Reviewer's report

Title: Association between UCP2 polymorphism A55V and risk of cardiovascular events in patients with multi-vessel coronary arterial disease.

Version: 1 Date: 23 March 2012

Reviewer: Vicky Cameron

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This candidate gene study explores the association between the A55V polymorphism in the uncoupling 2 protein (UCP2) gene and clinical outcomes in coronary disease patients enrolled in the Medical, Angioplasty or Surgery Study II (MASS II). The authors report significant associations in patients who are homozygotes for the minor allele, but only in the subgroup with dysglicemia. There are major issues with the rigor of the study design and presentation of methods and experimental findings as listed below.

Major Compulsory Revisions

1. There is no definition of “dysglicemia” or “glycemic disturbance.” Do the authors mean type 2 diabetes, glucose intolerance or insulin resistance? Please define these terms in the Methods. What the total number of patients with dysglicemia? Please state in Results how many in this subgroup.

2. The Introduction is too long and contains irrelevant information. In paragraph 2 it would be possible to keep only the first sentence and delete the rest of the paragraph. Also delete paragraph 7.

3. In the Methods chapter, more details are needed and the methods need to be more rigorously described. Please give details the ethnicites that constitute the patient group. On page 6 the authors state that events were tracked; how were they tracked? Under genotyping, what is the reference for the salting–out procedure of DNA extraction? The allele-specific PCR assay was modified from the published method in what way? The confirmation of genotyping results was performed on 32 samples; how were these repeat samples selected? The statistics section mentions haplotype analysis, but no haplotyping data are provided.

4. In the Results section, what was the justification for combining the major allele homozygotes and heterozygotes? Is there any previous evidence that the polymorphism effects fit a recessive model? Please explain the rationale for including the variables (hypertension, blood glucose, age, BMI, type of treatment, smoking status, coronary anatomy) in the multiple regression model.

5. The meaning of last paragraph of the Results section is unclear. At 5 years the authors observed no differences between the groups in what? The suggestion that “the predictive effect of UPC2 genotype in dysglycemic patients could be
related to the time since the glycemic status has been acquired" does not make sense. Surely the time of follow up started from the index admission for angina, not the time when the patients became dysglycemic?

6. The Kaplan-Meier survival curve was missing in my copy of the manuscript.

7. The Discussion needs to be rewritten. The first paragraph could be deleted as it adds nothing to the manuscript. The remainder of the Discussion needs to be re-formatted so that it follows a logical sequence. The English language needs to be corrected as many passages are unintelligible.

8. The tables are very difficult to read, with 8 font text, columns that do not line up and the text squashed up against the horizontal lines.

Minor Essential Revisions

Please note that there are numerous typographical errors and uses of non-colloquial English throughout the manuscript. Only a few examples are provided here.

Abstract

The first sentence should read “We have investigated the association…” “Patients” is spelled incorrectly (pacients) here and elsewhere in the manuscript. Please mention the method used for genotyping eg “using allele-specific polymerase chain reaction.”

Introduction

Page 3 paragraph 3, “ROS are…” (not is)
Page 3, second to last line, “Some studies have…” (not has)
Page 3, last line UCP “improves” (not improve) and on to page 4, “protects” (not protect)

Methods

Page 5, first line, “patients were selected…” (not The patients)
Page 5, line 8, “inclusion criteria” (not entry criteria)
Page 7, 1st line, “for continuous variables” (not variable)

Results

2nd sentence could be shortened to “The distribution of the A55V polymorphism in the study population was VV 31.5%…”

Results lines 3 and 4, use past tense throughout, ie “was similar” and “Allelic and genotypic distributions were…”

Page 7, final sentence could be shortened to “The Ala/Ala (AA) and Ala/Val (AV) genotypes were combined and compared with the Val.Val (VV) genotype group.”

Page 8, first sentence should read “There was no significant difference in baseline values between these groups (Table 1).”
Page 8, second sentence, “...as shown in Table 2.” (not showed)
Page 8, line 14, should read AMI p=0.0070 (not AIM)

Discussion
Too many stylistic errors to list.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

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.