Reviewer's report

Title: A novel mutation in the SH3BP2 gene causes cherubism

Version: 1 Date: 15 August 2006

Reviewer: Jan de Lange

Reviewer's report:

General
This is a descriptive study, analyzing a specific gene mutation in a family affected with cherubism. A mutation in SH3BP2 is evaluated by appropriate molecular biology methods. The study consists of DNA analysis and correlation with clinical and radiological findings.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

- This study is primarily confirmatory and not completely original since the location of the cherubism gene is already known. It is therefore more appropriate to present it as a case report.

- Although cherubism microscopically shows features of giant cell lesions, a characteristic perivascular collagen cuffing is sometimes present. This should be added to the introduction.

- Since the first report on the location of the cherubism gene in 2001, several point mutations have been described at amino acid number 415 to 420. The new mutation that is found in this study is in this well-known mutation hotspot and is therefore of relative significance. From the methods it is not clear if all 17 family members were analyzed. If all members were indeed analyzed, as the results and summary suggest, this should be clearly stated in methods and there should be more information on penetrance and expressivity of the mutation in the results. If not, it is a serious flaw because no information on penetrance or expressivity of this specific point mutation can be obtained.

- Patients III-8 and IV-5 should be more carefully characterized, if possible with panoramic X-rays in order to assess a possible difference in expressivity.

- The discussion is much too long and contains considerable information on molecular processes that are not relevant to the findings reported. Moreover, the information presented on the possible pathways in which the SH3BP2 gene is involved is mostly copied from earlier papers by other authors. There is no new insight or hypothesis regarding the molecular pathology of cherubism. The discussion should be made much shorter and limited to the findings of the study, i.e. penetrance and expressivity.

- Figure 3 does not give any additional information and should be removed. Instead the X-rays and images of the other two patients with cherubism should be added.

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

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.