Reviewer's report

Title: Curcumin activates the podocyte p38MAPK-HSP25 pathway in vitro but does not attenuate streptozotocin-induced diabetic nephropathy in vivo

Version: 1 Date: 17 August 2010

Reviewer: Sae kwang Ku

Reviewer's report:

This manuscript presents results of a study designed to examine the ability Curcumin to the podocyte p38MAPK-HSP pathway in vitro. However, author(s) did not revealed any favorable effects on streptozotocin-induced diabetic nephropathy in vivo.

This reviewer concluded as “Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)”

Despite the potential interest of this manuscript to the field, it is not possible to provide an adequate review of the manuscript in its current form due to the number of grammatical errors and some results are difficult to understanding. The author(s) are encouraged to describe or answers as following questions

Major comment: Why used streptozotocin-induced diabetic nephropathy in vivo only. There are numerous other nephropathy animal models; Before concluded Curcumin did not attenuate streptozotocin-induced diabetic nephropathy, author(s) should be test on other animal models, especially STZ-induced Rats or db/db mice. In addition, it seems to be need more detail explains on the Material and methods.

Statistical Analysis
This reviewer strongly suggest that used more sensitive statistical method such as ANOVA test, especially on In Vivo

Details
1. Seems to be need to change the ‘in vitro, in vivo’ with Italic

2. P3. Line 14. You said “previously showed in vitro that short-term incubation of podocytes in medium with a high glucose concentration resulted in phosphorylation of p38MAPK and downstream HSP25.” But we did not know when/where you said(quote the origin) and what time is short-term?

3. P4. Podocyte culture
Podocyte culture: briefly write the method of ‘conditionally immortalized mouse podocytes’

It seems to be need to write the ‘thermosensitive SV 40 transgene’ method: what kind(gene sequence) of promoter, terminator and others did you use. And how
do you check the transgene well-done.
Reference 23 is use ‘100 U/ml of the #-IFN’ but you use ‘50 U/ml’, explain why the dose is difference.

4. P6. DNase 1 inhibition assay for the measurement of F/G actin ratio
You could better changing number(24,25,18) to researchers’ name(blikstad I, papakonstanti EA, Dai T)
Need to write the full name of GA

5. Experimental animals
Need to write the detailed animal conditions (ages, donator or where do you purchased)
For the collecting the podocyte you must to kill the animals, so have to write the anesthesia method and IRB name & approval number.
Discretionary revisions: When you added the materials in food, it may be difficult to control the same dosage (mg/kg body weight). We suggest you to administer the materials using gastric gavage (Zondae) for accurate dosage

6. P7. In experimental I, you measured urine items on day 9 and 15. Why you measured on that day? And clear define the day of 9 and 15, define the day 1. Also in experiment 2, define the weeks 2, 4 and 7

7. P7. Numbers of animals in groups are different. Why do you have different number in your each group? And you measure the on 9 and 15 day but you did not write how many animal you kill on each days (9, 15)

8. P8. The sentence ‘to determine ~ subsequent experiments’ previously, and it is seems to be as a repetition stationery

9. P8. The pods changes in cur 60-70 min stimulation but we don’t know what/how the podocytes changes. You need to write the detail changes.

Line 3, check the DMcur0 value (2.8±07) and figure 3 does not indicate the 2.8 level
Line 20. You wrote the measurement were made from 5-11weeks but you just on one time values which is don’t know what weeks values
line 9. You did high concentration cur food experiment cause by thinking low dosage. But we think many cause ex) short-period administration, nullified effect, irregular cur-administration etc (P.18).

Line 23 how did you calculate ‘food intake was only ~50% higher’. In figure 5. I think the food intake volume is too much by a mouse.
Line 24,25, check the unit of creatinine ‘mcg’
Line 2. I think you collect the sample from the day 9 to 15 (during a week). If you do that, your samples have no consistency. Correctly explain when did you collect the renal sample.
Line 9. U 12-HETE/cr -> urinay 12-HETE/cr

Line 3,9 You need to quote reference.
Line 23. You argued Babu et al did not analyze the histological changes. But you also did not offer the histological analysis (glomeruli histomorphometry etc)

14. P17. Line 15. (6,93,94)(95) -> (6,93-95)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
I declare that I have no competing interests'