Research Week 2022

Bone derived bioink for 3D bioprinting

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Keywords

Biomaterials, tissue engineering, regeneration, human bone grafts, extracellular matrix, bioprinting, hydrogel, biomineralization,

Abstract

Bone defects may occur after trauma, infection, or oncologic resection. Autologous bone grafting is the current treatment option; however, grafting is limited in the case of more severe injuries, and the creation of donor site injuries may cause infection and scarring. Therefore, it is essential to develop biomaterials that are inherently osteoinductive and biologically active with live cells. We have recently found that embedding human mesenchymal stem cells (hMSCs) within nanoscale-mineralized collagen constructs can significantly promote osteogenic differentiation than conventional osteoinductive supplements. Recapitulating the extracellular matrix (ECM) of native human tissues may enhance the regenerative capacity and aid in the treatment of bone defects. Here, we developed an injectable microgels using bioinks formulated by mixing hMSCs with bone ECM derived hydrogel biomaterial (BoneMA) to study the osteogenic differentiation. We synthesized a photocrosslinkable bone ECM hydrogel – BoneMA, by enzymatic digestion and solubilization of demineralized, decellularized human bone fragments and functionalized with methacrylate groups. A digital light processing 3D printer was used to print square shaped microgels. These microgels were mineralized by treating with 9 mM $CaCl_2.2H_2O$, osteopontin (100 ug/mL), 4.2 mM K_2HPO_4, and Alpha-MEM media for three days. The mineralized microgels were characterized by alizarin red, and von Kossa staining. Live and dead stains showed hMSCs viability after three days of mineralization. Cell encapsulated mineralized microgels were cultured for further 7 more days and characterized for osteogenic differentiation using early osteocyte marker RUNX2. RUNX2 was highly expressed in mineralized microgels, indicating that the mineralization effectively enhances the osteogenic stem cell differentiation. We conclude that bioprinted mineralized BoneMA microgel may be a useful hydrogel system for regenerating defective bones. These findings pointed towards a promising strategy to develop treatment for bone defects using this novel bone derived bioink and bioprinting technology.