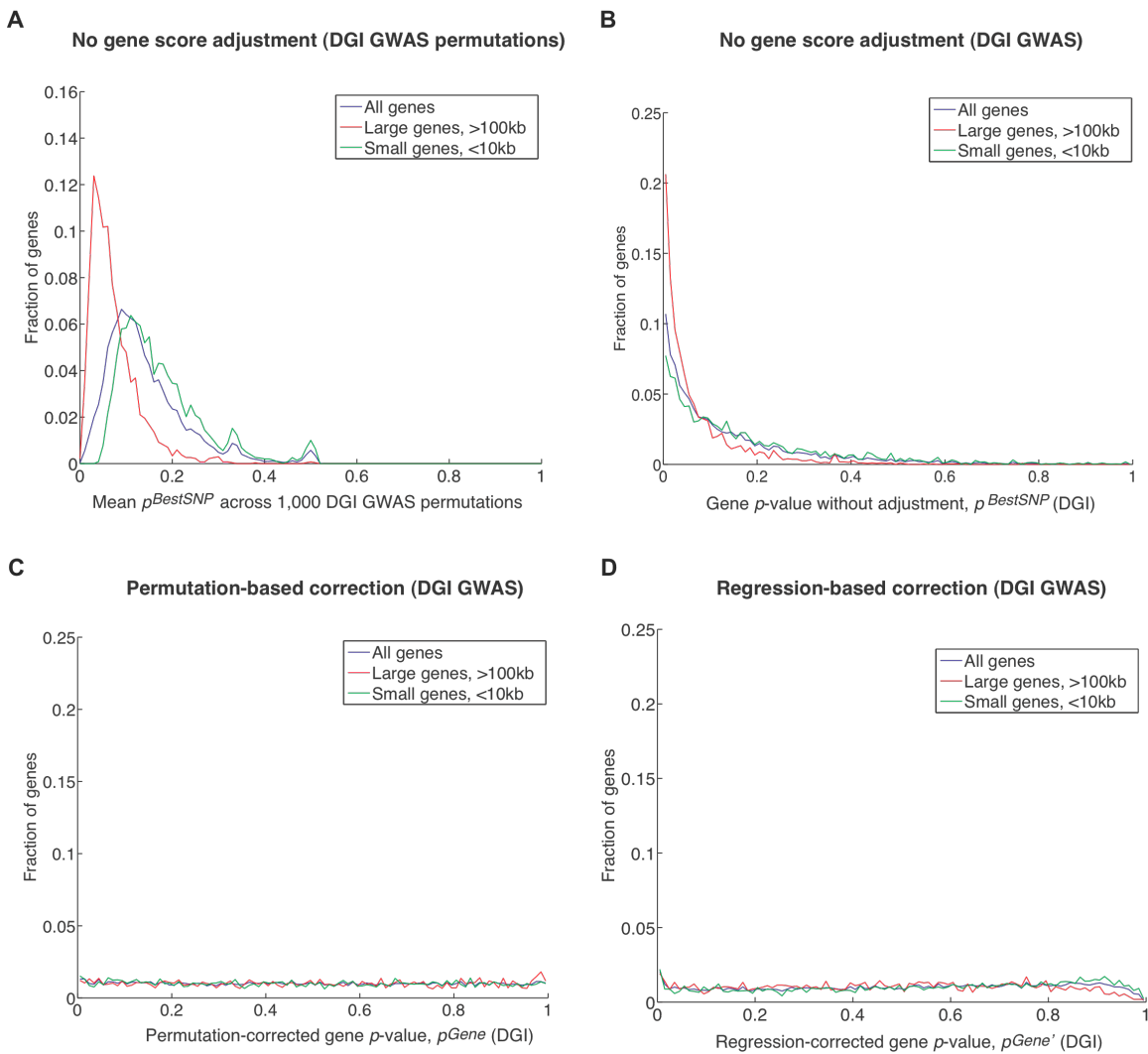


**Figure S2**

**Figure S2. Distribution of T2D gene  $p$ -values for small, large and all genes before and after correction for confounders.** (A) The distribution of the mean  $P_g^{BestSNP}$  (best SNP association  $p$ -value per gene  $g$ ) calculated across 1,000 phenotype permutations of the Diabetes Genetics Initiative (DGI) GWA study is shown for all genes in genome (blue line), only large genes ( $\geq 100$  kilobase (kb); red line), and only small genes ( $\leq 10$  kb; green line). Large genes tended to receive on average a more significant gene score (lower  $p$ -values) than all genes in the permuted datasets, and small genes tended to receive on average a less significant gene score (higher  $p$ -values) than all genes. (B-D)

The distribution of gene association  $p$ -values is shown for the actual DGI study for all gene sizes (blue line), large genes (red line) and small genes (green line) (B) before correcting for confounders ( $P_g^{BestSNP}$ ), and after correcting for confounders on  $P_g^{BestSNP}$ , such as gene size, using either (C) phenotype permutation analysis ( $P_g^{Gene}$ ) or (D) step-wise multivariate linear regression analysis ( $P_g^{Gene'}$ ). The regression-based correction transforms the gene  $p$ -values to a distribution that is close to uniform and removes the confounding effect of gene size, similar to the permutation-based correction, which corrects for all confounding effects without *a priori* knowledge of them. The regression correction seems to slightly over-correct the gene  $p$ -values of large genes (red line in D) in the high  $p$ -value end of the distribution ( $p > 0.8$ ). A bin of 0.01 was used for all four plots.