Dear editor:

Enclosed please find the revised manuscript No. 86498 “Advances in drug resistance of triple negative breast cancer caused by pregnane X receptor". We greatly appreciate the comments and have learned a lot from the reviewers. The critics have been addressed as following.

Reviewer #1:

1. The authors have discussed the three phases of the chemotherapy drug resistance mechanism caused by PXR in general (Figure-1). However, authors have superficially discussed the alterations of PXR regulated genes associated with the three phases of drug metabolism in TNBC.

A: Thank you for your valuable comments. We added several references and added further discussion about the alterations of PXR regulated genes associated with the three phases of drug metabolism in TNBC. All the modifications are marked RED.

2. The discussion should be made in detail with diagrammatic representation for better understanding of the role of PXR regulating genes in drug resistance in TNBC. This should be in concordance of title of the review.

A: Thank you for your valuable comments. We added a table (Table 1) help to illustrate the role of PXR regulating genes in drug resistance in TNBC. As the role of CYPs, GSTs, UGTs and ABCs in the mechanism of PXR-regulated TNBC drug resistance has not been fully confirmed, we didn’t add any more corresponding proteins in the figure. All the modifications are marked RED.

3. The conclusion of the review should be made in accordance of the discussion above.

A: Thank you for your valuable comments. We modified the conclusion and made it in accordance of the discussion. All the modifications are marked RED.

Reviewer #2:

1. The major drug metabolizing enzymes and transporters with sufficient evidences linked to chemotherapeutic resistance should be tabulated for a summary to shorten the narrative.

A: Thank you for your valuable comments. We added a table (Table 1) to illustrate the role of PXR regulating genes in drug resistance in TNBC and made it in concordance of title of the review.

2. Many important roles of PXR were not included in the manuscript as it highly relates to the manuscript title. This includes regulation of PXR and function of PXR independence of drug metabolism. Regulation of PXR is very important in that several chemicals and inflammatory mediators which likely occur in many cancers can regulate expression of PXR and PXR-regulated genes. PXR also acts independence of drug metabolism in regulation of various processes for instances, apoptosis, cell cycle progression and inflammation via p53, p21, NF-kB, STAT3. Moreover, many above effects can be tissue specific in that PXR acts differently in various tissues. These two aspects should be included in the manuscript.

A: Thank you very much for your precious and thought provoking advices. With no doubt PXR plays a certain role in the onset, progression, and outcome of cancer, but in this review, we are trying to focus our topic on "advances in drug resistance of triple negative breast cancer caused by pregnane X receptor". For this reason, we only elaborates on PXR in breast cancer-related drug metabolism. We added several references and further discussion, we also added "In the future, researchers should focus on improving our understanding of the mechanism of PXR in TNBC drug resistance, including regulation of PXR and function of PXR independence of drug metabolism." All the modifications are marked RED.

We feel that these changes are more persuasive and strongly support our statement in the manuscript. We hope the reviewers agree with our answers and the new version of this manuscript meets the standard of the prestigious World Journal of Clinical Oncology. Thank you very much for your consideration.

Sincerely yours

Author name been removed