Author’s response to reviews

Title: Diagnostic and Pathogenetic role of Cafe-au-lait macules in Nevoid Basal Cell Carcinoma Syndrome

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Author’s response to reviews: see over
Dear Editor,

We would like to resubmit our manuscript entitled “Diagnostic and pathogenetic role of Café-au-lait macules in Nevoid Basal Cell Carcinoma Syndrome” by Ponti G. et al., corrected and modified according to the suggestions and criticisms of the Reviewer for publication in “Hereditary Cancer in Clinical Practice”.

Reviewer 1

Major Revisions

1. Following your proposal we mentioned in the conclusion section that further research on the clinical association between CALS and NBCCS has to be done.

2. As suggested the title has been changed: “Diagnostic and pathogenetic role of Café-au-lait macules in Nevoid Basal Cell Carcinoma Syndrome”.

3. Molecular analysis of PTCH1 was performed as previously described (Molecular Characterization of Italian Nevoid Basal Cell Carcinoma Syndrome Patients. L. Pastorino, R. Cusano, S. Nasti, F. et al. Hum Mutat. 2005 Mar;25(3):322-3). We have added this reference in the revised version of the manuscript.
Total RNA was isolated from lymphoblastoid cell lines with TRIzol® (Invitrogen, Carlsbad, CA). cDNA synthesis was performed with the RevertAid™ H Minus First Strand cDNA Synthesis kit (Fermentas, Vilnius, Lithuania) using random hexamers. PCR primers were designed to cover exons 6–14 of the PTCH1 gene and the same primers were used for direct sequencing. Sequence numbering follows the recommendations of the Human Genome Variation Society (www.hgvs.org). All of the RT-PCR and sequencing experiments were performed twice to confirm the results.

Schematic representation of exon 8 skipping due to the c.1348-2A> G splicing mutation.
Reviewer 2

Minor Revisions

1. In Figure 1 (Table 1) a further column with internal signs and symptoms has been added.

2. In the third page, as the reviewer suggested, we left the abbreviation instead of the full meaning of KCOT.

3. We have added a sentence in the case presentation section regarding this specific PTCH1 mutation.

4. The PTCH1 mutation has already been detected by us in a young Tunisian patient and reported in the references section as note number 8.

5. Following your suggestion, we have added the NBCCS major and minor criteria in the conclusion section.

6. As suggested the language corrections have been done.

We thank very much the Assessors and the Editorial Board for their helpful suggestions, which contributed to improve the scientific quality of our paper. In our opinion the paper is now ready for a second evaluation by the Assessors. We therefore would like to resubmit the revised version of our manuscript.

Looking forward to hearing from you, best personal regards.

Sincerely yours

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