Establishment of a Three-Dimensional In Vitro Peri-Implant Bone-Mucosa Composite Model to Explore Host–Pathogen Dynamics

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Peri-implant health depends on balanced interactions between the implant, surrounding tissues, and oral microbiota. Pathogenic biofilm overgrowth disrupts this balance, leading to peri-implant disease. Conventional 2D models lack this complexity. Here, we developed a 3D in vitro peri-implant model combining soft tissue, bone, and a titanium implant, further integrated with multi-species biofilms to mimic infection and study host–pathogen interactions. As a hard tissue component, osteoblast-seeded HA/TCP scaffolds were combined with peri-implant mucosa to create a 3D in vitro peri-implant bone–mucosa composite model, which was cultivated for 2, 7, and 14 days. Structural integrity, osteoblast viability, and bone ECM characteristics were assessed by histology, live/dead staining, and collagen immunofluorescence. As proof-of-concept for infection simulation, an oral multispecies biofilm was integrated onto the implant within the composite model. Cell viability and osteoblastic phenotype were preserved throughout the study. Microscopic and histological analyses revealed a uniform architecture, with stratified epithelium overlying collagen-embedded human gingival fibroblasts in close contact with the underlying scaffold containing bone cells. When combined with a living multi-species biofilm, the model reproduced the key components characteristic of peri-implant infection. By combining oral soft tissue, hard tissue and a titanium implant in a 3D setup, this model represents an advanced and most complex model for evaluating innovative implant materials and novel treatment strategies as well as studying peri-implant disease progression. Incorporating diverse biofilms further increases its clinical relevance by enabling investigation of pro-inflammatory responses in a combined soft–hard tissue environment.

Index Terms—Bone Model, Oral Mucosa, Hard Tissue, Soft Tissue, 3D In Vitro Model, Organotypic Model, Peri-Implantitis