Supporting informations

Preliminary *in vivo* study of biodegradables PLA-PEU-PLA membranes in a rat Achilles tendon model: A new solution for the reduction of peritendinous adhesions

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Fig. S1 ¹H-NMR spectrum of (I) D-PACO1 membrane and (II) D-PACO2 membrane



Fig. S2 Histologic examination and higher magnification of images of Achilles tendon tissues by SHE stain at 2 weeks after surgery; a: control group (no surgery); b: Adhesions group (surgery, no treatment). S: skin, T: tendon, TC: tendon + cartilage (tendon enthesis), thick arrows indicate adhesions around fragments of tendon. Scale bare: 5 mm and 500 μm.



Fig. S3 Macroscopic images of the wound site in the Achilles tendons of rats before and after the dissection of peritendinous adhesions, 2 weeks after surgery (A) Control group and (B) Adhesions group. Scale bar: 2.5 mm.



Fig. S4 Macroscopic scoring evaluation of peritendinous adhesions 2 and 10 weeks after surgery. Six rats were included in each group: G2, adhesions group; G3, D-PACO1 group; G4, D-PACO2 group. The graph presents mean of macroscopic scoring ± SEM. Asterisks indicate significant difference with respect to the G2 group results (two-way ANOVA followed by Tukey test, *** p<0.001).</p>



(B) 10 weeks



Fig. S5 Histological examination and higher magnification of images of Achilles tendon tissues by SHE stain, (A) 2 weeks and (B) 10 weeks after surgery. G1: control group (no surgery); G2: Adhesions group (surgery, no treatment); G3: D-PACO1 treated group (surgery + D-PACO1 membrane); G4: D-PACO2 treated group (surgery + D-PACO2 membrane). S: skin, T: tendon, GT: granulation tissue, Thick arrows indicate adhesions between the skin and the granulation tissue surrounding and replacing the damaged tendon. Thin arrow in (A-G3) indicate a small band of fibrous connective tissue and the thin arrow in B-G2 points to mild granulomatous reaction around suture material. Scale bar: 500 μm. Two weeks after surgery, the untreated Achilles tendons in the adhesions group (G2) showed severe adhesions and abundant fibrous repair tissue between the damaged tendon and the surrounding tissues (A-G2). In animals treated with D-PACO1 membrane (G3) (A-G3) and D-PACO2 membrane (G4) (A-G4), the membranes created clear empty spaces between the skin and the damaged tendon. In D-PACO1 group G3 (A-G3), there was small irregular septa of connective tissue. For the D-PACO2 membrane (G4), there were no adhesions observed. D-PACO1 and D-PACO2 membranes elicited typical foreign body reactions that were mild to moderate with infiltration by mixed inflammatory cells. The tendons were replaced by large amounts of granulation tissue, with numerous fibroblasts, moderate neovascularization, and no difference in healing was observed between untreated (G2) and treated samples (G3 and G4). At 10 weeks after surgical trauma, there were no visible adhesions observed between the skin and the healing tendon of the treated animals (B-G3 and B-G4) compared to the adhesions group (B-G2). The foreign body reaction caused by the membranes was comparable in all surgical sections of the treated groups (G3 and G4) and reactions

occasionally increased due to incidental granulomatous inflammation around hair fragments or pieces of surgical material (gauze) (B-G2).



Fig. S6 Histological examination of Achilles tendon healing by SHE stain (A) 2 weeks and (B) 10 weeks after surgery. G1: control group (no surgery); G2: Adhesions group (surgery, no treatment); G3: D-PACO1 treated group (surgery + D-PACO1 membrane); G4: D-PACO2 treated group (surgery + D-PACO2 membrane) In G2, G3 and G4, the tendon is totally replaced by a large amount of mature granulation with moderate neovascularization. Arrows: examples of blood vessels. Scale bar: 100 µm. For tendon healing at 10 weeks after surgery, the number of fibroblasts and the number of blood vessels were lower in all groups compared to 2 weeks. The deposition of collagenous matrix in the D-PACO groups was almost at the same level of the control group (G1) without surgery.