Reviewer's report

Title: Implication of Xenobiotic Metabolizing Enzyme gene (CYP2E1, CYP2C19, CYP2D6, mEH and NAT2) Polymorphisms in Breast Carcinoma.

Version: 1 Date: 13 November 2007

Reviewer: RADHAKRISHNA PILLAI

Reviewer's report:

General
The authors have undertaken a study on “Implication of xenobiotic metabolizing enzyme gene (CYP2E1, CYP2C19, CYP2D6, mEH and NAT2) polymorphisms in breast carcinoma”.

The study has screened for polymorphisms in five genes, four from the CYP family and one phase II enzyme: NAT2. 560 subjects have been screened. Statistical analysis of the data is expressed as genotype frequency done using logistic regression. Survival analysis has been plotted according to Kaplan Meier.

The introduction part has laid emphasis on the importance of low penetrance genes in cancer. The role of xenobiotic metabolizing genes has been broadly looked into. A brief insight into incidence of breast cancer and its significance in the study would have further highlighted the importance of the work.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The materials and methods section has given details of the study subjects. But the genotyping details have excluded the PCR conditions, PCR enzymes, annealing temperatures and other certain particulars which are needed for reproducibility of the assays. The techniques are also not well described so as to replicate the work. The sentence “Genomic DNA was extracted from peripheral blood leukocytes by the salting-out procedure” is very vague. The brief procedure or at least reference to the procedure needs to be specified.

Clarifications are required for the sample size which was given as 246 controls and 314 patients in the materials and methods section but table 2 shows diverse numbers of controls for various genotypes. Also neither the tables nor the results section have mentioned the 95% confidence interval values, which is significant for understanding the statistical range of odds ratio. Survival analysis was done using Kaplan-Meier analysis. The curves illustrate interesting results. It is necessary to explain why axillary lymph node negative alone was selected for survival analysis over other tumor clinical-pathological characteristics.

Low penetrance genes are being suggested as candidate cancer susceptibility
genes but other lifestyle factors such as smoking, use of oral contraceptives and xenoestrogens act as confounding factors when effect of cancer susceptibility genotypes on breast cancer susceptibility and survival is being studied. These confounding factors need to be taken into account to make the genotyping data more sound.

There are various recent papers on similar epidemiological data on XMEs and cancer risk. It is suggested that more references be included in the text especially in the discussion section.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Name of the journal in reference no 24 needs to be italicized.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interestS.