Author's response to reviews

Title: TM4SF10 gene sequencing in XLMR patients identifies common polymorphisms but no disease-associated mutation

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Author's response to reviews: see over
Dear Editors,

I’m submitting here the revised version of the manuscript entitled “TM4SF10 gene sequencing in XLMR patients identifies common polymorphisms but no disease-associated mutation”, by C. Christophe-Hobertus, F. Kooy, J. Gecz, M.J. Abramowicz, E. Holinski-Feder, C. Schwartz and myself for consideration as a publication in BMC Medical Genetics. Here are our point-by-point responses to the reviewer’s comments:

-Maria G. Miano:
1) Description of the SNPs and genetic homogeneity of the families:
   A table describing the SNPs has been added (table 4) and a comment on the homogeneity of one of the families has been added in the text (Results and discussion section, Sequencing of TM4SF10 coding region, lines 9-12).
2) Linkage intervals sharing between the selected families:
   A table describing the linkage data has been added (table 1).
3) Specify if the gene is ubiquitously expressed:
   A sentence specifying the point has been added (Background section, lines 12-14).
4) Discuss regarding another level of alteration affecting TM4SF10 mRNA:
   This point was already discussed (see Conclusion section, lines 4-5).

-Carsten Bergmann:
1) Exclusion of the TM4SF2 gene:
   TM4SF2, as well as all other known candidate gene, was excluded on a routine basis, involving sequencing of the coding region in most cases. We do not think the point has to be detailed for each patient.
2) Information on the patients analyzed:
   A table (table 1) describing the major phenotypic traits for each patient has been added.
3) The reason to screen more than one affected patient in two pedigrees:
   As two samples were available from these two families, they were both included in the study in order to control for genetic homogeneity at this locus within these families. It is noteworthy that in one of the families a polymorphism in the TM4SF10
gene sequence was observed (see Results and discussion section, Sequencing of TM4SF10 coding region, lines 9-12).

4) Information on linkage analysis:
   A table (table 1) describing the linkage data has been added.

5) Chromosomal analysis and excluded genes other than TM4SF2:
   As already stated in our answer to comment 1), this is part of the routine analysis of the families that was performed in the different participating teams. We do not think the point justifies a lengthy description for each of the patients.

6) Allelic distribution of the SNPs:
   A table (table 4) describing all the SNP haplotypes determined in our study has been added.

Hoping you will find the present version of our manuscript acceptable for publication in BMC Medical Genetics,

Yours Sincerely,

Daniel Christophe, Ph.D.