Reviewer’s report

Title: Loss of heterozygosity at thymidylate synthase locus in Barrett’s metaplasia, dysplasia, and carcinoma sequences

Version: 2 Date: 23 January 2009

Reviewer: Rebecca Fitzgerald

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In their article, Kuromochi et al describe the presence of LOH at the thymidylate synthase locus. LOH was present in around 28% of BE and dysplasia samples and 40 in cancer samples. The mRNA expression of the enzyme was not different between thymidylate synthase genotype).

The presence of the locus is interesting since levels of thymidylate synthase are predictor of 5 FU chemotherapy. The significance of LOH is however not clear.

Major compulsory revisions:

1) The authors should add a short description of their methodology for RNA extraction and cDNA synthesis.

2) Figure 1: The screen grabs of the qPCR should be cleaned up to show only the graph not parts of the software window. Why did the authors choose to show the example of the 6bp insertion/deletion polymorphism?

3) Table 1 should be reformatted to present the data better. It should be divided into 2 tables: One for patient samples in which more information (age, gender, length of BE) and one for the patients with LOH.

4) LOH
   a. The authors should present a figure exemplifying sample with and without LOH since it is the main message of the manuscript.
   b. I would have expected to find data on the expression of thymidylate synthase between samples and without LOH. The authors should present this data.

5) In the abstract the conclusion that LOH is a “frequent” occurrence should be modified to “relatively frequent”

6) The findings do not need to be justified in terms of biomarkers to predict cancer risk. The data presented here are not sufficient to justify this and they are interesting in their own right. If anything it would be interest to explore whether loss of this locus predicts response to chemotherapy in this cancer.

Minor points:

1) Et al. is derived from Latin and should be italicised.
2) In the discussion paragraphs 1 and 2 should be inverted.
3) There are multiple grammatical errors throughout the text.

**Level of interest:** An article of importance 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.