Author's response to reviews

Title: APOA5 Q97X mutation identified through homozygosity mapping causes severe hypertriglyceridemia in a chilean consanguineous family.

Authors:

Catalina Dussaillant (cdussa@gmail.com)
Valentina Serrano (valenpaz@gmail.com)
Alberto Maiz (maiz@med.puc.cl)
Susana Eyheramendy (susana@mat.puc.cl)
Luis Rodrigo Cataldo (rcataldo@ciq.uchile.cl)
Matías Chávez (matchavezf@gmail.com)
Susan V Smalley (sysmalleym@gmail.com)
Marcela Fuentes (mfuentes@gmail.com)
Atilio Rigotti (arigotti@med.puc.cl)
Lorena Rubio (lnarubiog@gmail.com)
Carlos F Lagos (cflagos@uc.cl)
José A Martinez (jalfmtz@unav.es)
José Luis Santos (jsantos@med.puc.cl)

Version: 3 Date: 31 August 2012

Author's response to reviews: see over
RESPONSE TO REVIEWER

Thank you very much to the reviewer for the comments. Below are the point-by-point responses to these comments.

Regarding comment 1: "- the answer about the strategy of using linkage study instead of direct sequencing of genes classically involved in severe HTG is interesting but there is no answer about the cost of this strategy compared to sequencing".

Response to comment 1: Thank you for this comment. We have described the different pros and cons of the use of linkage analysis and direct sequencing in our study, giving emphasis to the complementary information of both approaches in finding deleterious causal mutations. We deliberately did not mention at all the specific costs of the different research strategies. The reason for this intentional omission is that the laboratory assays are constantly changing both in terms of cost and in terms of the amount and quality of the genetic data provided by new DNA technologies. Consequently, we considered that detailing specific amounts of money in the manuscript would result in information that is very likely to be out of date very soon. Instead, we have preferred to describe all the possible research strategies, providing the most relevant pieces of information in such a way that the reader would be able to find specific costs elsewhere.

Regarding comment 2: "in figure 1, subject 8 Q97X appears to carry S19W polymorphism as subject 9. But it is not indicated in results and discussion where only subject 9 is described".

Response to comment 2: Thank you for highlighting this omission. Subject 8 is the father of the index case and he is deceased. Therefore, the genotypes in this subject were inferred from the genotypes of first-degree family members. In fact, subject 8 is the only family member for whom the genotypes/haplotypes were inferred instead of directly measured. From this point of view, S19W genotype of subject 9 was the only heterozygous genotype of this polymorphism that was found in the available DNA samples of our study. In any case, we have modified the text (page 7) in order to mention genotypes of S19W polymorphism both in subject 8 and subject 9.

Regarding comment 3: "in discussion page 12, LPL activity are mentioned but not available in supplemental table S4".

Response to comment 3: Thank you for finding this error. In the first sentence of page 12, it is now stated that LPL activity is reduced in carriers of the Q97X mutation from previous studies. Therefore, information on LPL activity is not mentioned in the paragraph where table S4 is quoted. As a consequence of this, table S4 does not include information on LPL activity.