Reviewer's report

Title: Analysis of MLH1 and MGMT expression and promoter methylation on genomic instability in patients with thyroid carcinoma

Version: 2  Date: 2 January 2013

Reviewer: Chiara de Waure

Reviewer's report:

The paper “Analysis of MLH1 and MGMT expression and promoter methylation on genomic instability in patients with thyroid carcinoma” has been amended by the Authors but presents still several major concerns which make it unsuitable for publication.

Major concern

1. The objective of the paper has been clarified (study of the association between expression/methylation of MLH1 and BRAF V600E/MSI and expression/methylation of MGMT and IDH1/RAS mutation. Anyway, the following aspect remain still unclear:
   - Why the Authors did made a conclusion also on the association between MSI and histological pattern which was not included in the aim of the paper?
   - Why did the Authors evaluate also RET/PTC mutation?

2. In the statistical analysis there is not reference to the comparison between histological types and this is counteracting with the conclusion made in the abstract and in the discussion.

3. The recruitment process is not described at all: this is a relevant concern of the study.

4. The malignant samples are not 82 and not 92. I still do not understand why the Authors did include in the study also sample coming from benign lesion and normal tissue: in the aim the evaluation of differences between malignant and benign lesions was not listed.

5. Table 2 has to be amended: if a comparison between histological types has been made, I would expect to see only one p value for each of the two genes. In particular, I would like to see a unique value of p followed by a post-hoc analysis with a correction for multiple comparisons. I suggested doing it also in the previous review with no results (even though in the point to point answer Authors have told to do it). Furthermore, in the objective and in the methods the Authors did not mention the comparison between histological patterns as an aim.

6. Numbers in table 3 are still inconsistent with those in number 2 and each other.

7. I cannot understand totals reported in table 5 and 6: according to me numbers are still inconsistent.
8. Limits of the study are not discussed still in the amended version.
9. English has to be revised and sentence construction is sometime meaningless.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests