Reviewer's report

**Title:** Hsp90 inhibition differentially destabilises MAP kinase and TGF-beta signalling components in cancer cells revealed by kinase-targeted chemoproteomics

**Version:** 1  **Date:** 4 October 2011

**Reviewer:** Taeb Sim

**Reviewer's report:**

This manuscript entitled “Hsp90 inhibition differentially destabilizes MAP kinase and TGF-beta signaling components in cancer cells revealed by kinase-targeted chemoproteomics” would be of great interest as this manuscript proposes further Hsp90 clients and includes the impact of Hsp90 inhibition on a large number of kinases revealed by kinase-targeted chemoproteomics. It is also shown in this manuscript that BMP receptors are downregulated after Hsp90 inhibition. However, some errors in the text and figures are noted and the correction of these errors would upgrade this manuscript.

**Comments**

1) Page 7, line 24; “26 of 29 reported client kinases quantified in the reference Hs68 cell line showed significantly reduced level” It is required to put what are reported 29 client kinases.

2) Page 15, line 4; Authors mentioned that NQO1 influences on the antitumor activity of 17-AAG. It is required to explain briefly how NQO1 regulates the stabilization of Hsp90.

3) Page 8, line 22; It is required to clarify what is 60 data points.

4) Fig. 2; The resolution of western blot bands is not good. It should be better to represent the quantification value of western blot band.

5) In manuscript title; destabilises # destabilizes

6) Page 4, line 11; include the kinases (such as) SRC, CKD4, BRAF and ErbB2

7) Page 4, line 14; “degradation [5]..” one of two periods should be removed out.

8) Page 5, 12; It would be better to put full name (Receptor-interacting serine/threonine-protein kinase 2) of RIPK2.

9) Page 7, line 24 & 27 and page 10, line 6; space is required for 24h (24 h)

10) Page 8, line 23 and Page 10, line 1; it is recommended that “GA” is replaced by “geldanamycin”.

11) Page 9, line 1 ; it is recommended that “CK2a and CK2a’” is replaced by “two catalytic subunits (CK2a and CK2α') of CK2 holoenzyme”.

12) Comma and period are confusedly marked.
i.e.) Page 6, P-value < 0,05 # pvalue < 0.05 and page 5, 1,5mM # 1.5 mM
13) Page 12, line 11; stabilising # stabilizing
14) Space is required between value and unit (except %).
i.e.) page 5, 50mM Tris #50 mM Tris

**Level of interest:** An article of importance in its field

**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'