Reviewer's report

Title: Secretory Granule Neuroendocrine protein 1 (SGNE1) Genetic Variation and Glucose Intolerance in Severe Childhood and Adult Obesity

Version: 1 Date: 27 April 2007

Reviewer: Majambu Mbikay

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The work
This study investigates possible associations between SGNE1 single nucleotide polymorphisms (SNPs) and childhood obesity, adult obesity, type 2 diabetes or anomalies of glucose homeostasis. It is an extension of a previous genome-wide microsatellite analysis that linked susceptibility to obesity to the Chr 15 region encompassing the SGNE1 locus, making this gene a candidate for this phenotype. Data presented in this report failed to support the link, but an intron 1 SNP -1,701A>G showed strong association with anomalies of glucose homeostasis (glucose intolerance and insulin resistance).

Evaluation
This work is substantial, well designed and well conducted. The results support the conclusions. The discussion opens up future avenues of investigation. It suggests that SNP -1,701A>G may affects the functionality of transcription factor-binding in SGNE1 intron 1 (which reportedly influence 7B2 expression) without speculating on the direction of this effect. 7B2 is immunologically detectable in human plasma [1]. It might be worth mentioning the eventuality of a study to examine possible links between circulating levels of 7B2 and the variation in the putative element. Also worth of mention is the study showing an increase in pancreatic 7B2 in the ob/ob mouse relative to control mice [2]. There are indications that, besides facilitating PC2 activation, 7B2 may also affect regulated hormone secretion [3]. Except for a few typographic errors (see below), the manuscript is well written.


Major Compulsory Revisions: None

Minor Essential Revisions:

Page 3, paragraph 2, line 1: Replace micorsatellite with microsatellite.
Page 9, paragraph 2, line 9: Replace This data may... with These data may...
Page 10, paragraph 2, line 16: Replace pepetide with peptide.

Discretionary Revisions: None

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

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