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Bacterial-Cyclic Dinucleotides Regulate Human Osteoclast Differentiation.

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Objectives Bacteria and their virulence factors lead to local inflammatory reactions and activate the immune system that mediates alveolar bone loss, which is a hallmark of periodontitis progression. Cyclic dinucleotides (cyclic di-guanosine monophosphate (c-di-GMP) and cyclic di-adenosine monophosphate (c-di-AMP)) are important secondary signalling molecules, with which bacteria can sense and respond to environmental stress and stimulate the innate immune response. Our previous study showed that cyclic dinucleotides upregulate tumor necrosis factor receptor superfamily member 11B, which plays an essential role in bone metabolism and is a negative regulator of bone resorption, suppressing osteoclast activity in dental mineralized tissue. For that, the current study aims to study the effect of cyclic dinucleotides on the differentiation of human osteoclasts.
Methods Human osteoclast precursors were isolated from bone marrow samples of healthy donors. Osteoclasts precursors seeded in 96 well plates (0,3x10^{6}cells/ well) on Bovine cortical bone slices (Diameter: 6mm, Thickness: 0.4mm) with different concentrations of c-di-GMP and c-di-AMP (1, 10, and 100 µM) for two-time points. After one and two weeks of incubation, the differentiated cells adhering to the bone slices were stained by Tartrate-resistant acid phosphatase activity.
Results At one week of incubation, the highest concentration of c-di-AMP and all tested concentrations of c-di-GMP inhibited osteoclast differentiation. The same result was observed when osteoclast precursors were incubated with all concentrations of either c-di-AMP or c-di-GMP for two weeks.
Conclusions Cyclic dinucleotides exert inhibitory effects on osteoclast differentiation. Understanding this effect will aid in developing molecules that can inhibit bone resorption, which is a promising therapeutic approach to bone destruction in periodontitis.