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Bioprinting of Three-Dimensional Multicellular Skin Constructs (G)

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The production of functional skin equivalents derived from human cells holds promise for reconstruction of severe wounds and for modeling various skin pathologies. Although epidermal cells have the capacity to self-organize and form stratified structures in culture, it is often difficult to integrate these structures with dermal components. In recent years, cellular bioprinting has emerged as an efficient strategy for fabricating functional skin equivalents comprising both dermal and epidermal cells. Examples of bioprinting methods used for fabrication of functional skin equivalents include extrusion-based bioprinting, laser-assisted bioprinting, and inkjet printing. Here, we investigated the use of a layer-by-layer lab-on-a-printer technology for generating multi-cellular three-dimensional skin constructs. To efficiently print sheets of cells using this approach, we first examined the performance of several cross-linkable bio-ink formulations (e.g., alginate and chitosan) containing key extracellular matrix proteins hypothesized to improve cell attachment and growth (e.g., collagen I, collagen IV, fibronectin and laminin). Using these bio-inks, we demonstrate bioprinting of cell-laden sheets in various geometries such as squares and disks containing multiple layers of cells. We also demonstrate that it is possible to print cell-laden sheets using various fill patterns including rectilinear, concentric, and a combination of rectilinear and concentric. Furthermore, we demonstrate that it is possible to produce co-culture sheets consisting of dermal and epidermal cells using the lab-on-a-printer approach. Preliminary analysis of cell viability and organization within these bioprinted skin constructs is presented. Future work will optimize this approach to rapidly generate constructs that closely resembled the natural structure of skin.

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