Reviewer's report

Title: Common variants in the lipoprotein lipase (LPL) gene and type III hyperlipidemia.

Version: 1 Date: 26 February 2007

Reviewer: Michael Hoffmann

Reviewer's report:

General

The authors evaluated the impact of three common LPL mutations on the development of Type III HLP in Caucasians. In contrast to prior studies the authors recruited >100 patients, an impressive number taking the low prevalence of Type III HLP into account.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

- are all Type III HLP patients homozygous for E2/E2 or does this group include patients with other apoE mutations (e.g. Apo E Hamburg)? These patients should be excluded in the analysis.
- the authors ignored the publication of Brümmer et al. J Mol Med 76: 355-364, who described obviously a subgroup of the here analysed Type III HLP group; please integrate & discuss the data
- why do the authors look only for these SNP and not for mutations in exon 4-6 (like Gly188Glu)? Heterozygosity for a loss of function mutation of LPL is more likely a reason for Type III HLP than LPL SNP whose relevance for TG metabolism are rather low.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- a trigger for Type III HLP could be insulin resistance (de Beer et al. ATVB 22:294-99; Reference 5). LPL mass/activity are associated with the occurrence of insulin resistance. Do the authors have data about LPL mass/activity in the Type III HLP group?
- are in the lipid clinic population patients with LPL and ApoA5 mutation and if yes, do the mutations show an additive effect on TG?

Discretionary Revisions (which the author can choose to ignore)

- Abstract first line: homozygosity
- Method: UKE is not a common abbreviation
- reference 10: lipoproteins

What next?: Accept after minor essential 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