Author's response to reviews

Title: Analysis of the contribution of FTO, NPC1, ENPP1, NEGR1, GNPDA2 and MC4R genes to obesity in Mexican children

Authors:

Aurora Mejía-Benítez (amejia@cinvestav.mx)
Miguel Klünder-Klünder (klunderk@gmail.com)
Loïc Yengo (loic@good.ibl.fr)
David Meyre (meyred@mcmaster.ca)
Celia Aradillas (celia@uaslp.mx)
Esperanza Cruz (mcruzl@yahoo.com)
Elva Pérez-Luque (elvaleticaperez@yahoo.com)
Juan M Malacara (jmmalacara@hotmail.com)
Maria E Garay (enia911@hotmail.com)
Jesús Peralta-Romero (drijperalta@hotmail.com)
Samuel Flores-Huerta (floreshuertamd@gmail.com)
Jaime García-Mena (jgmena@cinvestav.mx)
Philippe Froguel (p.froguel@imperial.ac.uk)
Miguel Cruz (mcruzl@yahoo.com)
Amélie Bonnefond (amelie.bonnefond@good.ibl.fr)

Version: 4 Date: 29 November 2012

Author's response to reviews: see over
Reviewer comment

The authors have addressed nearly all the reviewers questions and comments. The only question whose answer should be further completed is that f power. Please estimate the power, given published OR and allele frequency in Mexican general population (maybe using 1000G) of the SNPs. The p-value for which the power should be estimated is at author’s choice but 5% corrected by the number of SNPs seems OK.

Response: Following the reviewer suggestion, we have now clarified this point in the Methods section of the revised manuscript. We have also added a supplementary table (Supplementary Table 1) that shows the expected statistical power for each SNP:

“To achieve a statistical power higher than 50%, with an odds ratio of 1.25, we only selected SNPs with minor allele frequencies ≥ 15% in the Mexican population (according to the HapMap database). These SNPs were identified by GWAS or meta-analyses of GWAS in European populations [6, 7, 9, 10]. Furthermore, we selected a SNP that was significantly associated with childhood obesity in a French population, according to a linkage association study [8]. The expected statistical power per SNP (estimated by Quanto software) is reported in Supplementary Table 1.”

Supplementary Table 1. Expected statistical power for reaching an odds ratio of 1.25 in the present obesity case-control study (Ncases=514; Ncontrols=949)

<table>
<thead>
<tr>
<th>SNP</th>
<th>RAF*</th>
<th>OR</th>
<th>Statistical Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC4R rs17782313</td>
<td>0.15</td>
<td>1.25</td>
<td>53%</td>
</tr>
<tr>
<td>NEGR1 rs2815752</td>
<td>0.73</td>
<td>1.25</td>
<td>67%</td>
</tr>
<tr>
<td>ENPP1 rs7754561</td>
<td>0.46</td>
<td>1.25</td>
<td>78%</td>
</tr>
<tr>
<td>NPC1 rs1805081</td>
<td>0.82</td>
<td>1.25</td>
<td>55%</td>
</tr>
<tr>
<td>GNPDA2 rs10938397</td>
<td>0.24</td>
<td>1.25</td>
<td>66%</td>
</tr>
<tr>
<td>FTO rs1421085</td>
<td>0.18</td>
<td>1.25</td>
<td>55%</td>
</tr>
</tbody>
</table>

*Risk allele frequency in the Mexican population, according to HapMap.