Author's response to reviews

Title: BAC array CGH in patients with Velocardiofacial-like features reveals genomic aberrations on chromosome region 1q21.1

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Author's response to reviews: see over
We enclose the comments of the reviewers and our reply to their points.

Reviewer's report
Title: BAC array CGH in patients with VCFS-like features reveals genomic aberrations on chromosome region 1q21.1
Version: 8 Date: 28 July 2009
Reviewer: Cédric Le Caignec

Reviewer's report:
Dear Editor,

Overall, Brunet et al. answered most of my criticisms. However, in general, I share the reservations with the two other reviewers concerning the deleterious effect of the 212 kb 1q21.1 microduplication. Patient V-5, in addition to the de novo 212 kb 1q21.1 microduplication presented with a de novo 1.15 Mb 1q21.1 microdeletion. Such microdeletion is known to be responsible for congenital heart defects (CHD). Therefore, it's rather speculative to write that this is the 212 kb 1q21.1 microduplication that likely contribute to the CHD. The second patient (case 112) carries a 212 kb 1q21.1 microduplication inherited from his phenotypically normal father. Incomplete penetrance is possible but, once again, the role of the duplication in CHD is unproven. Nevertheless, this 212 kb 1q21.1 microduplication is extremely rare in the general population, so, his presence in these two patients is surprising. Additional studies will contribute to delineate more precisely the role of this microduplication in CHD.

Discretionary revisions
In the Title: VCFS-like may be written as velocardiofacial syndrome-like
We have changed the title as suggested.

In the Abstract: Results, “... the same 212 kb microduplication”. “reciprocal to the TAR microdeletion syndrome” may be added.
We have added this information in the Abstract.

There are a number of typing errors, such as “sumbicroscopic” in the Results section, “for these reason”, “a rare the novo 1q21.1 microduplication”...
We have corrected this.

Level of interest: An article of limited interest
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.

Reviewer's report
Title: BAC array CGH in patients with VCFS-like features reveals genomic aberrations on chromosome region 1q21.1
Version: 8 Date: 27 July 2009
Reviewer: Andrew Sharp

Reviewer's report:
I believe that the final sentence of the abstract is too strong based on the
available data:
We report a 212-kb microduplication on 1q21.1, detected in two patients, which is likely to contribute to CHD.
The word 'likely' should be changed to 'may'.
We have changed ‘likely’ to may.

There are a few places in the manuscript that could benefit from a native English-language speaker reviewing and correcting to adjust syntax errors etc. This would not require much time but would make the manuscript read much better.
The manuscript has been reviewed by a native English-language speaker.

Level of interest: An article of limited interest
Quality of written English: Needs some language corrections before being published
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'

Reviewer's report
Title: BAC array CGH in patients with VCFS-like features reveals genomic aberrations on chromosome region 1q21.1
Version: 8 Date: 11 August 2009
Reviewer: Stefania Gimelli
Reviewer's report:
Concerning article 1544534040248275:
BAC array CGH in patients with VCFS-like features reveals genomic aberrations on chromosome region 1q21.1
Comments from Dr. Stefania Gimelli (stefania.gimelli@gmail.com):

The manuscript reports on a CNV analysis of 18 VCFS-like patients, not presenting the typical 22q11 microdeletion, using a whole genome and a chromosome 22-specific BAC array. The author discuss on the possible association of 1q21.1 duplication with heart defects which has been never described before and, in addition, refers on the potential role of some CNVs in the VCFS-like phenotype. The author has done some important modifications giving a new statement to the paper that appears now better organized and discussed with a less confusing message. Moreover the new discussion, more focalised on the possible correlation between the the 1q21.1 duplication and CHD, makes this study worthy of publication.

1) Major Compulsory Revisions:
Considering the high phenotypic variability of patients with VCFS and the apparent rarity of 1q21.1 duplications, I don’t agree with the author’s conclusion suggesting to consider this region in the MLPA screening of patients showing a VCFS-like phenotype as well as the ones with psychiatric diseases. I would better suggest a whole genome array-CGH should be proposed to such type of patients at least until more cases will be described, giving a better delineation on
a possible correlation between the 1q21.1 duplication and the VCFS phenotype.

We agree with the reviewer that a whole genome array-CGH is the best strategy for patients with VCFS-like phenotype without 22q11 microdeletion. We have removed the suggestion about consider this region in the MLPA screening.

2) Minor Essential Revisions
I would shorten the FISH materials and methods part, writing something like: “Fluorescent in situ hybridization (FISH) analysis was performed on metaphase chromosome spreads following standard procedures”
We shortened the description of FISH analysis as suggested in the Methods section.

Page 10 last line: I suggest to write the name of the patient (V5) instead of “this patient”
We have corrected this.

Page 11 line 19 “screened”
We have corrected this.

Page 12 line 10 loci
We have corrected this.

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' below. If your reply is yes to any, please give details below.