

Dear Ying Yu,

Thank you for editing our manuscript.

We have revised our manuscript as suggested by the editor and one of the referees. We enclose a point-to-point reply to the comments of reviewer #2. Please find uploaded the revised manuscript, revised figure 5 and figure 6, and an audio core tip.

We hope that after careful revision the manuscript is now suited for publication in **World Journal of Gastroenterology**.

Sincerely,

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## Reply to reviewer #2

Interesting paper with the novel idea how to learn more about genotype/phenotype correlations and potential genotype influence on reaction to therapy in WD. Rational and methods are clearly described . Presented results provide for a first time, that distribution in liver cells of ATP7B depends from mutation, as well from mutation depend copper toxicity. Most interesting is response to d-p and zinc. It is long way to practical implications. I am not sure that frequent use of zinc in Asian result from positive and better response in this population to zinc due to genetic reasons. In The Netherland and other countries where is predominance HQ mutation zinc is also preferred. Combination of two drugs in vitro and in vivo acts by different mechanism. This issue and other factors which can influence on phenotype as well response to drug should be mentioned.

We fully agree with the limitations of the observed results. The revised manuscript now includes a comment to the major issues raised by the reviewer (discussion, 2<sup>nd</sup> and 3<sup>rd</sup> last sentences).