Reviewer's report

Title: Molecular Diagnosis of Putative Stargardt Disease Probands by Exome Sequencing

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Reviewer: Stephen H Tsang

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This paper addresses the difficulties involved in diagnosing Stargardt disease due to the high phenotypic and allelic heterogeneity of the disease. Exome sequencing is proposed as a means to gain a better understanding of this condition’s genetic profile. Though most cases of Stargardt are caused by mutations in ABCA4, there are factors that complicate a precise molecular diagnosis. Although on clinical examination, these patients reportedly all had features of the disease, especially peripapillary sparing, in three of the patients no mutation of ABCA4 was present. Authors of the study found mutations in the RDS/PRPH2 gene, which has previously been observed to be pathogenic.

This study’s findings have immediately applicable clinical value. When conducting genetic sequencing to check for classic Stargardt disease, clinicians might face instances in which the ABCA4 mutation cannot be found and seemingly enough information does not exist to make a diagnosis. In these cases, this paper highlights the importance of checking for PRPH. One unexpected finding in this study was the fact that patients with peripapillary sparing had the PRPH mutation. As the paper found, exome sequencing can detect mutations in putative Stargardt patients, and these tests provided important diagnostic information.

Supplementary Fig 8 and 9 are identical.

Some minor changes would provide more information in the tables. For instance, patients’ clinical phenotypes were described in table 1 but not table 5; including this information would help. In addition, the last 4 rows of patients found in table 5 were not listed in table 1.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests