Reviewer's report

Title: MC1R variants predisposing to concomitant primary cutaneous melanoma in a monozygotic twin pair

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Reviewer: Veronique Bataille

Reviewer's report:

This is an interesting report and shows the role of genetic factors in the aetiology of melanoma. However the role of MC1R variants in the causation of the 2 melanomas in this twin pair cannot be confirmed and the authors should acknowledge that many individuals have several variants of the MC1R and will never develop a melanoma. To put things into context may be the authors should give the prevalence of one or two variants in individuals with fair skin. In the introduction, the authors mention the role of rare and high penetrance genes in melanoma and only one common low penetrance gene such as MC1R. However, there are many other low penetrance genes recently discovered which confer an increased risk of melanoma and many of those are pigmentation genes which the authors should mention and discuss the fact that these were not genotyped but may have been involved. Nevus genes have also been identified and this is relevant as the twins have an excess number of nevi. The authors should also mention the possible screening bias as the second twin is more likely to come forward for screening or be called back for screening because the co-twin has just been diagnosed with melanoma. The second twin indeed has a very thin melanoma and these lesions can be very borderline pathologically especially with a Breslow thickness of 0.33 mm. In patients with the atypical mole syndrome, it is not uncommon to remove lesions which did not look that suspicious clinically and find melanomas which are borderline with very low Breslow thickness. This should also be discussed.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests: I declare that I have no competing interests