# Functionalisation of a 'Tendon Repair Augmentation Device' to support tissue regeneration and repair

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## Introduction

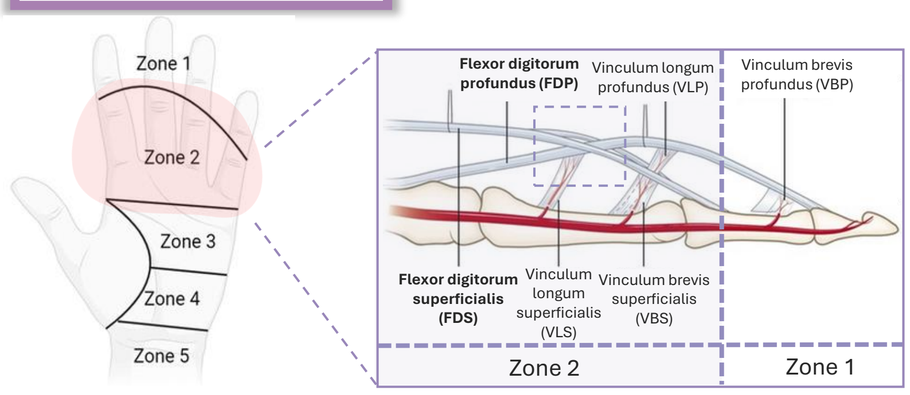


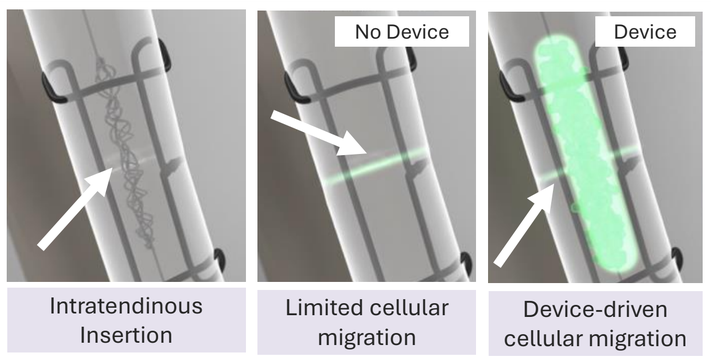

**Figure 1. Verdan Classification of the Hand and Flexor Tendon Anatomy.** (Adapted from[1, 2])

Conservative & surgical intervention

Zone 2; prominent biomechanical challenge [4, 5]

11% require secondary tenolysis or surgery [3]

Adhesion formation & insufficient mechanical functionality [6]




Intratendinous Insertion | Limited cellular migration | Device-driven cellular migration

**Figure 2. Implantation of ReTendon Ltd Tendon Repair Augmentation Device (TRAD) to support device-driven cell migration and tissue repair (US 2022/0176014 A1 [7]).**

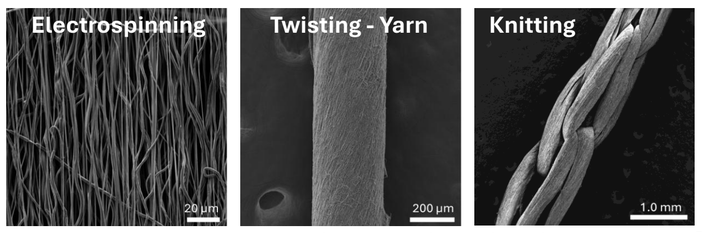



**Figure 3. Manufacture of the Tendon Repair Augmentation Device (US 2022/0176014 A1 [7]).**

## Research Aims

**Aim:** Functionalise the established TRAD, developed by ReTendon Ltd, to encourage **cellular migration** and **extracellular matrix production (ECM)** to improve tissue healing following injury.

**Biomimetic | Mechanical Support | Cellular Interactions**

Material Manufacture | Functionalisation | Research Areas | Cell Culture | Mechanical Testing

This research to functionalise the established product is currently under Intellectual Property agreements with the University of Manchester.

## Screening & Incorporation

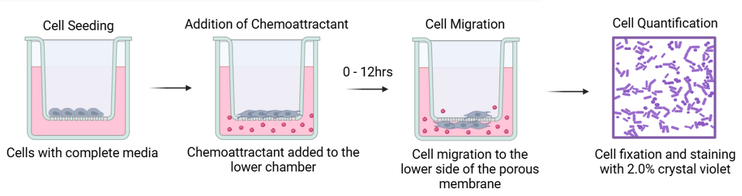



**Figure 4. Schematic of Transwell Migration Assay protocol**

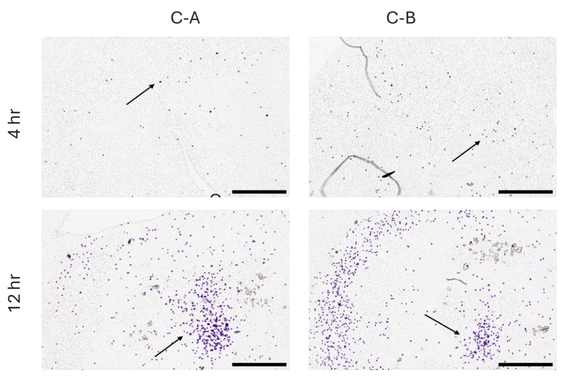



**Figure 5. The application of Chemoattractant A (C-A) and B (C-B) using a Transwell Migration Assay.** *Scale bar; 1 mm.*

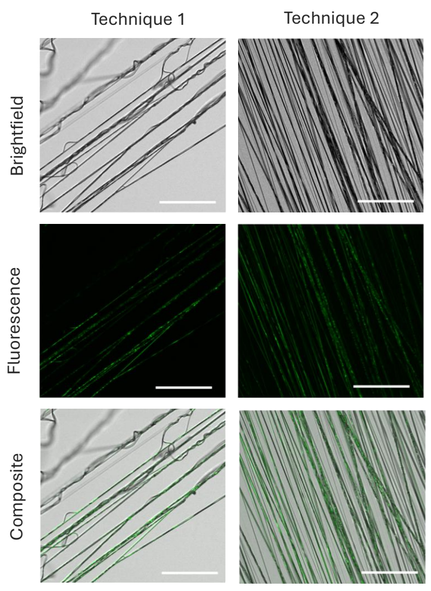
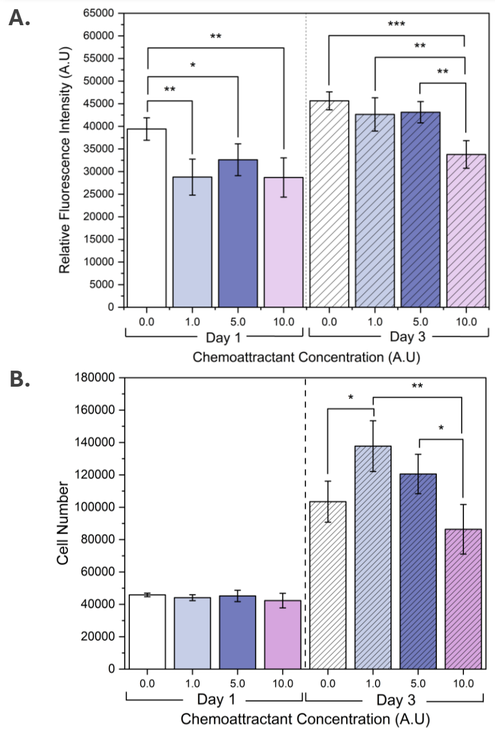



**Figure 6. Confocal microscopy of a fluorescent protein conjugate to assess successful functionalisation of electrospun materials.** *Scale bar; 50 µm.*

Chemoattractant Optimisation | Incorporation Techniques | Confocal Microscopy

## Supplemented Media



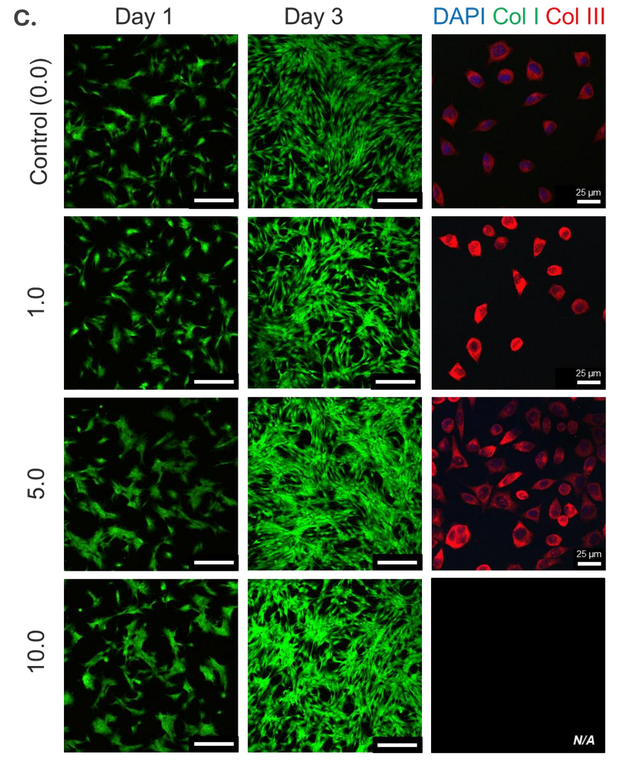




**Figure 7. Cell viability analysis following the incubation of Human Foreskin Fibroblasts (HFF-1) with Chemoattractant-A.** ***(A.)*** *alamarBlue; metabolic activity.* ***(B.)*** *PicoGreen; dsDNA quantification.* ***(C.)*** *Live/Dead and Immunofluorescence; viability and collagen production. Scale bar; 250 µm.*

## Live-cell Tracking

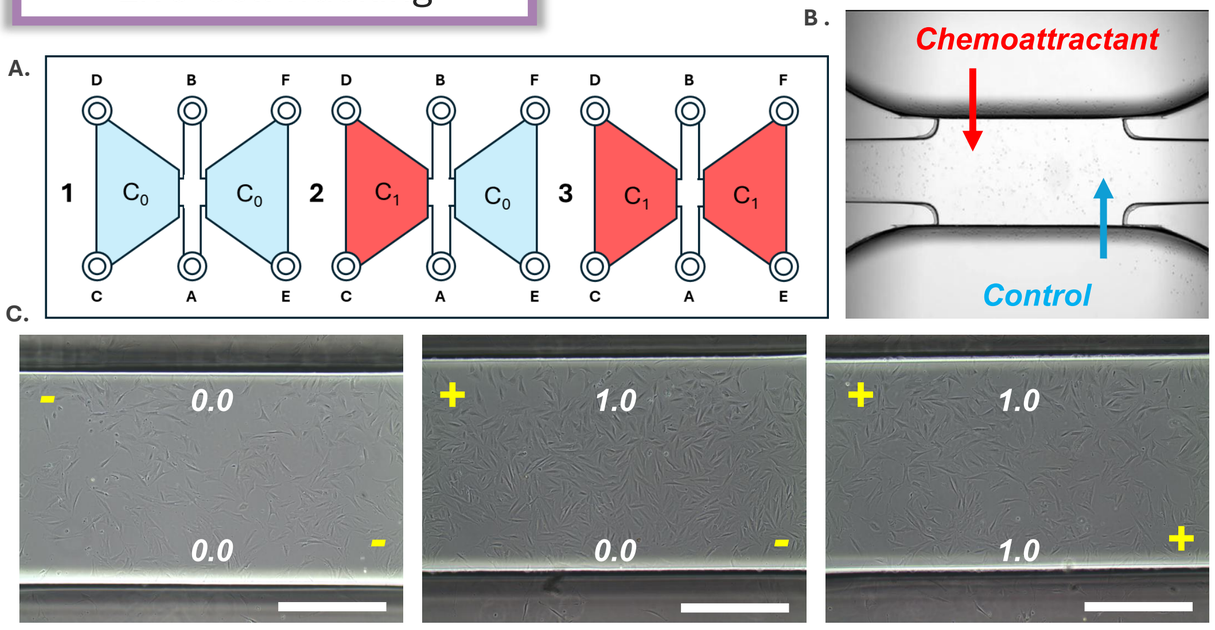



**Figure 8. Preliminary research for the live-cell tracking of HFF-1 cells across 48-hours using controlled release microfluidics (ibidi µ-Slide).** ***(A.)*** *Schematic of ibidi µ-Slide layout.* ***(B.)*** *Brightfield image of cell seeding chamber with respective chemoattractant and control reservoirs.* ***(C.)*** *Brightfield live-cell tracking of HFF-1 migration across 48-hours in response to controlled release of +/- controls and chemoattractant.*

Cell Migration | Real-time Cellular Interactions | Dose-dependant Response Analysis

## Transcriptomics

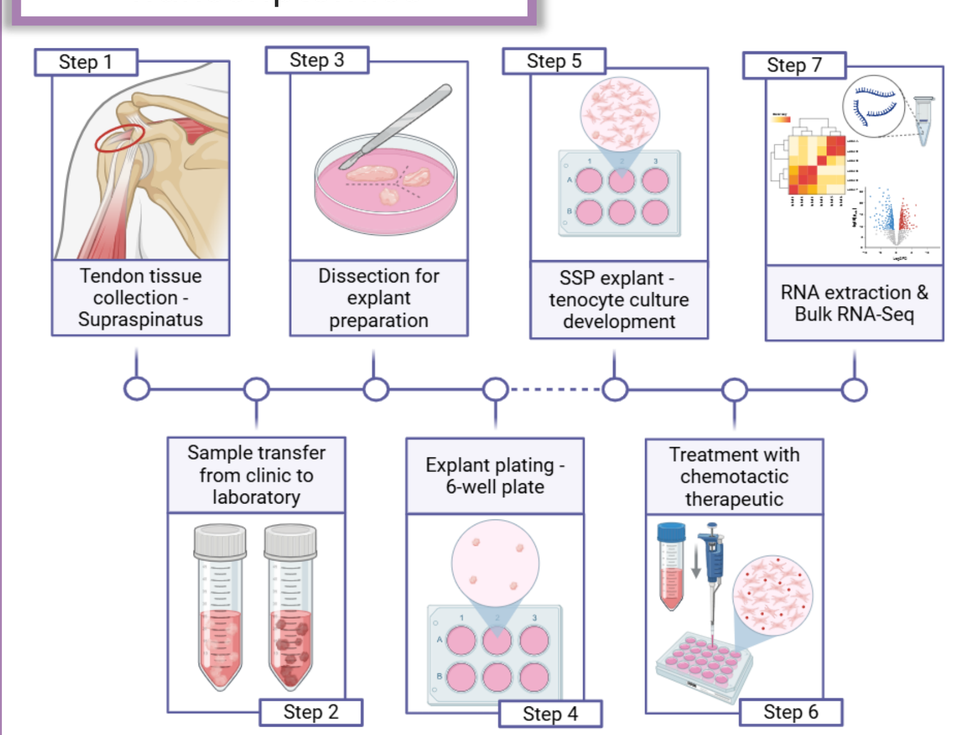



**Figure 9. Schematic of the experimental workflow investigating how the incubation with the chemoattractant effects genetic expression of HFF-1 and Primary Human Supraspinatus (SSP) Tenocytes using Bulk RNA-Sequencing**

**Bulk RNA-Sequencing** of **HFF-1** and **Supraspinatus** (SSP) primary tenocytes.

Gene expression; **cell migration pathways** & **ECM components.**

Whole **transcriptome** analysis for **clinical translation** and applicability.

## Ongoing Research

The next phase of this research includes assessing and optimising the **elution profile** of the product in nanofiber mats, yarn and knitted scaffold morphologies to coincide with **native healing timeframes**. This will provide the basis for the assessment of **cellular responses** upon incubation with the functionalised product with respect to **cellular migration** and **extracellular matrix** component production.

**Optimisation of the elution profile of electrospun and knitted materials** → **Assess cellular responses to the functionalised material in real-time.** → **Analyse genetic expression profiles following dose-dependant incubation.** → **Development of a surgical technique for TRAD delivery.**

**Rotator cuff device design development and new clinical target isolation.**

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