Reviewer's report

Title: Absence of mutations in NR2E1 and SNX3 in MMEP (microcephaly, microphthalmia, ectrodactyly, and prognathism) and related phenotypes

Version: Date: 16 March 2007

Reviewer: Annick Raas-rothschild

Reviewer's report:

General

- I would suggest to see that the manuscript has been shortened and modified before publication.

1. Is the question posed by the authors new and well defined?
The question is new in part and defined

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
Yes

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data? Not completely.

6. Do the title and abstract accurately convey what has been found? No
I would add the number of patients studied

7. Is the writing acceptable? Manuscript should be shortened.

Kumar et al reported the study of SNX3 and NR2E genes in 4 patients with MMEP syndrome and one patient with a translocation including the breakpoint 6q21.
One patient with related MMEP harbored the g.21502T>C change previously reported in a patient with Microcephaly who also had additional NR2E sequence mutations.
The authors already showed in a former paper [genes brain behavior 2006] that NR2E1 coding mutations do not contribute to cortical and behavioral abnormalities in patients with Microcephaly.
I would suggest writing that the patient with ulnar aplasia was included in the work only because of the translocation breakpoint locus.

The manuscript should be shortened:
The background first paragraph could be synthesized for example.
In this work SNX3 was sequenced in 4/5 patients although no mutation had been found in one previous MMEP patient. This should be stated clearly.

Information such as "...33.5 kb sequence data" [page 7]; "we confirmed this variant by sequencing both strands etc..." are not needed.

The g.21502T>C change was reported in the paper by Kumar et al, as a candidate regulatory mutation and not a mutation as it is stated in page 7, in addition to two more mutations which is different from the present report. I would suggest adding this.
I would suggest adding to the discussion that the unaffected father in the paper by kumar [2006] was a g.21502T>C carrier.

Did the author sequenced pax 6 in the studied patients? It would be interesting to add the information.
Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)