Author's response to reviews

Title: Analysis of the XRCC1 gene as a modifier of the cerebral response in ischemic stroke.

Authors:

Ana V Dutra (dutracacd@hotmail.com)
Hsiu-Fen Lin (sflin@kmu.edu.tw)
Suh-Hang H Juo (hjuo@c2b2.columbia.edu)
Harvey Mohrenweiser (hmohrenw@uci.edu)
Souvik Sen (SenS@glial.med.unc.edu)
Raji P Grewal (rgrewal@solarishs.org)

Version: 3 Date: 18 September 2006

Author's response to reviews: see over
Dear Sir:

We are grateful to the reviewers for their comments regarding our manuscript entitled “Analysis of the \textit{XRCC1} gene as a modifier of the cerebral response in ischemic stroke”.

We are gratified that they both feel that the article represents “an article of importance in the field” and, furthermore, that Reviewer #2 feels that this paper “is a significant contribution to the field of genetics and stroke and should be accepted for publication”.

We have revised the manuscript taking into account the criticisms of both reviewers.

One general comment raised by both reviewers concerns the relatively small sample size of our study population. We would suggest that given that we have found a significant effect of the \textit{XRCC1} gene in this sample size, it is possible that there is a major rather than minor gene effect. We agree that independent replication with a larger sample size is warranted for verification of our results. In response to Reviewer #2 “discretionary revisions”, we have made changes regarding this issue. On page 10, 3\textsuperscript{rd} paragraph of the revised manuscript, we have discussed in more detail our small sample size and the need for further study.

Comments specific to Reviewer #1-

1) Major compulsory revisions

-There were concerns raised about not including the one individual with the TT genotype. As suggested, we have included this individual in all of the analysis and the revised results. These revisions are reflected in both the abstract, results and Table 2. The addition of this individual with the TT genotype does not change the significance of our results or the main conclusion of the study.
2) Minor essential revisions

- In the Methods section, as suggested by the reviewer, the order of paragraphs as been changed from “Samples for variation screening” with “Identification of XRCC1 variants”.

- In the Methods section, the hanging 4 has been eliminated.

- In the Discussion section, 3rd paragraph, in the last sentence, “then” has been changed to “than”

Comments specific to Reviewer #2-

1) Major Compulsory Revisions

Changes have been made to both of the Tables following the recommendations of this reviewer.

- In Table 1, the mean age is now not given to 2 point accuracy and the ethnicity numbers of the patients add up to 134. Raw numbers are provided; not just the %.

- Table 2, the SD is given with the stroke volume and another column with statistical results is provided. In addition, another row demonstrating the sub-type analysis is provided.

1) Minor essential revisions

- The reviewer suggests that there is an error in the calculation of the T allele frequency; however we have reviewed the raw data and find there is no error in this calculation.

- Reference #14 has been corrected.

- Finally, the reviewer has doubts about the size of an ischemic stroke which is small and appears to have been a lacunar stroke. However, the clinical (in the setting of new onset atrial fibrillation) and radiological data (location of the lesion) on diffusion imaging MRI do not support a lacunar stroke.

We thank the reviewers for their comments, many of which have been incorporated into this revised manuscript. We hope the changes are acceptable.

Sincerely:

Raji Grewal MD,
Associate Professor of Neurology