Mechanical stimulation for tissue engineering: characterising load-induced changes by the 'collagen barcode'

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Introduction

Differentiated cells can be characterized by the composition of collagen isoforms that they produce in response to specific mechanical loads – effectively a 'collagen barcode' that functionally defines engineered tissues.

Collagen is one of the major structural proteins within the body, currently known to exist as 28 different isoforms that are each associated with specific functions in the tissue, such as mechanical resilience, structure, proteoglycan-binding and cell fate regulation. The combinations and ratios of collagen types vary across all tissues, e.g. Type I,III,V,XI,XII,XIV in tendon; Type II,IV,V,VI,IX,XI in cartilage.

Materials and Methods

We have used 3D printing to generate bespoke bioreactor components which apply mechanical stimulus to cells seeded within 3D constructs. We have customised our culture components around an EBERS TC3 bioreactor and replicated individual chambers at low cost.

The mechanical stimuli that have been applied at this stage is cyclic tensile force at 3, 5 and10% strain, 1Hz for 5 hours per day over 3 weeks. Western blot was used to quantify collagen isoforms produced at different stages of the loading regime. Supplementary data was collected using qPCR, histology, TEM and two-photon/second harmonic generation to visualize structure.

Results

Our early results show that in response to cyclic tensile loading hMSCs alter the collagen composition of the extracellular matrix they produce. Collagen I and III were upregulated, whilst V was suppressed, versus unloaded controls. Collagens XI, XII and XIV were detected in both loaded and controls, but at low concentrations – these will be investigated in more detail in future experiments.

Discussion

Defining 'optimal' loading conditions may help generate engineered tissues with comparable ratios of collagen types as found in healthy native tissue, and thus improved functionality and integration as implants. Using total collagen isoform expression to characterize these tissues in comparison to native, functional tissue is a novel approach which sheds light on developmental processes recapitulated in tissue engineering and allows us to better define successful bioengineered implants.