

## Supplemental information

### Identification of novel type 1 and type 2 diabetes genes by co-localization of human islet eQTL and GWAS variants with *colocRedRibbon*

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# Identification of novel type 1 and type 2 diabetes genes by co-localization of human islet eQTL and GWAS variants with *colocRedRibbon*

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## SUPPLEMENTAL INFORMATION

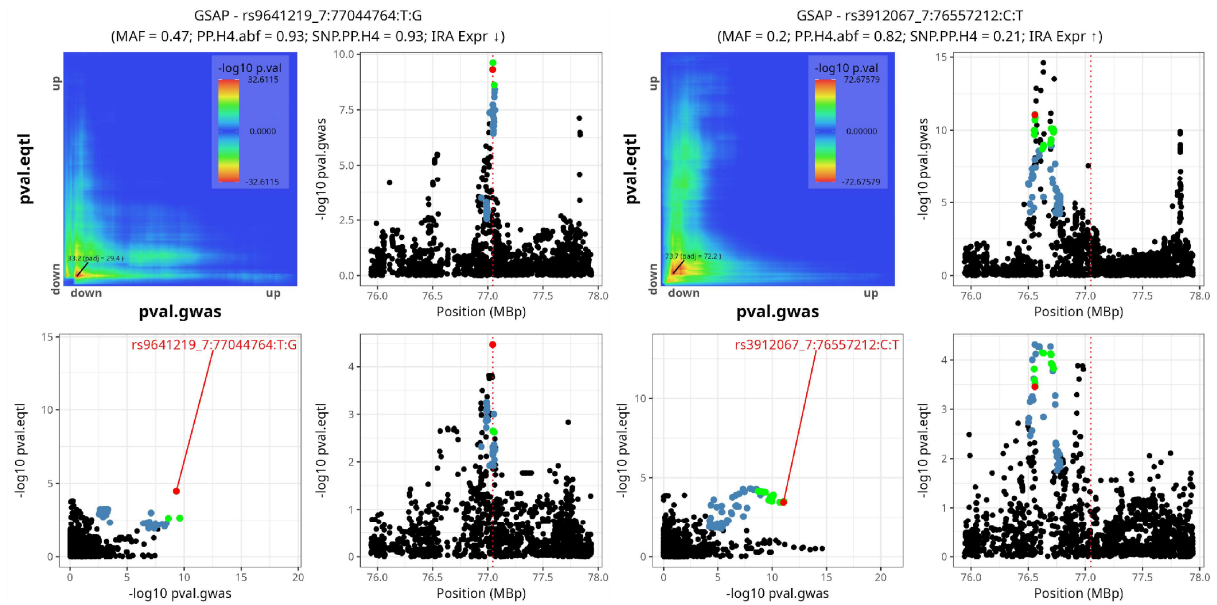


Figure S1. Co-localization plots for GSAP eQTL and type 2 diabetes GWAS, Related to Figure 3. The lead SNP is shown in red, the 99% credible set in green and RedRibbon overlap in blue. GSAP presents two distinct co-localizations in the same region with opposite risk allele expression regulation. SNPs are referenced by rsids, PP.H4 abf and SNP PP.H4 are the posterior probability for coloc tool hypothesis 4, MAF is minor allele frequency. Arrows pointing up or down indicate increased or reduced gene expression, respectively.



Figure S2. Co-localization genes are enriched in important pathways, Related to Figure 4 and Tables S17-18. Directional Gprofiler2 enrichments in co-localizing genes for type 2 diabetes and glycemic trait GWAS. (A) Enrichment for genes upregulated by lead risk allele. (B) Enrichment for genes downregulated by lead risk allele. (C-E) Enricher enrichments for co-localizing genes of type 2 diabetes and glycemic trait GWAS. Top 10 enriched terms from BioPlanet, WikiPathways, and Reactome gene

set library are displayed by increasing *P*-Value. (F) Metascape enrichment for co-localizing genes of type 2 diabetes and glycemic trait GWAS.

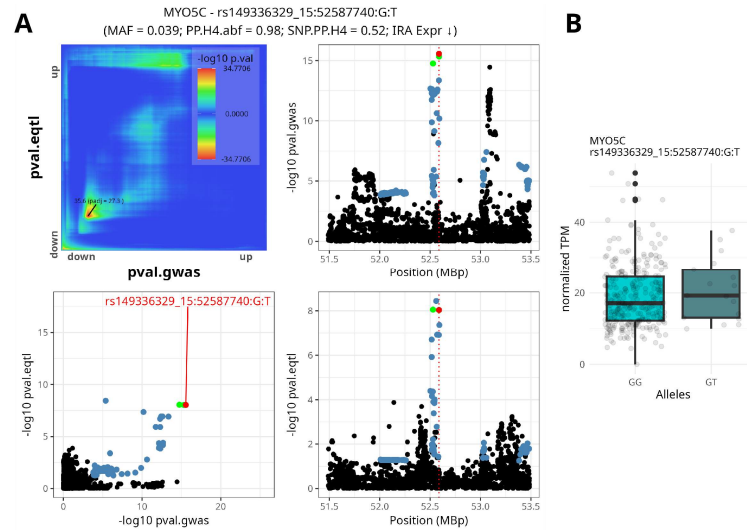


Figure S3. Identification of MYO5C as a novel type 2 diabetes gene, Related to Figure 4H. (A) Co-localization plots for MYO5C, showing lead SNP in red, 99% credible set in green and RedRibbon overlap in blue. The red dotted line is the gene transcription start site. (B) Expression plot for co-localizing SNP. SNPs are referenced by rsids, PP.H4 abf and SNP PP.H4 are the posterior probability for coloc tool hypothesis 4, MAF is minor allele frequency, Increasing Risk Allele expression regulation direction; an arrow pointing down means decreased gene expression for the risk allele

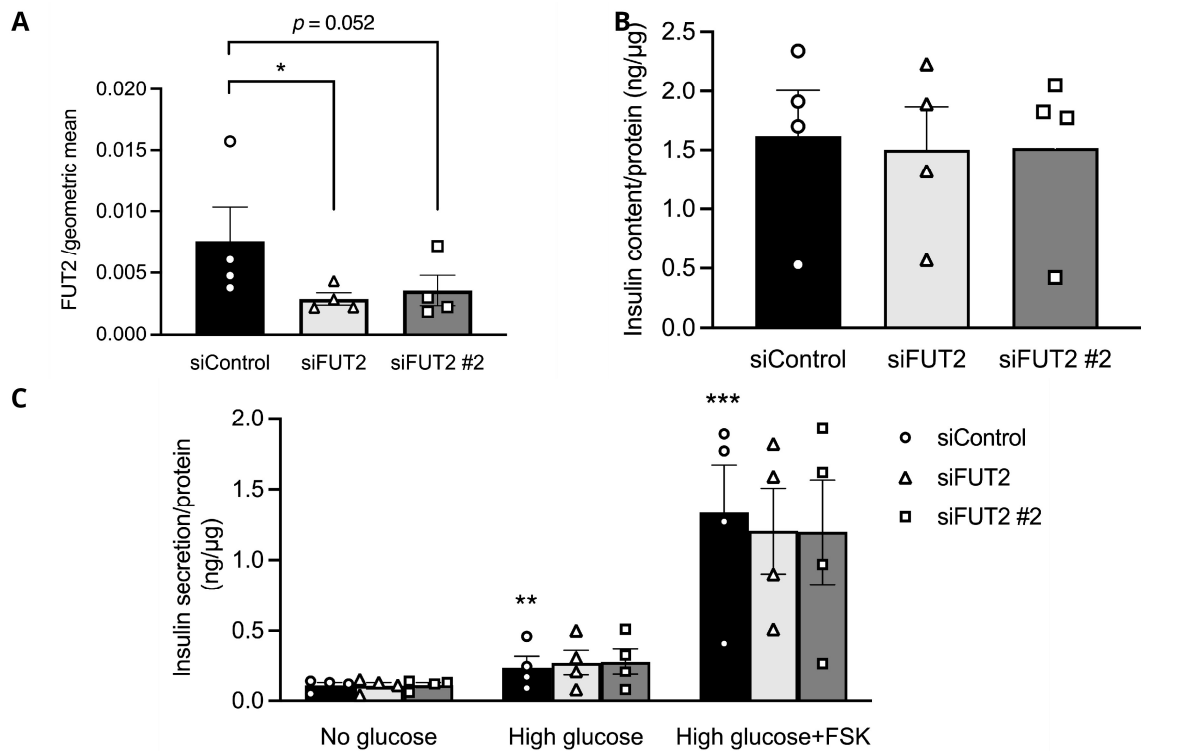


Figure S4. FUT2 depletion does not alter beta-cell function, Related to Figure 5. (A) *FUT2* mRNA expression in EndoC-βH1 cells 48 hours after transfection with siControl or *FUT2* siRNAs (siFUT2 or siFUT2 #2), normalized to the geometric mean of reference genes *ACTB* and *VAPA* (n=4). (B) Insulin content of cell lysates. (C) Insulin secretion induced by 0 or 20 mM (high) glucose or 20 mM glucose + 10 μM forskolin (FSK) (n=4). Statistical analysis by (A-B) one-way or (C) two-way ANOVA followed by Dunnett post hoc test for pairwise comparisons GraphPad software. Data are presented as mean ± SEM, with individual points representing independent experiments. \*\*\**P*-Value ≤ 0.001, \*\**P*-Value ≤ 0.01, \**P*-Value ≤ 0.05.

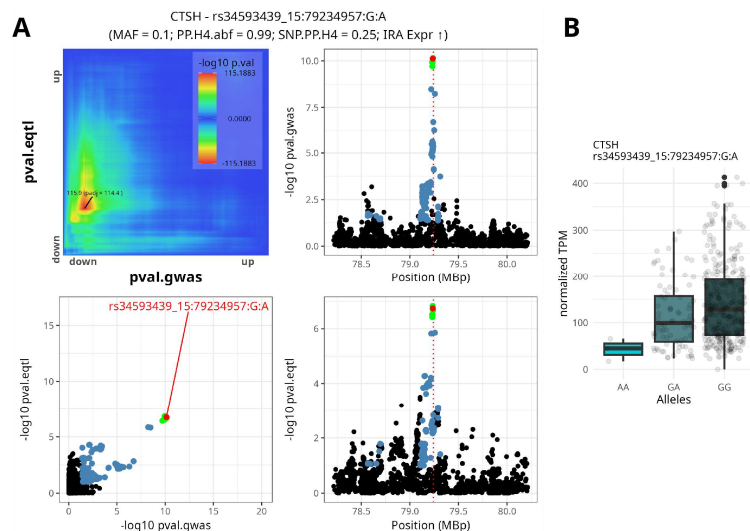


Figure S5. Co-localization for *CTSH* eQTL and type 1 diabetes GWAS, Related to Figure 2. (A) Co-localization plots for *CTSH*, showing the lead SNP in red, the 99% credible set in green and RedRibbon overlap in blue. The red dotted line is the gene transcription start site. (B) Expression plot for co-localizing SNP. SNPs are referenced by rsids, PP.H4 abf and SNP PP.H4 are the posterior probability for coloc tool hypothesis 4, MAF is minor allele frequency, IRA indicates the Increasing Risk Allele expression regulation direction; an arrow pointing up means increased gene expression for the risk allele.

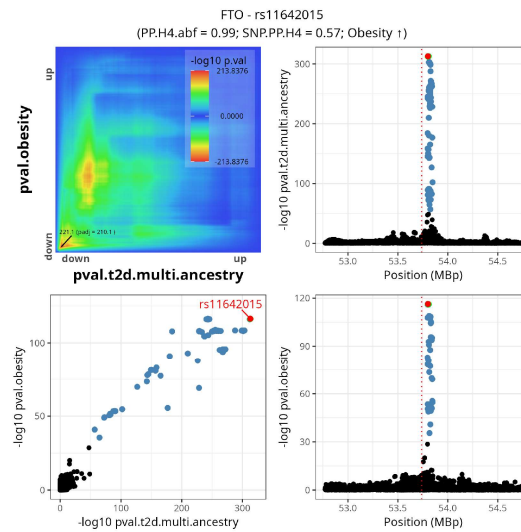


Figure S6. Co-localization for *FTO* region between obesity GWAS and multi-ancestry type 2 diabetes GWAS, Related to Figure 2. Co-localization plots for *FTO*, showing the lead SNP in red, the 99% credible set in green and RedRibbon overlap in blue. The red dotted line is the gene transcription start site. SNPs are referenced by rsids, PP.H4 abf and SNP PP.H4 are the posterior probability for coloc tool hypothesis 4; an arrow pointing up means increased gene expression for the risk allele.

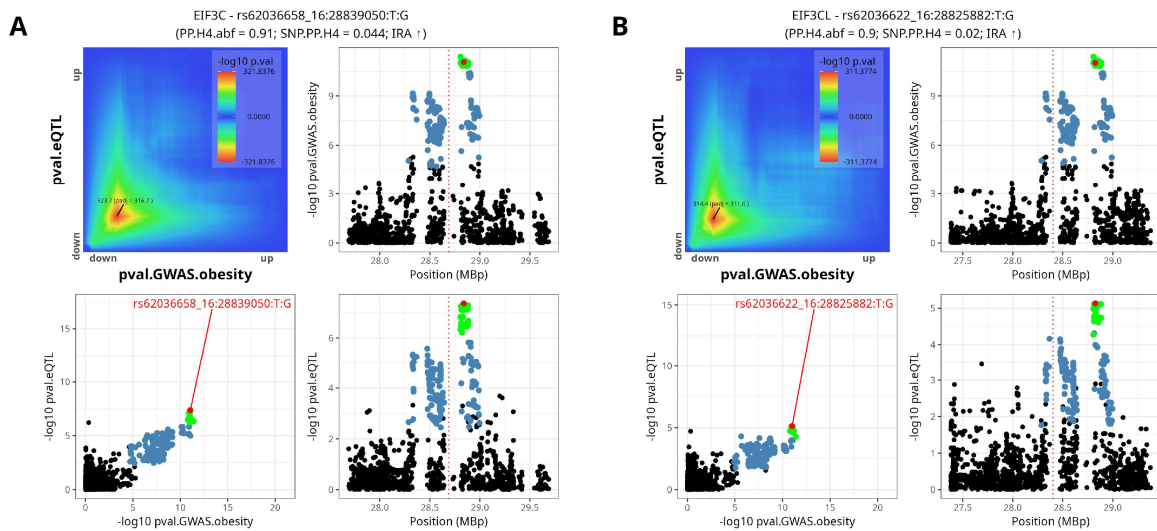


Figure S7. Co-localization for *EIF3C* and *EIF3CL* pancreatic islet eQTL and obesity GWAS, Related to Figure 2 and Graphical Abstract. Co-localization plots for (A) *EIF3C* and (B) *EIF3CL*. The lead SNP in red, 99% credible set in green and RedRibbon overlap in blue. The red dotted line is the gene transcription start site. SNPs are referenced by rsids, PP.H4 abf and SNP PP.H4 are the posterior probability for coloc tool hypothesis 4, IRA indicates the Increasing Risk Allele expression regulation direction; an arrow pointing up means increased gene expression for the risk allele.

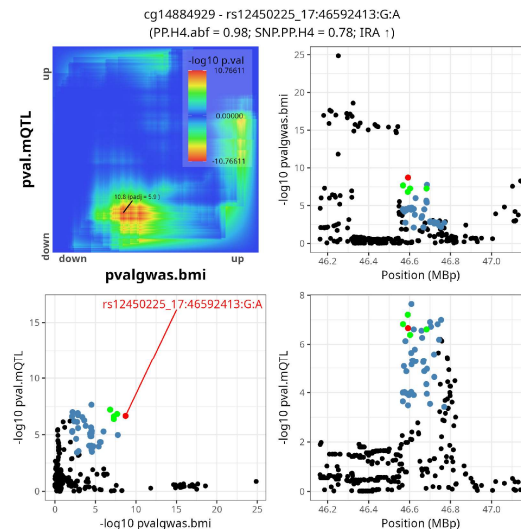


Figure S8. Co-localization for methylation site cg14884929 meQTL and BMI GWAS, Related to STAR Method Key Resources Table and Graphical Abstract. The lead SNP in red, 99% credible set in green and RedRibbon overlap in blue. PP.H4 abf and SNP PP.H4 are the posterior probability for coloc tool hypothesis 4, IRA indicates the Increasing Risk Allele; an arrow pointing up means increased DNA methylation for the risk allele.



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