Reviewer's report

Title: An Intronic Alteration of the Fibroblast Growth Factor 10 Gene Causing ALSG- (aplasia of lacrimal and salivary glands) Syndrome

Version: 1 Date: 17 December 2007

Reviewer: Bernd Wollnik

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The paper by Scheckenbach et al. reports a novel splice site mutation in FGF10 causing autosomal dominant aplasia of lacrimal and salivary glands (ALSG) in a German family with several affected individuals. The clinical symptoms of the patient are nicely described in detail and documented. The identified mutation most likely abolishes splice site recognition leading to an aberrant transcript. Quantitative analysis of FGF10 expression levels suggested a reduced expression level caused by the mutation.

Minor Essential Revisions

(1) Transcript analyses and quantitative expression analysis: it is not clear, if the amplified FGF10 RNA was completely sequence and if there might be a heterozygous SNP seen that would help to distinguish both alleles. In addition, was there any heterozygous exonic SNP found on genomic level, which is not present on RNA level? Also this would strength the view that the mutated allele is not stable. Furthermore, the expression of patient’s transcript levels as shown in figure 3 is much more than 50% reduced as would be expected from a heterozygous loss of function mutation. How this might be explained? These data are not convincing. The expression changes should be verified by a second quantitative method or more carefully discussed.

(2) In general, the putative effect of the splice site mutation is discussed in the result part in too much detail. This should be shortened.

(3) It was recently shown that haploinsufficiency is one mechanism of LADD FGF10 mutations. This should be discussed. There are no FGF10 mutation yet described showing a dominant negative effect. This statement should be omitted from the last part of the discussion.

(4) Citations should be checked.

(5) In the conclusion it should be mentioned that there is no functional difference yet described for ALSG versus LADD FGF10 mutations.

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, the manuscript does not need to be seen by a statistician.

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