated with systemic inflammatory conditions like atherosclerosis and rheumatoid arthritis.

A new study led by University of Pennsylvania School of Dental Medicine researchers demonstrates that a protein called Del-1, can inhibit bone loss associated with periodontitis. They also found the protein curbs the activity of osteoclasts, cells that absorb [bone tissue](#), leading to a mechanistic explanation of how Del-1 can prevent [periodontal bone loss](#).

The finding paves the way for therapeutic interventions to treat periodontitis and possibly other conditions.

"This is not just important for periodontitis," said George Hajishengallis, senior author on the work and the Thomas W. Evans Centennial Professor in the Department of Microbiology at Penn Dental Medicine. "It could also have implications for other inflammatory diseases where bone loss is involved, like osteoporosis and [rheumatoid arthritis](#)."

Additional Penn Dental Medicine collaborators included co-lead authors Jieun Shin and Tomoki Maekawa, as well as co-authors Toshiharu Abe, Evlambia Hajishengallis, Kavita Hosur and Kalyani Pyaram. The Penn team collaborated with Triantafyllos Chavakis and Ioannis Mitroulis from Germany's Technical University of Dresden.

"The findings underline the therapeutic potential of this endogenous anti-inflammatory factor, Del-1, in further human pathologies where the levels of Del-1 are reduced," Chavakis said.

The paper appears in the journal *Science Translational Medicine*.

Previous studies by Hajishengallis and colleagues have demonstrated the important role that Del-1 plays in inhibiting the movement and accumulation of neutrophils in gum tissue in mice, and they have found a similar mechanism occurs to reduce inflammation in the central nervous system. In both scenarios, Del-1 is able to restrain the

recruitment of neutrophils, which prevents damaging inflammation. The Penn scientists demonstrated that applying Del-1 to the gums can inhibit inflammation and bone loss in a mouse model of periodontitis.

But evidence from those studies also suggested that Del-1's effect on bone loss was not solely due to its inhibition of neutrophil recruitment.

"When we compared Del-1 with a small-molecule inhibitor of neutrophil recruitment side by side, we found that Del-1 was much more effective at inhibiting bone loss," Hajishengallis said. "That suggested to us that Del-1 may have an additional mechanism to inhibit bone loss, perhaps by acting directly on the osteoclasts."

Del-1 is known to be expressed on various soft tissues, such as the gums, brain and lungs, but, to confirm their suspicions that it might also be involved in bone preservation, the research team stained bone tissue for the molecule. They found evidence of Del-1 in the same areas as osteoclast activity, then followed up by generating human and mouse osteoclasts in vitro and found Del-1 mRNA and protein expressed at high levels.

Osteoclasts from mice that lacked Del-1 or from cell lines lacking the protein could be differentiated faster and stronger.

"In fact, Del-1 doesn't block the formation of osteoclasts, but it does put the brakes on the process," Hajishengallis said.

Further experimentation in vitro with human osteoclasts and in vivo in mice identified a portion of the Del-1 protein that was particularly important for containing osteoclast activity, though additional parts of the molecule were needed to have the most potent inhibition of inflammation and bone loss. In further mechanistic experiments using different parts of the protein, the researchers were able to dissociate the

anti-inflammatory action of Del-1 from its anti-osteoclastogenic action.

"Even when we administered Del-1 after the peak recruitment of neutrophils, we were still able to significantly inhibit bone loss," Hajishengallis said.

With this new understanding of how Del-1 can inhibit periodontal bone loss—both by reducing inflammation and by restraining the activity of osteoclasts that resorb bone tissue—the researchers tested it, in a preclinical model of [periodontitis](#) observing that Del-1 significantly reduced [inflammation](#) and tissue damage and that there was significantly less [bone loss](#).

Hajishengallis and colleagues have implicated Del-1 in other inflammatory diseases, including multiple sclerosis, and are beginning to examine its possible involvement in rheumatoid arthritis and osteoporosis. Unlike some drugs used to treat these diseases, Del-1 is a protein that the human body already produces, so administration of a Del-1-based drug would likely be safer than some of the alternatives, especially for local [inflammatory diseases](#).

"I'm convinced that this is a drug that could work in humans," Hajishengallis said.

More information: DEL-1 restrains osteoclastogenesis and inhibits inflammatory bone loss in nonhuman primates, [stm.sciencemag.org/lookup/doi/ ... scitranslmed.aac5380](http://stm.sciencemag.org/lookup/doi/...scitranslmed.aac5380)

Provided by University of Pennsylvania

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