

polymorphism with high myopia. *Invest Ophthalmol Vis Sci* 2010; **51**: 96–102.

- 3 Lin HJ, Wan L, Tsai Y, Chen WC, Tsai SW, Tsai FJ. Muscarinic acetylcholine receptor 1 gene polymorphisms associated with high myopia. *Mol Vision* 2009; **15**: 1774–1780.
- 4 Wittke-Thompson JK, Pluzhnikov A, Cox NJ. Rational inferences about departures from Hardy-Weinberg equilibrium. *Am J Hum Genet* 2005; **76**: 967–986.
- 5 Nakanishi H, Yamada R, Gotoh N, Hayashi H, Yamashiro K, Shimada N *et al*. A genome-wide association analysis identified a novel susceptible locus for pathological myopia at 11q24.1. *PLoS Genet* 2009; **5**: e1000660.

JA Guggenheim¹, T Zayats^{2,3}, C Hammond^{4,5}
and TL Young⁶

¹School of Optometry & Vision Sciences, Cardiff University, Cardiff, Wales, UK

²MRC Centre for Causal Analyses in Translational Epidemiology, University of Bristol, Bristol, UK

³Department of Social Medicine, University of Bristol, Bristol, UK

⁴Twin Research and Genetic Epidemiology, King's College London, St Thomas' Hospital, London, UK

⁵West Kent Eye Centre, Bromley Hospitals NHS Trust, London, UK

⁶Duke University Center for Human Genetics, Durham, NC, USA

E-mail: Guggenheim@cf.ac.uk

Eye (2010) **24**, 1411–1412; doi:10.1038/eye.2010.55;
published online 23 April 2010

Sir,
Reply to Guggenheim *et al*

We thank Guggenheim *et al*¹ for their critical comments on our recently published papers.^{2,3} We would like to reply to their comments as follows. Myopia is a multigenetic condition involving several overlapping signalling pathways. Therefore, the effects of lumican (*LUM*) and muscarinic acetylcholine receptors 1 (*CHRM1*) in myopia are likely to be different between Taiwanese patients and those from other ethnic origin because of differences in environment and race.⁴ *LUM* was initially described as a proteoglycan responsible for the control of collagen fibrillogenesis and interaction. The *LUM* gene is located at 12q21-23 (*MYP3*), which is a locus associated with high-grade myopia. However, the association between *LUM* gene and myopia is controversial. We performed two independent studies to identify the association between myopia and *LUM* gene. The one published in *Eye* is actually a study that was completed more than 2 years ago. The paper submission and publication process was long and complicated. After completion of the previous study, we tried to identify the possible functional roles of *LUM* in the pathogenesis of myopia, for which we performed whole gene sequencing analysis on *LUM* gene and identified one novel polymorphism. The influence of

this newly identified polymorphism on the expression levels of *LUM* was also studied. Taken together, the single-nucleotide polymorphisms in *LUM* genes may have multiple effects on the expression level of *LUM*. We have thoroughly studied and listed the association between *LUM* and myopia in a manner that is not biased on account of using few patients or only one SNP. We must admit that we made errors in the statement of Hardy-Weinberg equilibrium (HWE). The text in one of our reports reads:⁵ 'In the test of HWE, there were departures from HWE for S1 in both the control and high myopia groups ($P = 0.048$ and 0.023 , respectively) and for S2 in the control group ($P = 0.012$).' These values were not P values but were the results of $HWE\chi^2$. Consequently, the exact statement of the sentence must be changed to 'In the test of HWE, there were no departures from HWE for S1 in both the control and high myopia groups ($HWE\chi^2 = 0.048$ and 0.023 , respectively) and for S2 in the control group ($HWE\chi^2 = 0.012$). The S3 and S4 polymorphisms were not in HWE.' We had explained the possible problems about departures from HWE in the fourth paragraph in the text,⁵ and hoped this could decrease the doubt on genotyping or population stratification. Definitely, we must make painstaking efforts in our future studies.

Conflict of interest

The authors declare no conflict of interest.

References

- 1 Guggenheim JA, Zayats T, Hammond C, Young TL. Lumican and muscarinic acetylcholine receptor 1 gene polymorphisms associated with high myopia. *Eye* 2010; **24**: 1411–1412 (this issue).
- 2 Lin HJ, Wan L, Tsai Y, Chen WC, Tsai SW, Tsai FJ. The association between lumican gene polymorphisms and high myopia. *Eye* 2009; doi:10.1038/eye.2009.254.
- 3 Lin HJ, Kung YJ, Lin YJ, Sheu JJ, Chen BH, Lan YC *et al*. Association of the Lumican gene functional 3' UTR polymorphism with high myopia. *Invest Ophthalmol Vis Sci* 2010; **51**: 96–102.
- 4 Lin HJ, Wan L, Tsai Y, Chen WC, Tsai SW, Tsai FJ. Muscarinic acetylcholine receptor 1 gene polymorphisms associated with high myopia. *Mol Vision* 2009; **15**: 1774–1780.
- 5 Nakanishi H, Yamada R, Gotoh N, Hayashi H, Yamashiro K, Shimada N *et al*. A genomewide association analysis identified a novel susceptible locus for pathological myopia at 11q24.1. *PLoS Genet* 2009; **5**: e1000660.

H-J Lin^{1,2,3}, L Wan^{1,2,3}, Y Tsai^{1,2,3}, W-C Chen^{1,2,3}, S-W Tsai^{1,2,3}
and F-J Tsai^{1,2,3}

¹Department of Ophthalmology, China Medical University Hospital, Taichung, Taiwan

²Department of Medical Genetics, China Medical University Hospital, Taichung, Taiwan

³School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan

E-mail: d2396@mail.cmuh.org.tw

Eye (2010) **24**, 1412; doi:10.1038/eye.2010.56;
published online 23 April 2010