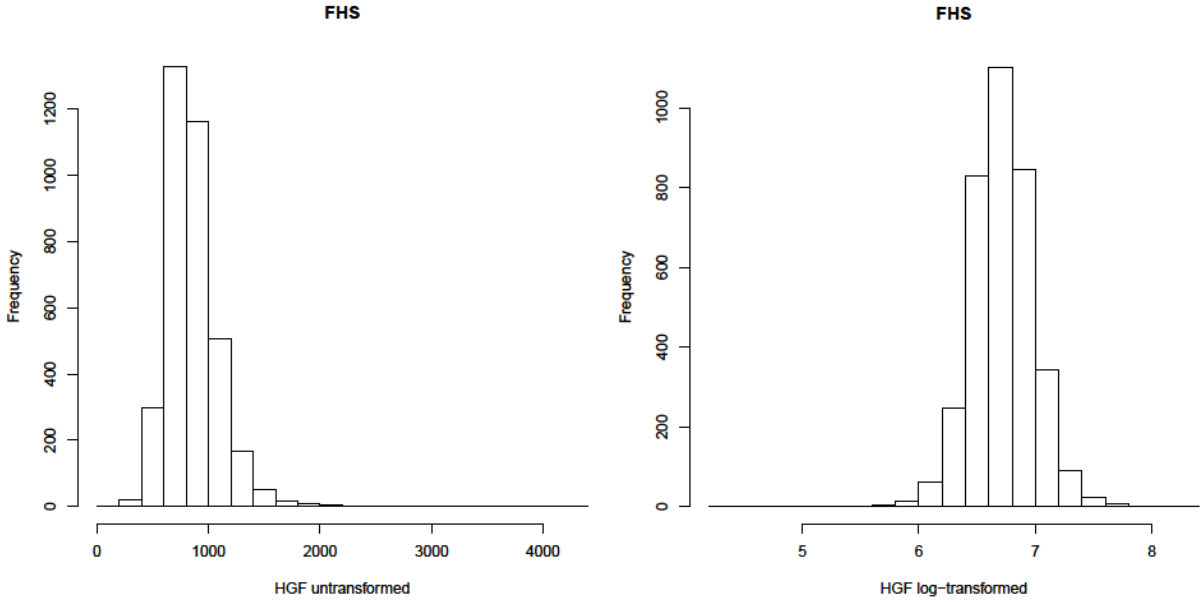
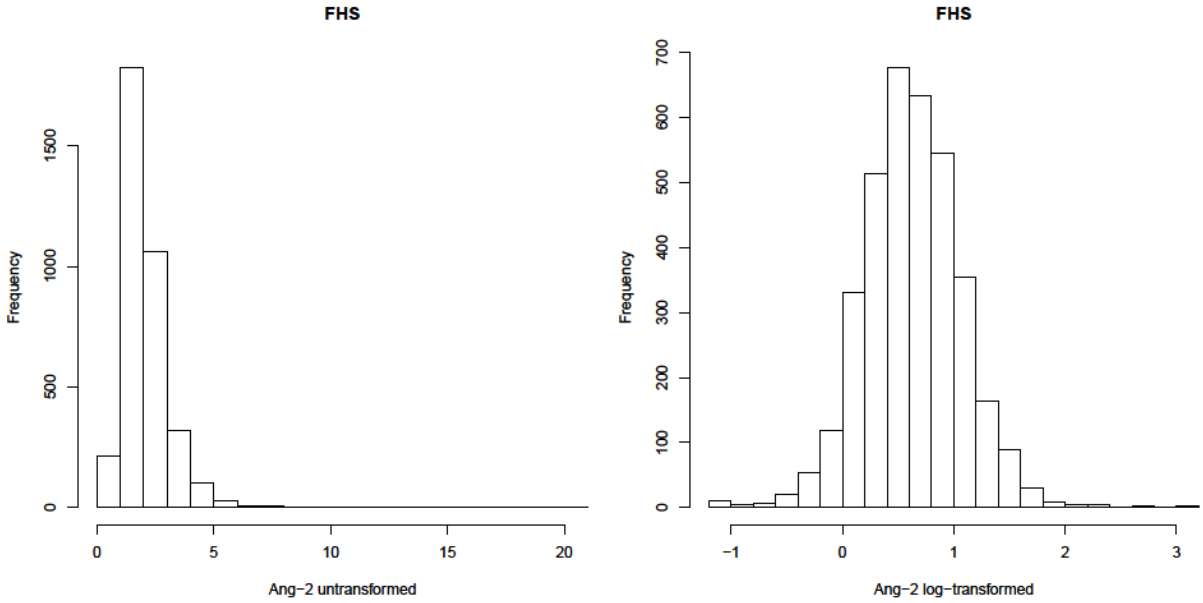
SUPPLEMENTAL MATERIAL

Supplementary Figure 1. Untransformed and transformed HGF concentrations (pg/mL) in the Framingham Heart Study (FHS).

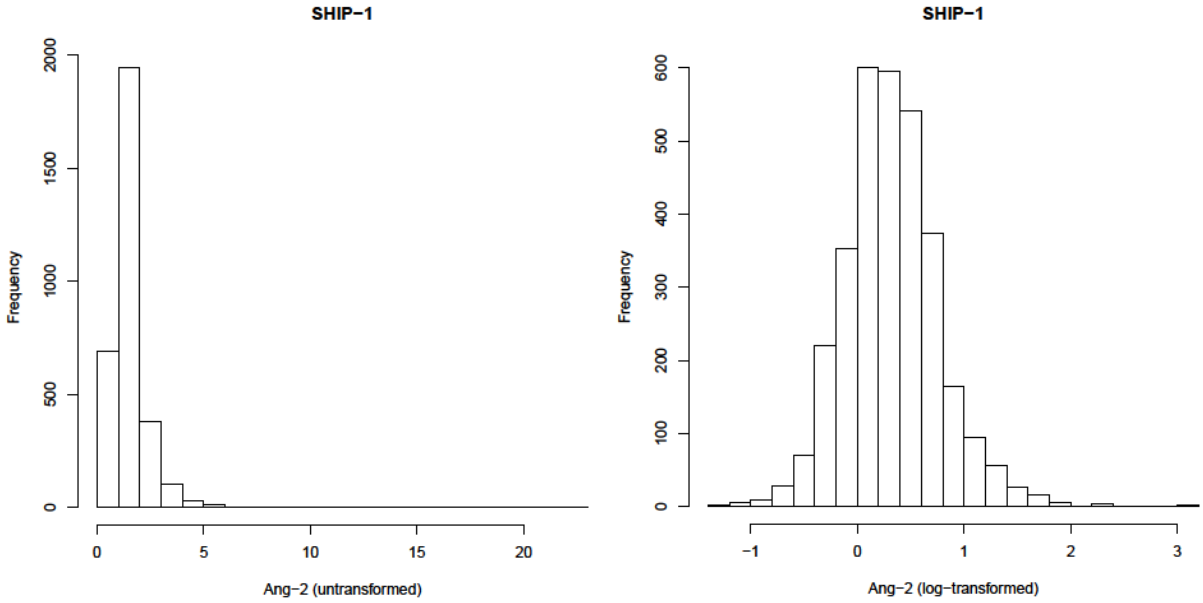


Supplementary Figure 2. Untransformed and transformed Ang-2 concentrations (ng/mL) in the Framingham Heart Study (FHS) sample (**Panel A**) and in the SHIP (Study of Health in Pomerania) sample (**Panel B**).

Panel A

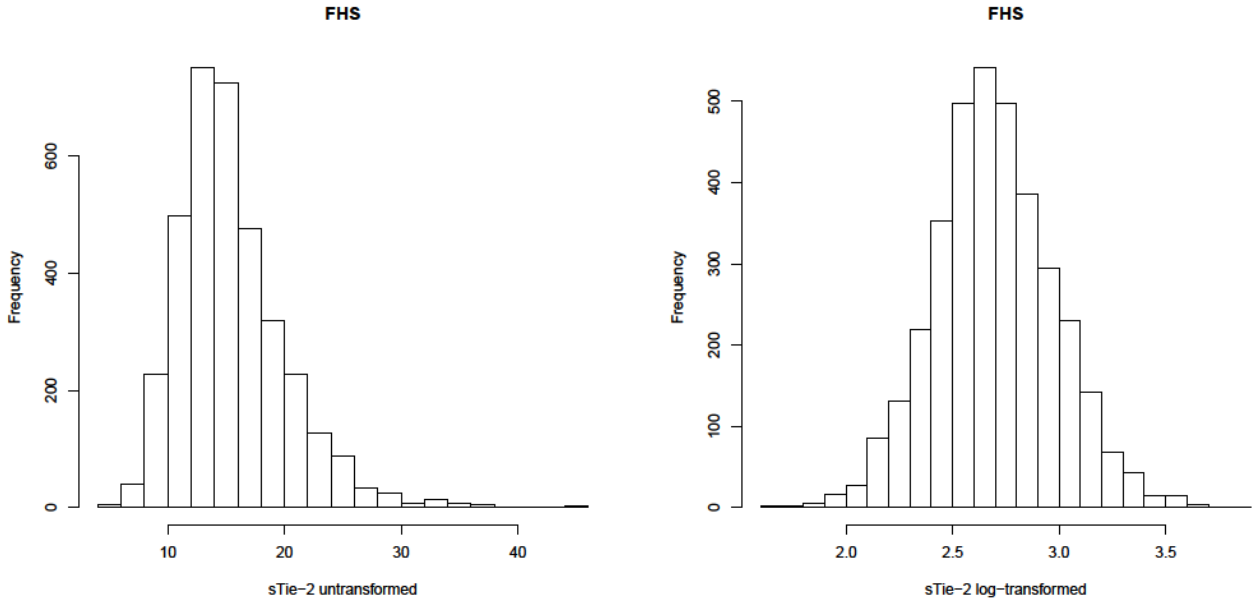


Panel B

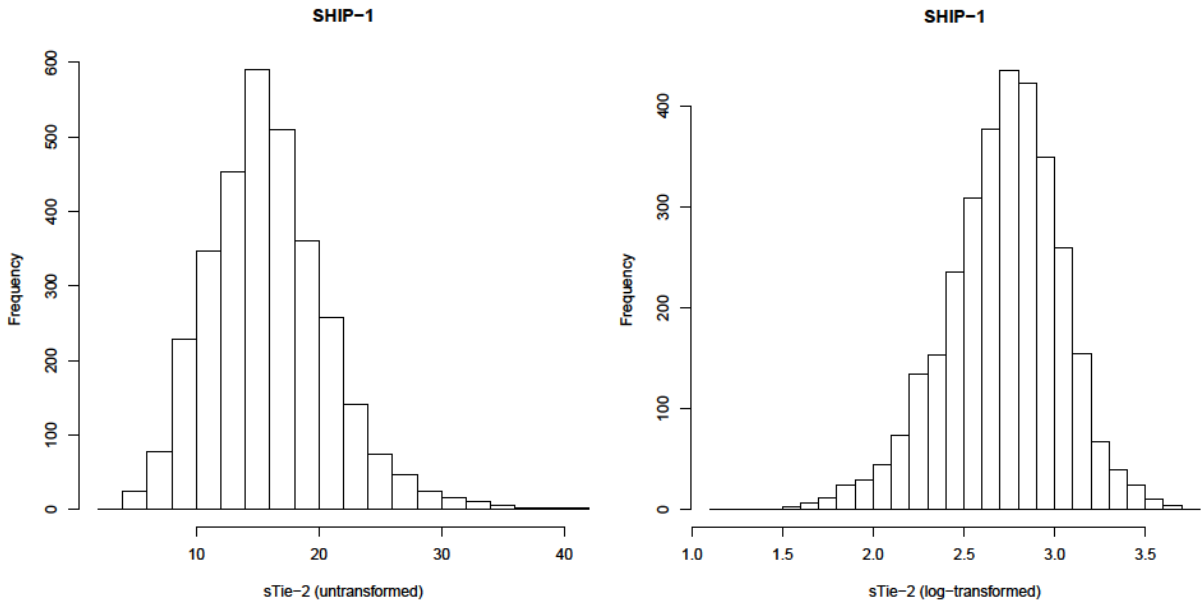


Supplementary Figure 3. Untransformed and transformed sTie-2 concentrations (ng/mL) in the Framingham Heart Study (FHS) sample (**Panel A**) and in the SHIP (Study of Health in Pomerania) sample (**Panel B**).

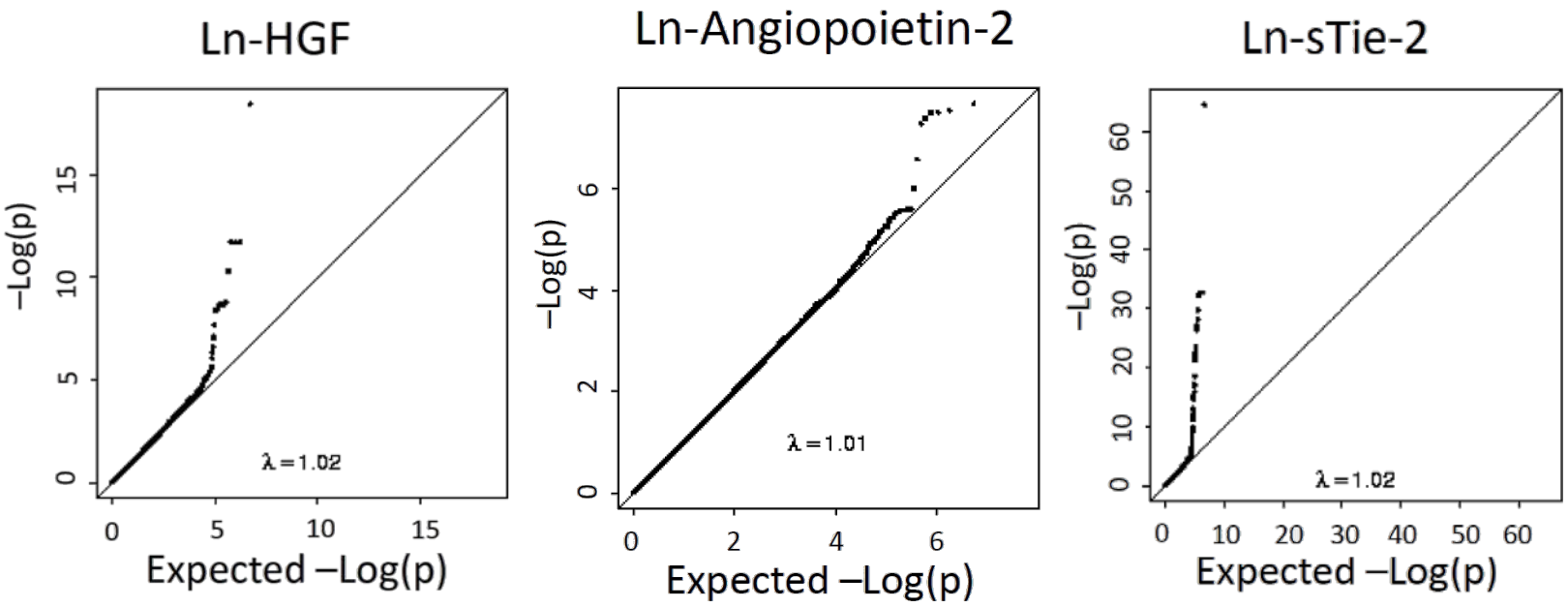
Panel A



Panel B

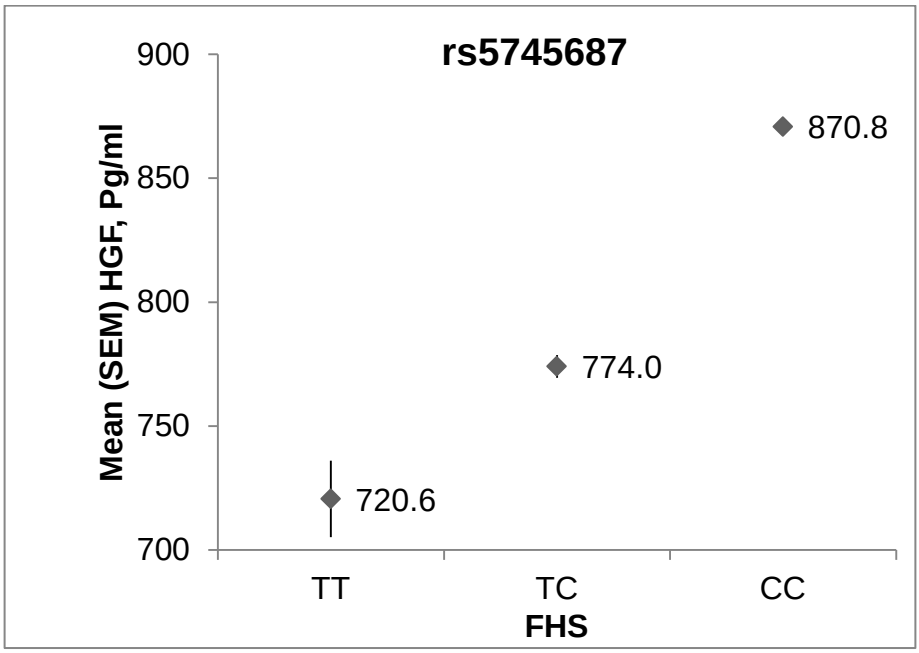


Supplementary Figure 4. Quantile-quantile plots comparing the observed against the expected –log10 (p-value) distributions associating common genetic variants to circulating levels of hepatocyte growth factor (**HGF**), angiopoietin-2 (**Ang-2**), and Tie-2 (**sTie-2**), respectively, in the Framingham Heart Study.



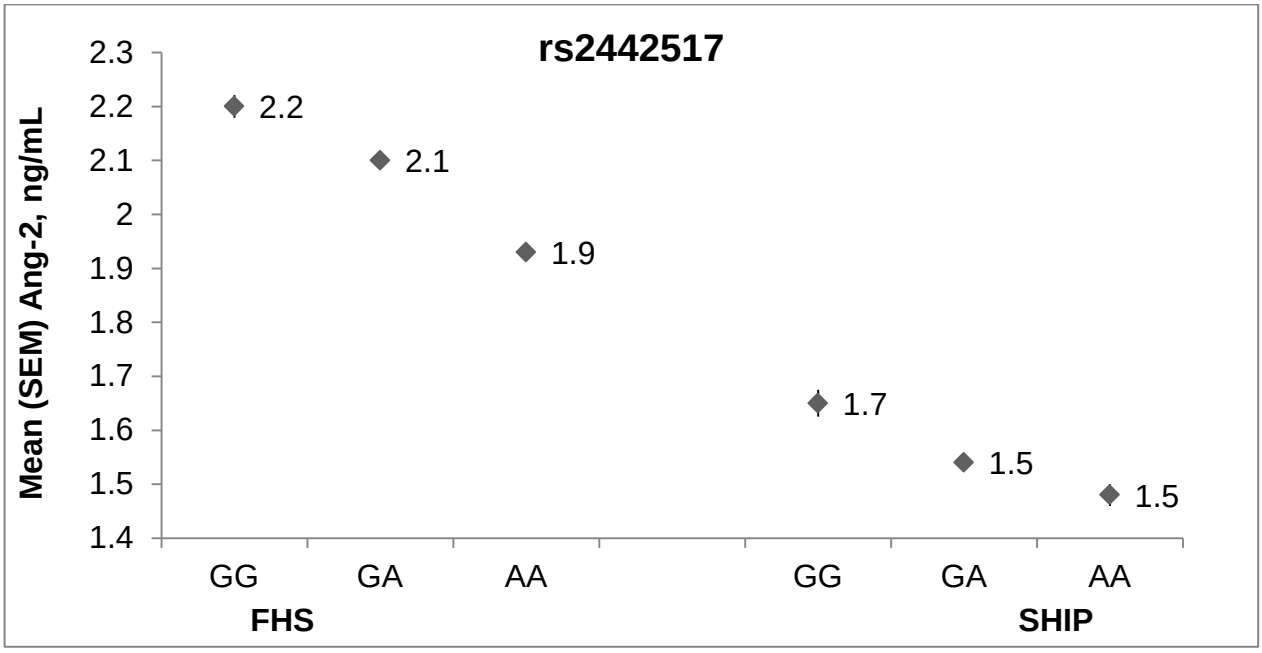
Ln, biomarkers were logarithmically transformed (to the base e) prior to genetic analyses

Supplementary Figure 5. Circulating concentrations of hepatocyte growth factor (HGF), stratified by rs5745687 genotype in the Framingham Heart Study (FHS) sample.

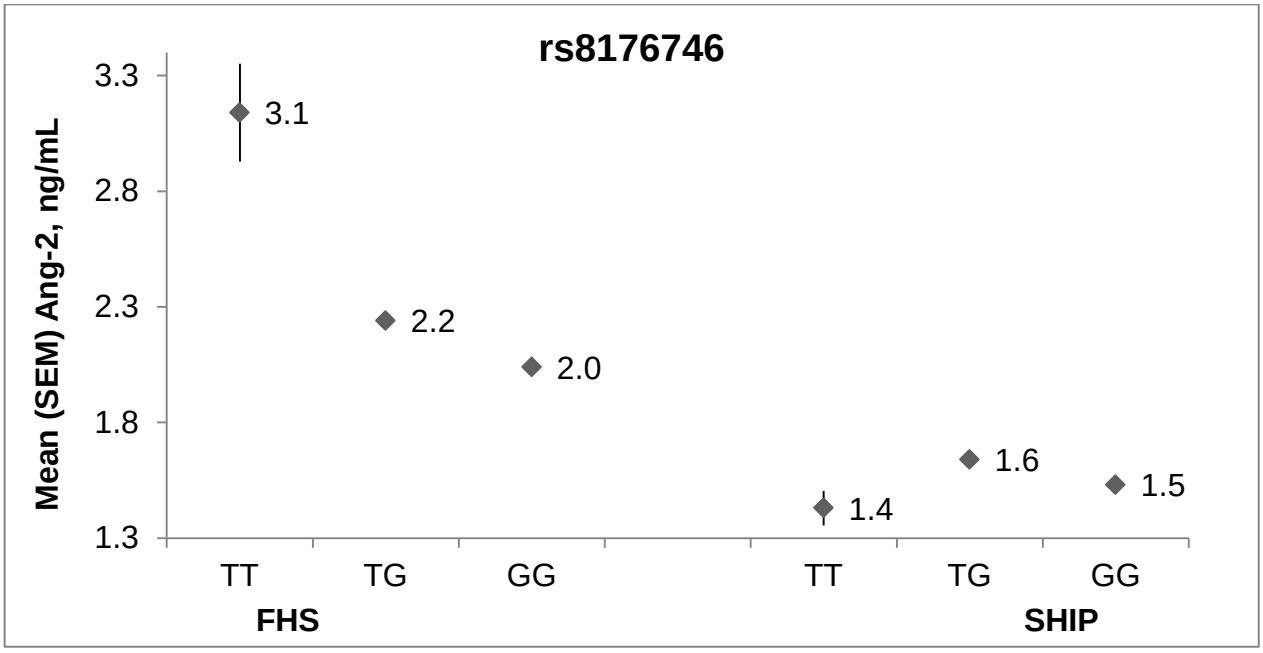


Supplementary Figure 6. Angiopoietin-2 (Ang-2) concentrations stratified by rs2442517 genotypes (**Panel A**) and stratified by rs8176746 genotypes (**Panel B**) in the Framingham Heart Study (FHS) sample and in the SHIP (Study of Health in Pomerania) sample.

Panel A

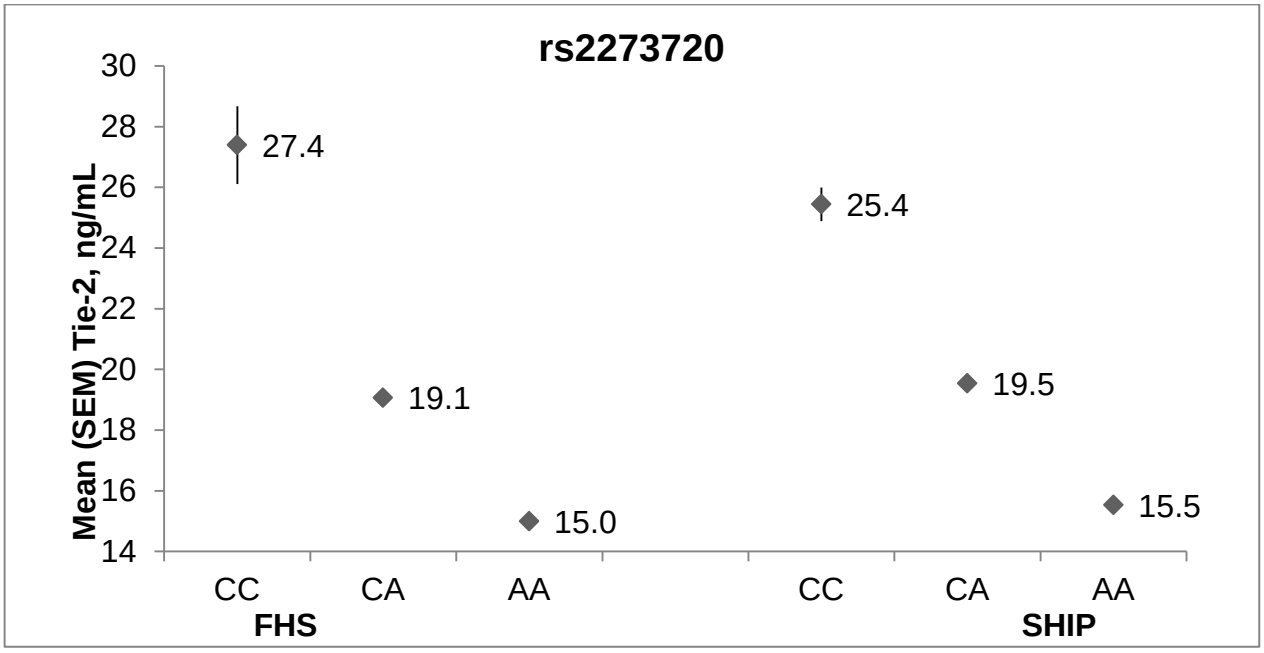


Panel B

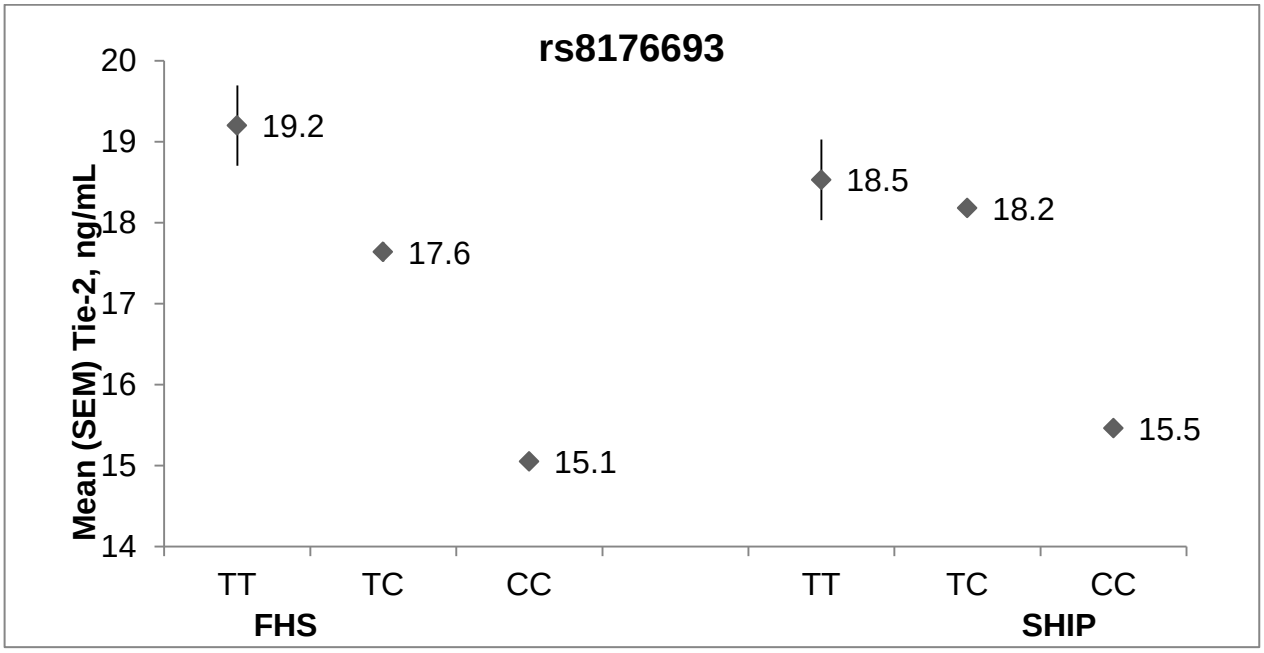


Supplementary Figure 7. Tie-2 concentrations stratified by rs2273720 genotypes (**Panel A**) and stratified by rs8176693 genotypes (**Panel B**) in the Framingham Heart Study (FHS) sample and in the SHIP (Study of Health in Pomerania) sample.

Panel A



Panel B



Supplementary Table 1. Top 5 enriched canonical pathways for hepatocyte growth factor (HGF).

Name	p-value	Ratio
mTOR Signaling	1.7E-05	10/198 (0.051)
Amyotrophic Lateral Sclerosis Signaling	5.2E-05	7/103 (0.068)
Regulation of eIF4 and p70S6K Signaling	9.7E-05	8/164 (0.049)
EIF2 Signaling	4.3E-04	8/192 (0.042)
Small Cell Lung Cancer Signaling	6.4E-04	5/85 (0.059)

mTOR denotes mammalian Target of Rapamycin; eIF2 *(*Eukaryotic Initiation Factor-2*)*

Supplementary Table 2. Frequency of the minor allele of rs5745687 in different ethnic subgroups in the 1000 Genomes data[1] (http://www.1000genomes.org/data).

Population/ Sample	T-Allele frequency
CEU (Utah Residents (CEPH) with Northern and Western European Ancestry)	0.0647
GBR (British in England and Scotland)	0.0730
IBS (Iberian population in Spain)	0.1071
MXL (Mexican Ancestry from Los Angeles USA)	0.0547
CHB (Han Chinese in Bejing, China)	0.0052

References

1. Abecasis GR, Altshuler D, Auton A, Brooks LD, Durbin RM, Gibbs RA, Hurles ME, McVean GA. A map of human genome variation from population-scale sequencing. *Nature*. 2010;467:1061-1073.