Reviewer's report

Title: Pitavastatin suppresses diethylnitrosamine-induced liver preneoplasms in male C57BL/KsJ-db/db obese mice

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Reviewer: NEERAJ SAXENA

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The manuscript by Shimizu et. al. entitled "Pitavastatin suppresses diethylnitrosamine-induced liver preneoplasms in male C57BL/KsJ-db/db obese mice" investigated the effect Pitavastatin on DEN induced hepatocacinogenesis in Leptin receptor deficient db/db mice. Pitavastatin belong to a class of stanins which acts as an inhibitor of HMG-CoA resductase, an enzyme responsible for cholesterol synthesis. This medicine has been in use to treat hyperlipidemia especially cholesterol. Authors have demonstrated a dose dependent inhibitory effect of Pitavastatin on DEN induced heaptocarcinogenesis being recorded as premalignant lesions and FCA in liver. Pitavastatin resolved liver steatosis, decreased free fatty acids and total cholesterol. Authors have concluded that obesity-related liver tumorigenesis can be inhibited by Pitavastatin.

Although its an interesting study but it lack novelty, as role of Pitavastatin in obesity induced colorectal cacinogenesis has already been reported. Hepatic steatosis resolution by Pitavastsnin has also been reported earlier in 2003.

There are some major discrepancies in presentation and/or interpretation of some of the results as pointed out below. The manuscript needs more in-depth analysis of results, that would enhance the enthusiasm for its acceptance for publication in this journal.

Conclusions are not very clear and don’t go with the results, especially the statistical analysis with respect to the standard-deviation in the values.

Major compulsory revisions:

Figure 1, FCA values shows significant decrease at 1ppm (p<0.05) and 10ppm (p<0.001). SD bars basically nullifies eachother and shows no differences between the three groups. Same thing is true for Data in Figure 2 for FFA and total cholestrerol levels.

Very importantly, control experimentation using wild type mice needs to be included in this study to show the importance and relevance of obesity in DEN induced hepatocarcinogenesis.

Minor Essential Revisions:

Improvement in adipocytokines imbalance (increased adiponectin and decreased leptin) is a cause or the effect of Fat resolution?
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'