Reviewer's report

Title: Effect of sulfasalazine on human neuroblastoma: analysis of sepiapterin reductase (SPR) as a new therapeutic target

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Reviewer: Jianhua Yang

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In the submitted manuscript by Lisette P.Yco et al., the authors investigated the function and clinical relevance of sepiapterin reductase (SPR) in human neuroblastoma (NB). SPR expression was showed to correlate with unfavorable NB characteristics and therapeutic treatment by blocking SPR with sulfasalazine (SSZ) led to potent anti-proliferation activity in vitro. In addition, the manuscript identified sulfasalazine in combination with DFMO as a novel therapy for NB patients.

Although this study is interesting with carefully designed experiments, some points should be clarified.

Major points:

1. In figure 3, manuscript showed that “SPR and ODC (2 log) expression values for each sample are visualized with red circles and black rectangles”, but there is no red circles and black rectangles in figure. In addition, even though the p value is very significant, but the R value is only 0.225, which showed very weak correlation between SPR and ODC. Therefore, the rationale of targeting SPR and ODC together is not well established.

2. For drug synergy, the synergism means that combing two drugs together can enhance or magnify the effects of these drugs. It doesn’t depend on drug concentration. Otherwise, how to explain that using same drugs with different concentrations can get different effects (synergy or antagonism)?

3. Fig.4 should include the link of significant difference and Descriptions of statistical methods.

Minor points:

1. Line-115 should be “P values < 0.05”