Reviewer’s report

Title: Synthetic Lethal Screen Identifies NF-kappaB as a Target for Combination Therapy with Topotecan for patients with Neuroblastoma

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Reviewer: Darran O’Connor

Reviewer’s report:

Here the authors set out to identify drug targets to synergise with topotecan in neuroblastoma using a synthetic lethal RNAi screen. All of the experiments are clearly described, well controlled and results interpreted correctly. The authors conclusion that inhibiting the NF-kB pathway in combination with topotecan treatment seems rational based upon their results. It would be interesting to see if NF-kB activation occurs in neuroblastoma patients treated with the same regimen, and this could be readily achieved using commercial assays for NF-kB DNA binding, however, inclusion of this data is not required for the publication of these initial findings. It is a very straightforward study that addresses an outstanding clinical need and derives clear and unambiguous results. In all, an excellently performed screen with well validated hits. I have no major revisions to suggest (though it would be nice to see the actual data from the screens rather than just the list of validated hits). A second siRNA in their final analyses would also be useful, however, given that the same results are derived through chemical inhibition of the pathway, the potential for off target effects looks small. No minor revisions required either.

Level of interest: An exceptional article

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests