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Editorial: Scaffold-free cell-based approaches in biomedicine and biotechnology

Scaffold-free systems in tissue engineering is an emerging subdiscipline with broad applications and significant impact in biomedicine and biotechnology. In this special issue of *Biotechnology Journal*, we highlight several scaffold-free systems with exciting applications in areas such as cell therapies for tissue regeneration [1], in vitro functional tissue and disease models for drug sensitivity testing [2], bioscreening [3], cell-based biosensors [4], and drug delivery [5] (Fig. 1).

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In the absence of scaffolding materials, such as hydrogels, scaffold-free cell-based approaches allow generation of functional tissues, in which cells can survive, grow and recapitulate native tissue characteristics. Deeper understanding of cellular microenvironment has revealed that tissue functionality arises from the synergistic collaboration of multiple factors including cell-extracellular matrix interactions, contact with other cells, biomechanical cues, and biochemical signals. The influential factors on cell fate require significant consideration in developing physiologically relevant cell microenvironments, which establish the groundwork of scaffold-free cell-based systems. A comprehensive comparison of scaffold-free and scaffold-based approaches for cell-based therapies in tissue engineering is presented in this issue by Demirbag et al. [1].

To foster cost-effectiveness and to minimize animal testing in pharmaceutical and cancer research, there is a need for in vitro tissue models, which mimic the microenvironment and the functionality of the native tissues [2]. Scaffold-free cell-based approaches have had a significant impact in functional tissue models, which allow systematic, quantitative investigation and screening of drugs, supporting rapid pharmacokinetic and pharmacodynamic analyses. High-throughput (HT) bioscreening is essential for rapidly evaluating biochemical compound libraries against biological targets, which has been widely used in drug discovery, engineering of new biomaterials, and genomics research over the past few decades. Since throughput is critical in these applications, high-throughput assembly and fabrication technologies with precise compositional and spatial control over cells to establish scaffold-free cell-based platforms are needed, as highlighted by Rodríguez-Dévora et al. [3].

Cells in natural tissues are embedded in a three-dimen-

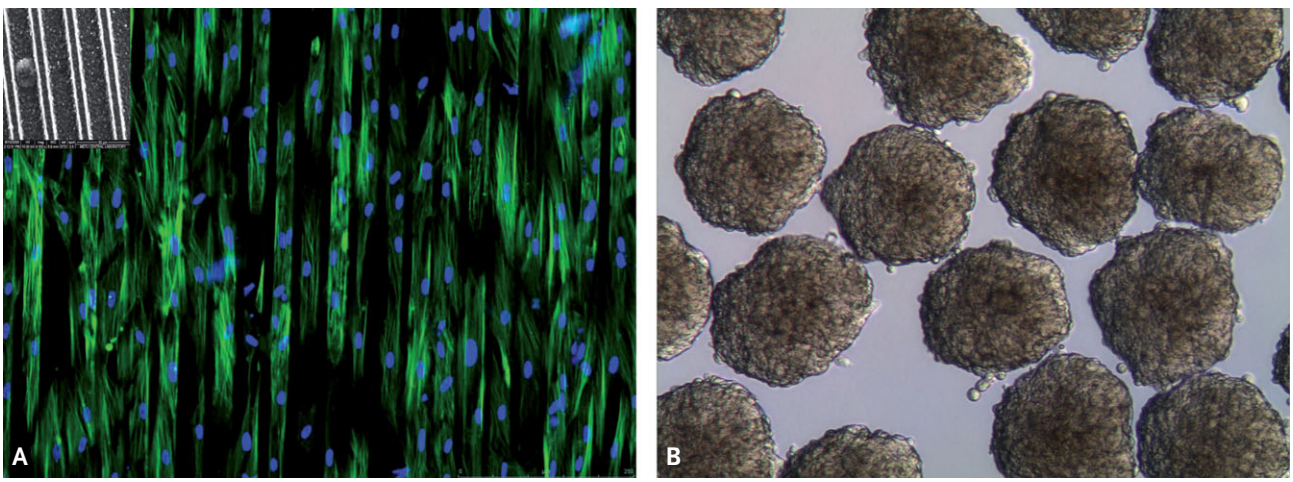

Figure 1. Scaffold-based and scaffold free tissues. (**A**) Wharton Jelly Mesenchymal Cells seeded on biodegradable polymeric films stained for the cytoskeleton and nuclei [1]; (**B**) prostate tumor microtissues [2].


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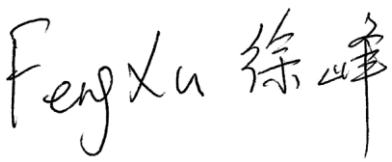
sional (3D) microenvironment. When cultured in a two-dimensional (2D) setting, cells display significant perturbations in gene expression, unlike the cells in native tissues and in 3D culture conditions. These differences between the 2D and 3D culture conditions have been recognized in the cancer research field, which widely employ scaffold-free microtissue models of tumors in vitro. The extensive need for scaffold-free 3D tumor microtissues that effectively mimic the native tumor characteristics has been recognized by Drewitz et al. [2], who present an automated production platform for tumor microtissues in this issue.

Scaffold-free approaches integrated with nano- and microfabrication technologies have generated a synergistic outcome triggering multiple significant applications in biosensors and drug delivery systems. Cell-based biosensors (CBBs) have emerged as promising microfabricated tools in biotechnology as scaffold-free systems, in which various types of cells act as sensing units to detect external stimuli [4]. In a review by Zhou et al. [4], the authors describe the emerging hydrogel-based CBBs via scaffold-free approaches and their applications in areas such as pathogen/toxin detection. On the other hand, in a review by Pan et al. [5], the authors present particulate drug-delivery systems with focus on emerging scaffold-free microfabrication techniques to generate micro-/nanoparticles with a highly controllable architecture.

The guest editors thank all the authors for their contributions and insights in the field, which make this special issue a valuable resource for the readership of *Biotechnology Journal*. We hope that this issue will stimulate future work at the frontiers of scaffold-free systems in biomedicine and biotechnology.



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