Reviewer’s report

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

Version: 1 Date: 23 June 2006

Reviewer: Sima Salahshor

Reviewer’s report:

General

Recent studies indicate that the levels and status of DNA repair genes is a predictor of survival and degree of respond or resistance to different therapies in cancer patients. However, there are some conflicting results and therefore, more studies are required to address these issues.

In this study authors have examined the mRNA levels of two DNA repair genes and one gene involved in apoptosis in adenomas and carcinomas extracted from colorectal cancer patients and found higher levels of these genes in adenomas and tumors compared to corresponding normal tissues and conclude that increased expression of DNA repair genes is an early event in colorectal carcinogenesis.

-----------------------------------------------------------------------------------------------

Major Compulsory Revisions

1) DNA repair mechanisms are complex and involve more than 100 genes. In the Background Section is not clear why authors choose to study specifically these two DNA repair genes.

2) A number of studies have examined the levels of these three proteins in different forms of cancer, including colon cancer which should be cited in this paper.

3) OGG1 gene is coding for over 8 different splice variants. Are the primers used for quantitative RT-PCR detects all the variants or some of them? (Genbank Accession number?)

4) As mentioned in the text there is 5-10 fold variation in mRNA ERCC1 and OGG1 levels measured in healthy volunteers (Page 11- Ref. 23). If you measure mRNA levels in tumors/adenomas compared to the corresponding normal tissue (for each case), in how many cases do you find statistically significant difference?

-----------------------------------------------------------------------------------------------

Minor Essential Revisions

1) The page numbers is missing in some of the references. Reference number 33 is published in 2006 and not 2005.

2) Please provide the full-names of OGG1 and ERCC1 in the beginning of the paper.

-----------------------------------------------------------------------------------------------

Discretionary Revisions

1) It has been suggested that the mRNA and protein levels of DNA repair genes correlate. Immunohistochemistry or western blot analysis of OGG1, ERCC1 and RAI in tumors and corresponding normal tissues would provide evidence whether increased mRNA level in tumors is also an indicator of higher levels of protein.

2) Authors suggest that the low level of DNA repair genes in normal tissue is a risk factor for adenoma formation. Have they compared the expression level of these genes in normal tissue in general population (control) with their levels in normal tissue from cancer patients?
3) Are there any clinical data available to assess whether the high level of DNA repair genes in the cases studied there is a predictor of survival or respond to therapy?

4) Have authors any explanation why cases with low expression of these DNA repair genes in normal tissue show increase expression in tumors? It is possible that these results indicate that ERCC1, OGG1 and RAI are functioning normal and are activated in tumors as a result of the disease?

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

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: No

Declaration of competing interests:

I declare that I have no competing interests.