Reviewer's report

**Title:** DNA hypermethylation and upregulated miRNA-21 expression leads to decreased mRNA expression of MAL, PRIMA1, PTGDR and SFRP1 in left-sided colorectal adenoma and cancer

**Version:** 2  
**Date:** 12 March 2015

**Reviewer:** Christos Kontos

**Reviewer's report:**

This is an excellent original research study providing convincing evidence that hypermethylation of specific genes (COL1A2, SFRP2, SOCS3) and/or miR-21 overexpression may result in reduced expression of these genes and hence contribute to colorectal carcinogenesis. The study is very well designed and performed, experimental methodology is appropriately used, the results are very promising and the conclusions are solid. Moreover, the subject of the study is original and very interesting and the manuscript is of high scientific quality. However, there are a few issues that should be addressed to improve the manuscript:

**Minor Essential Revisions**

1. The introduction is rather short. Moreover, important introductory information (e.g. on miRNAs) is missing. The authors should consider enriching appropriately the Introduction section.

2. Was the current study performed in accordance with the ethical standards of the revised Declaration of Helsinki? If so, this should be mentioned in the Materials and Methods section.

3. The authors should discuss the role of miR-21 in more detail (end of the Discussion section). It is also advisable to add some information about the epigenetic regulation of miR-21 in colorectal cancer.

4. The whole manuscript should be carefully checked for English language (grammatical and syntax) errors and these should be corrected; e.g. last sentence of the introduction "… we aimed to confirm…".

**Level of interest:** An article of outstanding merit and interest in its field

**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.