

Manuscript Title: Phenethyl isothiocyanate inhibits the carcinogenic properties of hepatocellular carcinoma Huh7.5.1 cells by activating MAPK/PI3K-Akt/p53 signaling pathways

Manuscript ID: 96427

The authors of this research article tried to explore potential of Phenethyl isothiocyanate to inhibit the carcinogenic properties of Huh7.5.1 cells. The work done is extensive and explanatory. However, some inadequacy was noted in the manuscript which needs to be addressed for the improvement of the quality of the research article considering the publication criteria of the highly esteemed journal like PeerJ. The comments are given below:

1. It is not clear that how Huh 7.5.1 cells are different from that of HepG2 and SkHep-1 cells. The authors should justify the same in the Introduction part.
2. Did the author check for CD81, a plasma membrane protein essential for viral replication?
3. The authors didn't check the effect of PEITC in normal cell line.
4. Why the authors have kept incubation time for 48 hours?
5. Identification and characterisation of genomic markers in human hepatoma cells have already been done (Ref: Kawamoto M, Yamaji T, Saito K, Shirasago Y, Satomura K, Endo T, Fukasawa M, Hanada K, Osada N. Identification of Characteristic Genomic Markers in Human Hepatoma HuH-7 and Huh7.5.1-8 Cell Lines. *Front Genet.* 2020 Oct 9;11:546106. doi: 10.3389/fgene.2020.546106. PMID: 33193621; PMCID: PMC7581915). What are the novel findings of this paper is not clear?
6. The authors should mention the p53 status of Huh 7.5.1 cells at basal levels.
7. It is not clear from the western blot results that how come when I κ B α is high then NF κ Bp65 is also high because I κ B α is supposed to inhibit the expression and activation of NF κ B.
8. IC₅₀ of PEITC in Huh 7.5.1 cells is 29.61 μ M. Then basis for selecting 15 and 30 μ M is not clear.
9. Some grammatical errors are noted which needs rectification.

Considering these issues in my opinion the research article needs revision for better precision and interpretation.