

AB0079

### EFFECT OF HYALURONIC ACID LOCAL INJECTIONS ON ACHILLES TENDINOPATHIES: AN OBSERVATIONAL STUDY ON TENDON VISCOELASTIC PROPERTIES AND THEIR RELATIONSHIPS WITH CLINICAL OUTCOMES

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**Background:** Effect of hyaluronic acid local injections on Achilles tendinopathies: an observational study on tendon viscoelastic properties and their relationships with clinical outcomes.

**Objectives:** Achilles tendinopathy (AT) affects athletes, recreational exercisers and also inactive people, where it is sometimes associated with arthritic phenotypes. The aim of this study was to evaluate the efficacy of a three-local injections regimen of hyaluronic acid (HA) in middle aged patients with a diagnosis of AT; the relationships of the functional, biochemical and clinical outcomes with the viscoelastic properties of the tendon were also studied

**Methods:** 8 patients previously diagnosed for monolateral AT were enrolled. AT was confirmed before the first local HA injection (T0) by clinical examination, MRI and thermography. At T0 patients were assessed for maximal voluntary isometric contraction (MVI) involving Achilles tendon (both injured and healthy), and pain level with a Likert scale; Achilles tendon viscoelastic state, i.e. tone and stiffness, were then measured at relaxed state and at 10% of MVI with MyotonPro (Myoton Ltd, UK). Finally patients received the first HA injection (RegenFlex T&M, a blend of 2 to 1000 KDa HA, Regenyal, IT). All the measurements were repeated at T1 (15 days after the first injections and immediately prior the second), at T2 (15 days after the second injection and prior the third) and at T3 (15 days after the third injection), i.e. over a total of 45 days in which clinical visits were also performed. Furthermore, before each injection, injured tendon exudates were collected by needle aspiration and the levels of IL-1 $\beta$  and matrix metalloproteinase 3 (MMP-3) were determined with an ELISA test.

**Results:** At T0, pain score and MVI were significantly higher and lower in injured tendons, respectively. Accordingly, tone and stiffness values were significantly different between injured and contralateral tendons, especially when measured at the relaxed state. Interestingly, the above differences gradually disappeared at T1, 2 and 3. In keeping with these results, tendon exudates volumes also decreased over time, as well as the levels of IL-1 $\beta$  and MMP-3.

**Conclusion:** RegenFlex T&M promoted a progressive healing of AT, with recovery of clinical, functional and tendon's viscoelastic state.

#### REFERENCES

- [1] P. Sestili, M. Gervasi, E. Barbieri, I. Capparucci, G. Annibaldi, S. Contarelli, D. Sisti, S. Amatori and Department of Biomolecular Sciences, University Urbino Carlo Bo, via A. Saffi 2, 61029 Urbino, Italy

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AB0080

### THE INHIBITION OF IL-25 TO THE EFFECT OF IL-17 TO ERK1/2 AND MMP-3 IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIALCYTES

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**Background:** Rheumatoid arthritis (RA) is a common chronic systemic autoimmune diseases characterized by the inflammation in joint and synovium. Synovitis leads to the destruction of cartilage and bone in joint subsequently joint dysfunction and even disability eventually. Recently, IL-25 has been found to play a role in regulating inflammation through Th1 and Th17 responses in inflammatory diseases<sup>[3]</sup>. However, the function to fibroblast-like synoviocytes and its signaling pathway are not clear. This study aims to probe the effects of IL-25 on the expression of ERK1/2 and MMP-3 in RA fibroblast-like synoviocytes.

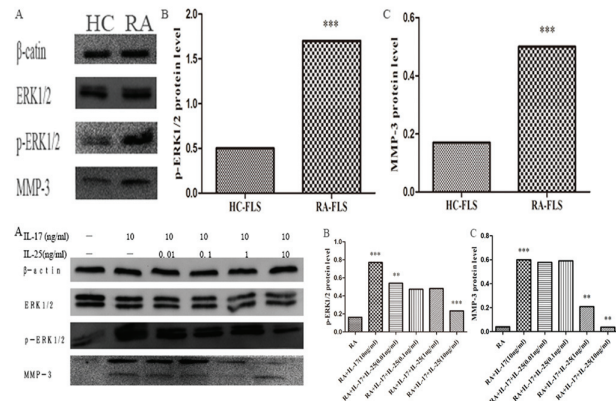
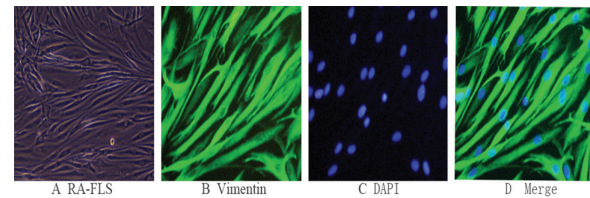
**Objectives:** To study the function of IL-25 for rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS) differentiation as well as to the effects on the expression of extracellular regulating protein kinase (ERK) and matrix metalloproteinases-3 (MMP-3).

**Methods:** The differences on ERK1/2 and MMP-3 protein levels were tested in RA-FLS and healthy controls, then IL-17A (10ng/ml), different concentrations of IL-25 (0.01, 0.1, 1 and 10ng/ml) and IL-17A(10ng/ml) to co-stimulate the RA-FLS for 24 hours respectively. The expression of ERK1/2 and MMP-3 protein were detected by the Western blot. The results were expressed by  $\pm$ s, *t* test was used for the comparison between different groups.

**Results:** The expression of ERK1/2 (1.71 $\pm$ 0.17) and MMP-3 (0.50 $\pm$ 0.13) proteins in RA-FLS was higher than the healthy controls (0.50 $\pm$ 0.15, 0.17 $\pm$ 0.05)(*t*=9.13, *P*<0.001 and *t*=4.10, *P*<0.05), because of the stimulation of IL-17A, the expression of ERK1/2 (0.77 $\pm$ 0.22) and MMP-3 (0.59 $\pm$ 0.13) proteins in RA-FLS were increased compared with untreated groups (0.18 $\pm$ 0.35, 0.04 $\pm$ 0.03)(*t*=

4.69, *P*<0.01 and *t*=-7.47, *P*<0.01). with the increase of the concentration on IL-25, the level of ERK1/2 (0.54 $\pm$ 0.26, 0.48 $\pm$ 0.18, 0.48 $\pm$ 0.23, 0.23 $\pm$ 0.06) and MMP-3 (0.58 $\pm$ 0.09, 0.59 $\pm$ 0.14, 0.21 $\pm$ 0.04, 0.04 $\pm$ 0.02) in RA-FLS which stimulated by IL-17A was decreased slowly (*t*=4.22, *P*<0.05 and *t*=4.95, *P*<0.01 and *t*=7.47, *P*<0.01).

**Conclusion:** IL-25 can inhibit the stimulation of IL-17A on ERK1/2 and MMP-3 fractionally, which imply that it may take part in the development of RA through this pathway and may play as a target for the RA treatment on IL-17A.



**Disclosure of Interests:** None declared

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AB0081

### NOVEL COOPERATION BETWEEN CCL26 AND CX3CL1 VIA CX3CR1 IN THE INJURY OF SMALL BILE DUCT IN PRIMARY BILIARY CIRRHOSIS

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**Background:** CX3CL1-CX3CR1 pathway has been found to be critically involved in the pathogenesis of primary biliary cholangitis (PBC)<sup>1</sup>. As a novel ligand to CX3CR1, CCL26 can promote chemotaxis of CX3CR1+ immune cells but its role in PBC remains elusive<sup>2</sup>.

**Objectives:** This study aimed to explore the role of CCL26, together with CX3CL1-CX3CR1 pathway, in the pathogenesis of PBC.

**Methods:** We recruited 40 patients diagnosed with PBC in the Peking Union Medical College Hospital from Jan 2018 to May 2018 and 18 age and sex-matched healthy controls (HCs). Peripheral blood and liver tissue samples were collected. The plasma level of CX3CL1 and CCL26 were determined by ELISA. Flow cytometry was used to measure the percentage of CX3CR1+ cells in various subsets of PBMCs. The expression of CX3CL1 and CCL26 in liver tissues was revealed by immunohistochemical staining. Using ELISA and flow cytometry, the change of CX3CL1/CCL26-CX3CR1 pathway expression in human intrahepatic biliary epithelial cells (HIBECs) upon stimulation of various cytokines was studied.

**Results:** The plasma level of CX3CL1 and CCL26 was higher in patients with PBC than HCs with a *P* value of 0.044 and 0.104 respectively. The increased level of CCL26 was positively correlated with peripheral eosinophils, basophils and CRP level. In comparison with HCs, the expression of CX3CR1 was significantly higher in NKT-like and CD4+ T cells in PBC patients. In liver samples from PBC patients, CX3CL1 and CCL26 were significantly over-expressed in intrahepatic bile ducts and CCL26 also tended to be abundant in hepatocytes near portal areas and gradually weakened in distant regions. This distribution pattern was not observed in HCs. Upon stimulation of IFN- $\gamma$ , the expression of CX3CR1 on HIBEC surface and CX3CL1 in culture supernatant was significantly up-regulated, while the expression of CCL26 was increased upon IL-4 and IL-13 stimulation.

**Conclusion:** CCL26 may cooperate with CX3CL1 to mediate the immune injury of intrahepatic bile ducts via CX3CR1 in PBC.