Reviewer's report

Title: Why the short alleles (<35 repeats) of the 3’APOB-VNTR polymorphism are rare in centenarians? A possible answer given by the study of the allele-average effect on lipidemic parameters.

Version: 1 Date: 3 December 2003

Reviewer: Francesco Panza

Reviewer's report:

General
The Authors investigated the possible role on longevity of the 3’APOB-VNTR genotype and in particular the homozygous SS genotype studying 409 subjects aged 20-102 years and comparing, out of 409 subjects, 105 healthy subjects characterized by a low level of serum HDL-C (40 subjects) or by a high level of serum LDL-C (40 subjects). The results of this study may be potentially interesting for scientists involved in research on genetics of longevity, but some methodological aspects should be improved.

Minor Essential Revisions
The Friedwald’s formula should be correct in the footnote of table 2

The raw mean Tg values (±DS) in table 2, 3, and 5 should be reported together the log transformed TG values.

Abbreviations should identify univocally the pathology of interest. CAD identifies, according to international guidelines, Coronary Artery Disease. Then to attribute CAD to other “pathologies” could yield confusion in an inexpert reader.

Major Compulsory Revisions
Description of study population and setting are incomplete. The patients were recruited at the Italian National Research Center on Aging (INRCA) in Cosenza (Calabria, Southern Italy) but the Authors didn’t report if the clinical setting of the enrolment was ambulatory, and/or hospital and/or day-hospital. Moreover the data were adjusted for age, sex, and BMI but:
- How the body height was measured? which stature was collected (past or present, calculated by knee/height). Why the results on the BMI are not presented ?
- The only sample of healthy subjects has been stratified for age and sex, why not for CADH and CADL patients

Concerning the statistical methods should be indicated:
a. kind of chi-squared test was used for the statistical analysis of the results.
b. chi-squared values and degree of freedom in Hardy-Weinberg equilibrium evaluations for either patients or controls.
In particular at page 13 in the footnote of Table 4 the degrees of freedom (df) for Hardy-Weinberg equilibrium is 3 and p=0.328, instead of 2 df and p=0.179

The Authors should specify what methodological approach they used to select healthy subjects to match it with CADH and CADL patients.

The Authors should clearly report what it is the meaning of a low level of serum HDL-Cholesterol
(HDL-C) and an high level of serum LDL-Cholesterol (LDL-C). In other words what was the criteria to categorize HDL-C < 35 mg/dL and LDL-C > 170 mg/dL: Cardiovascular Atherosclerotic Disease according to international criteria (NCEP-ATP III, European Guidelines on CVD Prevention, or others)? Low HDL-C and High LDL-C quartiles of their data? The reason that the Authors dichotomized, the way they did, is not obvious and it is a tremendous waste of information.

**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**: Acceptable

**Statistical review**: No

**Declaration of competing interests**: None