Comment on homozygosity mapping of a consanguineous Pakistani family affected with oculocutaneous albinism to *Tyrosinase* gene

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Received: 2016-07-22 Accepted: 2017-01-04

DOI:10.18240/ijo.2017.05.29

Khan MA. Comment on homozygosity mapping of a consanguineous Pakistani family affected with oculocutaneous albinism to *Tyrosinase* gene. *Int J Ophthalmol* 2017;10(5):826

Dear Editor,

I have carefully read the article entitled "Homozygosity mapping of a consanguineous Pakistani family affected with oculocutaneous albinism to *Tyrosinase* gene", published by Shakil *et al*[1] in 2016 and found it very interesting for the scientific community. I will consider it a significant contribution of authors toward the development of molecular diagnosis and better management of oculocutaneous albinism (OCA). In that article, Shakil *et al*[1] analyzed 10 Pakistani families with OCA and determine the association of one AL03 family with *TYR* locus, while rest of the families were excluded from the known OCA loci and suggest the involvement of novel genetic factors in disease etiology.

I fully agree with the medico-genetic outcomes of the present study. However, with due respect, I have few technical concerns that I believe will further improve this article and make it interesting for the readers. My first concern is regarding the title of this article "Homozygosity mapping of a consanguineous Pakistani family affected with oculocutaneous albinism to *Tyrosinase* gene", which reveals that they analyzed single OCA family, while in the text body authors have described that they screened 10 families (see also conclusion). My second concern is regarding the linkage analysis of family AL03, which shows two point logarithm of odd (LOD) score of 1.80 at marker D11S1367 at zero recombination fraction. In statistical term, for association of a locus with disease phenotype (autosomal recessive) the LOD score should be 3.0 at zero recombination fraction, while the current analysis does not meet the statistical criteria of linkage analysis. Nevertheless, the LOD score can be regarded as suggestive of linkage to disease. Moreover, they did not perform sequence analysis of *TYR* gene for mutation identification. Given the low value of LOD score (less than 3) and no mutation analysis may reduce the significance of *TYR* gene linkage to disease phenotype.

However, I would like to add few minor suggestions to this commentary regarding the linkage and mutation analysis of AL03 family associated with *TYR* gene locus. In order to positively justify the suggestive LOD score value, author should perform simulation analysis to determine the total linkage power of this family and then compare the actual LOD value with simulated value, which should come close to each other. Or, they can achieve significant LOD score of 3 by enrolling additional affected individuals from fifth generation (V-1 and V-2). Regarding the sequence analysis, the authors should consider the sequencing of few common *TYR* gene mutations that are reported by Jaworek *et al*[2] in Punjabi ethnic Pakistani families. Mutation analysis of the *TYR* gene in AL03 family will be their significant contribution in personalized healthcare and devising an ethnic specific molecular diagnostic test for genetic counseling of Pakistani families.

ACKNOWLEDGEMENTS

Conflicts of Interest: Khan MA, None.

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