Reviewer's report

**Title:** Array-CGH in patients with Kabuki-like phenotype: Identification of two patients with complex rearrangements including 2q37 deletions and no other recurrent aberration

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**Reviewer:** damien Sanlaville

**Reviewer's report:**

The article proposed by Cusco et al. consists in a study of 10 patients with Kabuki syndrome (KS) using array CGH and the search for an association between some CNV and KS.

It is an interesting and actual subject, nevertheless, I have several major compulsory revisions

**METHOD**

In abstract, introduction and methods, the authors mention a study of 16 patients. For example in the abstract: "We have studied 16 Spanish patients â#¿, to search for genomic imbalances using genome-wide array technologies." In fact only 10 patients were analysed using array CGH. This causes confusion in the article.

16 patients were clinically investigated, but only 10 were correctly studied at molecular level.

This study should report only 10 patients.

**CLINICAL**

16 patients with clinical manifestations overlapping with the KS phenotype were included in this study.

Clinical findings were well developed in table 1. However, I suggest that the authors clearly indicate in table 1 which patients were studied using array CGH from the others (clinically different groups?). In addition, the authors should indicate the frequency of each sign in their cohort and the reported frequency in the literature. Now major series have been published and the frequency of each clinical sign typically found in KS patients is well known.

The authors decided not to use strict clinical inclusion criteria with the idea that the molecular characterization of patients with overlapping phenotypes may provide clues to the final identification of the molecular basis of the specific syndromes. It is true, all the more since a recent study has found only a single abnormality in KS patients using array CGH (Maas et al, J Med Genet 2007). Nevertheless, the clinical criteria for inclusion are not well defined especially with regard to the "peculiar face". However, careful look at Figure 1 shows that the KS14 patient (Figure 1b) did not have a typical Kabuki face. In my opinion, the
facial gestalt of this patient is characteristic of 2qter deletion. Patients KS7 and KS12 have a Kabuki-like face. It is less obvious in KS2 patient. Hence inclusion of KS2 and KS14 in this study is debatable. Along the same limit, in the text of the conclusion, the authors confirmed that a 2q deletion was suspected in these two patients: "inclusion of two patients in which a terminal 2q37 deletion syndrome could have been clinically suspected."

Minor Essential Revisions

Patient KS 14 had a balanced translocation inherited from his mother. Gribble et al. showed in 2005 the complex nature of constitutional de novo apparently balanced translocations in patients presenting with abnormal phenotypes. J Med Genet. 2005 Jan;42(1):8-16. These results were confirmed recently by De Gregori et al. (J Med Genet. 2007 Oct 11). The authors should discuss this point.

The authors used GenePix Pro 6.0 software. Generally this software was used to extract and analyze expression data. In particular, Feature Extraction ® and CGH Analytics® were used to analyze Agilent slides. The authors should explain their choice.

The authors studied patients using array CGH. This technique can detect the 8p duplication described by Milunsky and Huang. It is therefore difficult to understand why a systematic study of the 8p region 8 p has been carried out using microsatellite markers. Even if they had found such a duplication, array CGH would have been carried out to exclude another imbalance in the genome.

The authors study 10 patient using HSBA and oligo array. They could compare and discuss their advantages, sensitivity, discordance, between the two types of array. It is not very clear in table 2 and not discussed in the discussion part.

Discretionary Revisions

Table 2, gain and losses detected in KS patients were not confirmed using Agilent array ? (confirmed by 1 : FISH and 2 : Microsatellite markers)

Table 2 : No BAC were abnormal for the KS6 patient (14q23.1 gain) ? (12 Agilent Probes with gain).

In supplementary Table 4, total control samples vary from 30 to 270. Why ?

The authors should precise how many BAC clones or oligo are present on the slide for the 20p12.1 region (in particular for the c20orf133 gene)

It lacks some space in the text.

De novo should be written in italics.

References did not fit the editor recommendations