Reviewer’s report

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

Version: 1 Date: 26 April 2007

Reviewer: Kui Zhang

Comment:

The authors conducted a study to investigate other genetic factors other than APOE gene that may contribute to the development of Type III hyperlipidemia (Type III HLP). They focused on three common variants in the LPL gene: D9N, N291S, and S447X and did not find statistically significant difference in the frequencies of these variants between APOE2/2 patients and controls. They concluded that it is unlikely that common variants in the LPL gene play an important role in the development of Type III HLP. Their conclusions are different from other studies using a small number of patients.

Major Comments:

1. As the authors stated in the paper, “Although APOE2/2 genotype is required for the development of Type III HLP only approximately 1-10% of APOE2/2 subjects suffer from the condition implying that additional genetic and/or environmental factors are necessary for its expression [1-2].” Since APOE2/2 genotype is required for the development of Type III HLP, I think the authors should also compare the allele frequencies between the Type III HLP patients with APOE2/2 genotype and the healthy blood donors and patients with hyperlipidemia without APOE2/2 genotype.

2. More detailed descriptions regarding these samples are needed. First, it is not clear if 102 patients from the lipid clinic, UKE are all Type III HLP patients from the paper. Second, it is not clear if all the 200 blood donors have APOE2/2 genotypes. Third, it is not clear if 1197 patients with hyperlipidemia are all Type III HLP patients.

3. Since the allele frequencies for three SNPs in the LPL gene are quite low, the power to detect the statistically significant difference in the frequencies between different groups of samples may also be low. The authors should conduct the power calculation to see what the power is in different conditions using the current number of samples. Only if the power is quite high using the current number of samples, we can safely draw the same conclusions as the paper.

Minor Comments:

1. Several abbreviations were used without definitions or before they were defined in the paper (e.g., APOE, APOA5).
2. Both APOE 2/2 and APOE2/2 were used in the paper. The authors should use one of them throughout the paper.
3. On Page 3, “As the authors comment meaningful conclusions…” should be “As the authors’ comment meaningful conclusions…”.
4. On Page 4, “or other patients from the lipid clinic (5.3%)” This should be “or other patients from the lipid clinic (4.3%).” from table 1.
5. On Page 4, “In the case of the S447X SNP, the frequency in APOE2/2 patients (16.8%) was the same as in blood donors (17.0%), although the frequency in lipid clinic patients was lower this was not statistically significant.” Please consider revising this sentence.

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: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.