Reviewer’s report

Title: Li-Fraumeni-like syndrome associated with a large BRCA1 intragenic deletion

Version: 2 Date: 23 March 2012

Reviewer: Jenny Leary

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This study by Goncalves Silva et al. reports on their investigations of large genomic rearrangements in 3 highly penetrant cancer susceptibility genes associated with both the inherited breast cancer susceptibility and Li Fraumeni-like cancer phenotypes- BRCA1, BRCA2 and p53. 23 patients presenting with early onset breast cancer in families with additional tumours that may be indicative of a Li Fraumeni-like syndrome and who tested negative for p53 point mutations were analysed. A single BRCA1 deletion (36.4 kb) was detected in a family meeting the Eeles 1 criteria for Li Fraumeni-like syndrome but that also presents with a strong breast cancer susceptibility phenotype.

Whilst acknowledging that the deletion-positive family meets criteria for the Li Fraumeni-like syndrome, this same deletion has been observed in an Italian breast/ovarian cancer family and the discussion should acknowledge the potential that this large genomic deletion may represent a breast cancer susceptibility allele rather than a more general cancer susceptibility allele of the Li Fraumeni-syndrome. This will only become evident when/if further testing is performed in this family in the clinical/diagnostic setting.

Nevertheless, this re-submission is a much improved representation of the results and issues with comprehensive and sound data that has been well presented. The study will positively add to the literature for families with Li Fraumeni-like syndrome.

Major Compulsory Revisions- nil
Minor Essential Revisions- see above
Discretionary Revisions- nil

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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