Loss of Tissue Regenerative Capacity in Aging – the Tendon

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1. Introduction

✓ Tendon aging is a complicated process following similar mechanisms of other tissues[1]

✓ Tendon structure and cellular composition is also unique, which makes scientific research a very specific and select task

✓ Tendon cells include[2] →

- Tenocytes - differentiated tendon cells

- Mesenchymal Stem Cells (MSCs), which include Tendon/Stem Progenitor Cells (TSPCs) – capable of clonogenicity, multipotency and self-renewal according with stimuli and respective cellular adaptation[3]

2. Objectives

✓ Discuss the current evidence on tendon aging and its treatment

✓ Identify potential targets to be considered for future therapies

3. Design

Analytical review conducted through *PubMed* database

"tendon cell aging" and "tendon cell regeneration"

English written original articles only

No year of publication restrictions

4. Results

- Moderate exercise ameliorates the depletion of TSPCs and it is beneficial for delaying the undesirable effects of age[4]
- Mechanical stretching improved the tenogenic differentiation of both induced pluripotent stem cells (iPSCs) and pre-MSCs[3]
- When tenocytes are exposed to a certain amount of NSAIDs, the differentiation of MSCs to tenocytic lineage gets impaired and drawn toward adipocytic lineage[5]
- Different concentrations of ascorbic acid have been used in tenocyte cultures to enhance collagen synthesis[5]
- Ultrasonication and shock wave were experimentally confirmed to be beneficial for promoting the differentiation and proliferation of MSCs[6]
- An important role for increased Rho has been reported, associating coiled-coil forming protein kinase (ROCK) activity in accelerating the ageing progress of aged TSPC[7] →

A changing back to a morphology similar to young TSPCs

Upon treatment with Y-27632, a common ROCK inhibitor[7]

5. Conclusions

✓ In tendon injuries there is no optimal treatment strategy till this day

✓ Limited studies have been done to explore all the elaborate cell repair mechanisms in the tendon

Tendon aging can be correlated with TSPC aging ⟷ Tendon MSCs may be the main orchestrators directing tendon-regenerative processes

✓ It is of atmost importance to understand how the tendon ages → create alternative guided treatment strategies

References

1. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. *The hallmarks of aging*. Cell. 2013;153 (6):1194–1217.
2. Costa-Almeida R, Calejo I, Gomes M. *Mesenchymal Stem Cells Empowering Tendon Regenerative Therapies*. Int. J. Mol. Sci. 2019, 20, 3002; doi:10.3390/ijms20123002.
3. Dai GC, Li YJ, Chen MH, Lu PP, Rui YF. *Tendon stem/progenitor cell ageing: Modulation and rejuvenation*. World J Stem Cells 2019 September 26; 11(9): 677-692 DOI: 10.4252/wjsc.v11.i9.677.
4. Zhang J, Wang JH. *Moderate Exercise Mitigates the Detrimental Effects of Aging on Tendon Stem Cells*.; PLoS One 2015; 10: e0130454; DOI: 10.1371/journal.pone.0130454.
5. . Chiu CH, Chen P, Chen AC, Chan YS, Hsu KY, Rei H, and Lei KF. *Real-Time Monitoring of Ascorbic Acid-Mediated Reduction of Cytotoxic Effects of Analgesics and NSAIDs on Tenocytes Proliferation*. Dose-Response: An Interna DOI: 10.1177/1559325819832143.
6. Chen et al. *Effect of Low-Intensity Pulsed Ultrasound After Autologous Adipose-Derived Stromal Cell Transplantation for Bone-Tendon Healing in a Rabbit Model*. The American Journal of Sports Medicine; 2019;47(4):942–953 DOI: 10.1177/0363546518820321.
7. Kohler J, Popov C, Klotz B, Alberton P, Prall WC, Haasters F, Müller-Deubert S, Ebert R, Klein-Hitpass L, Jakob F, Schieker M, Docheva D. *Uncovering the cellular and molecular changes in tendon stem/progenitor cells attributed to tendon aging and degeneration*. Aging Cell 2013; 12: 988-999; DOI: 10.1111/acel.12124.