Author's response to reviews

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

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We would like to thank the reviewers for their time and efforts. Responses to specific points raised by each reviewer are given below.

Dr. Cleaver:

We have kept the manuscript as balanced as possible between the patient diagnosis and characteristics and the NER results. In deference to Dr. Sgambato’s review we have expanded the discussion of NER by 2 sentences in the Abstract, 2 sentences in the Background and by a paragraph in the Discussion. We have not removed any of the non NER-related material, nor have we rearranged the order of discussion of the various aspects of the report.

Dr. Sgambato – Major points:

1a) We appreciate the reviewer’s focus on the NER results in the manuscript, and, to a degree, we agree that this is the most interesting aspect of the study since we identified it in the title. On the other hand, we feel that we must identify the patient as being diagnosed by low power MRI in case her results prove to be non-representative of BRCA1 carrier patients (or their tumors) in general.

1b) We believe there are two reasons that MRI-diagnosed tumors may include some tumors of unusual or even novel etiology. The first, which applies to our current patient, is that the basis for the cancer predisposition observed in women with dense breasts is not known, and may affect or even direct the molecular pathway of carcinogenesis in these patients. Second, there is also the possibility that MRI will uniquely detect early tumors even in women with normal breast
density. Such “low density” tumors might include mucinous or inflammatory breast cancer or even presently unknown subclasses. This second possibility does not directly apply to our patient, however, and will only be addressable if MRI or other complementary screening methods are applied in general population screening.

1c) Although we have not reduced the indication to MRI, we have increased the background and discussion of the NER results, effectively putting the patient data into a lesser context.

Minor points:

3) We have rewritten the sentence in question to clarify its meaning. Initial cultures are of mixed cell types, although epithelial cells can distinguished morphologically and persist through passaging and sub-culture.