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Journal Name:	Journal of Pharmaceutical Research International
Manuscript Number:	**Ms_JPRI_51352**
Title of the Manuscript:	**A review of Genetic polymorphism of GSTs (glutathione –s transferase) genes in breast cancer**
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	**Although this manuscript has the potential to be quite interesting given the title, the material contained within varies greatly away from the original idea. Very few areas of the manuscript have a focus upon breast cancer, and even in the sections detailing the isoforms/alleles of the GST genes, the authors have undercited references and have not made clear the links to breast cancer.** **Initially in the manuscript, when discussing the incidence rates, the listing of several statistics becomes confusing. Creating a figure or table of this data would greatly benefit the introductory section. The same can be stated for the data regarding incidence in Iran, much of which has gone uncited.** **There is much redundancy when discussing the glutathione and hydrophobic binding sites, and these are defined after their abbreviations are utilized. The authors mention evolution and conserved areas amongst mammals, but this detail may not be important as the focus of this review was supposed to be on cancer.** **The start of the first full paragraph on page five alludes to environmental risk factors, yet the paragraph has nothing to do with this. This is followed by discussion of an experiment that is not**	

	cited. Beyond this, the terminology is not defined. What are the "p" and "m" isoforms? What are PHAs? What is NacetoxyPhIP? This confusion is followed in the subsequent paragraph by a discussion of glutathione peroxidases, not GSTs. **On page 5-6, the author begins to explain several of the mutations that have been identified. This explanation contains several errors. For example, the distinction stated by the author for the difference in GSTA1*A and GSTA1*B is a substitution of a Proline residue; however, the cited table states it is a promoter point mutation (and promoters do not contain amino acids).** **When discussing the GSTZ gene, the final sentence in the paragraph on the top of page 9 mentions a mutation that results in human death, yet no reference is cited.** **The paragraph on GSTM is very confusing. Some of the genes listed in the paragraph are not included in Table 2. There is no mention of any reproductive cancers in this paragraph.** **The Theta class paragraph is the first real mention of the impact on these genotypes on breast cancer incidence. However, it is unclear whether the author is intending to speak regarding all mutations and genotypes or just the theta class ones; the author specifically mentions Mu class again in this paragraph. The discussion of the theta class then goes further to mention benefical mutations where cancer risks are lowered.** **The most beneficial of the discussion of the types**	

	of GSTs is that of the pi class, as that is the one that has an impact on breast cancer. Following this, the null phenotype paragraph and the discussion of the GSEC Study offers conflicting information that loss of GST expression either increases one's risk of developing cancer, or is beneficial in its reduction in the processing/clearance of chemotherapeutics. **Several times the authors make reference to differential tissue or organ expression of the different forms of GST, yet they do not provide any type of table that clearly states the expression patterns and/or main function of each type. They then go further to mention different classes (such as k) that is neither mentioned nor discussed earlier in the lengthy section on GST classes.** **On page 13, a lengthy run-on sentence tries to discus GSTA3-3, which is not listed in Table 2. This does not fully fit into the paragraph on estrogen metabolism and exposure.** **If you are going to hypothesize that increased estrogen exposure is responsible for many breast cancers (in actuality, only 2/3 are hormone-dependent), then you should report some actual data related to either GST levels or activity related to increased estrogen levels and concrete evidence that this alters cell function.** **You state that BRCA1 and BRCA2 mutations only account for up to 5% of all breast cancer cases – this is not entirely true. There are some populations with up to 10% of breast cancers having a mutation in BRCA1 alone (those of Ashkenazi Jewish**	

	ancestry), and these mutations are found in up to 40% of breast cancers in men. **For a review of the literature, this manuscript is severely lacking. There are only 24 cited references, and only three of those were published within the last 5 years. In contrast, a search in Google Scholar identifies over 18,000 manuscripts published since 2014 that highlight GSTs in breast cancer.**	

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Minor REVISION comments	• There are several spelling and grammatical errors throughout the manuscript. Many of these include run-on sentences that are difficult to comprehend, or left out spaces that causes several words to run together. A thorough spell- and grammar-check need to be performed to correct these errors. • Were the tables copied and pasted from other sources? If not, why are the genes listed in different orders between the two tables, and why does the order not match the text? • Why is there a second copy of Table 1 included at the end of the manuscript?	
Optional/General comments		

PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

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If plagiarism is suspected, please provide related proofs or web links.	Although a copy/paste style of plagiarism may not have taken place, there are several areas throughout where citation is needed. other than literature is not cited as much as needed.	

Reviewer Details:

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