Reviewer's report

Title: Interaction of functional NPC1 gene Polymorphism with smoking on coronary heart disease

Version: 2 Date: 12 April 2010

Reviewer: Pawel Niemiec

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Major Compulsory Revisions
1. WHOLE TEXT
   a) Authors analyze only one polymorphism of NCP1 gene (A644G), but they write in abstract, materials and methods and the discussion sections that examining many.
   b) The names of genes should be written in italics, but there is no standardization in this respect in the text. The name of NCP1 peptide is sometimes written with small letters (Ncp1) sometimes with large (NCP1).
   c) The quality of English is unsatisfactory. There are many grammatical and syntax errors. Some sentences are unintelligible, e.g:
      - “...plays critical roles in vascular injure, which is involved in the progressed of coronary heart disease”...
      - “…These findings may provide evident that in gene status NPC1 contributes to lipid accumulation in human macrophages and interacts with smoking environment factor in the pathogenesis of CHD”...
      - “Moreover, in smokers, carriers of NPC1 GG had a decrease age- and sex-adjusted coronary heart disease as compared with those carrying AA and AG.”

2. MATERIAL AND METHODS
   The authors should give a references to recommendations and standards used in the classification of traditional risk factors (including hypercholesterolemia and smoking habit), MI and CAD.

3. RESULTS
   a) The groups are not sex matched (84.0% vs 70.8%)
   b) table 1:
      - there is no number of individuals in the case of gender, cigarette smoking, hypertension and DM history
- There is no Odds Ratios values for classical risk factors of CAD
c) table 2.
- The table is incomprehensible. Place the groups in the columns and genotypes in the lines. The ORs and p values assign to concrete genotypes and show in additional column. At present, the left and right sides of table do not correspond.
- Authors did not present crude ORs (from the univariate logistic regression analysis) but only the adjusted values.
- The alleles frequencies (n, %) and the results of comparison between groups (ORs, p) should be inserted
d) NCP1 polymorphism – cigarette smoking interactions
There is the weakest part of the text (unclear in all the sections, from abstract to discussion). The logistic regression is not appropriate tool for gene-environment interactions analyses. You must use the 4 x 2 tables approach. Please add the amounts of interaction by using: I. SI - synergy indexes, II. AP - attributable proportion due to interaction and III. RERI - relative excess risk due to interaction, together with their 95% confidence intervals.
e) Because of the NPC1 protein role Authors should give the results of gene-hypercholesterolemia interactions

4. DISCUSSION
The discussion section is too long and should be focused on NPC1 gene, the A644G polymorphism, and explanation of possible gene-smoking, gene-hypercholesterolemia interactions

The conclusion “We investigated the gene-environment interaction and found carriers of NPC1 GG had a decrease risk of coronary heart disease as compared with those carrying AA and AG in smokers. This result brings an indirect evidence for a repression of NPC1 expression in AHs–exposed macrophages.” is unclear and written in “baaaaad” English. I suggest to wait for the results of the gene-environment analyses.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

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