RESTORING DISORGANISED TENDINOPATHIC TISSUE USING MAGNETIC TOPOGRAPHICAL CUES

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Introduction

Tendons, which connect muscle to bone, are comprised of longitudinally-packed collagen type I fibres at length scales that range from the nano to the macroscale [1]. The main cell type, specialised fibroblasts called tenocytes, are arranged in between these collagen structures [2]. The strong anisotropy of the tendon's collagen matrix results in a high cell aspect ratio, co-aligned with the collagen, ideal for proper tendon functioning [3]. However, in tendinopathy, i.e., tendon disease, cell and matrix anisotropy are lost, affecting tissue function and thus increasing rupture risk. As cells are known to be able to manipulate collagen organization [4], it is hypothesised that recovering the lost cell alignment promotes functional remodelling to an anisotropic and healthy tendon. The aim was thus to control cell aspect ratio and orientation, using injectable magnetic rods, in an isotropic collagen matrix, to promote functional tissue remodelling towards strong tissue anisotropy.

Methods

Super Paramagnetic iron-oxide nanoparticles in polymeric MicroRods (SPµRs) [5] were used to provide topographical cues to the cells. Cells that encounter the rods can align their longitudinal axis to the rods'.

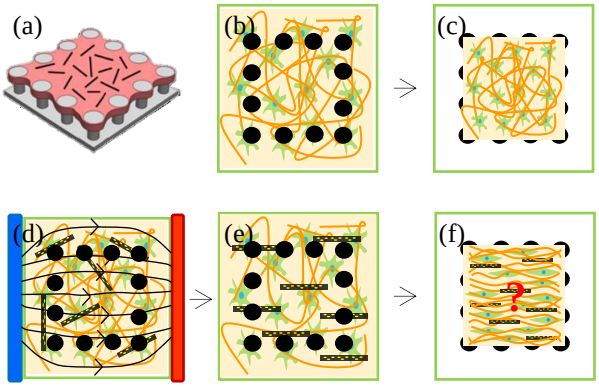

Figure 1: (a) in-vitro 3D isotropic tissue; (b-c) formation of isotropic microtissue; (d-f) formation of microtissues with SPµRs.

3D tendon microtissues (fig 1a) that mimic a tendinopathic isotropic tissue (fig 1b) were created in-vitro using a gel mixture of collagen type I and tendon like-cells. The isotropy was created in the tissue by restricting contraction of the collagen (orange) by the cells (green) in all directions using 12 black posts (fig 1c). In the same isotropy setup, SPµRs (black) were added to override the isotropy and promote anisotropy (fig 1d). Using a magnetic field, the SPµRs were aligned in the direction of the magnetic field (fig 1d) after which collagen was allowed to polymerise (fig 1e). Subsequently, the alignment response of the cells to the SPµRs was monitored (fig 1f).

Results

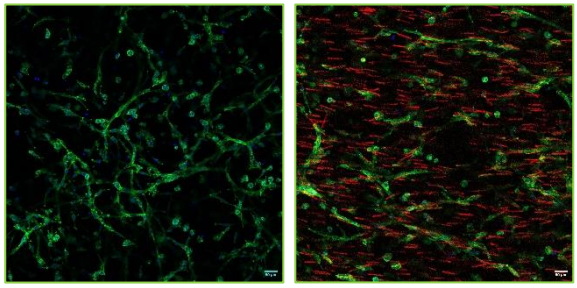

Figure 2: (a) Isotropic arrangement of cellular actin stress fibres (b) Anisotropic arrangement of actin fibres

In the absence of SPµRs, an isotropic distribution of cellular actin stress fibres (green) developed in the microtissues (fig 2a). Whereas in the presence of magnetically aligned SPµRs (red), microtissues displayed preferential cellular co-alignment (fig 2b). It was shown that the cellular orientation can be manipulated to anisotropy using SPµRs in 3D microtissues, which would be isotropic without SPµRs.

Discussion

The cellular co-alignment was exhibited roughly throughout the tissue. A major variable at play was the concentration of rods to cells. The ratio of rods to cells has to be optimised to achieve complete and strong alignment throughout the tissue. The effect of the aligned cells on the existing collagen, the orientation of cell-secreted collagen and the effect of uniaxial cyclic load to investigate the strength of the topographical cues against strain avoidance, are also being assessed.

References

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