Proceedings Paper:
Walker, F., Da Silva, C.F., Ingham, E. orcid.org/0000-0002-9757-3045 et al. (1 more author) (2023) Cellular Interactions at the Decellularised Scaffold:Tissue Interface in an Ex-Vivo Organ Culture Model. In: Tissue Engineering Part A. TERMIS 2023 – European Chapter Manchester, 28-31 Mar 2023, Manchester, UK. Mary Ann Liebert, Inc. .

https://doi.org/10.1089/ten.tea.2023.29043.abstract

Cellular Interactions at the Decellularised Scaffold:Tissue Interface in an Ex-Vivo Organ Culture Model

Fiona Walker[1], Carolina Franco Da Silva[2], Eileen Ingham[1], Helen Berry[1]

[1]Institute of Medical and Biological Engineering, School of Biomedical Sciences, Faculty of Biological Sciences, University of Leeds, UK.

[2]School of Medicine, Faculty of Medicine and Health, University of Leeds, UK.

INTRODUCTION:

Modulation of the cellular response to decellularised biological scaffolds towards an immuno-regulatory (M2) phenotype has been suggested to be a determinant of regenerative outcomes in vivo[1]. A key role in recellularisation of functional decellularised heart valve scaffolds was revealed for macrophages during 6-month[2] and 12-month[3] in vivo ovine models. CD163+ (M2) macrophages were shown to pioneer the initial cellular response to porcine decellularised bladder scaffold in a human tissue organ culture model[4]. The aim of this study was to develop an ex-vivo organ culture model for decellularised cardiovascular scaffolds, that could replicate the initial innate and stromal cell response seen at the in-vivo tissue:decellularised scaffold interface.

METHODS:

An interface was established between decellularised porcine pulmonary artery scaffolds and native ovine pulmonary artery. The constructs were maintained in culture for 0, 2, 6, and 11 days (n = 4 at each time point). Haematoxylin and eosin (H&E) staining, and immuno-histochemistry, was used to characterise the cellular response at the tissue:scaffold interface; using primary antibodies for macrophages, smooth muscle cells, proliferating cells, progenitor cells, endothelial cells and connective tissue growth factor. Manipulation of the ovine ex vivo cellular response was investigated by exposing decellularised scaffolds to two concentrations of a carbodiimide cross-linker prior to organ culture.

RESULTS:

Observation of H&E stained histological sections revealed a time dependent infiltration of cells into the non-crosslinked scaffolds. This was a heterogeneous population, expressing markers for stromal and progenitor cells. A striking number of cells within the scaffold and at the tissue:scaffold interface were CD163+ (M2 macrophage marker). Analysis of the cellular response towards the cross-linker treated decellularised scaffolds revealed that the ovine cellular response was attenuated in comparison to the non-crosslinked scaffolds. The cells appeared to collect at the interface, similar to the encapsulation response, rather than crossing into the scaffold.

DISCUSSION & CONCLUSIONS: The striking CD163+ cell presence, in combination with the recruitment of site specific stromal cells and progenitor cell types, indicates that this ex-vivo model may provide a valuable tool for investigating the mechanisms of an early regenerative cellular response. Further investigation of the cell infiltrate and mechanisms of recruitment and polarisation of macrophages at the scaffold interface is required.

REFERENCES:

1. Badylak S.F., et al.,Tissue Eng Part A, 2008. 14(11): p. 1835-42.
2. Paniagua-Gutierrez, J.R., et al.,Tissue Engineering Part A, 2015. 21(1-2): p. 332-42.
3. Vafaee, T., et al., J Tissue Engineering. 2022;13.
4. Bullers, S.J., et al., Tissue Engineering Part A, 2014. 20(17-18): p. 2390-401.

Keywords: Decellularised matrices, Cardiovascular