Author's response to reviews

Title: The contribution of the ABCG2 C421A polymorphism to cancer susceptibility: a meta-analysis of the current literature

Authors:

Pin Chen (chenpin1987@126.com)
Lin Zhao (postletterplant@163.com)
Peng Zou (isdwhzp@126.com)
Haitao Xu (haibao.44@163.com)
Ailin Lu (LIUNING0853@YAHOO.COM.CN)
Peng Zhao (zhaopeng@njmu.edu.cn)

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Author's response to reviews: see over
Dear Prof Zhao,

Your manuscript has now been peer reviewed and the comments are accessible in PDF format from the link below. Do let us know if you have any problems opening the file.

Editorial request:
- MOOSE guidelines

BMC Cancer supports initiatives aimed at improving the reporting of biomedical research. We recommend authors refer to the EQUATOR network website for further information on the available reporting guidelines for health research. Authors are requested to make use of these when drafting their manuscript and peer reviewers will also be asked to refer to these checklists when evaluating these studies. Checklists are available for a number of study designs, including systematic reviews (PRISMA), meta-analyses of observational studies (MOOSE).

We would be grateful if you could address the comments in a revised manuscript and provide a cover letter giving a point-by-point response to the concerns.

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

We look forward to receiving your revised manuscript by 4 August 2012. If you imagine that it will take longer to prepare please give us some estimate of when we can expect it.

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Please don’t hesitate to contact me if you have any problems or questions regarding your manuscript.

With best wishes,

Christina
Christina Chap, PhD
Senior Executive Editor
BMC-series
BioMed Central
236 Gray's Inn Road
London WC1X 8HB
Email: editorial@biomedcentral.com
Dear Editors and Reviewers,

We highly appreciate the detailed valuable comments of the referees on our manuscript of ‘MS: 5178335687095852’. The suggestions are quite helpful for us. We have modified the manuscript accordingly, and the responses to the quests are listed below point by point.

The major changes are highlighted in the revised manuscript. We hope the Reviewers and the Editors will be satisfied with the revisions for our manuscript.

Thanks and Best Regards!

Yours sincerely,

Peng Zhao

July 26, 2012

Responses to the quests:

Replies to Reviewer #1: Dr. Deborah Rund

Minor discretionary:

1. Regarding the relationship between ABCG2 and malignancy predisposition, I suggest in the Introduction, second paragraph, that the word "immature" be added to the phrase "hematopoietic tissues" since ABCG2 was found in immature cells but not mature cells of this tissue, as stated in the references that the authors quote (8-9).

Furthermore, in the discussion, they can mention that the tissue distribution of the malignancies is in concert with the tissues in which there is significant expression of ABCG2, supporting a mechanistic role for this transporter in prevention of damage by xenobiotics to these diverse tissues.

Thanks for the good advice. We have added "immature" to the phrase "hematopoietic tissues" in the Introduction part (second paragraph) to make it clear.

2. The English is really quite good but here and there, a preposition is used incorrectly. I do not want to note every spot in which this occurs, perhaps the authors can go over the English one more time with a native English speaker. Similarly there are places where a space is missing (between the last word and a citation).

Many thanks for the reviewer’s comments. We have gone over the English with the help of a native English speaker and then corrected the spelling and syntax errors. The space-missing places
have also be added.

3. I think that the title would be more attractive if the word meta-analysis was added rather than simply saying "evidence from the current literature. The authors' analysis was rigorous and not just a casual glance, which is what the title implies. I suggest it read: "The contribution of the ABCG2 C421A polymorphism to cancer susceptibility: meta-analysis of the current literature".

Thanks for the reviewer's wonderful suggestion, which is valuable in improving the quality of our manuscript. We have modified the title to "The contribution of the ABCG2 C421A polymorphism to cancer susceptibility: a meta-analysis of the current literature" accordingly.

Minor essential:

1. In the last paragraph of the Methods, the = sign (equal sign) in the description of the level of significance (p=……) is written as a small box.

Thanks for the reviewer’s careful insights! We have corrected the typographical error in our revised manuscript.

Replies to Reviewer #2: Dr. Csaba Szalai

Major compulsory revisions

1. I recalculated some of the results and for an unknown reason I received slightly other numbers found in the paper, although it did not influence significantly the conclusion. But, e.g. in the paper of Semsei et al. the A allele in the C421A polymorphism has higher frequency in the cases (10.6%) than in the controls (9.4%), and still the figure 2 shows an odds ratio value of 0.94, i.e. below 1, which is contradictory to the frequencies. If a frequency of an allele in the cases is higher than in the controls, the OR must be above 1. All the statistical calculations must be recalculated, and the results must be modified accordingly.

Thanks for the reviewer’s professional recommendation, which is undoubtedly helpful to our manuscript. According to the reviewer’s advice, we have reviewed the procedure of the data extraction and recalculated all the statistical results carefully, and found a mistake in the calculation of the A allele frequency in the C421A polymorphism, which resulting in the inaccuracy of the additive model comparison. We are so sorry for this. After three-times recalculation, all the statistical results are verified and corrected now and revised accordingly in the manuscript and table 2.

Simultaneously, we have updated Figure 2 (the forest plot of additive model) and Figure 3. Above all, a significant association between the ABCG2 C421A polymorphism and decreased cancer risk was still found in the additive model (A allele versus C allele).

Minor essential revisions

1. In table 2 there are superscripts (a, b), but there are no explanations for them.

Many thanks for the reviewer’s suggestion. We have provided the explanations for superscripts (a, b) in table 2 according to the editor’s advice.
2. There are several disturbing minor grammatical mistakes in the paper, e.g. ‘dates’ instead of ‘data’, and ‘Begger’s funnel plot’ instead of ‘Begg’s funnel plot’, etc.

Many thanks for the reviewer’s good suggestion. We have modified the grammatical mistakes in the manuscript accordingly.

Discretionary revisions

1. It would be interesting to evaluate and discuss, whether the number of the A allele carried by an individual influence the risk to ALL (i.e. AA vs AC)?

Thanks for the reviewer’s good advice. In our meta-analysis, we found that there was a significant association between the ABCG2 C421A polymorphism and cancer risk in the additive model, dominant effect model and heterozygote model. However, among all 10 studies included, only one study focused on acute lymphoblastic leukaemia (ALL), so we did not evaluate and discuss the association of the A allele carrier and the risk of ALL development (AA vs AC). Your suggestion is really helpful to our further work.