Directing tissue morphogenesis via self-assembly of vascular mesenchymal cells

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1. Introduction

Regenerative medicine aims at cell-based therapy to heal or restore tissue function that has become impaired by chronic degeneration or physical damages [1,2]. The reconstruction of tissue function requires the orchestration of its constituent cells, soluble chemical factors, and extracellular matrix into a spatiotemporal pattern. For example, cardiac function requires the cardiac fibers to assemble into layers with specific orientation angles [3]. Similarly, biochemical and detoxification functions of the hepatic lobule require hepatocytes organizing into a radial network for fluidic transportation of the metabolites [4]. Thus, in addition to providing proper cell types for different applications [5,6], the development of tissue/biomaterial with structural features mimicking the specific spatial pattern is also crucial in tissue regeneration.

To date, considerable efforts have been invested into constructing scaffolds that allow cell attachment, migration and delivery of biochemical factors [7]. To reconstruct tissue architectural features in microenvironments, diverse attempts have been made to fabricate the scaffold with specific structure to guide cell spreading [8], assemble layers of cultured cell sheets [9,10], directly deposit cells or move cells to chosen locations [11–13]. However, the structural complexity is limited by the mechanical precision of those approaches. Additionally, cellular self-organization, an essential feature in tissue development that uses mechanisms such as cell migration [14] and cell–cell alignment [15], would also defeat and frustrate such artificial attempts, eventually disorganizing the defined morphology.

In natural development, embryogenesis and wound healing heavily rely on self-organized activities. In this manner, tissue-level