Reviewer's report

Title: Serum 25-hydroxyvitamin D3 levels and Vitamin D Receptor variants in melanoma patients from the Mediterranean area of Barcelona

Version: 3 Date: 27 September 2012

Reviewer: Anna Brozyna

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This is an interesting, extensive, well-designed and executed study that most of melanoma patients from sunny Mediterranean area had insufficient vitamin D3 level and that some VDR SNPs can protect against multiple melanomas. The study was performed using appropriate techniques in a sufficient number of tissue samples in SNPs analysis, with smaller group in vitamin D study. The discussion and conclusions are balanced and reasonable. Overall, this is a well-written paper reporting results of a comprehensive, carefully done experimental work.

Vitamin D level depend on many independent factors (age, season, diet, sunscreen use and others), thus the lack of relationship between vitamin D level and Breslow thickness can result from small cohort of melanoma patients.

I have additional recommendations for revision of the paper:

Major Compulsory Revisions
1. Page 10. Melanomas at stage IIIA is not localized disease. At this stage patient has lymph node metastases. Thus it should be clarified.

2. Summarize patients characteristic in table – it would be more clear.

3. Add a table summarizing clinic and pathologic data for melanomas (stage, Breslow, site).

4. Some studies showed that vitamin D level affect survival in cancer patients (including melanoma patients) thus I think this paper’s impact would be increased by examining the disease free survival and overall survival in relation to vitamin D3 level and SNPs (at least for significant SNPs).

Minor Essential Revisions
1. List the analyzed SNPs in method section.

2. Fig. 1 legend – explain meaning of circles and asterisk.

3. Some grammar and syntax corrections are needed, e.g.:
Page 2: “comparing melanoma patients 150 with low and 113 with high nevus number”
Page 7: “We selected 11 SNPs based on linkage disequilibrium (LD) with 0.5> r^2 >1 for Caucasians using Hapmap (http://www.hapmap.org) and the Tagger program. We included SNPs that had at least one independent validation criterion as established in dbSNP (https://www.ncbi.nlm.nih.gov/snp) and reported minor allele frequencies (MAF) ≥0.05”

Discretionary Revisions

1. Nevus size is one of risk factor for melanoma development. In his paper there is lack of information regarding nevi size in studied cohorts. Please clarify what was the nevi size (minimal, maximal, mean). There were any differences in group with low and high nevi number?

2. Please clarify when nevi were counted, at the time of melanoma diagnosis or after?

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.