Reviewer's report

Title: DNA repair deficiency in peripheral blood lymphocytes of endometrial cancer patients with a family history of cancer

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Reviewer: Adi Baumgartner

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RE: The manuscript by Buchynska et al. “DNA repair deficiency in peripheral blood lymphocytes of endometrial cancer patients with a family history of cancer”.

The question posed by the authors is well defined and the method is appropriately described with some lapses in detail. The data seem to be sound. The manuscript adheres to the relevant standards for reporting and data deposition and the discussion & conclusions are well balanced and adequately supported by the data. The limitations of the work, however, have to be more clearly stated such as the small samples size. Any work upon which they are building was acknowledged by the authors. The title and the abstract accurately convey what has been found and the writing is acceptable.

- Major Compulsory Revisions

1) The number of healthy control donors is with only ten individuals 4.5-times lower than the number of endometrial cancer patients. This needs to be addressed in more detail in the discussion. I strongly recommend having a higher number of age-matched healthy individuals. If this is impossible it has to be at least shown by the authors that the sample size is sufficient to yield good statistical power.

2) The authors need to address confounding factors such as life style, work environment, medication, alcohol consumption and smoking status of the blood donors by elaborating on the individuals’ questionnaire in the material and methods section. These variables may need to be addressed in the statistical analysis.

3) Did the patients receive radio- and/or chemotherapy? If yes, was blood taken before the start of the treatment?

- Minor Essential Revisions

1) Abstract:

- The authors should mention that the difference of the levels of spontaneous DNA damage (= baseline damage) in lymphocytes of patients and healthy
individuals was indeed significant as stated in the results section.

2) Introduction:
- It should read “… increased frequencies of chromosomal aberrations and breaks at fragile sites …”

Cytogenetic damage generally includes numerical abnormalities (e.g. due to an aneugen) and chromosomal aberrations (e.g. due to a clastogen) and I assume the authors meant the latter.

There are more than 120 known fragile sites in the human genome. Did the authors intend to say that their actual number increases in lymphocytes of cancer patients?

3) Patients & Methods:
- State the exact number of patients with a familial history of cancer.
- It should read “… low-melting point agarose …”
- Write “… treated with bleomycin (20 µg/ml) in phosphate buffered saline (PBS), # 7.4, for …”
- It is not clear when the treatment occurred. The way it is written it indicates a treatment and recovery of the cells while being embedded in agarose. Is this correct?
- Please state the exact conditions of the recovery phase in PBS such as temperature etc.
- Write “…with a significance level of p#0.05.”

4) Results:
- Give p-values when showing significances.
- The authors wrote “… we found differences after we removed bleomycin and studied DNA damage in a time course sampling …” Do you mean DNA damage repair?
- Is there any significance between the repair capacity of lymphocytes from patients with and without a familial history of cancer? If yes, state it with p-value.

5) Discussion:
- Exchange “depressed” with “suppressed” or “reduced”
- Two recent articles are addressing the sensitivity of lymphocytes from cancer patients. The authors should include the following articles in their discussion:
  Kurzawa-Zegota et al. (2012; in Food Chem Toxicol 50(2):124-129) which stated that lymphocytes from colon cancer patients had greater baseline DNA damage compared to those from healthy individuals and this higher level of damage was also observed throughout in vitro treatment with genotoxins.
  Najafzadeh et al. (2012; in Mutagenesis 27(3):351-357) which identified peripheral lymphocytes from patients with cancers (malignant melanoma and colorectal cancer) or their precancerous states to be more sensitive to a generic
mutagen than lymphocytes from healthy individuals.

6) Tables 1&2:
- Add an extra column before the “Removed DNA damage” column indicating the measured DNA damage in % tail DNA after the 15 min recovery. I assume this value has been compared to the baseline damage for statistics.
- In the footnote it must read p#0.05.
- Please use decimal points and not commas.
- The number n of patients should be stated in the description of the rows.
- Please use the wording “healthy individuals” instead of “control”.