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Supplemental Data

**Dynamic Role of *trans* Regulation
of Gene Expression in Relation to Complex Traits**

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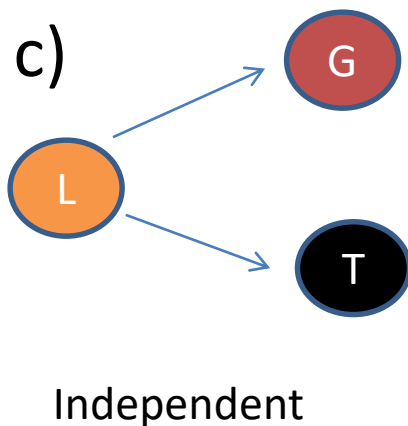
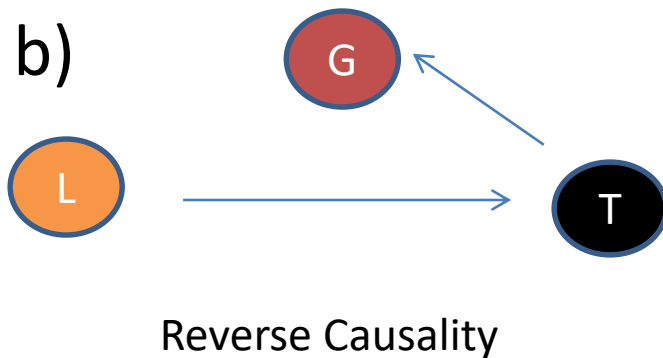
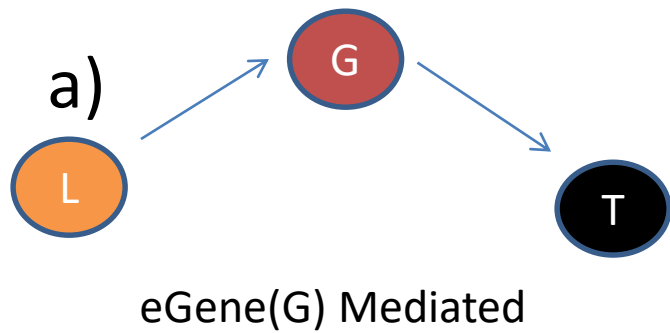


Figure S1. Possible relationships between a causal factor (L), a potential mediator (G) and an outcome (T).

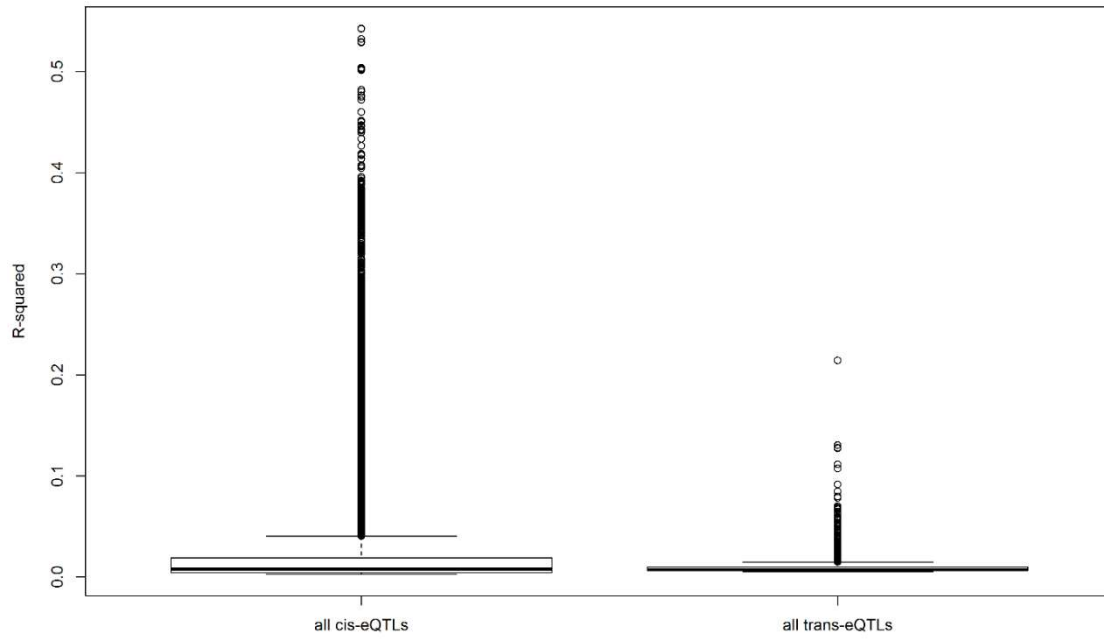
A) The eGene-mediated relationship, in which genotype (L) acts on phenotype (T) through gene expression (G).

B) The reverse causality model, in which gene expression changes (G) are the consequence of phenotype (T).

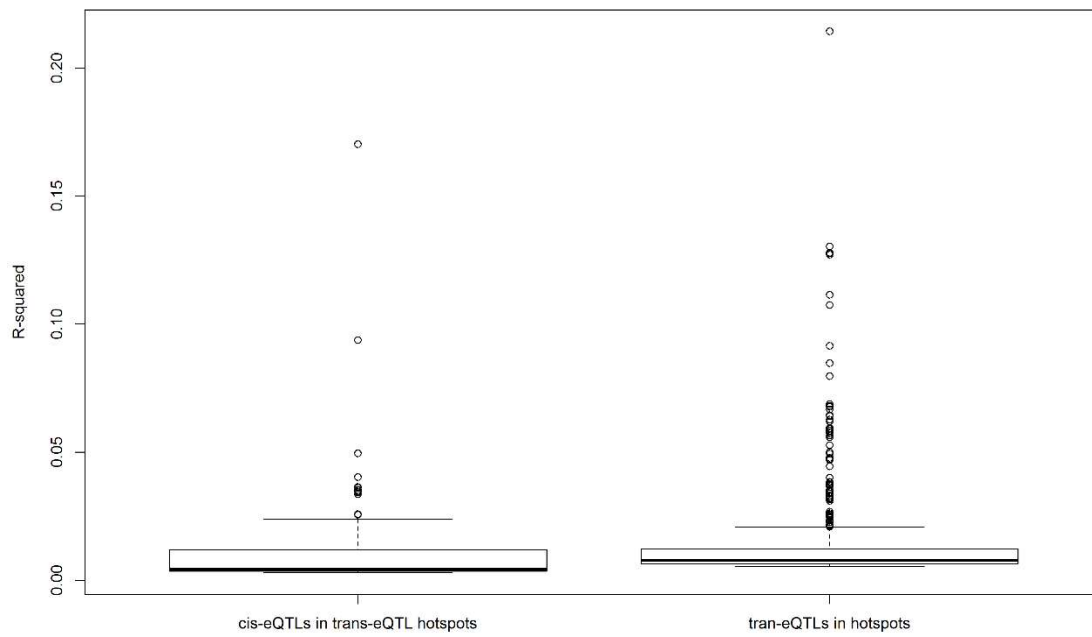
C) The independent model, in which the genotype affects gene expression (G) and phenotype (T) independently.

If gene expression is a consequence of T (Fig. S1b) or independently affected by L (Fig. S1c), rather than a mediator in the path from G to T (Fig. S1a), the estimated effect of L on T should not be affected by conditioning on G. However, if gene expression is indeed a mediator, this conditioning should drastically reduce the observed effect of L on T (Fig. S1a).

Figure S2 . Genetic effects of A) cis-eQTLs, trans-eQTLs; B) cis-eQTL on trans-hotspots, and trans-eQTLs on trans-hotspots.



(A)



(B)

Figure S3. Protein-protein interactions of *cis*-eGenes (red) and their interaction proteins (blue)

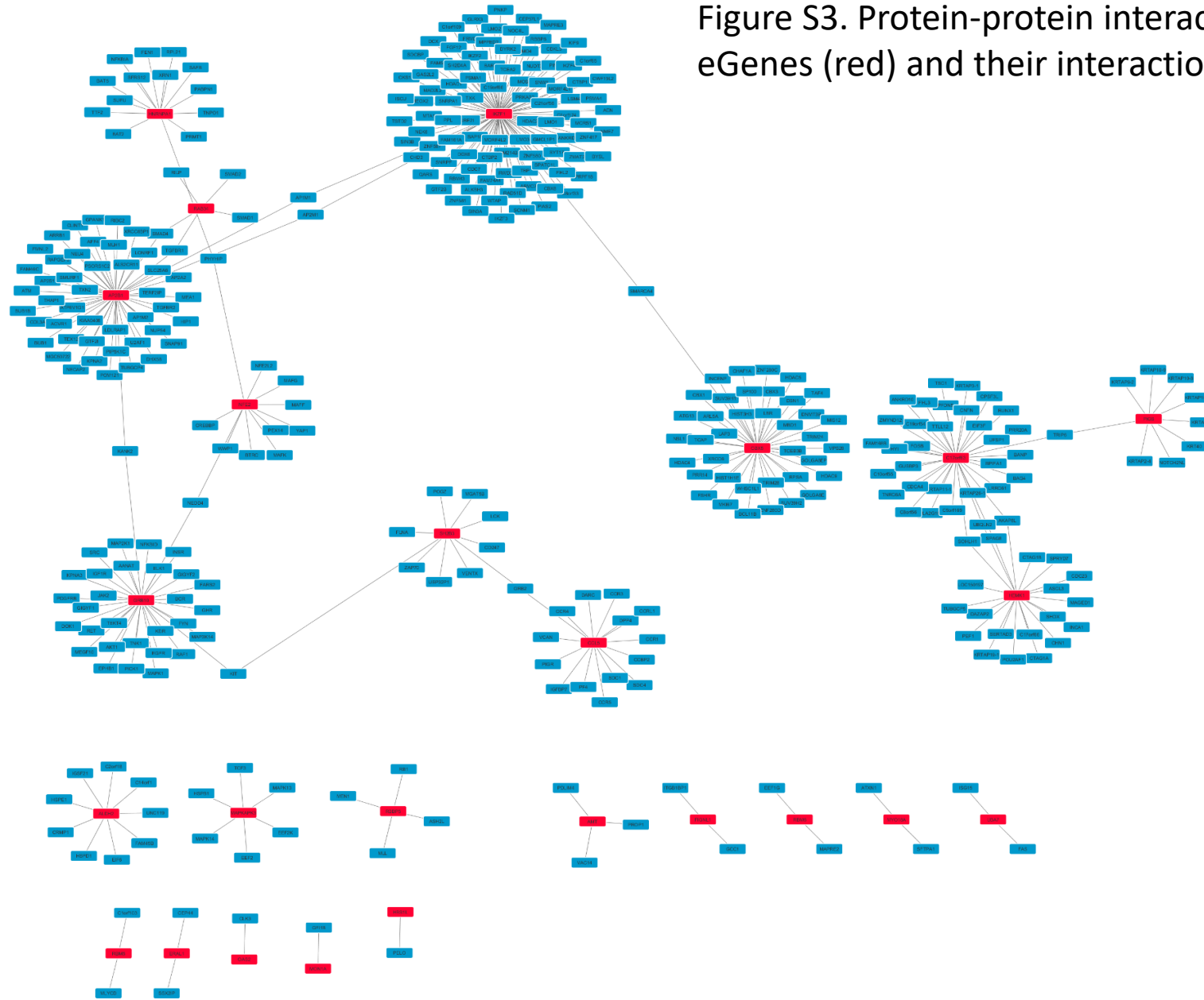


Table 1. Clinical Characteristics of the Framingham Heart Study Participants

Clinical Trait	Mean (SD)	Clinical Trait	Mean (SD)
Age, years	51 (15.7)	Total cholesterol, mg/dL	188 (36.3)
Sex, male (percentage)	46 %	Triglycerides, mg/dL	116 (83.5)
Fasting blood glucose, mg/dL	100 (21.5)	HDL cholesterol (HDL-C), mg/dL	56 (17.0)
Body mass index(BMI), kg/m ²	27.5 (5.5)	Hypertension*, (%)	40%
Systolic blood pressure (SBP), mm Hg	122 (16.6)	Diabetes mellitus*, (%)	8%
Diastolic blood pressure (DBP), mm Hg	74 (9.9)	Lipid treatment, (%)	28%
Current Smoker	13%	Non-drinkers	29%