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Smart/Stimuli-Responsive Antimicrobial System for Soft Tissue Integration

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Objectives Soft-tissue integration is crucial for the long-term success of dental implant rehabilitation. Our preliminary studies validated the drug incorporation method into our layer-by-layer (LbL) system on titanium (Ti) substrate. Here, we developed a stimuli-responsive film onto our LbL system with excellent *in vivo* adhesive capacity to prevent biofilm formation and to improve soft tissue seal on abutment surfaces.

Methods Detailed multilayer coating characterization was performed by different microscopy and spectroscopy approaches to probe physical and chemical properties. The drug-delivery capacity of the LbL system was proven over 15 days. Microbiology experiments were carried out with human saliva to uncover the broad-spectrum of the drug against bacteria involved in implant infection. Additionally, the effect of stimuli-responsive film on cell behavior was evaluated by cells in monolayer and collagen matrix. Finally, the inflammatory response of degradation products and the collagen deposition by fibroblasts into the surrounding tissue, were assessed in a rat subcutaneous implantation model.

Results The stimuli-responsive film instability in acidic environment over time was identified through changes in roughness and wettability values. The antibacterial capacity of stimuli-responsive film was confirmed with a higher concentration of drug released at acidic pH up to 15 days. Quantitative and qualitative assessments demonstrated the non-cytotoxic effect over a sufficient period to measure the hazard potential. *In vivo* experiments revealed the absence of inflammation and confirmed an increase in collagen production in the stimuli-responsive film group compared to Ti.

Conclusions Stimuli-responsive film is a novel dual-function coating that promotes soft tissue seal and preserves antibacterial activity of the LbL system. Conveniently, the film discloses a slight capacity of controlling the drug release under neutral condition. From a clinical point of view, these unique properties enable the stimuli-responsive film on LbL system to be applied as a potential coating to abutment surfaces addressed to patients diagnosed with peri-implant mucositis.