Development of biosynthetic implants and models for the treatment of ocular diseases

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INTRODUCTION

Diseases of the eye are numerous and debilitating for the many who suffer from them. Diseases such as glaucoma can be initiated by dysfunctional trabecular meshwork (TM) tissue, which typically regulates the fluid levels in the eye to maintain intraocular pressure. With aging, loss of functional TM cells can cause fluid to be retained which causing pressure in the eye to rise significantly. This can go on to cause compression of the optic nerve and irreversible sight loss. Treatments currently include topical eye drops, laser surgery or insertion of micro stents to actively drain ocular fluid; though none of these treatments aim to regenerate and restore the TM and often require further intervention [1]. In corneal disease, such as Fuchs' endothelial dystrophy (FED), endothelial cells are lost and when this reaches a critically low level, fluid accumulates in the corneal stroma (oedema), causing cloudiness, corneal thickening, and blurred vision. FED is currently treated with a corneal transplant that typically uses cadaveric tissue in a 1 to 1 ratio of donor to recipient.

Our aim is to use 3D bioprinting to design and create biosynthetic grafts from printed hydrogels that may also incorporate fibrous scaffolds to closely mimic structures of eye and improve surgical outcomes for patients.

MATERIALS AND METHODS

We have used PεKMA peptides a naturally occurring poly-lysine, which we have methacrylated (MA) to allow use of a photo initiator (LAP) cross linking method for hydrogel production, as well as purchased CELLINK bioinks in these studies. The BIONOVA X will allow more flexibility in the creation of hydrogels in terms of thicknesses, mechanical properties transparencies and shapes that are achievable. Our own material can be printed using the BIONOVA X , the gel along with CELLINK PEGDA and GEL photo ink, were also printed around electrospun or melt electrowritten scaffolds placed within the wells. These fibres were encapsulated within the hydrogels which could essentially be used to create a more realistic TM model system for lab-based experiments or possibly developed into a future implant if loaded with TM cells, for replacement surgeries

RESULTS AND DISCUSSION

We have shown that our PεKMA peptides can be used as printable bioinks. Furthermore, fibre-gel composites were produced for the first time with fibres fully encapsulated by the printed gel. To our knowledge, this is the first time the BIONOVA X has been employed to create these innovative composite structures and without impeding the bioprinter's function.

CONCLUSIONS

We have demonstrated that the BIONOVA X can support printing of PεKMA hydrogels and it's copolymers to create potential carriers to deliver cells into patients for corneal eye diseases. We have also successfully demonstrated the ability to create fibre-gel composite structures that are more typical of a tissue's extracellular matrix (a natural fibre-gel composite). This ability could be used to create biomimetic TM implants that aim to regenerate diseased tissue (1).

In this study, we have established the utility of the Bionova X to create bioprinted grafts that may be used to treat different ocular diseases. Further research is required but this study presents a positive step forward in tackling the issues around long waiting times, inadequate treatments and poor outcomes for patients suffering from ocular diseases.

ETHICAL STATEMENTS (IF ANY)

REFERENCES

[1] Crouch, D.J., Sheridan, C.M., D'Sa, R.A., Willoughby, C.E. and Bosworth, L.A., 2021. Exploiting biomaterial approaches to manufacture an artificial trabecular meshwork: A progress report. *Biomaterials and biosystems*, *1*, p.100011.

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