Reviewer’s report

Title: A novel germline PALB2 deletion in Polish breast and ovarian cancer patients

Version: 1 Date: 20 September 2009

Reviewer: William Foulkes

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This is an interesting ms on the identification of a putative founder PALB2 mutation in central Poland.

Major revisions
Please check “basal” markers in the medullary PALB2+ breast cancers – CK5, CK14, EGFR and KIT would be good markers to choose from. HER2 should be completed if at all possible.

Minor revisions
Abstract: Methods – I do not think the word “random” in “random ovarian cancer patients” is quite right. What exactly do you mean? Non-consecutive, incident, prevalent, consecutive, non-selected etc? Please clarify.


Methods: page 6 – it is not clear what is meant by “ovarian cancer samples and respective blood samples, as well as control samples were screened for PALB2 alterations...”. Do you mean the DNA from the tumors was screened at the same time as was DNA from lymphocytes? Or was lymphocyte DNA analysed first with results checked in the tumors? If not, the somatic mutations identified only in the tumors should be presented.

Were the controls screened for all mutations? This should be clarified in this section, rather than later. This is not really made clear in the paper.

Page 7 - the primers should be in a table.

Page 8 – the sensitivity of SSCP is well known to be well below 95%. Please comment on this and reference several relevant papers.

Results - page 10 – was it possible to test any other individuals, or pathology blocks from the family of patient 293? It would be very helpful if the segregation of the two mutations could be better studied. The presence of both a BRCA2 and PALB2 mutation in the same person obviously makes it very hard to interpret the significance of the overall findings with respect to OC risk in PALB2 carriers. Is it clear that the families of the two PALB2 mutation carriers are not fairly closely related?

Page 10: Please show the presumptive haplotype of the seven women with the putative founder mutation
Discussion: page 12 – frequency of PALB2 in breast and ovarian cancers was said to be the same, but the presence of one BRCA2 mutation in one of the two cases must be included at this point in the discussion.

Page 13: Mention Tischkowitz study at ref 14.

Discretionary revisions –

Page 14: it is quite notable that Heikkinen also found 2 breast cancer patients who were double mutants for PALB2 and BRCA2. Based on the gene frequency of each gene in controls in Finland, can the authors speculate on how often this would occur by chance? 2/104 seems somewhat high to me: it would support their own data if the observed ~2% were significantly different from the expected number.

Typographical errors
Page 14, first line: Garcia, not Gracia. There are other scattered typos and an editorial check of English usage would be worthwhile.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

i declare that I have no competiing interests