Author's response to reviews

Title: Molecular breakpoint cloning and gene expression studies of a novel translocation t(4;15)(q27;q11.2) associated with Prader-Willi syndrome

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In response to the reviewer’s comments we have made the following revisions:

1. In the legend to figure 1c the word “grey” was replaced with “orange”.
   Figure 5: Regarding the separation of the 10kb and 11.5 kb bands in lane 4, the following sentence was added to the legend: “The two bands are not well resolved on the rendition of this blot”. The “12.6 kb” was a marker and has been removed, as it is not relevant.

2. In the original submission, we did not say that the patient lives independently, and we did state that hyperphagia is a problem for him. We added the following sentences: “He lives with his parents who help to control his food intake. He has never been on growth hormone treatment”.

   Regarding the patient’s intellect, we had stated that the developmental delay was assessed in comparison to his older siblings and that his IQ was measured as 111 on the WISC. We revised this sentence: “At the age of 22, he is attending a mainstream high school requiring extra time and assistance in completing a diploma in information technology.”

Discretionary revisions:

1. Sentence was revised to read: “In about 1 % of the cases, the disease is due to aberrant imprinting and gene silencing. Of these, 14% have small deletions in the imprinting center (IC) region of the paternal allele that abolish the expression of all imprinted paternally-expressed genes in cis. In the remainder no demonstrable DNA sequence changes have been observed”. A new reference was added: Buiting K, Gross S, Lich C, Gillessen-Kaesbach G, El-Maarri O, Horsthemke B: Epimutations in Prader-Willi and Angelman Syndromes: A Molecular Study of 136 patients with an Imprinting defect. Am J Hum Genet 2003, 72:571-577.

2. This suggested change was not made. We strongly believe that there must be targets for these snoRNAs because their sequences are highly conserved in mammalian evolution.

3. Corrections were made

4. Correction was made

5. In the revised figure 1, two minor corrections were made

Formatting changes requested by editor:

Competing interests - we added: ‘The authors declare that they have no competing interests’.

Tables – They have been organized into portrait format and incorporated into the manuscript file and placed after the figure legends. The vertical rules were deleted.
Patient identifiable information – It is not necessary to anonymize the patient. He has provided written consent to have this information published.