Reply to: Could leptin-deficient mice be good novel models for diabetic Achilles tendinopathy?

Sirs,

We appreciate your interest in our work. Your suggestion will stimulate us to further efforts.

First question: obesity had been recognised as the independent risk factor of Achilles tendinopathy in human-beings. The excess body weight of ob mice should be taken into consideration in the pathogenesis of Achilles tendinopathy.

Clinical researches (1, 2) show that structure disorder change of Achilles tendon exists in diabetic patients, there is a tendency towards spontaneous rupture. At the same time, the leptin-deficient (ob/ob) mouse is a new animal model of peripheral neuropathy of type 2 diabetes and obesity (3, 4). Therefore, we believe that the Achilles tendon of ob mice has a similar pathologic structure change as diabetes patients. Our research confirmed our hypothesis (5).

We also think that mechanical factors play a very important role in the development of Achilles tendinopathy (6, 7). Diabetes patients often suffer from obesity, therefore, pathological changes of the Achilles tendon in ob mice were studied in order to research Achilles tendinopathy in diabetic patients. Therefore, we are not merely setting up an animal model of Achilles tendinitis.

Second question: could decompensated leptin-signalling represent the changes of leptin signalling during the development of diabetic Achilles tendinopathy?

Leptin-deficient leads to a series of endocrine function change, such as hyperglycemia, hypercholesteremia and insulin resistance symptoms, in addition to characterisation of manifestations and pathogenetic mechanicsms of peripheral diabetic neuropathy (PDN) (8). At present, our study just demonstrates that there are structural abnormalities in the Achilles tendon of diabetic model mice. Perhaps leptin-resumption of ob mice delays the onset of the Achilles tendon disease? This provides new thought for our further research.

Moreover, leptin-signalling on neuropathy for the prevention of diabetic Achilles tendinopathy should consequently arouse more interest (9, 10). Whether leptin delays and protects the diabetes nerve and tendons (9, 10), is subject to further study.

As Achilles tendinitis occurred in the Achilles tendon resection model, the question as to whether leptin delays Achilles tendinitis developing caused by mechanical factors is also a research direction.

Finally, thank you again for your interest in our work.

J. JI[1]
Q. JIANG[1,2]

[1]The Center of Diagnosis and Treatment for Joint Disease, Drum Tower Hospital Affiliated to Medical School of Nanjing University; [2]Laboratory for Bone and Joint Diseases, Model Animal Research Center, Nanjing University, Jiangsu, China.

Address correspondence and reprint requests to: Qing Jiang, MD, PhD, The Center of Diagnosis and Treatment for Joint Disease, Drum Tower Hospital Affiliated to Medical School of Nanjing University, 321 Zhongshan Road, Nanjing, Jiangsu, 210009, P.R. China.
E-mail: qingj@nju.edu.cn

Clin Exp Rheumatol 2017; 35 (Suppl. 104): S4.

Competing interests: none declared.

References

1. BATISTA F, NERY C, PINZUR M *et al*.: Achilles tendinopathy in diabetes mellitus. *Foot Ankle Int* 2008; 29: 498-501.
2. GILL GV, ENGLISH PJ, EYES B, *et al*.: Painless rupture of the Achilles tendon in a diabetic patient with sensory neuropathy. *Pract Diab Int* 2007; 24: 29-30.
3. VIKTOR R, DREL, NAZAR MASHTALIR *et al*.: The leptin-deficient (ob/ob) mouse a new animal model of peripheral neuropathy of type 2 diabetes and obesity. *Diabetes* 2006; 55: 3335-43.
4. HALUZIK M, COLOMBO C, GAVRILOVA O *et al*.: Genetic background (C57BL/6J versus FVB/N) strongly influences the severity of diabetes and insulin resistance in ob/ob mice. *Endocrinology* 2004; 145: 3258-64.
5. JI J, WANG Z, ShI D, GAO X, JIANG Q: Pathologic changes of Achilles tendon in leptin-deficient mice. *Rheumatol Int* 2010; 30: 489-93.
6. WANG L, HUANG MJ, YIN GH *et al*.: Characterization of a novel calcific Achilles tendinopathy model in mice: contralateral tendinopathy induced by unilateral tenotomy. *J Surg Res* 2013 in press doi:10.1016/j.jss.2013.10.059.
7. HOLMES GB, LIN J: Etiologic factors associated with symptomatic Achilles tendinopathy. *Foot Ankle Int* 2006; 27: 952-9.
8. ALYSSA H, HASTY, HITOSHI SHIMANO *et al*.: Severe hypercholesterolemia, hypertriglyceridemia, and atherosclerosis is in mice lacking both leptin and the low density lipoprotein receptor. *J Biol Chem* 2001; 276: 37402-8.
9. FOLCH J, PEDRÓS I, PATRACA I *et al*.: Neuroprotective and anti-ageing role of leptin. *J Mol Endocrinol* 2012; 49: R149-56.
10. DE OLIVEIRA RR, MARTINS CS, ROCHA YR *et al*.: Experimental diabetes induces structural, inflammatory and vascular changes of Achilles tendons. *PLoS One* 2013; 8: e74942.