Reviewer's report

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

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Reviewer: Daniel Sem

Reviewer's report:

Haupt et al present a chemoproteomic analysis assessing changes to the kinome in cancer cells treated with the Hsp90 inhibitor, geldanamycin. The concept behind this study is of scientific and practical interest, as one would expect a destabilization of kinases, particularly in cancer cells, due to inhibition of Hsp90. This effect could explain efficacy of such inhibitors as potential anti-cancer agents, and off-target effects might also help to explain toxicity issues.

As is typical in such proteome-wide analyses, there are errors and issues with reproducibility, so careful attention to such matters is important – using proper controls, statistical analysis, as well as experimental verification. In this regard, one nice feature of this study is the attempt to confirm changes to protein levels using Western analysis. Unfortunately, the Western analysis did not reveal very clear trends in changes in protein levels. Also, overall it seems like the changes in protein levels were not dramatic enough (20-25%), when comparing cell lines, to permit strong conclusions regarding effect of drug in cancer versus non-cancer cells. Of course, this is of some interest as well.

But, on the whole this study seems like it might be better suited for a more specialized journal, focused perhaps on proteomics.

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.