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Professor Fang-Fang Ji
Science Editor
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World Journal of Virology

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Dear Professor Ji,

Thank you and your colleague for reviewing our manuscript entitled "Expression of HBV surface antigens induces defective gonad phenotypes in *Caenorhabditis elegans*".

The reviewers' comments are well taken. Please see the point-to-point responses attached in the next page. We hope this paper will be interested by virologists who are seeking a heterologous system for studying virus-host interaction and viral pathogenesis.

Sincerely yours,

Szecheng J. Lo, Ph.D.
Professor
Department of Biomedical Sciences
Chang Gung University

Point-to-point responses

Reviewer 1

The paper Expression of HBV surface antigens induces defective gonad phenotypes in *Caenorhabditis elegans* described an useful platform for protein-protein interaction, specially in the viral-host frame. The paper is well written, but should be carefully reviewed because it have some mistakes. Examples: Page 5, line 6 Revise the use of word “fulminate” . I think that the correct is “fulminant” Page 5, line 25 Revise this part of the phrase “... interaction of HBx and CED-9, a human homolog of BCL-2.” . It is not better to say: a homologue of human Bcl-2? Page 6, line 17 Change “excited” by “excised”

Thanks for the reviewer 1 pointing two typos, “fulminate” and “excited”. Both are changed into fulminant and excised in the revised manuscript. We also changed “..interaction of HBx and CED-9, a human homolog of BCL-2” into “interaction of HBx and CED-9, a homologues of human Bcl-2”.

Reviewer 2

I would like to see a different control that expresses some "nontoxic" protein to fairly high levels in the 2nd cistron. If you can do that then I think this is a great paper and a real contribution to the field. The writing is pretty clear.

Thanks for the reviewer’s comment for adding a nontoxic protein in the second cistron. We did express worm’s rps-15 (non-toxic protein) as the second cistron and reported in *Gene* 455, 16-21 (2010).

Reviewer 3

The authors constructed 3 plasmids that were able to express the large, middle, and small forms of HBsAg (LHBsAg, MHBsAg, and SHBsAg, respectively) driven by a fib-1 and 3 plasmids that were able to express SHBsAg driven by different tissue-specific promoters and microinjected these plasmids into *C. Elegans*, demonstrating that SHBsAg can induce observable phenotypes. This work is interesting and may have provided a new platform for studying the pathogenesises of HBV and other viruses.

The paper is well organized and the findings were clearly presented. “fulminate hepatitis” may be replaced by “fulminant hepatitis”.

Thanks for the reviewer’s positive comments. Yes, we changed the mis-spelled “fulminate hepatitis” into “fulminant hepatitis”.