Decellularisation: A method of recycling unsuitable donor corneas for transplantation?

[Abstract]

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Decellularisation: A method of recycling unsuitable donor corneas for transplantation?
S.L. Wilson*, L.E. Sidney, S.E. Dunphy, H.S. Dua, A. Hopkinson
Academic Ophthalmology, Division of Neuroscience, University of Nottingham, Queen’s Medical Centre Campus, NG7 2UH, UK

Rationale: There is a significant clinical need for reliable and quality biomimetic corneas that are as effective, preferably superior to cadaveric donor tissue. The current worldwide cornea shortages have led to the development of feasible, long-term substitutes to cadaveric donor tissue including keratoprostheses, tissue engineered constructs, xenografts, and the use of acellular matrices. With respect to corneal regeneration, there are many challenges, not least that the corneal structure is unique and difficult to replicate. When manufacturing corneal tissues, the choice of material is vital as the list of requirements is extensive. They must be biocompatible, (preferably) optically transparent, flexible, and strong, as to withstand manipulation in culture, potential suturing, irrigation and handling during surgery. The manufacturing process needs to be simple and consistent, preferably at high speed and low cost.

Decellularised matrices are advantageous when compared to synthetic or semi-synthetic engineered tissues in that the complex native milieu can potentially be preserved to retain intrinsic biological cues including growth factors, cytokines and glycosaminoglycans (GAGs). However, the decellularisation protocols need to sufficiently eliminate cellular material with minimal disruption to tissue architecture. To date, there is currently no effective, standardised decellularisation protocol suitable for human corneas. Therefore, the purpose of this work was to provide a systematic evaluation of common decellularisation methods in terms of efficacy, reproducibility, reliability and ability for manufacturing upscale.

Methods: Corneal eye-bank tissue deemed unsuitable for transplantation was utilised to determine an optimal human specific decellularisation technique. Hypertonic sodium chloride (NaCl); ionic detergent, sodium dodecyl sulphate (SDS); non-ionic detergent, Triton-X100, mechanical agitation, followed nuclease treatments were investigated. Removal of detectable cellular and immune reactive material was evidenced by immunofluorescence and quantitative assays. Preservation of optical properties and light transmittance was evaluated. Retention of corneal architecture and GAGs was assessed via histological, immunofluorescence and quantitative analysis.

Results: No currently employed decellularisation techniques successfully removed 100% of cellular components. The techniques which had the least residual DNA were most structurally compromised. GAG analysis demonstrated the stripping effects of the different decellularisation treatments.

Conclusion: The ability to utilise, reprocess and regenerate tissues deemed “unsuitable” for transplantation allows us to salvage valuable tissue. Reprocessing the tissue has the potential to have a considerable impact on addressing the problems associated with cadaveric donor shortage, which would have a significant economic benefit. Patients would directly benefit by accessing greater numbers of corneal grafts and health authorities would fulfill their responsibility for the delivery of effective corneal reconstruction to alleviate corneal blindness.