Reviewer's report

Title: MDM2 SNP309 is associated with high grade node positive breast tumours and is in linkage disequilibrium with a novel MDM2 intron 1 polymorphism

Version: 2 Date: 12 June 2008

Reviewer: Sharon Pine

Reviewer's report:

This is a well written report showing the MDM2SNP309 is not associated with breast cancer among Scottish women, but is associated with poor prognostic variables.

1. How were the controls for this study recruited? Were there any differences in demographic variables between those who agreed and disagreed to participate?

2. A table comparing the demographics of the cases versus controls is needed, including age, menopausal status, family history of breast cancer, household income, and education level.

3. Please indicate the referent group for each analysis shown in Table 2.

4. Is there an association between SNP309 and tumor histology?

5. The 20 cases with DCIS should not be included in the risk assessments or in the comparisons to clinical characteristics in Table 2, because DCIS patients may not represent a true breast cancer population. Alternatively, stratify risk analysis by DCIS versus invasive breast cancer, and/or justify why DCIS patients are included in analyses. The lack of the 309G/G genotype among DCIS patient is of merit and supports its association with high tumor grade and should still be included.

6. On page 10, in the “Additional MDM2 intron 1 polymorphisms” section, SNP285C was shown to be associated with breast cancer risk. Were the male controls included in the analysis? Please show the N values for each allele in the cases and controls.

7. The discussion on page 11 states that 275 cancer free controls were used in the study to correlate MDM2 SNPs with age of diagnosis, pathological variables, and clinical outcome. However, this is not the case. First, the controls were not used for correlating the SNPs with age at diagnosis, or pathological variables. Second, clinical outcome was not reported.

8. Please state the limitations of the study in the discussion, in particular, that the numbers of cases and controls are low (especially in association between the SNP309 homozygous variant group and prognostic variables) and are not matched on demographic features.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

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