Reviewer's report

Title: Haploinsufficiency for BRCA1 is associated with normal levels of DNA nucleotide excision repair in breast tissue and blood lymphocytes

Version: 2 Date: 8 March 2005

Reviewer: Alex sgambato

Reviewer's report:

General
In this manuscript the nucleotide excision repair (NER) activity is evaluated in normal blood cells and breast tissue from a breast cancer patient carrying a BRCA1 mutation. The results obtained demonstrate that BRCA1 haploinsufficiency does not affect NER activity in these tissues.

The paper is of interest because it evaluates the proposed hypothesis (see ref. 19) that an association exists between BRCA1 mutation and the development of NER deficiency.

The technical aspects of the report are fine.

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

Only one case is analyzed and results might not be reliable. Authors should confirm their results on more than one case of BRCA1 mutation carrier patients before reliable conclusions could be drawn.

One of the hypotheses to be tested is that BRCA1 mutations might be responsible for NER deficiency observed in sporadic breast cancer patients: it would have been easier to look for BRCA1 mutation in the cases with NER deficiency amongst the available series of sporadic breast cancer and normal adjacent tissues to which Authors often refer to.

The Authors continuously refer to a previous work in which they analyze a series of normal breast epithelial samples: however, this is often not appropriate. In the paragraph “Functional analysis of NER capacity” the Authors refer to a series of 33 normal samples of blood lymphocytes which have never been previously described and whose origin is unclear.

They also refer to previous abstracts and this makes it difficult to understand some of their results. It might be appropriate to include all the information in one manuscript being the results of this study a completion of the previous ones.

The Authors seem to suggest the use of their assays to identify mutation carriers among the sporadic breast cancer population: however, this appears extremely difficult to realize (if not impossible) considering the difficulty and the cost of the assays to be performed routinely for sporadic breast cancer patients.

The Authors conclude speculating on the importance of NER deficiency and on the advantage of having breast tumors from hereditary patients with NER deficiency, despite the fact that the results of the study show that this is not the case.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discussion can be easily shortened by avoiding useless repetition (as is the case for the first paragraph). Moreover, all the manuscript can be simplified avoiding useless information and repetition.

There are some typos through the manuscript.

Legends to Figs. 1 and 2 should be more detailed and better described.

In Fig. 3 is not clear whether both panels show cells from patient or not and whether they are from ipsilateral or contralateral breast.

The patient is reported to be 35 years old in the Results section and 36 years old in the Materials and Methods section.

Discretionary Revisions (which the author can choose to ignore)

Most of the information reported in the Results section from Patients description to Final Pathology, treatment plane and outcome are irrelevant for this study and can be eliminated.

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