Direct 3D-bioprinting of human functional cardiac tissues

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Biofabrication is a young field with the potential to produce human tissues/organs to replace animal models and for therapeutic use in humans. Heart disease (HD) is the most common cause of death. Despite decades of research, no effective treatment exists to induce functional recovery from HD and no system mirroring the complexity of the human heart is available to reliably predict drug efficacy and cardiotoxicity. Current pre-clinical studies rely on animal models and 2D in vitro human cell culture systems, which showed to have an insufficient predictive value. These model limitations have led to target exhaustion and low chances of drug success in clinical trials. In addition, current engineered cardiac tissues have shown promise to restore heart function in preclinical models. As shape is very important for function, a major aim is to engineer materials that allow to fabricate hierarchically structured tissue constructs, and at the same time, prevent unwanted post-fabrication changes in construct shape. Recently, we developed a method to directly 3D-bioprint human induced pluripotent stem cell (hiPSC)-derived cardiomyocytes embedded in a collagen-hyaluronic acid ink, generating centimeter-sized functional ring- and ventricle-shaped cardiac tissues in an accurate and reproducible manner. The printed tissues contain hiPSC-derived cardiomyocytes with well-organized sarcomeres and exhibit spontaneous and regular contractions, which persist for several months and are able to contract against passive resistance. Importantly, beating frequencies of the printed cardiac tissues can be modulated by pharmacological stimulation. Currently, we work on the integration of chitosan in this system for in vivo applications as it is biocompatible supporting cell adhesion, mimics the extracellular matrix, evokes minimal foreign body response and minimal fibrous encapsulation, and exhibits hemostatic, antibacterial, and antioxidant activities, reducing infection risks in tissue scaffolds. The polycationic nature and reactive groups of chtisoan allow easy modifications and tuning of its degradation. In the future, we will utilize glycol-chitosan as it is soluble in water at physiological pH and cytocompatible. Our approach opens up new possibilities for generating complex functional cardiac tissues as models for advanced drug screening or as tissue grafts for organ repair or replacement.