Supplementary Text S1

Discovery P-values

The original report of association with obesity of 220 kb deletions of the chr16:28.73-28.95 Mb region preceded our publications demonstrating that a nearby 593 kb region was itself strongly associated with morbid obesity, independent of the 220 kb locus. Two of 5 cases used by Bochukova, et al. to calculate the discovery-stage P-value carried extended deletions spanning both regions, and a further 4 cases and 4 controls carried the 593 kb deletion alone. Due to carrying a known obesity-causing variant, therefore, these individuals were uninformative concerning a putative obesity association for the smaller region. In the light of this information, not available at the time of the original report, we have recalculated the P-value at discovery. Excluding the 10 uninformative subjects yields initial significance of $P=4.51 \times 10^{-4}$ for the 220 kb deletion (3 carriers out of 278 cases; 2/7362 controls), a value that no longer survives correction for multiple testing – over 300 rare variants were identified in the discovery cohorts. Combining the discovery data with those reported for the replication obesity cohort (2/1062 cases) gives an overall $P$-value of $1.37 \times 10^{-3}$ (Fisher’s exact test), as shown in Table 1.

$P$-values at discovery for GSVs identified in subjects with common obesity by Glessner, et al., as shown in Table 1, were determined using Fisher’s exact test applied to the aggregate of the data from the two cohorts used in this study.