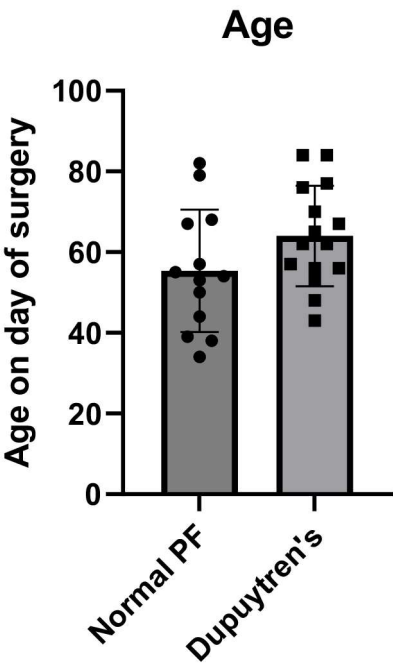
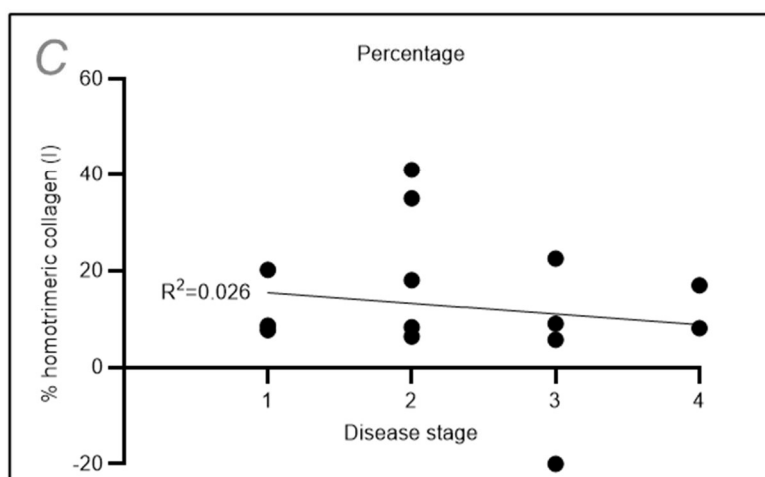
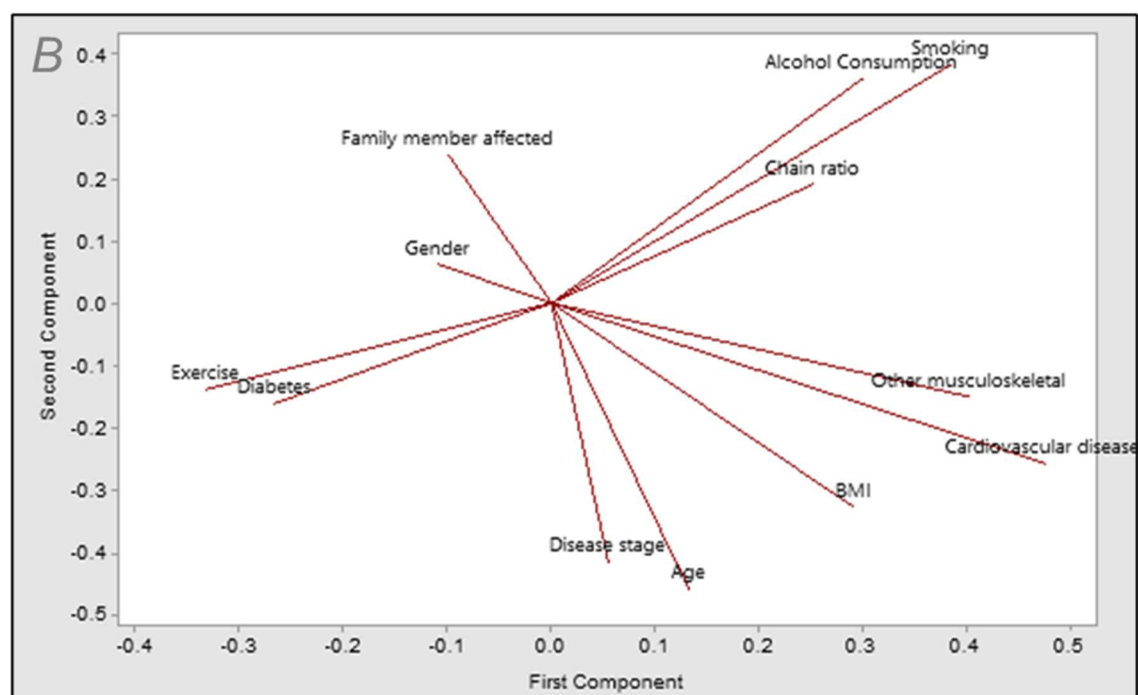
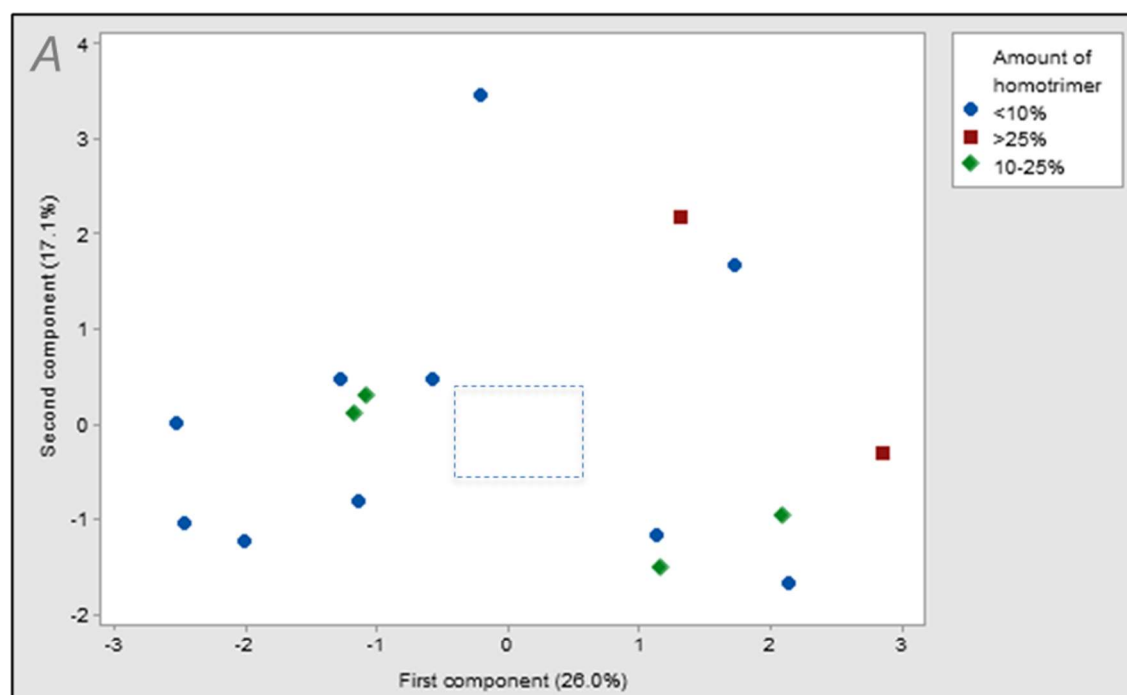


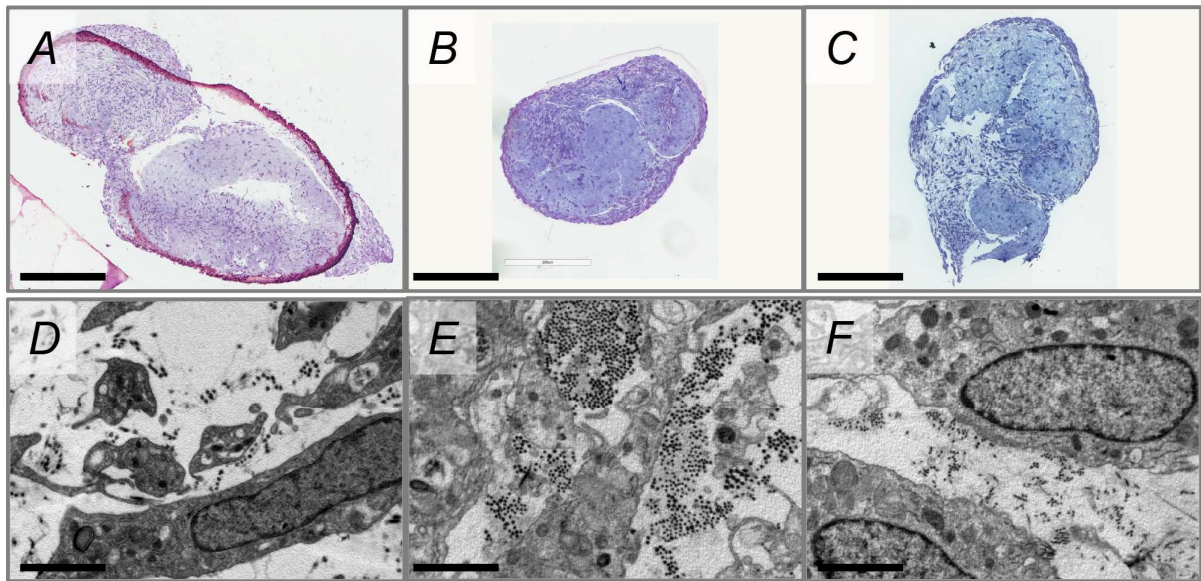
Supplementary Figures



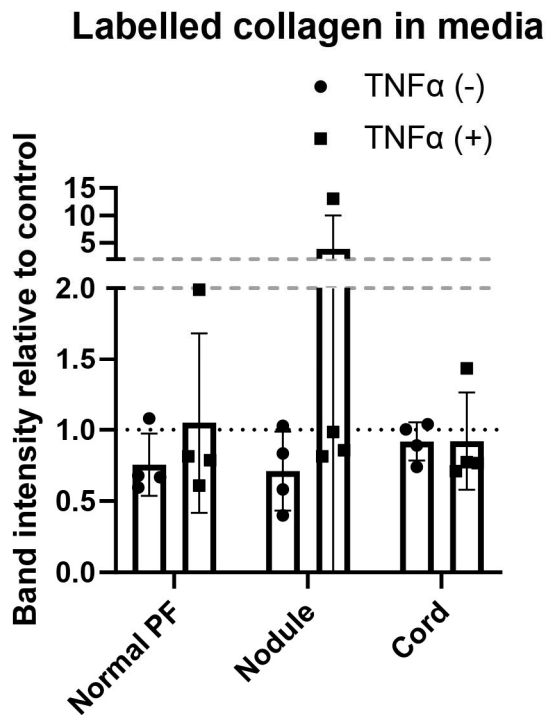
**Figure S1: Age distribution of tissue samples used for qRT-pCR.** No significant difference in the age of the patients on the day of surgery, when normal PF from carpal tunnel decompression (n=13) and Dupuytren's (n=15) samples were collected, was detected between the groups using a t-test.



**Figure S2: Principal components analysis of the relationship between demographic factors and the proportion of homotrimeric collagen synthesized by a sub-set of the human Dupuytren's surgical samples with disease stage information.** A: Score plot grouped by lower (<10%), medium (10-25%) and higher (>25%) percentages of type I collagen homotrimer (n=16). The box indicates the relative scale on the loading plot (B). C: Plot of % homotrimeric collagen (I) versus disease stage reveals a very low inverse correlation ( $R^2 = 0.026$ ).



**Figure S3: *De novo* collagen fibrils are present within tendon-like structures in 3D culture of normal palmar fascia and Dupuytren's cells.** A-C: Semi-thin toluidine blue-stained sections of 3D tendon-like constructs (bar 200 μm). D-F: Transmission electron microscopy images of 3D tendon-like constructs (bar 2 μm). Constructs were derived from normal palmar fascia cells (A&D), Dupuytren's nodule (B&E) or Dupuytren's cord (C&F). Sample IDs are shown in Supplementary Table 3.



**Figure S4. Comparison of the amount of labelled collagen in the media of tendon-like constructs treated with TNF $\alpha$  in the absence or presence of serum.** Densitometric quantification of the relative amounts of radiolabelled (pro)collagen present in conditioned media from normal PF, Dupuytren's nodule and Dupuytren's cord cells (n=4) after TNF $\alpha$  treatment, as compared to control treatments, in serum free conditions (-) and in the presence of 10% FCS (+). Data are derived from Figures 6 I & L and were analysed by 2-way ANOVA.



**Figure S5. 3D tendon-like constructs formed in a 24 well plate.** Image of a 24-well plate containing fully-formed 3D tendon-like constructs between pinned sutures (black) in each well.

## Supplementary Tables

**Supplementary Table 1: Dupuytren's human surgical samples used for collagen synthesis assays.**

| Sample ID               | Age | Gender | Methods (pulse-chase: $^{14}\text{C}$ ) | Demographics<br>A, B, C | Data shown in Figure: (lane number) |
|-------------------------|-----|--------|-----------------------------------------|-------------------------|-------------------------------------|
| 140227-56-F             | 56  | F      | qPCR, $^{14}\text{C}$                   | No                      | 1A-G, D(12), 3A(12)                 |
| 140227-81-M             | 81  | M      | $^{14}\text{C}$                         | -                       | 1D(13), E-F, 3A(13)                 |
| 140310-67-M             | 67  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1A-G, D(14), 2A-D, 3A(14)           |
| 140310-76-M             | 76  | M      | qPCR, $^{14}\text{C}^{\text{D}}$        | +                       | 1A-G, D(15,16), 2A-D, 3A(15,16)     |
| 140312-43-M             | 43  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1A-G, D(17), 2A-D, 3A(17)           |
| 140318-48-M             | 48  | M      | qPCR, $^{14}\text{C}$                   | No                      | 1A-G, D(18), 3A(18)                 |
| 140320-56-M             | 56  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1A-G, D(19), 2A-D, 3A(19)           |
| 140327-68-F             | 68  | F      | $^{14}\text{C}$                         | -                       | 1E-F, 2A-B                          |
| 140331-71-M             | 71  | M      | $^{14}\text{C}$                         | +                       | 1E-F, 2A-D                          |
| 140331-76-M             | 76  | M      | $^{14}\text{C}^{\text{E}}$              | -                       | 1E-F, 2A-B                          |
| 140423-68-M             | 68  | M      | $^{14}\text{C}$                         | +                       | 1E-F, 2A-D                          |
| 140423-69-M<br>Nodule   | 69  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1E-F, G, 2A-D                       |
| 140512-47-M             | 14  | M      | $^{14}\text{C}$                         | +                       | 1E-F, 2A-D                          |
| 140528-52-M<br>Nodule   | 52  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1E-F, G, 2A-D                       |
| 140529-58-M             | 58  | M      | $^{14}\text{C}^{\text{F}}$              | -                       | 1E-F                                |
| 140714-84-M             | 84  | M      | qPCR                                    | No                      | 1A-C                                |
| 140804-71-M             | 71  | M      | $^{14}\text{C}$                         | +                       | 1E-F, 2A-D                          |
| 140804-84-M             | 84  | M      | qPCR                                    | No                      | 1A-C                                |
| 140811-50-M<br>Nodule   | 50  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1E-F, G, 2A-D                       |
| 140929-57-M             | 57  | M      | qPCR                                    | No                      | 1A-C                                |
| 141006-67-M<br>Cord     | 67  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1E-F, G, 2A-D                       |
| 141016-66-M             | 66  | M      | $^{14}\text{C}$                         | -                       | 1E-F, 2A-B                          |
| 141016-76-M             | 76  | M      | $^{14}\text{C}$                         | -                       | 1E-F, 2A-B                          |
| 141103-62-M             | 62  | M      | qPCR, ( $^{14}\text{C}^{\text{G}}$ )    | No                      | 1A-C, D(20), 3A(20)                 |
| 141113-65-M             | 65  | M      | $^{14}\text{C}^{\text{H}}$              | -                       | 1D(21,22), E-F, 2A-B, 3A(21,22)     |
| 141120-65-M             | 65  | M      | qPCR, $^{14}\text{C}$                   | -                       | 1A-G, D(23), 2A-B, 3A(23)           |
| 141120-80-F             | 80  | F      | $^{14}\text{C}$                         | -                       | 1D(24), E-F, 2A-B, 3A(24)           |
| 150319-70-F             | 70  | F      | ( $^{14}\text{C}^{\text{I}}$ )          | -                       | 1D(25)                              |
| 150611-62-F             | 62  | F      | qPCR                                    | No                      | 1A-C                                |
| 150618-61-M-1<br>Nodule | 61  | M      | $^{14}\text{C}^{\text{J}}$              | +                       | 1E-F, 2A-D                          |
| 150819-77-M             | 77  | M      | qPCR, ( $^{14}\text{C}^{\text{G}}$ )    | No                      | 1A-C                                |
| 150910-53-M             | 53  | M      | qPCR, $^{14}\text{C}^{\text{K}}$        | +                       | 1E-F, G, 2A-D                       |
| 150917-52-M             | 52  | M      | qPCR, $^{14}\text{C}$                   | +                       | 1A-C, E-F, G, 2A-D                  |
| 150950-70-M             | 70  | M      | qPCR                                    | No                      | 1A-C                                |
| 151015-72-M<br>Nodule   | 72  | M      | qPCR, $^{14}\text{C}^{\text{L}}$        | +                       | 1E-F, G, 2A-D                       |
| 160618-78-M             | 78  | M      | ( $^{14}\text{C}^{\text{G}}$ )          | -                       | NA                                  |

Table footnotes: A: 'No' indicates no demographics information. B: '-' indicates demographics without disease stage. C: '+' indicates that demographics include disease stage. D: Sample from thumb (16) was sufficiently labelled for quantification, sample from little finger (15) was not. E: Sample from thumb was sufficiently labelled, samples from ring and little finger were not. F: Mean value for cord and nodule utilised for quantification. G: Not sufficiently labelled for quantification. H: Mean value for cord (22) and nodule (21) utilised for analysis. I: Samples from neither the 4th (25) or 5<sup>th</sup> phalanges were sufficiently labelled for quantification. J: Cord was insufficiently labelled for quantification. K: Mean value for cord and nodule utilised. L: Cord was insufficiently labelled

**Supplementary Table 2: Human normal Palmar Fascia (PF) surgical samples used for collagen synthesis assays.**

| Sample ID   | Age | Gender | Methods (pulse-chase: $^{14}\text{C}$ ) | Data shown in Figure: (lane number) |
|-------------|-----|--------|-----------------------------------------|-------------------------------------|
| 140723-82-F | 82  | F      | qPCR, $^{14}\text{C}$                   | 1A-C, D(4), 3A(4)                   |
| 140821-38-M | 38  | M      | qPCR, $^{14}\text{C}$                   | 1A-C, D(2), 3A(2)                   |
| 140821-39-F | 39  | F      | qPCR, $^{14}\text{C}$                   | 1A-C, 3A(11)                        |
| 140822-54-F | 54  | F      | qPCR, $^{14}\text{C}$                   | 1A-C, D(3), 3A(3)                   |
| 140822-55-F | 55  | F      | qPCR, $^{14}\text{C}$                   | 1A-C, D(1), 3A(1)                   |
| 140822-68-F | 68  | F      | qPCR, $^{14}\text{C}$                   | 1A-C, D(6), 3A(6)                   |
| 140911-48-M | 48  | M      | $^{14}\text{C}$                         | 1D(10), 3A(10)                      |
| 141002-44-F | 44  | F      | qPCR                                    | 1A-C, D(7), 3A(7)                   |
| 141003-79-F | 79  | F      | qPCR                                    | 1A-C                                |
| 141007-57-F | 57  | F      | qPCR                                    | 1A-C                                |
| 141009-25-F | 25  | F      | $^{14}\text{C}$                         | 1D(8)                               |
| 141013-34-M | 34  | M      | qPCR                                    | 1A-C                                |
| 141013-67-M | 67  | M      | qPCR                                    | 1A-C                                |
| 141103-51-F | 51  | F      | $^{14}\text{C}$                         | 1D(9)                               |
| 141125-77-F | 77  | F      | $^{14}\text{C}$                         | 1D(5)                               |
| 141128-50-F | 50  | F      | qPCR                                    | 1A-C                                |
| 141218-53-M | 53  | M      | qPCR                                    | 1A-C                                |



**Supplementary Table 3. Human surgical samples used for cell culture and treatments.**

| Sample ID   | Age | Gender | Tissue type               | Data shown in Figure:                                                                 |
|-------------|-----|--------|---------------------------|---------------------------------------------------------------------------------------|
| 161012-62-F | 62  | F      | Dupuytren's Cord & Nodule | 4, 5 E& H(nodule), F,I(cord), 6 A-F(cord), G-H & J-K(nodule), I, L, 7 A&C(nodule), 7B |
| 161109-70-M | 70  | M      | Dupuytren's Cord & Nodule | 4, 5B (nodule, 6-11), 6 A-F(cord), G-L, 7 A-C                                         |
| 161130-65-M | 65  | M      | Dupuytren's Cord & Nodule | 4, 5C (nodule, 12-17), 6 A-F(nodule), G-L, 7A-C                                       |
| 161130-76-M | 76  | M      | Dupuytren's Cord & Nodule | 4, 5A (cord, 1-4), 6 A-L, S3 B&E(nodule), D&F(cord), 7 A-C                            |
| 170201-67-M | 67  | M      | Normal Palmar Fascia      | 4, 6 A-F, I, L, 7B, D                                                                 |
| 170206-69-M | 69  | M      | Normal Palmar Fascia      | 4, 6 I, L, 7B, D                                                                      |
| 170301-61-F | 61  | F      | Normal Palmar Fascia      | 4, 5, 6 A-F, S3A, D, , 7B, D                                                          |
| 170313-57-F | 57  | F      | Normal Palmar Fascia      | 4, 5 D&G, 6 A-F, I, L, 7B, D                                                          |
| 181126-71-M | 71  | M      | Dupuytren's               | 8                                                                                     |
| 190109-66-F | 66  | F      | Dupuytren's               | 8                                                                                     |
| 190313-63-M | 63  | M      | Dupuytren's               | 8                                                                                     |
| 190501-65-F | 65  | F      | Dupuytren's               | 8, 9                                                                                  |
| 190604-62-M | 62  | M      | Dupuytren's               | 8, 9                                                                                  |
| 190614-69-M | 69  | M      | Dupuytren's               | 8, 9                                                                                  |
| 170403-68-M | 68  | M      | Dupuytren's Cord & Nodule | 10                                                                                    |
| 170403-86-M | 86  | M      | Dupuytren's Cord & Nodule | 10                                                                                    |
| 170412-51-M | 51  | M      | Dupuytren's Nodule        | 10                                                                                    |
| 170412-68-F | 68  | F      | Dupuytren's Nodule        | 10                                                                                    |
| 170508-76-M | 76  | M      | Dupuytren's Cord & Nodule | 10                                                                                    |
| 170515-65-M | 65  | M      | Dupuytren's Cord & Nodule | 10                                                                                    |
| 170802-80-M | 80  | M      | Dupuytren's Nodule        | 10                                                                                    |
| 170816-73-F | 73  | F      | Dupuytren's Cord          | 10                                                                                    |
| 170816-78-M | 78  | M      | Dupuytren's Nodule        | 10                                                                                    |