Reviewer's report

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

**Version:** 2  
**Date:** 19 March 2015

**Reviewer:** Vincenzo Marotta

**Reviewer's report:**

This is an innovative paper clearly demonstrating that berberine could represent a potential tool for the treatment of MTC (namely aggressive forms). This could led to the development of in vivo and then human studies about the efficacy and safety of this compound in MTC.

Several lab techniques have been used in this research, thus rendering the article of high quality. All aspects and potentials criticisms are solved by dedicated experiments.

Minor points:
- in the discussion authors should better explain how berberine blocks RET transcription. Particularly, it is not clear for me (by the experiments regarding Berberine on RET promoter activity) if it acts on the G-quadruplex or its activity is indipendent by these structures.
- in the discussion authors should address whether they this selective action ciuld be better as compared with multifunctional action of cabozantinib and vandetanib.

Congratulations for your research.

**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:**

no conflict of interest