076

EXTRACELLULAR MATRIX HYDROGEL DERIVED FROM DECELLULARISED INTESTINAL TISSUE FOR THE 3D-CULTURE OF PRECURSOR CELLS IN TISSUE ENGINEERING.

Claire Crowley[1], Luca Urbani[1], Martina De Santis[1], Vivien Gaillet[1], Francesca Onofri[1], Laween Meran[1,3], Sang Eun Lee[1,3], Sara Campinoti[1], Paola Bonfanti[1], Alan Burns[1,4], Vivian Li[3], Martin Birchall[2], Simon Eaton[1], Paolo De Coppi[1]
[1]UCL Institute of Child Health and Great Ormond Street Hospital,, London, UK, [2]UCL Ear Institute, Royal National Throat Nose and Ear Hospital and UCL, London, UK, London, UK, [3]The Francis Crick Institute, Mill Hill Laboratories, The Ridgeway, London, UK, [4]Department of Clinical Genetics, Erasmus Medical Center,, Rotterdam, The Netherlands

Aim: Anatomical/functional loss of the small intestine can require the use of total parenteral nutrition or indeed the need for an intestinal transplant. Both options unfortunately have a high associated risk. A hydrogel derived from decellularised intestine, thereby possessing the extracellular matrix (ECM) information of the native tissue, would be beneficial for many applications within intestinal tissue engineering, including; cell delivery to restore function, 3D-culture of organoids for the repopulation of decellularised scaffolds or as a hybrid engineered intestinal replacement. Here, we develop and characterise such a hydrogel focusing on its ECM preservation, rheology and cytocompatibility investigating its potential in tissue engineering.

Methods: Pig intestine was decellularised with the Detergent Enzymatic Treatment (DET) and ECM components were quantified. A gelation protocol was developed, involving drying, milling and digestion followed by neutralisation to physiological pH and temperature. Whole intestine and mucosa alone were compared examining gelation properties, conductivity and ECM composition. Finally the gel was investigated for its potential to support intestinal organoids in 3D-culture conditions.

Results: The pig intestine was successfully decellularised with a significant reduction of DNA quantified and immunofluorescence staining showing no nuclei. Quantification of the ECM components showed Collagen, Elastin and GAG were preserved after decellularisation. A hydrogel was successfully formed as evident in turbidimetric tests showing normalised absorbances forming sigmoidal curves typical of gelation. The mucosa alone formed a more stable and consistent gel than the whole intestine with a faster gelation time of 20minutes. Oscillation rheology showed both tissues to have a high storage modulus of 100-1000Pa. The gel successfully supported the 3D-culture of intestinal organoids maintaining cell viability and comparable morphologically to Matrigel®.

Conclusion: This study reports the optimisation of an ECM hydrogel derived from non-immunogenic intestinal tissue with encouraging potential in organoid culture, tissue engineering and cell delivery for intestinal repair and regeneration.