Reviewer's report

**Title:** Increased mRNA expression levels of ERCC1, OGG1 and RAI in colorectal adenomas and carcinomas.

**Version:** 1  **Date:** 22 June 2006

**Reviewer:** Tamotsu Sugai

**Reviewer's report:**

**General**
The author indicates that increased expression of defense genes ERCC1 and OGG1 is an early event in the progression of colorectal neoplasia. In addition, the author suggests that low level expression of DNA repair genes in the normal mucosa is a risk factor for colorectal adenoma. Although this manuscript is generally well presented, several minor points are suggested below:

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

1. The adenoma-carcinoma sequence model is generally accepted for polypoid tumors since it is common to find both adenomatous and carcinomatous lesions within such tumors. However, an increasing number of superficial or flat colorectal tumors have been reported, particularly in Japan. Recent molecular analysis indicates that there are two broad categories of colorectal tumors: superficial and conventional polypoid tumors. In contrast to polypoid lesions, which follow the adenoma-carcinoma sequence, superficial colorectal tumors have distinct histological and genetic characteristics. The findings in this report suggest that colorectal adenomas are not homogeneous tumors. If possible, the author should examine expression levels of the three suggested genes not only in polypoid adenomas, but also in superficial adenomas.

2. Colorectal carcinoma sometimes invades into the submucosa from the mucosa. If the author clarifies the point at which these two tumor grades (intramucosal cancer and submucosal cancer) of colorectal carcinoma acquire high expression levels of the genes examined, this manuscript could potentially contribute to the understanding of the underlying pathogenesis of colorectal tumors.

3. Colorectal tumors frequently contain considerable intervening stroma between neoplastic glands. The presence of nonneoplastic tissue also technically compromises mRNA expression analysis since the proportion of tumor cells in the specimen is reduced and DNA from nonneoplastic cells can complicate interpretation of mRNA expression data. Therefore, many of the problems limiting interpretation of mRNA expression analysis stem from contaminating nonneoplastic cells, which can lead to inaccurate analysis. The author should clarify the ratio of tumor cells to nonneoplastic cells.

4. For the same reason, low expression levels of DNA repair genes in the normal mucosa may be influenced not only by normal crypt cells, but also by low level expression of interstitial cells. The author should discuss expression of the three genes in normal crypt cells.

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**Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)**

1. The Introduction is rather long and should be shortened.

2. There are a few missed characters in this manuscript.

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**Discretionary Revisions (which the author can choose to ignore)**

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions