Reviewer’s report

Title: Role of t-PA and PAI-1 Variants in Temporal Lobe Epilepsy in Chinese Han Population

Version: 0 Date: 25 Jul 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: In this study, the authors tested for a relationship between incidence of temporal lobe epilepsy (TLE) and two specific polymorphisms in the tissue plasminogen activator (t-PA) gene and one polymorphism in the plasminogen activator inhibitor 1 (PAI-1) gene. The rationale for this study is based on previous findings that t-PA and PAI-1 mRNA expression has been shown to increase in human patients and animal models of TLE. TLE patients and healthy controls had peripheral blood sampled and genotype for each of these polymorphisms checked using PCR. The authors report a significantly higher incidence of each of the two t-PA polymorphisms in TLE patients that controls but no significant difference in occurrence of the PAI-1 polymorphism and TLE. These novel findings provide insight into the genetic contribution to sporadic TLE.

This study was a pleasure to read because the authors addressed an interesting and relevant question based on experimental findings in animal models and post-mortem tissue. This study was very straightforward and easy to follow based on the text. These findings will provide a useful contribution to the literature, but the current presentation could be improved to facilitate the reader’s understanding of the findings, as outlined below. Briefly, further information in the introduction section and interpretation in the discussion section and clarification of the tables would help the manuscript.

ADDITIONAL REQUESTS/SUGGESTIONS:

1. In the introduction section, the authors should provide some statement as to what t-PA and PAI-1 are, what they does under normal circumstances, and how alterations in expression could promote the occurrence of seizures. Such information will strengthen the rationale of the study.

2. In the introduction, the authors describe increased expression of t-PA and PAI-1 following seizures in animal models and in human postmortem tissue. Therefore, one would predict that
that the t-PA polymorphisms described in this study would lead to increased expression of t-PA and/or increased t-PA release, as the authors briefly mention in the discussion section. Please discuss the nature of the polymorphisms and how they might lead to increased occurrence of TLE in further detail in the discussion.

3. In the last paragraph of the discussion, the authors wrote, "Unfortunately, we failed to find a significant difference in genotypic and allelic frequencies of polymorphic site PAI-1 in rs1799768 between TLE and control groups." I suggest you delete the word "unfortunately", as use of this word suggests a bias approach to the study.

4. In the current form, Tables 2 and 3 are quite difficult to interpret. I suggest splitting each table into one table for genotype and one table for allele. Also, I suggest a footnote under each allele table or an indication at the top of each allele table indicating the number of subjects and the number of alleles (i.e., "Cases (242 alleles across 121 subjects (% of population)"). In the current form, it is confusing to the reader why the total number of samples for the bottom three rows of each of Tables 2 and 3 totals greater than the number of samples listed at the top of the column.

5. This manuscript would benefit by editing.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript
Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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