



Letter to the editor

Can urinary titin be used for predicting Duchenne muscular dystrophy?



We appreciate “Letter to the editor” for comments on our 2 papers published in *Clinica Chimica Acta*. Responses to comments are described below.

- 1) We have published 2 papers on urinary titin relating to Duchenne muscular dystrophy (DMD) in a short time period. Though both were published in the year of 2018, the first and second study was performed in 2015–2016 and 2018, respectively. We are afraid that this makes confusion in understanding. In the first paper [1], 113 DMD patients aged 3–29 y were examined for their urinary titin levels at 145 points. This was the hospital-based study, and urine samples were obtained at the time of their visit to the outpatient clinic. In the hospital, it was difficult to obtain control urine samples. Therefore, only 9 urine samples were obtained from controls aged from 4 to 16 years. This was the limitation of this study. In the second paper [2], we examined a possibility to screen DMD using urinary titin as a biomarker since the results obtained in the first paper suggested the possibility. Then, the community-based study was implemented to enroll 100 apparently healthy 3-year-children. Urinary titin levels of healthy children were found within a very narrow range. To examine the applicability to screen DMD, 4 urinary titin values of 3-year-old DMD patients were obtained from the results published in the first paper and revealed in the afterward study. There found strongly elevated urinary titin levels in DMD.
- 2) Early detection of DMD is an emerging issue. We desired to set the optimal thresholds to screen DMD. However, we believe that it is too early to set the thresholds. Because, numbers of samples of both 3-

year-old DMD patients and controls were small. By enlarging the number of DMD patients, we wish to set the threshold in near future.

- 3) Urinary titin values of 3-y-old DMD patients were remarkably high and far separated from that of controls. This indicated very severe titin degradation in DMD. In the first report the number of control was small, even though we tried to collect urine samples as many as possible during the study period. In the second report, we set the number of samples to 100 in the study plan, since this was a preliminary study. As a whole, we never selected the controls intentionally in these 2 separated studies.

References

- [1] H. Awano, M. Matsumoto, M. Nagai, T. Shirakawa, N. Maruyama, K. Iijima, Y.I. Nabeshima, M. Matsuo, Diagnostic and clinical significance of the titin fragment in urine of Duchenne muscular dystrophy patients, *Clin. Chim. Acta* 476 (2018) 111–116.
- [2] M. Matsuo, T. Shirakawa, H. Awano, H. Nishio, Receiver operating curve analyses of urinary titin of healthy 3-y-old children may be a noninvasive screening method for Duchenne muscular dystrophy, *Clin. Chim. Acta* 486 (2018) 110–114.

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