Reviewer's report

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

Version: 1 Date: 2 July 2012

Reviewer: William Bruno

Reviewer's report:

In their paper, Pellegrini and colleagues describe a case of monozygotic twins who developed nearly concomitant cutaneous melanomas. The authors point out that only two similar cases have been reported so far, and that their study is the first that includes molecular analysis of melanoma susceptibility genes in the patients.

The twins were analyzed for presence of mutations in high-risk genes CDKN2A, CDK4, and low/intermediate risk genes MC1R and MITF. The authors attempted to identify both the behavioural and genetic risk factors shared by the twins, and found that they harboured two R MC1R variants but had a different history of sun exposure.

Minor Essential Revisions

1) This referee thus agrees that "the concordance for cutaneous melanoma as well as the congruence for its location and identity of the age of onset in monozygotic twins support the role of genetic rather than environmental factors" in the development of melanoma. However, a number of low-penetrance melanoma genes have been identified to date. Furthermore, previous findings on the rare Y152X variant suggest that despite its truncating effect this variant may not only require additional MC1R variants but also other genetic/environmental risk factors to actually increase risk (i.e., Galore et al. Melanoma Research 2007, a reference that could be added).

The authors should therefore reduce the emphasis they place on the contribution of MC1R variants to melanoma susceptibility in these patients, and add a concluding sentence that leaves the door open to the possibility that other known or as yet unknown genetic risk factors may be involved.

Discretionary Revisions

2) This referee suggests to substitute “the importance of low penetrance genes” in the final line with “the contribution of” or “the role of”.

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