Reviewer's report

Title: Two polymorphisms (rs699947, rs2010963) in the VEGFA gene and diabetic retinopathy: An updated meta-analysis

Version: 1 Date: 10 June 2013

Reviewer: Dongfeng Zhang

Reviewer's report:

Comments to the Author

Lu Y et al. investigated association of two polymorphisms (rs699947, rs2010963) in the VEGFA gene and diabetic retinopathy by conducting an update meta-analysis. 8 studies with 1204 cases and 1198 controls for rs699947 polymorphism and 10 studies with 1666 cases and 1782 controls for rs2010963 polymorphism were included in this meta-analysis. They concluded that rs699947 polymorphism might be associated with the risk of DR among Europeans but not among East Asians; rs2010963 polymorphism was not associated with DR. However, I have several important issues in this meta-analysis.

Major Compulsory Revisions

1. Exploring the potential sources of heterogeneity is the essential part of meta-analysis. In the present analysis, significance of heterogeneity was found across all studies and subgroups. So how did the authors explain the source of heterogeneity across studies? Besides the authors should conduct the further analysis after excluding the articles that caused the heterogeneity.

2. The authors performed multiple comparisons, i.e. homogeneous co-dominant model and heterogeneous co-dominant model. But this multiple comparisons could result in the risk of an inflated Type I error rate. How do the authors deal with this problem in this manuscript?

3. The authors referred the homogeneous co-dominant model, heterogeneous co-dominant model, dominant model and recessive model. The authors should explain the models in the article. Besides, co-dominant model should be added.

4. The authors did not include all qualified studies. (for example: Association of vascular endothelial growth factor 2 634C/G polymorphism and diabetic retinopathy in type 2 diabetic Han Chinese. Experimental Biology and Medicine 2010; 235: 1204 – 1211). The authors should identify all possible studies fully.

5. We do not think literature and search strategy is suitable with only PubMed and EMBASE literature databases. Please supplement the qualified articles from other databases.

6. The authors say that this was an update meta-analysis. Two meta-analyses by Abhary et al. [17] and Zhao et al. [18] have investigated association of VEGFA gene and DR. However, another meta-analysis by Qiu et al. have assessed
VEGF# 634G>C (rs2010963) polymorphism and DR risk in 2013, and this meta-analysis had shown significant association between rs2010963 polymorphism and DR. The current meta-analysis by Lu Y et al added only two new studies and the result changed to no significant association between rs2010963 polymorphism and DR under all genetic models. Please explain the results.

Minor Essential Revisions
1. You state that two researchers extracted data with the inclusion and exclusion criteria independently and reached a consensus. Please clarify if two investigators searched articles as well.
2. The flow chart was not clear.
3. About table 3 and 4, please indicate that which pooled ORs and 95%CIs were for REM and which were for FEM.

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests