Reviewer's report

Title: Influence of maternal and own genotype at tanning dependence-related SNPs on sun exposure in childhood

Version: 0 Date: 06 Feb 2018

Reviewer: Gloria Ribas

Reviewer's report:

The manuscript is based on The Avon Longitudinal Study of Parents and Children (ALSPAC) which is a large, prospective mother-child cohort study set on 1992 with Local Research Ethics approval and informed consent from child's mothers. They recruited more than 14500 pregnant women and followed them and their children for years. When the children reached the age of 8 years old, about 7300 mothers responded to a long questionnaire (it contains some questions related to sun exposure, sun protection and related habits). The cohort has been extensively used in different studies, the web page of the association shows the full list of the articles published.

Although the cohort is impressive and the initiative has given rise to hundreds of articles in other subjects, in this particular context, the results identified are not strong and even the authors called them weak findings. These make me have some concerns about the hypothesis and aims.

The hypothesis is based on the attractiveness of becoming tanned, process that has severely increased in the last decades. Tanning, then, can be seen for some (particularly women) a way to be healthier and more attractive, and several studies shown that those individuals can become tanning dependent (TD). In this particular case, the authors tried to demonstrate the influence of maternal genotype, in addition to the genotype of the children, at tanning dependence-related SNPs on sun exposure in childhood. The hypothesis is based on the fact that the tanning dependent behavior of the mothers may regulate their children's sun exposure.

Concerns:

- The design of the experiment is not clear: For one side, authors declare to have selected 20 SNP-genes based on previous published studies; in the next paragraph they specified the use of GWAS data for the children and genotyping arrays for the mothers. In the following paragraph the authors mention that the final number of SNPs studied was of 17 located in 13 different genes (they explain the reduction from 20 to 17). Authors need to make clear that as I have guessed; they have accessed to hundred thousands of SNPs but only used the data from a few. This could have statistical implications. I would like to have this clear in the text.

- The whole cohort presents several weaknesses, some are mentioned in the text others are ignored:
a- I missed information on pigmentation characteristics both from mothers and kids (can be different from mothers). Pigmentation (skin, hair, eyes, freckles, tanning ability, etc) has been previously involved in susceptibility to sunburns and tanning. Several SNPs related to pigmentation are well documented and could have been available in the GWAs and genomic data. Mothers with genetic (and phenotypic) susceptibility to sunburn should be more prone to protect their children. None of these is neither studied nor mentioned in the manuscript and to my opinion is very relevant.

b- Fathers are not included in the equation. Both their behavior and also their pigmentation may introduce some confusion to the results.

c- They report the number of days the child was in the sun for 4 or more hours at 8 years. Maximum value is 40. Is that during the week, on weekends? In holidays? Holidays in the same country or abroad? In spring-summer? For the whole year? All this information should be better explained in the manuscript. Chronic sun exposure has been related with protection to sunburns, however, acute sun exposure is indeed a risk activity. All this can introduce biases to the responses. Authors should explain better the subgroups and the conditions.

d- The study was initially intended to study the mothers. And so, different platforms have been used, and most probably different set of SNPs have been analyzed. Genotyping has been performed at distinct institutions: children, at the Wellcome Trust Sanger Institute, and the Laboratory Corporation of America-23andMe; mothers at the Centre National de Génotypage, France. The genotyping more likely has been done at different times. All this together with different technologies and sets of SNPs may add some difficulty in the combination of the data. Could the authors comment on that and how they have minimize any bias for all the mentioned above.

e- Mothers responded on child habits and exposure to sun, which is highly modulated by mothers themselves, independent tanning addiction in children, is difficult to evaluate. When children of the cohort reach adulthood would be more accurate to evaluate their addictiveness.

Table 1 "Characteristics of the children in the study population". Title should be changed. Which characteristics are described? The table summarizes the information related to sun exposure, sunburns and sun protection habits of the children in the ALSPAC cohort given by their mothers. Refer to characteristics to the children induce to errors. The table should show statistical significance for the different subgroups in all categories.

- They highlighted the findings of two SNPS located in two corresponding genes that were associated to several sun exposure variables, and a third variation was associated to an increased likelihood of using sun cream, the conclusions shown weak evidence to tanning dependence.
Taking into account that the results have been obtained using more than 7000 samples from the kids and their corresponding mothers, I think the significance obtained is pretty low.

-Table 2: Is difficult to understand. Authors should described which are the sun exposure variables they have obtained, those explained in table 1? In the text is said that the 13 genes studied are shown in table 2, however nothing more is said about number of sun exposure variables associated to exactly what? The genes? Why one of the genes, LY75, then has zero

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
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Are the conclusions drawn adequately supported by the data shown?
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