Acta Biomaterialia 8 (2012) 3723–3731

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Synthetic collagen fascicles for the regeneration of tendon tissue

S.J. Kew [a,*], J.H. Gwynne [b], D. Enea [c], R. Brookes [c], N. Rushton [c], S.M. Best [b], R.E. Cameron [b]

[a] Tigenix Ltd., Byron House, Cambridge Business Park, Milton Road, Cambridge CB4 0WZ, United Kingdom
[b] Department of Materials Science and Metallurgy, University of Cambridge, Pembroke Street, Cambridge CB2 3QZ, United Kingdom
[c] Orthopaedic Research Unit, University of Cambridge, Box 180, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, United Kingdom

ARTICLE INFO

Article history:
Received 28 January 2012
Received in revised form 11 June 2012
Accepted 12 June 2012
Available online 21 June 2012

Keywords:
Tendon
Regeneration
Collagen
Fibre
Tissue

ABSTRACT

The structure of an ideal scaffold for tendon regeneration must be designed to provide a mechanical, structural and chemotactic microenvironment for native cellular activity to synthesize functional (i.e. load bearing) tissue. Collagen fibre scaffolds for this application have shown some promise to date, although the microstructural control required to mimic the native tendon environment has yet to be achieved allowing for minimal control of critical in vivo properties such as degradation rate and mass transport. In this report we describe the fabrication of a novel multi-fibre collagen fascicle structure, based on type-I collagen with failure stress of 25–49 MPa, approximating the strength and structure of native tendon tissue. We demonstrate a microscopic fabrication process based on the automated assembly of type-I collagen fibres with the ability to produce a controllable fascicle-like, structural motif allowing variable numbers of fibres per fascicle. We have confirmed that the resulting post-fabrication type-I collagen structure retains the essential phase behaviour, alignment and spectral characteristics of aligned native type-I collagen. We have also shown that both ovine tendon fibroblasts and human white blood cells in whole blood readily infiltrate the matrix on a macroscopic scale and that these cells adhere to the fibre surface after seven days in culture. The study has indicated that the synthetic collagen fascicle system may be a suitable biomaterial scaffold to provide a rationally designed implantable matrix material to mediate tendon repair and regeneration.

1. Introduction

Regeneration of damaged tendon tissue remains an underserved medical need for the field of orthopaedics. These highly specialized and aligned tissues provide the structural support necessary in order to maintain appropriate biomechanical function in all joints of the human body. The properties of ligament and tendon vary substantially by anatomical location, with concomitant variation in structure and configuration. However, an invariant feature of these tissues is that they are substantially oriented type-I collagen fibre structures, providing load bearing and force transfer parallel to the direction of orientation. Once damaged, tendons and ligaments lose their ability to protect the joint from biomechanical loading patterns which can damage articular cartilage and may expedite the onset of degenerative changes such as osteoarthritis [1]. Furthermore, the loss of function and pain associated with injuries to tendon carries a significant societal burden via patient morbidity, notably in the Achilles [2] and shoulder rotator cuff tendons [3]. Current approaches to the surgical treatment of tendon injuries rely on fixation devices such as bone-anchoring sutures and biomaterial grafting in combination with various suture techniques to reattach tissues and restore function to the damaged area. However, bone anchors and (bio)synthetic grafting are limited to providing a purely mechanical solution to what is often a biological problem, with degenerated or ruptured tendon tissue often found either prior to, or as a result of, a tendon injury [4]. However, autografting and muscular transfers are limited by a noticeable morbidity, and allografting may cause immunoreactions and spread infective diseases. Hence structural repairs often fail: for example in the case of massive rotator cuff repairs an estimated 13–68% will re-rupture (see Ref. [5] and references therein). Therefore, the ability to provide a biological augmentation, which enhances the quality of the repaired tendon tissue in concert with the structural repair, is a promising methodology by which to reduce the significant problem of longevity in the current repair modalities. A multitude of approaches have been proposed towards the overall goal of regenerating tendon tissue, with combinations of biological species such as growth factors, stem cells, blood concentrates both with and without biomaterials all attracting significant current research interest.

Clinical attempts to provide a biomaterial scaffold that enables the recapitulation of tendon tissue have, to date, focused on use of decellularized extracellular matrix (ECM) materials [6]. However, these materials are unlike the tissues they aim to regenerate, being non-axially oriented and retain allergenic or xenogenic epitopes

* Corresponding author. Tel.: +44 (0)1223 438254.
E-mail address: sjkew@hotmail.com (S.J. Kew).

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http://dx.doi.org/10.1016/j.actbio.2012.06.018