Spatio-Temporal Control of 3D-Bioprinted Light Activated Hydrogels for Regenerative Medicine Applications

Khoon S. Lim[1]

[1]Light Activated Biomaterials Research Group, Department of Orthopaedic Surgery and Musculoskeletal Medicine, University of Otago, New Zealand

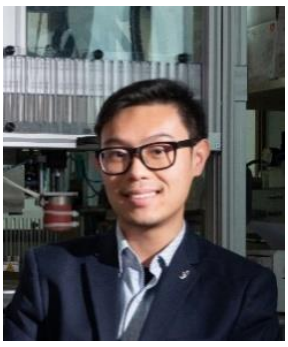
Engineering multi-scalar vascular network is the key to fabricate functional tissues/organs. Although current bioprinting approaches have demonstrated promise in recapitulating the macro-scale (100-1000µm) regions of vascular network, spatial-patterning of the microscale (5-10µm) aspects remains an unmet challenge [1]. Microscale vasculogenesis, which is typically driven through cell-directed capillary-like network formation, requires a cell-permissive environment, typically provided by hydrogels exhibiting low-stiffness properties. This is however problematic as current low-stiffness bioink formulations inherently possess low viscosity, which is not compatible with most biofabrication approaches [2]. Therefore, the aim of this study is to develop vascular bioinks that simultaneously allow spatial patterning of macroscale vessels, as well as capillary-like vessel formation. Physicochemical (mass-loss) and mechanical (compressive modulus) properties were screened in allylated-gelatin (Gel-AGE, 3-5wt%) hydrogels (Ø5mm, 1mm height), photo-polymerised (5.4 kJ/cm2) with initiators ruthenium (0.2-1mM) and sodium persulfate (5-10mM). Thiolated crosslinkers used were dithiothreitol (DTT) or 8-arm thiol-functionalized poly(ethylene glycol) (PEG-8-SH). Rheological properties were measured and bioinks were directly printed through extrusion-based bioprinting (Bioscaffolder, Sys+Eng, 19-23G, speed 300-700 mms-1). Cell viability (Live/Dead®), capillary formation and macroscale vessel lining (CD31/F-actin) were investigated in a co-culture of human umbilical cord endothelial cells ($5x10^6$mL-1) and mesenchymal stromal cells (1x106mL-1), after 7-14 days culture in endothelial growth media. Gel-AGE hydrogels of low stiffness (5-20kPa) were tailorable through crosslinker size and concentration. Rheological assessment revealed favorable viscosity (3-4Pa·s) and shear-thinning behavior for extrusion-based bioprinting. High cell viability (80-90%) and subsequent capillary-like networks were obtained within the bioprinted constructs. Moreover, macroscale channels were successfully included in engineered constructs and long-term shape stability was observed. Thiol-ene clickable bioinks allowed a wide window of physicochemical properties and provided flexibility in flow properties for various biofabrication methods. This was successfully leveraged towards vasculogenesis, demonstrating that thiol-ene bioinks hold great potential for micro- and macroscale vasculogenesis for tissue engineering.

Keywords: Hydrogel, 3D bioprinting, photopolymerization, tissue engineering

References

1.Kolesky D et al. PNAS. 2016;113(12). 2. Datta P et al. Acta Biomater. 2017;15(51). 3. Bertlein S et.al. Adv Mater. 2017;29(44)

Khoon S. Lim
Associate Professor
Department of Orthopaedic Surgery and Musculoskeletal Medicine, University of Otago, New Zealand
Phone: +642108492312; E-mail: khoon.lim@otago.ac.nz



Personal History:

2022 Research Associate Professor
2018-2022 Senior Research Fellow (beyond the bar)
2016-2018 Research Fellow
2014-2016 Postdoctoral Fellow

Research interests: visible light, 3D bioprinting, biofabrication, hydrogels