













percholesterolemic rats treated with statin compared to controls. However, this result could be interpreted as in support of our hypothesis. Perhaps most importantly, the drug was administered at pharmacological doses and no evidence of adverse effects in the Achilles tendon due to such treatment was found. Therefore, results support the possibility that simvastatin treatment may not majorly compromise Achilles tendon health in hypercholesterolemic individuals.

### Conflicts of interest

The Author (LJS) has a patent related to hypercholesterolemia and tendinous injuries (US9427437). No other conflicts of interest exist that might be construed as affecting the conduct or reporting of the work presented.

### References

1. Mozaffarian D, Benjamin EJ, Go AS, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2015 Update: A Report from the American Heart Association. *Circulation*. 2015;131(4):e29-322.
2. Klemp P, Halland AM, Majoos FL, Steyn K. Musculoskeletal manifestations in hyperlipidaemia: a controlled study. *Ann Rheum Dis*. 1993;52:44-48.
3. Tsouli SG, Kiortsis DN, Argyropoulou MI, Mikhailidis DP, Eljaf MS. Pathogenesis, detection and treatment of Achilles tendon xanthomas. *Eur J Clin Invest*. 2005;35:236-244.
4. von Bahr S, Movin T, Papadogiannakis N, et al. Mechanism of accumulation of cholesterol and cholesterol in tendons and the role of sterol 27-hydroxylase (CYP27A1). *Arterioscler Thromb Vac Biol*. 2022;22:1129-1135.
5. Mathiak G, Wening JV, Mathiak M, Neville LF, Jungbluth K. Serum cholesterol is elevated in patients with Achilles tendon ruptures. *Arch Orthop Trauma Surg*. 1999;119:280-284.
6. Beason DP, Hsu JE, Marshall SW, et al. Hypercholesterolemia increases supraspinatus tendon stiffness and elastic modulus across multiple species. *J Shoulder Elbow Surg*. 2013;22:681-686.
7. Istvan ES, Deisenhofer J. Structural mechanism for statin inhibition of HMG-CoA reductase. *Science*. 2001;292:1160-1164.
8. Chazotte P, Hayem G, Hamza S, Best C, Ziza JM. Four cases of tendinopathy in patients on statin therapy. *Joint Bone Spine*. 2001;68:430-433.
9. Pulla RC, Gharla MR, Karas RH, Alsheikh-Ali AA, Thompson PD. Tendon rupture associated with simvastatin/ezetimibe therapy. *Am J Cardiol*. 2007;100:152-153.
10. Savvidou C, Moreno R. Spontaneous distal biceps tendon ruptures: are they related to statin administration? *Hand Surg*. 2012;17:167-171.
11. Schaafsma D, Dueck G, Ghavami S, et al. The mevalonate cascade as a target to suppress extracellular matrix synthesis by human airway smooth muscle. *Am J Respir Cell Mol Biol*. 2011;44:394-403.
12. Contractor T, Beri A, Gardiner JC, Tang X, Dwamena FC. Is Statin Use Associated With Tendon Rupture? A Population-Based Retrospective Cohort Analysis. *Am J Ther*. 2015;22:377-381.
13. Marie I, Delafenêtre H, Massy N, Thuillez C, Noblet C. Network of the French Pharmacovigilance Centers. Tendinous disorders

- attributed to statins: a study on ninety-six spontaneous reports in the period 1990-2005 and review of the literature. *Arthritis Rheum*. 2008;59:367-372.
14. Teichtahl AJ, Brady SR, Urquhart DM, et al. Statins and tendinopathy: a systematic review. *Med J Aust*. 2016;204:115-121.
15. Lin TT, Lin CH, Chang CL, Chi CH, Chang ST, Sheu WH. The effect of diabetes, hyperlipidemia, and statins on the development of rotator cuff disease: a nationwide, 11-year, longitudinal, population-based follow-up study. *Am J Sports Med*. 2015;43:2126-2132.
16. Freedman BR, Gordon JA, Soslowky LJ. The Achilles tendon: fundamental properties and mechanisms governing healing. *Muscles Ligaments Tendons J*. 2014;4:241-251.
17. de Oliveira, Vieira CP, Guerra FD, Almeida MS, Romel ER. Structural and biomechanical changes in the Achilles tendon after chronic treatment with statins. *Food Chem Toxicol*. 2015;77:50-57.
18. Kaleağasioğlu F, Olcay E, Olgun Y. Statin-induced calcific Achilles tendinopathy in rats: comparison of biomechanical and histopathological effects of simvastatin, atorvastatin and rosuvastatin. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(6):1884-1891.
19. Tucker JJ, Soslowky J. Effect of simvastatin on rat supraspinatus tendon mechanical and histological properties in a diet-induced hypercholesterolemia model. *J Orthop Res*. 2016;34(11):2009-2015.
20. Beason DP, Tucker JJ, Lee CS, Edelstein L, Abboud JA, Soslowky LJ. Rat rotator cuff tendon-to-bone healing properties are adversely affected by hypercholesterolemia. *J Shoulder Elbow Surg*. 2014;23:867-872.
21. Paulo J, Oliva F, Frizziero A, Maffulli N. *Muscles, Ligaments and Tendons Journal - Basic principles and recommendations in clinical and field science research: 2016 update*. MLTJ. 2016;6(1):1-5.
22. Favata, M. Scarless healing in the fetus: implications and strategies for postnatal tendon repair. PhD Thesis, Bioengineering. University of Pennsylvania, Philadelphia. 2006.
23. Bey MJ, Song HK, Wehrli FW, Soslowky LJ. A noncontact, nondestructive method for quantifying intratissue deformations and strains. *J Biomech Eng*. 2002;124:253-258.
24. Descamps OS, Leysen X, Van Leuven F, Heller FR. The use of Achilles tendon ultrasonography for the diagnosis of familial hypercholesterolemia. *Atherosclerosis*. 2001;157:514-518.
25. Rolf CG, Fu BS, Pau A, Wang W, Chan B. Increased cell proliferation and associated expression of PDGFRbeta causing hypercellularity in patellar tendinosis. *Rheumatology (Oxford)*. 2001;40(3):256-261.
26. Rufai A, Benjamin M, Ralphs JR. Development and ageing of phenotypically distinct fibrocartilages associated with the rat Achilles tendon. *Anat Embryol (Berl)*. 1992;186(6):611-618.
27. Eliasson P, Svensson RB, Giannopoulos A, Eismark C, Kjær M, Schjerling P, Heinemeier KM. Simvastatin and atorvastatin reduce the mechanical properties of tendon constructs in vitro and introduce catabolic changes in the gene expression pattern. *PLoS ONE*. 2017;12(3):e0172797.
28. Nakano A, Kinoshita M, Okuda R, Yasuda T, Abe M, Shiomi M. Pathogenesis of tendinous xanthoma: histopathological study of the extremities of Watanabe heritable hyperlipidemic rabbits. *J Orthop Sci*. 2006;11:75-80.
29. Abboud JA, Beason DP, Soslowky LJ. Emerging ideas: the effect of hypercholesterolemia on tendons. *Clin Orthop Relat Res*. 2012;470:317-320.
30. Kuklina EV, Shaw KM, Hong Y. Vital Signs: Prevalence, Treatment, and Control of High Levels of Low-Density Lipoprotein Cholesterol - United States, 1999-2002 and 2005-2008. *Morbidity and Mortality Weekly Report, CDC*. 2011;6:109-114.