

**Reviewer no. 01221925:**

This is an interesting paper reviewing HBV promoter mutations and their correlation with genotypes and liver disease severity. Could the authors please respond to the following questions/comments? 1) The author uses a “first person – narrator” approach, ie “Now I will discuss..”. May wish to reconsider this for a paper. 2) The author may wish to consider adding a discussion section where the potential clinical utility and any efforts to-date in that direction are discussed 3) Could the author elaborate on how these mutations interact with other mutations at other parts of the virus?

**Reply:**

1. In manuscript first person sentences like ie “Now I will discuss.”, is removed.
2. I have added discussion section with potential clinical utility and any efforts to-date in that direction.
3. I have added information about how these mutations interact with other mutations at other parts of the virus.

**Reviewer no. 04770380:**

The submitted manuscript entitled “Xihuang pills induce apoptosis and growth inhibition in hepatocellular carcinoma cells by suppressing the PI3K/Akt/mTOR signalling pathway” by Teng YJ et al aimed to study proapoptotic role of Xihuang pills (XHP) in HCC cell line. However, there is a great concern regarding experimental design of this study. First of all, the authors used SMMC-7721 human cell line, which was identified as belonged to false and cross-contaminated cell lines (see Ye F, Chen C, Qin J, Liu J, Zheng C. Genetic profiling reveals an alarming rate of cross-contamination among human cell lines used in China. FASEB J. 2015 Oct;29(10):4268-72. doi: 10.1096/fj.14-266718). Second, SMMC-7721 cell viability and apoptosis as well as PI3K/Akt/mTOR signalling were investigated using a XHP extract that is composed of a mixture of different compounds, and it is difficult to judge which compound cause these effects. Instead, the authors are recommended to use any purified XHP component identified by mass- spectrometry. The above-mentioned circumstances make the results obtained in this study invalid and can lead to harmful therapeutic strategies.

**Reply:**

1. I have removed old references i. e. 1990s and their findings and also added new reference findings as reviewer said.
2. I have added correct descriptions of various mutations.
3. I have organized the manuscript well now and removed repetitions.
4. I have checked and corrected Grammar and style of the manuscript as said by reviewer.
5. All figures are removed.

**Reviewer no. 04770380:**

Accept.

**Reply:**

Thanks for your comments.

**Reviewer no. 05224602:**

Accept.

**Reply:**

Thanks for your comments.