Reviewer's report

Title: Selective repression of RET proto-oncogene in Medullary Thyroid Carcinoma by a natural alkaloid berberine

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Reviewer: anna ivana Scovassi

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The manuscript by Kumarasamy et al. focuses on the effects of the plant drug berberine on a cell line derived from a medullary thyroid carcinoma, possibly mediated by a direct action on the proto-oncogene RET.

Although addressing a hot topic and being well conceived, the manuscript can be further improved by a number of revisions.

Major Compulsory Revisions

1. In my opinion, the main goal of the MS is not to depict the effect of berberine on G-quadruplexes, but to demonstrate that the drug is effective on the medullary thyroid carcinoma cell line. In this respect, the description of the Results must start with the biological data, i.e. with the effect on cell viability and on cell cycle distribution. Otherwise, one cannot understand why the authors searched for the berberine action on RET.

2. Cell cycle distribution: the evident arrest in G1 is not commented; the three conditions illustrated in Fig. 6D require a quantitative analysis, and the presentation in a uniform way, in order to see the 3 conditions at the same size.

3. In M&M, a section named Chemicals must be added, reporting the source of berberine and other drugs, the preparation of the stock solutions, and the solvent. The concentration is sometimes expressed in µg/ml and sometimes in µM, please uniform. The standard treatments (concentrations, times) have to be clearly stated.

4. The specific effect of berberine on cancer cells is not mentioned. Parallel experiments on normal thyroid cells are required.

5. Are the effects of berberine reversible?


7. To better discuss the already published data on berberine and G quadruplexes, check the papers listed at:

Minor Essential Revisions

M&M: why there is a so different % of serum (9 vs 15%) in the culture media?
Note that the singular of media is medium, so DMEM 1640 medium etc.
Check for English, a cell line was (not were) cultured.
Pag. 8, lines 4-5: abcam is in fact Abcam. Tagged is in fact conjugated, last sentence is truncated.
Pag. 9, line 1 96 well dish is a 96-well plate. Line 2: wide range: specify.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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