Reviewer's report

Title: Effects of polymorphisms in ERCC1, ASE-1 and RAI on the risk of colorectal carcinomas and adenomas: a case control study

Version: 1 Date: 19 April 2006

Reviewer: Gregory Tranah

Reviewer's report:

General

Effects of polymorphisms in ERCC1, ASE-1 and RAI on the risk of colorectal carcinomas and adenomas: a case control study. Skjelbred et al.

My main concerns involve the epidemiologic study design (see below). The selection of genes is of interest due to previous findings and in general the author’s interpretation of the data is cautious and appropriate.

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

Study design:
The description of the study design and case-control selection needs to be presented in substantially more detail. A more thorough description of how do the resources of the KAM biobank fall into the larger context of NORCCAP would be very useful. For instance, are the cases and controls presented in this analysis the total number available from NORCCAP or the KAM biobank? The authors also state that the study consists of 1044 individuals with adenoma, 160 with carcinoma and 400 cases and that additional patients diagnosed with colorectal cancer at two hospitals are included. How many patients are from the screening group and how many are from the hospital?
The authors state that there are ‘available’ blood samples from 981 adenoma cases, 156 carcinoma cases and 399 controls. Please state why blood is not available for all samples listed above.

Control subjects:
The authors state that there are 400 healthy ‘controls’ available for this study. Why 400? Are these the only disease-free individuals in the biobank that are available or is this number chosen for another reason? This is an atypically low number of controls for a study that includes over 1,000 cases. This must limit the power of this study. Are the controls matched to cases by any criteria? In the analysis the controls are younger and have a different sex distribution ‘how is age matching done in the analyses? The authors need to provide more detail about the controls being appropriately matched to cases.

Analysis:
Information regarding smoking, alcohol intake and exercise is also available. Since these are all risk factors for colorectal adenoma and carcinoma were they considered for adjustment in the logistic regression analyses? Also, since two of the genes are involved in DNA repair and inflammation it would be interesting to see if there are any gene*environment interactions with smoking and alcohol intake (even with retrospective ascertainment of these behaviors).

Haplotype:
The authors state that they performed haplotype analysis. Did they computationally derive haplotypes (based on genotypes) for the analysis? It seems like they considered the homozygous carriers of specific alleles for each of the three genes as their haplotype. Was the comparison group all other remaining individuals? Please clarify.

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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)
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

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests