Reviewer’s report

Title: Aberrant allele-specific replication, independent of parental origin, in blood cells of cancer patients

Version: 2 Date: 12 September 2008

Reviewer: Rui Henrique

Reviewer’s report:

In this study, Dotan and co-workers examined the modification of replication pattern of biallelically and monoallelically expressed genes in peripheral blood lymphocytes of prostate cancer patients, using lymphocytes of patients with benign prostatic hyperplasia as controls. They found that the normal pattern of replication was reversed and that the addition of azacytidine was able to restore the normal pattern in cancer patients but did not change the replication pattern of cells from non-cancer patients. Overall, the methodology is sound and appropriate for the aims of the study.

The findings are interesting although not completely novel, as the authors have previously addressed this theme in previous publications.

Major compulsory revisions

1. The manuscript is too long and detailed in almost all sections (Background, Results, Discussion, Material and methods) and would benefit from substantial shortening. Moreover, some paragraphs are somewhat misplaced (e.g., the 2nd and 3rd paragraphs of page 6 seem more appropriate for the Results and Discussion). In addition, there is no clear statement of the aims of the study in the introductory section.

2. The authors used the SD frequency as a measure of the replication pattern. However they do not define the normal limits (although CEN15 is used for that purpose). For Kitsberg et al. (reference 21) loci with SD frequencies of 10-20% are considered synchronous and 25-40% are considered asynchronous. Notably, CEN15 (used as an example of synchronous replication in BPH patients) displays an intermediate value (although more close to 20%). The authors should clearly state which were the “normal” limits defined for this study.

3. Along the text, including the Abstract, the authors state that their findings might be used as potential markers for cancer-drug evaluation. Could they specify this hypothesis?

Minor essential revisions

1. The manuscript is not structured according to the BMC Cancer style:
   a. A “Methods” section is missing in the Abstract
   b. In the main body of the text, the “Material and methods” section is placed at the end and not after the “Introduction”, as it should
2. In the Abstract, the authors state that “malignancy disrupts...”; however, they do not demonstrate a causal effect between cancer and alteration in replication pattern in lymphocytes. So, they can only state that there is an association between these two conditions.

3. In the statistical methods, the level of significance is not stated.

4. There are some typing errors:
   a. Pg. 12, line 21: “hypermethylation”
   b. Pg. 13, line 6: “retino-blastoma”
   c. Pg. 15, line 12: “baiallelical”
   d. Pg. 15, line 19: “epigentic”
   e. Pg. 21, line 21: “conceived of the study”
   f. Pg. 29, line 13: “(PBH)”

Discretionary revisions
1. Abstract, line 12: “resurrect” might be replaced by “restore”
2. Abstract, line 22: “a solid tumor” would more appropriately be replaced by “prostate cancer”

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

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