Reviewer's report

Title: The low penetrance of retinoblastoma for the V654L mutation in RB1 gene

Version: 1 Date: 3 February 2011

Reviewer: Annemarie Hedwig H van der Hout

Reviewer's report:

The authors describe a large Taiwanese family with a mutation in the RB1 gene, which has in this family an extremely low penetrance. The mutation is found in 11 relatives, of whom only four develop retinoblastoma, at extremely high ages. This mutation has been described in other families, in which the penetrance was much higher. Therefore, the most interesting question is: why is the penetrance of this mutation so low in this particular family. However, the authors do not really answer this question, they only sum up what other authors have written as possible explanations why other RB1 mutations show low penetrance.

Major Compulsory Revisions

1. The manuscript should be edited to improve the use of the English language. As it is, it is at places hardly understandable what the authors mean.

2. Because it is hardly believable that persons survive up to 46 years with untreated retinoblastoma, pathology reports or other proof that the tumors are really retinoblastoma should be added.

3. In the pedigree all family members tested should be marked, also those who do not show the mutation.

4. Given the late age at diagnosis, the age of mutation carriers without retinoblastoma should be given. The chance that these will develop retinoblastoma later on should be discussed.

5. The references are not properly chosen. e.g. Zhang et al., Hum Mutat. 29 (2008) 475-484 describe that the mutation V654L is in fact a splice mutation, this article is not mentioned. References 14-17 describe low penetrance RB mutations, but not extreme low penetrance. In the LOVD RB1 mutation database much more RB1 mutations are listed than in HGMD which is used by the authors.

6. The authors should address the question: why is the penetrance of this mutation so low in this particular family

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

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'