Author's response to reviews

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

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Author's response to reviews:

June 13, 2011
Dr Andrzej K. Bednarek,
Section Editor, BMC Cancer,

Re: Re-revision of BMC Cancer manuscript MS # 5930295664816320:
"Pitavastatin suppresses diethylnitrosamine-induced liver preneoplasms in male C57BL/KsJ-db/db obese mice"

Dear Dr. Bednarek,

Thank you for your email of June 3, 2011, indicating our manuscript needs to answer Dr. Saxena comments before final acceptance for publication in BMC Cancer. Enclosed please find our revised manuscript, which we believe addresses all of the concerns raised by Dr. Saxena, and a point-by-point list of our responses to the criticisms.

We thank you and the reviewer for these very helpful and constructive criticisms and we would like to request that our revised paper may again be considered for publication in BMC Cancer.

With best personal regards,

Sincerely,

Masahito Shimizu, M.D., Ph.D.

Responses to Reviewer #1 (Dr. Neeraj Saxena)
We wish to thank Dr. Saxena for reviewing our manuscript. In the overall comment, this reviewer initially suggested that our findings that there is no decrease in serum levels of total cholesterol and triglyceride after pitavastatin treatment (Fig. 3C) are in contradiction to the results of previous report (Egawa T. Lipids 2003, Ref. #15). We understand the importance of this suggestion. We presume that lipid-lowering effects of pitavastatin might depend on the animal strain and experimental procedure (Refs. #15, 21, and 29). We also speculate that HMG-CoA reductase activity might be inhibited by pitavastatin in this study because previous studies have indicated that pitavastatin potently inhibits de novo cholesterol synthesis without affecting serum lipid levels (new Refs. #30 and 31). Cholesterol synthesis enzymes were also remarkably induced by feedback regulation in rodents, which might mask the lipid-lowering effects of statin (new Ref. #32). We revised the “Discussion” section in light of these points (Page 15, line 14 to Page 16, line 5). We deeply appreciate your very important suggestion.

Next, this reviewer raised questions about the results of statistical analysis in Fig. 2B. In order to clarify this point, we performed real-time RT-PCR analysis and conducted a statistical analysis again (new Fig. 2B and Page 11, lines 3 to 6). In addition, we emphasized the novelty of present study in the “Discussion” section because this reviewer suggested that overall our study lacks it. We believe that this study is novel and clinically significant since it provides the first detailed evidence that statin is effective in preventing the development of obesity-related liver tumorigenesis. (Page 14, lines 13 to 19). We thank your constructive suggestion again.