Correction

Correction: Genome-Wide Associations between Genetic and Epigenetic Variation Influence mRNA Expression and Insulin Secretion in Human Pancreatic Islets

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Due to errors in production, Figure 2 and Figure 4 are incorrect. The correct versions are provided here.

Citation: The *PLOS Genetics* Staff (2014) Correction: Genome-Wide Associations between Genetic and Epigenetic Variation Influence mRNA Expression and Insulin Secretion in Human Pancreatic Islets. *PLoS Genet* 10(12): e1004886. doi:10.1371/journal.pgen.1004886

Published December 12, 2014

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Figure 2: Depiction and distance analysis of associations between genotype and DNA methylation of significant mQTLs in human pancreatic islets. Depiction of (A) the most significant *cis*-mQTL; rs1771445 vs. cg02372404, and (B) the least significant *cis*-mQTL; rs196489 vs. cg06433283, among all identified *cis*-mQTLs in human pancreatic islets. Data is presented as Box and Whisker plots with P-values adjusted for multiple testing. (C) Distance analysis between SNPs and CpG sites of significant *cis*-mQTLs plotted as the number of identified mQTLs within each distance bin. Distance summary: minimum = 0 kb, 10%ile = 1.88 kb, 25%ile = 7.62 kb, 50%ile = 26.31 kb, 75%ile = 74.76 kb, 90%ile = 164.5 kb, maximum = 499.6 kb. (D) The strength of associations plotted against the distance between SNPs and CpG sites of significant *cis*-mQTLs after correction for multiple testing. Depiction of (E) the most significant *trans*-mQTL; rs17660464 vs. cg22968622, and (F) the least significant *trans*-mQTL; rs6440971 vs. cg10438649, among all identified *trans*-mQTLs in human pancreatic islets. Data is presented as Box and Whisker plots with P-values adjusted for multiple testing. (G) Quantile-Quantile plots (Q-Q plots) of $-\log_{10}(\text{P-value})$ illustrating the distribution of P-values for all analyzed SNP-CpG pairs in the *cis*- (red dots) and *trans*- (blue dots) mQTL analysis in relation to a theoretical null distribution (grey diagonal line). Bold dots indicate significant mQTLs identified in the *cis*- (red dots) and *trans*- (blue dots) mQTL analysis after correction for multiple testing.
doi:10.1371/journal.pgen.1004735.g002

Mathematical conditions fulfilled to conclude causality in CIT:

- *G* and *E* are associated
- *G* is associated with *M* after adjusting for *E*
- *M* is associated with *E* after adjusting for *G*
- *G* is independent of *E* after adjusting for *M*
- Causal hypothesis at FDR 5% (*Q*-value < 0.05)

Figure 4: CIT analysis identifies mQTLs where DNA methylation potentially mediates genetic associations with mRNA expression in human pancreatic islets. (A) Depiction of possible relationship models between genotype as a causal factor (*G*), DNA methylation as a potential mediator (*M*) and islet mRNA expression as a phenotypic outcome (*E*). Left diagram: The causal or methylation mediated model. Middle diagram: The reactive or methylation-consequential model (reverse causality). Right diagram: The independent model. (B) Illustration of the study approach to identify if DNA methylation of CpG sites potentially mediates the causal association between SNPs and islet mRNA expression. Left: Workflow steps. Middle: Tested relationships between *G*, *M* and *E* in the different steps. Right: Number of identified sites in each step. Bottom: Conditions that must be fulfilled to conclude a mathematical definition of a causal relationship between *G*, *M* and *E*. Significantly called as causal at 5% FDR (causal hypothesis *Q* < 0.05).

doi:10.1371/journal.pgen.1004735.g004

Reference

1. Olsson AH, Volkov P, Bacos K, Dayeh T, Hall E, et al. (2014) Genome-Wide Associations between Genetic and Epigenetic Variation Influence mRNA Expression and Insulin Secretion in Human Pancreatic Islets. *PLoS Genet* 10(11): e1004735. doi:10.1371/journal.pgen.1004735