Developing dextran-based bioinks for visible light-aided 3D bioprinted cartilage tissue mimics

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INTRODUCTION

Despite its avascular, aneural nature and single cell type population, articular cartilage has yet to be fully replicated *in vitro* due to its complex extracellular matrix architecture and depth-dependent biomechanical properties. Spatial-temporal bioprinting methodologies used alongside stem cell differentiation and growth factor delivery regimes may provide a solution [1]; nonetheless, the complexity and cost of these biological procedures underscore the need for user-friendly and bioactive bioinks. At present, the selection of printable materials that possess optimal properties for cell encapsulation is modest. These materials are commonly crosslinked using ionic or chemical means to form viscoelastic gels; however, shortcomings include lengthy crosslinking kinetics, lack of cellular support, and thermosensitivity [2]. Our objective is to develop bioactive, visible-photocrosslinkable bioinks for cell encapsulation and cartilage-based bioprinting. For this, we have formulated a semi-interpenetrating network consisting of hyaluronic acid (HA), a principal component of cartilage and various other tissues, and glycidyl methacrylated-dextran (DexGMA). We hypothesise that DexGMA-HA bioinks will provide a simple approach in fabricating viscoelastic hydrogels that are adept in: (1) replicating heterogeneous tissues by utilising pressure-assisted bioprinting and visible light, and (2) supporting encapsulated cells, particularly during chondrogenic differentiation of stem cells (SCs).

MATERIALS AND METHODS

DexGMA, or a combination of DexGMA with HA, was solubilised at a total solid concentration between 5-10% (w/v). SCs were incorporated within the pre-gel and were either pipetted into silicone moulds or 3D bioprinted into a suspension bath using a pneumatic printhead installed in a BIOX6 bioprinter. The printed constructs were reticulated using lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) and the Sarspec© UniLight 405 nm LED light source for <1 minute. The viability of encapsulated cells was qualitatively recorded using fluorescent microscopy with calcein-AM and NucRed Dead to stain live cells green and dead cells red, respectively. The chondrogenic potential of the cell-encapsulated hydrogels was assessed using RT-qPCR and histological staining. The rheological properties of DexGMA and DexGMA/HA were characterised before, during, and after crosslinking, and the mechanical and time-dependent swelling properties were measured following reticulation and incubation.

RESULTS AND DISCUSSION

Cell viability of encapsulated cells remains high over the course of 14 days in both bioprinted DexGMA and DexGMA/HA hydrogels. Oscillatory rheology confirmed that HA improves the elastic resistance of reticulated DexGMA, while the compressive moduli was calculated from mechanical testing. Repetitive low-high strain oscillatory rheological tests revealed the recovery potential of DexGMA-based hydrogels. Gene expression and histological analysis confirm the chondrogenic potential of DexGMA-based bioinks, which will open the opportunity for deeper longer-term explorations into cartilage tissue generation.

CONCLUSIONS

Overall, DexGMA-based bioinks offer a convenient and user-friendly approach for fabricating cell-laden cartilage constructs. By harnessing the spatial-temporal control of extrusion-based bioprinting, we aim to use DexGMA-based bioinks to create heterogeneous 3D constructs for developmental and disease models, as well as tissue regeneration.

REFERENCES

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