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Bioengineered Models in Oral Health: From Development to Clinical Applications

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Abstract: Oral bioengineered models have emerged as a leading platform for oral health research because they can closely resemble the structure, biology, and function of native oral tissue. Through the combination of living cells with sophisticated biofabrication technologies and smart biomaterials, these models outperform other model systems, such as conventional 2D *in vitro* cultures and animal models. This article summarizes recent advances in the generation and characterization of bioengineered oral models, as well as their applications in modeling human oral diseases, regenerative dentistry, and biomaterial testing. The actual limitations and forthcoming opportunities towards translational and personalized oral care is also emphasized.

Keywords: Bioengineered models; Oral health; Tissue engineering; Biomaterials; Regenerative dentistry.

Until now, studies on oral health have primarily made use of animal models and cell cultures in two dimensions. The above techniques have greatly furthered scientific understanding but are limited in their ability to recreate the well-organized three-dimensional structure, cellular diversity and mechanical environment of oral tissues. Therefore, bioengineered models have received attention as more physiologically relevant systems for studying oral biology, pathology and therapeutic responses [1].

Successful bioengineered oral model development depends on the unification of appropriate cell sources, biomaterials and fabrication technologies. The most commonly used cells are human oral keratinocytes, gingival fibroblasts, periodontal ligament cells and dental pulp stem cells due to their regenerating capacity and clinical relevance. Scaffolds to mimic the extracellular matrix need to be composed of natural biomaterials (collagen, gelatin, chitosan) or synthetic biodegradable polymers. With the recent progress in 3D bioprinting and microfluidic techniques, it is now possible to achieve better spatial control over cell placement, enhanced cell–cell interaction and fluid flow-based dynamic culture [2].

Stringent characterization is critical for the biological relevance and the reproducibility of bioengineered models. Histological staining and state-of-the-art imaging are used for morphologic identification. Gene and protein expression for tissue-specific markers are examined by molecular analyses. Functional testing includes tests for cell proliferation, differentiation, inflammation and mineralization. It is even more important for the oral tissues because they are exposed to forces produced by mastication [3].

Oral bioengineered models are broadly used for investigating periodontal diseases, dental caries, oral mucosa related pathologies and oral cancer. In regenerative dentistry, such models enable the study of regeneration of dental pulp, periodontal and alveolar

bone. They additionally represent established bases for biomaterials testing, testing of dental implants, drug screening and the development of individualized therapies.

Even with these benefits, bioengineered oral models suffer from production expenses, technical complexity, limited vasculature and are an incomplete immune system representation. The upcoming research will be likely directed toward organ-on-a-chip rights, multi-tissue integration, and the use of artificial intelligence-supported analysis to enhance the translational significance [4].

Bioengineered models are an innovative aspect of oral health research. Rapid progress in biomaterials science, stem cell biology and biofabrication technologies is likely to improve further their predictive potential and medical relevance.

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