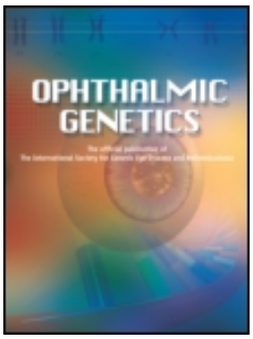

Ophthalmic Genetics

ISSN: 1381-6810 (Print) 1744-5094 (Online) Journal homepage: informahealthcare.com/journals/iopg20

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To cite this article: Lei Liu (2016) Additional Comments on "Ten SNPs of PAX6, Lumican, and MYOC Genes are not Associated with High Myopia in Han Chinese", Ophthalmic Genetics, 37:1, 119-120, DOI: 10.3109/13816810.2014.889170

To link to this article: https://doi.org/10.3109/13816810.2014.889170

Published online: 19 Feb 2014.

Ophthalmic Genetics, 2016; 37(1): 119–120

ISSN: 1381-6810 print / 1744-5094 online
DOI: 10.3109/13816810.2014.889170

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LETTER TO THE EDITOR

Additional Comments on "Ten SNPs of PAX6, Lumican, and MYOC Genes are not Associated with High Myopia in Han Chinese"

Lei Liu

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I have read with profound interest the article "Ten SNPs of PAX6, Lumican, and MYOC genes are not associated with high myopia in Han Chinese" by Dai and colleagues.[1] The commentary found that there were no significant associations between PAX6, Lumican, and MYOC genes and high myopia in Han Chinese. To our knowledge, the results for the association between PAX6 and high myopia in Chinese were not consistent.[1–5] Although the authors have pointed out some possible reasons for the discrepancy in results at the end of their article, I wish to point out some additional possible reasons which account for this discrepancy. First, the conclusions of these recent reports are equivocal due to the complex etiology of myopia. Second, in the study by Tsai and colleagues,[5] although the genotype distribution of rs667773 was not statistically different between the high myopia and control groups, when they examined extreme myopia (<10.0 D) patients in the total high myopia group, the results revealed that the distribution of genotype and allelic frequency was significantly different, and demonstrated an association of the rs667773 polymorphism with extreme myopia. Hence, their failure to find an association between PAX6 and myopia was most likely due to the less severe degree of myopia in the study group. Third, selection bias may be another reason. As previously shown, people with higher education have a higher prevalence of myopia than people in the general population.[6] The age, sex and education level of the sample under study is not mentioned. The results would have been more reliable if the study had been carried out on a sample of similar age group, sex and education level. Fourth, the choice of tagged SNP may be another possible reason. The study could have been strengthened by ensuring that full genetic coverage of the gene was obtained.

In addition, I have conducted a meta-analysis to verify the association between PAX6(RS667773) and myopia in Chinese with extreme myopia (<10.0 D). I searched Pubmed, Medline, Embase, the Cochrane Library, Chinese Biological Medicine, China National Knowledge Infrastructure, Wang Fang Data and Chongqing VIP database using the terms "paired box 6 or PAX6," "RS667773," "myopia" and "polymorphism, variant or mutation." After reviewing the full texts, a total of three studies were included in the meta-analysis. The results indicated no significant relationship of RS667773 polymorphism with extreme myopia risk (OR = 0.48, 95% CI = 0.14–1.65, $I^2 = 95\%$, $p < 0.01$ for C versus T by random-effects model; OR = 0.41, 95% CI = 0.05–3.41, $I^2 = 82\%$, $p < 0.01$ for CC versus TT by random-effects model; OR = 0.47, 95% CI = 0.13–1.66, $I^2 = 93\%$, $p < 0.01$ for CC versus TC by random-effects model; OR = 0.44, 95%CI = 0.11–1.73, $I^2 = 95\%$, $p < 0.01$ for CC versus CT + TT by random-effects model; OR = 0.53; 95% CI = 0.10–2.76, $I^2 = 72\%$, $p = 0.03$ for CC + CT versus TT by random-effects model). The genotype distributions of the control population were not in Hardy-Weinberg equilibrium (HWE) in the study by Tsai and co-authors.[5] There was no heterogeneity when I excluded this study. However, I found there was no significant relationship of RS667773 polymorphism with extreme myopia risk for all genetic models. Although the results of this meta-analysis could be used as a reference for the

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association between PAX6(RS667773) and myopia in Chinese people with extreme myopia (<10.0 D), further studies are also needed.

In addition, I would also encourage the editors and reviewers of the presented work to look at Table 2 and Table 3 in the article,[1] and there may be some spelling errors in both tables. In Table 1, the name of the tag was RS667773, but it had been changed to RS66773 both in Table 2 and Table 3. I think it should be RS667773 instead of RS66773.

DECLARATION OF INTEREST

The author reports no conflicts of interest. The author alone is responsible for the content and writing of this article.

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