

**Table S1.** Correlation of 7 traits in WTCCC

	<b>T2D</b>	<b>BD</b>	<b>CAD</b>	<b>CD</b>	<b>HT</b>	<b>RA</b>	<b>T1D</b>
<b>T2D</b>	1.00	0.34	0.39	0.36	0.39	0.36	0.32
<b>BD</b>		1.00	0.36	0.36	0.37	0.33	0.29
<b>CAD</b>			1.00	0.35	0.39	0.37	0.31
<b>CD</b>				1.00	0.36	0.34	0.32
<b>HT</b>					1.00	0.36	0.32
<b>RA</b>						1.00	0.43
<b>T1D</b>							1.00

BD, CAD, CD, HT, RA, and T1D denote bipolar disorder, coronary artery disease, Crohn's disease, hypertension, rheumatoid arthritis, type 1 diabetes and type-2 diabetes, respectively.

**Table S2.** Correlation of 4 traits in Global Lipids

$\rho$	<b>TG</b>	<b>HDL</b>	<b>LDL</b>	<b>TC</b>
<b>TG</b>	1.00	-0.42	0.27	0.38
<b>HDL</b>		1.00	-0.08	0.16
<b>LDL</b>			1.00	0.88
<b>TC</b>				1.00

TG, HDL, LDL, and TC denote triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and total cholesterol, respectively.

**Figure S1.** Simulated distribution of Pleiotropy Index for 6 hematologic and 3 blood pressure traits. The left panel is for the *SH2B3* region and the right panel is for the *BRAP* region. A total of 200 million simulations were performed. A dotted red line is drawn across the y-axis at a value of 10 simulations. A simulated Pleiotropy Index below this line indicates genome-wide significance, i.e.,  $P_T$  less than  $10/200$  million =  $5 \times 10^{-8}$ . A Pleiotropy Index not observed at all simply means that the  $P_T$  is less than  $1/200$  million =  $5 \times 10^{-9}$ , while the exact simulated  $P_T$  value is unknown.

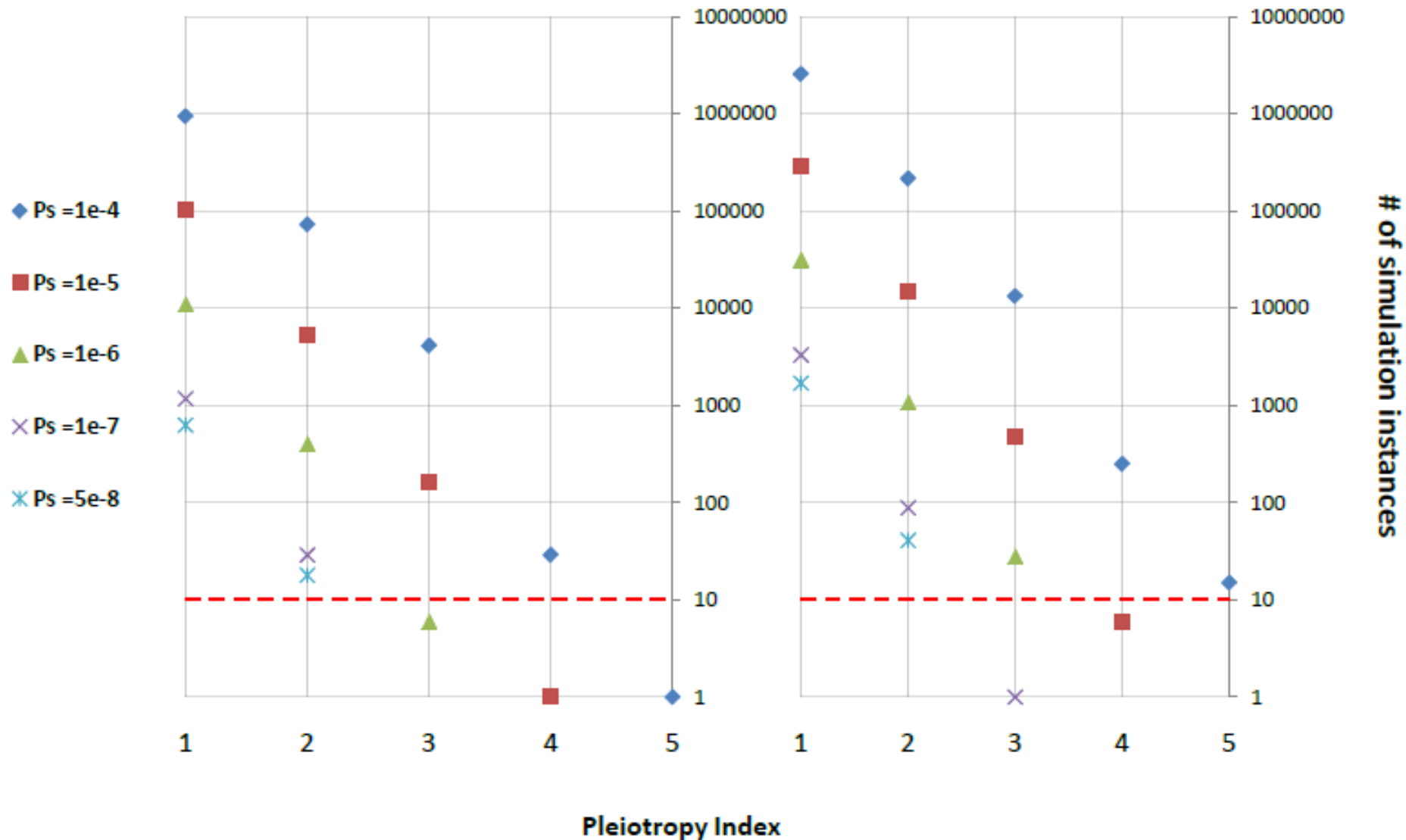
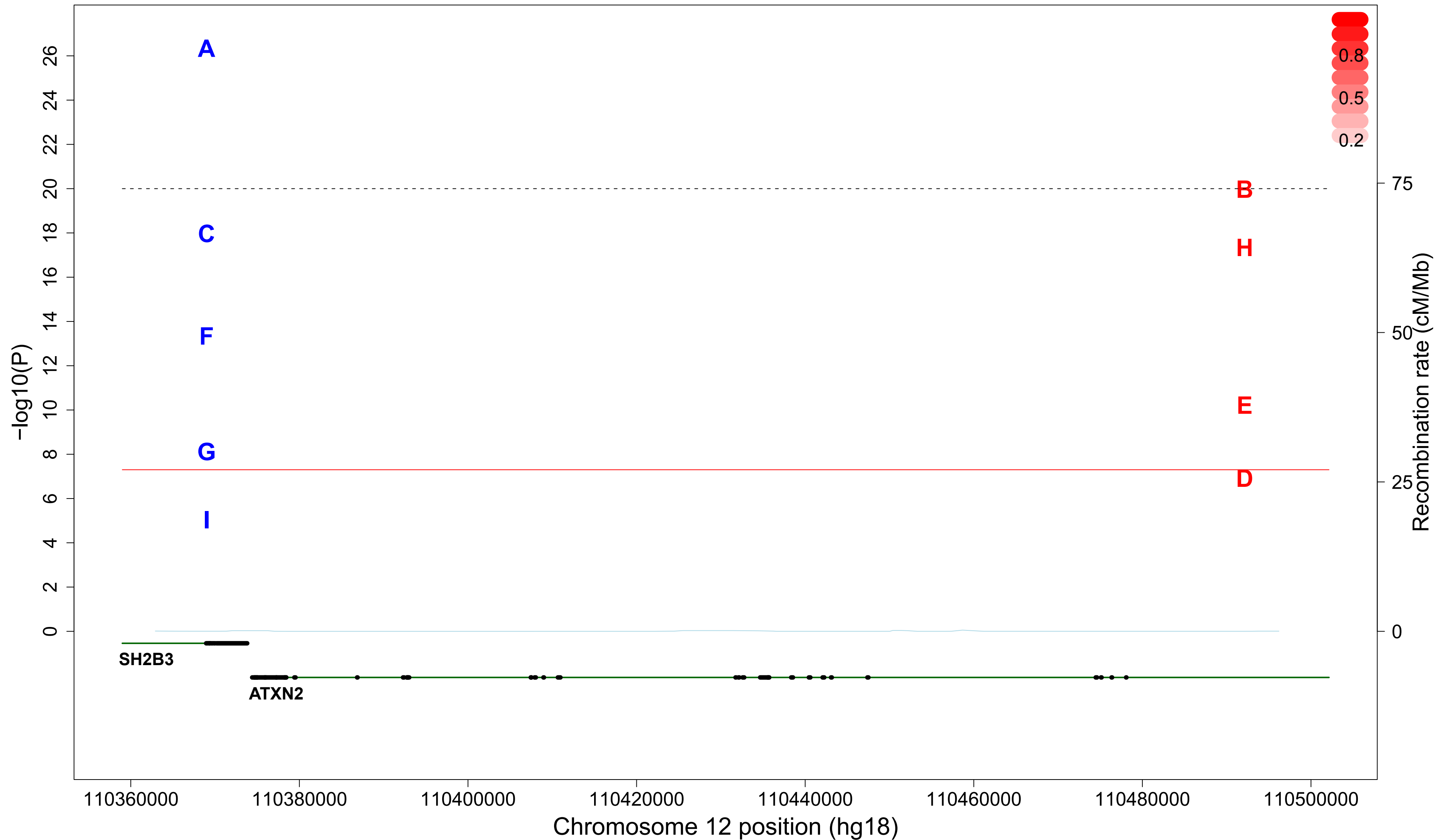


Figure S2: Pleiotropy Index: 9; driver SNP (in blue): rs3184504; passenger LD threshold: 0.8

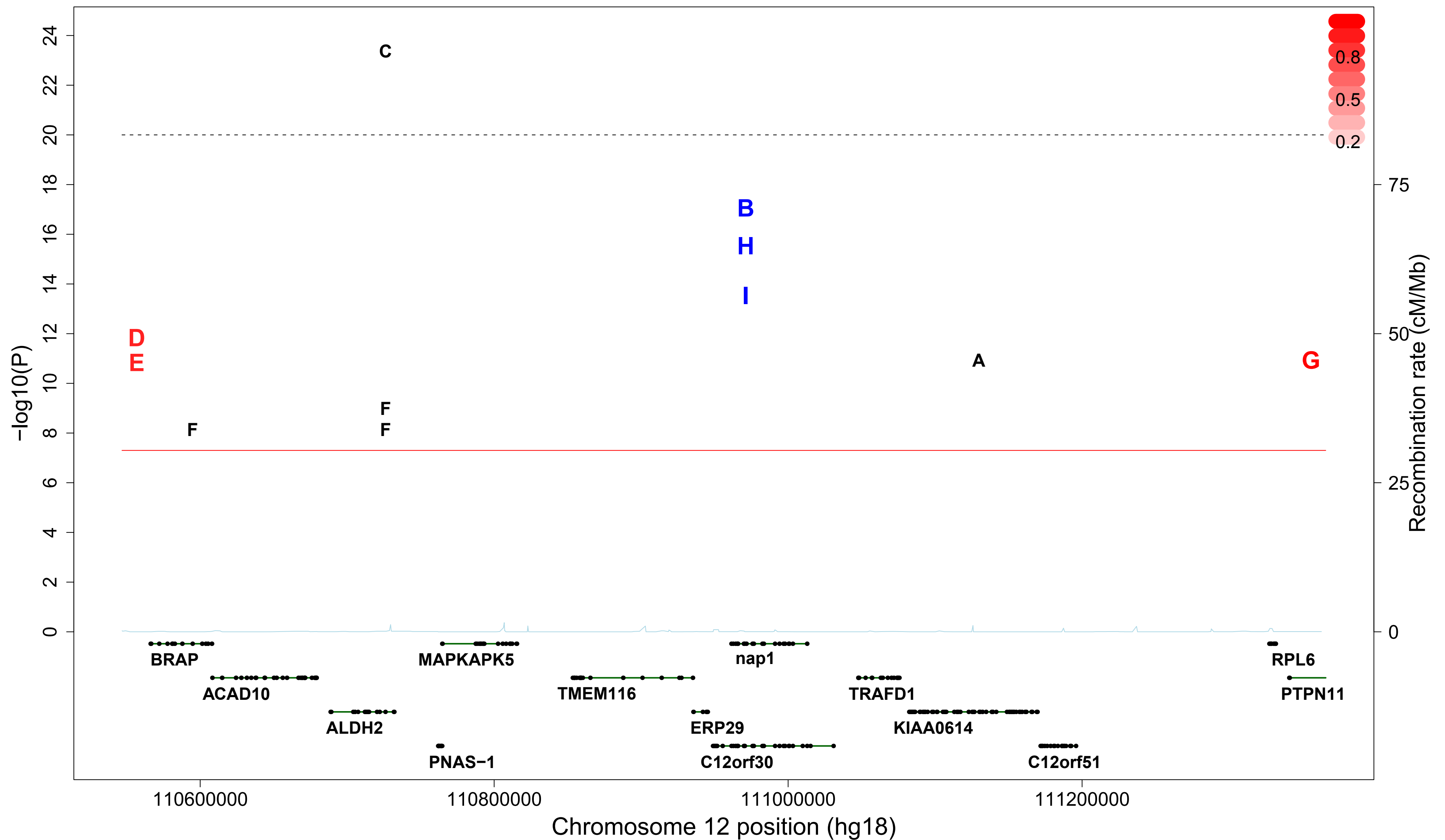


A. Barrett(19430480)(Type\_1\_diabetes)  
B. Dubois(20190752)(Celiac\_disease)  
C. Gudbjartsson(19198610)(Eosinophil\_count)

D. Hunt(18311140)(Celiac\_disease)  
E. Kottgen(20383146)(Chronic\_kidney\_disease)  
F. Levy(19430479)(Diastolic\_blood\_pressure)

G. Levy(19430479)(SBP)  
H. Newton-Cheh(19430483)(DBP)  
I. Stahl(20453842)(Rheumatoid\_arthritis)

Figure S3. Pleiotropy Index: 9; driver SNP (in blue): rs17696736; passenger LD threshold: 0.8



A. Cho(19396169)(Biomedical\_QTL)

B. Cooper(18978792)(Type\_1\_diabetes)

C. Cui(19698717)(Esophageal\_cancer)

D. Ganesh(19862010)(Hematocrit)

E. Ganesh(19862010)(Hemoglobin)

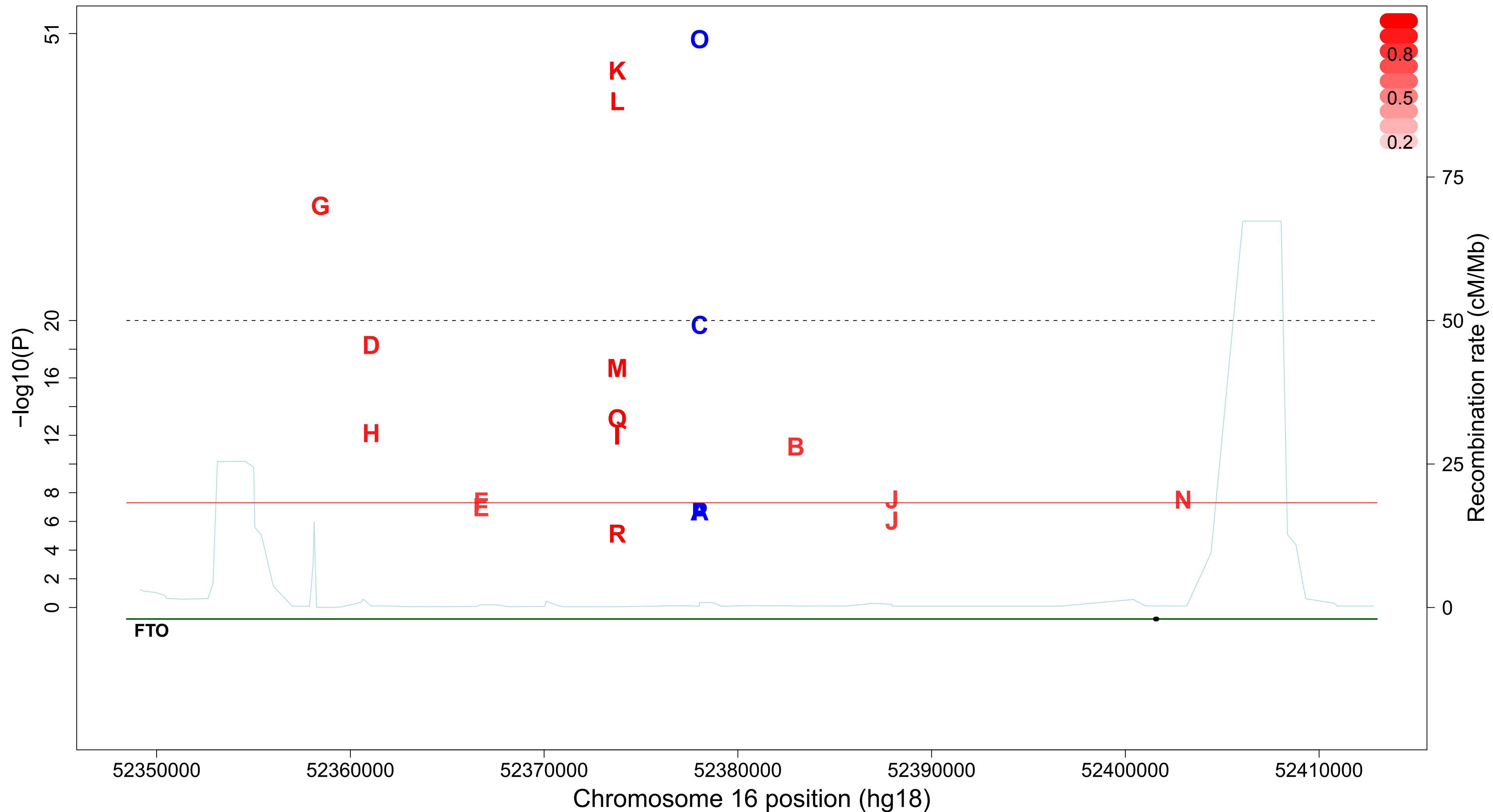
F. Kamatani(20139978)(Hematological\_traits)

G. Soranzo(19820697)(Hematological\_paramete

H. Todd(17554260)(Type\_1\_diabetes)

I. WTCCC(17554300)(Type\_1\_diabetes)

Figure S4. Pleiotropy Index: 15; driver SNP (in blue): rs9939609; passenger LD threshold: 0.8



A. Cho(19396169)(Biomedical\_QTL)

B. Cotsapas(19553259)(Obesity)

C. Frayling(17434869)(Body\_mass\_index)

D. Heard-Costa(19557197)(Waist\_circumference)

E. Hinney(18159244)(Obesity)

F. Loos(18454148)(Body\_mass\_index)

G. Meyre(19151714)(Obesity)

H. Scherag(20421936)(Obesity)

I. Scott(17463248)(Type\_2\_diabetes)

J. Scuteri(17658951)(Obesity)

K. Thorleifsson(19079260)(Body\_mass\_index)

L. Thorleifsson(19079260)(Weight)

M. Timpson(19056611)(Type\_2\_diabetes)

N. Voight(20581827)(Type\_2\_diabetes)

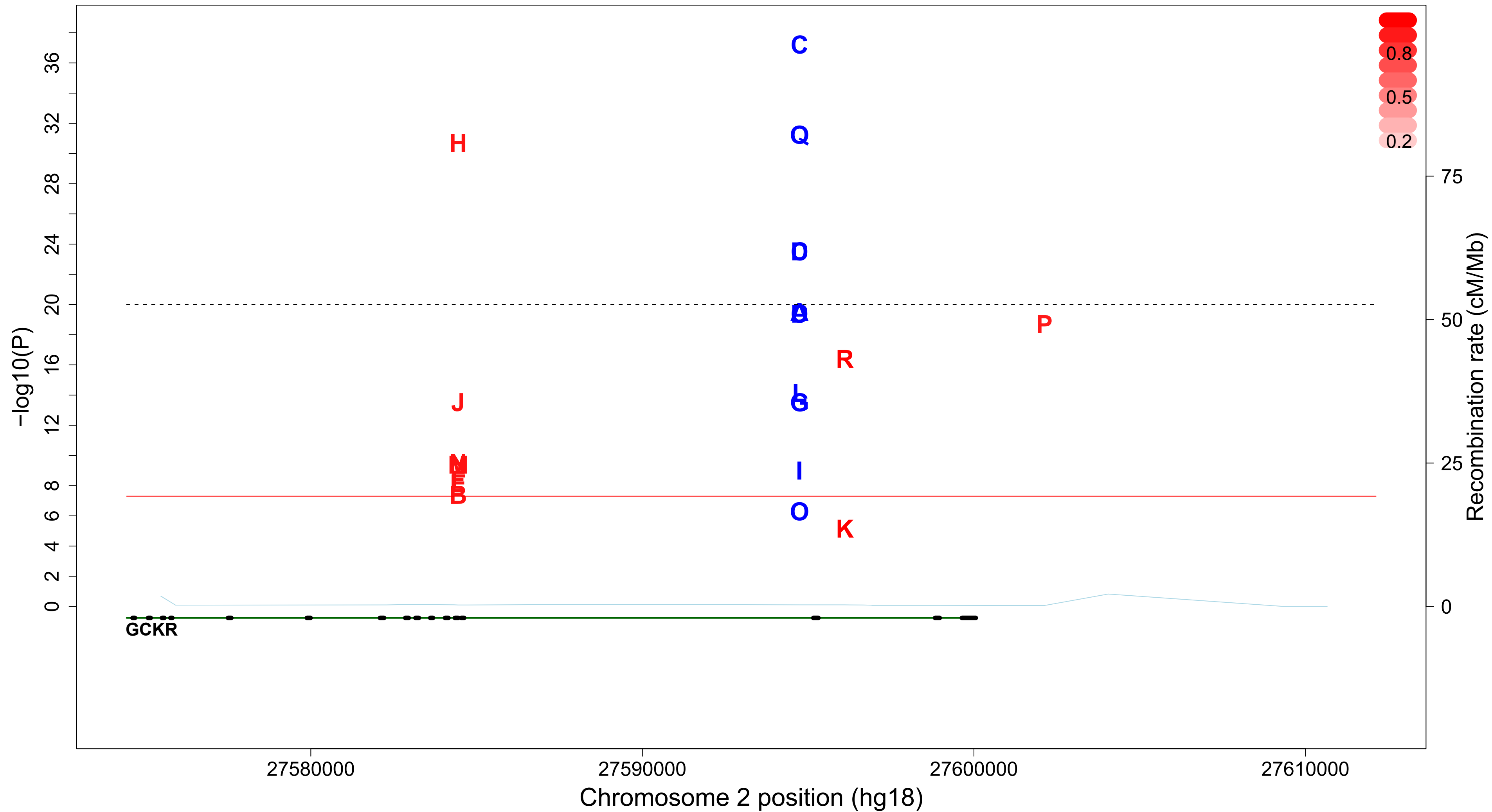
O. Willer(19079261)(Body\_mass\_index)

P. WTCCC(17554300)(Type\_2\_diabetes)

Q. Zeggini(17463249)(Type\_2\_diabetes)

R. Zeggini(18372903)(Type\_2\_diabetes)

Figure S5. Pleiotropy Index: 18; driver SNP (in blue): rs780094; passenger LD threshold: 0.8

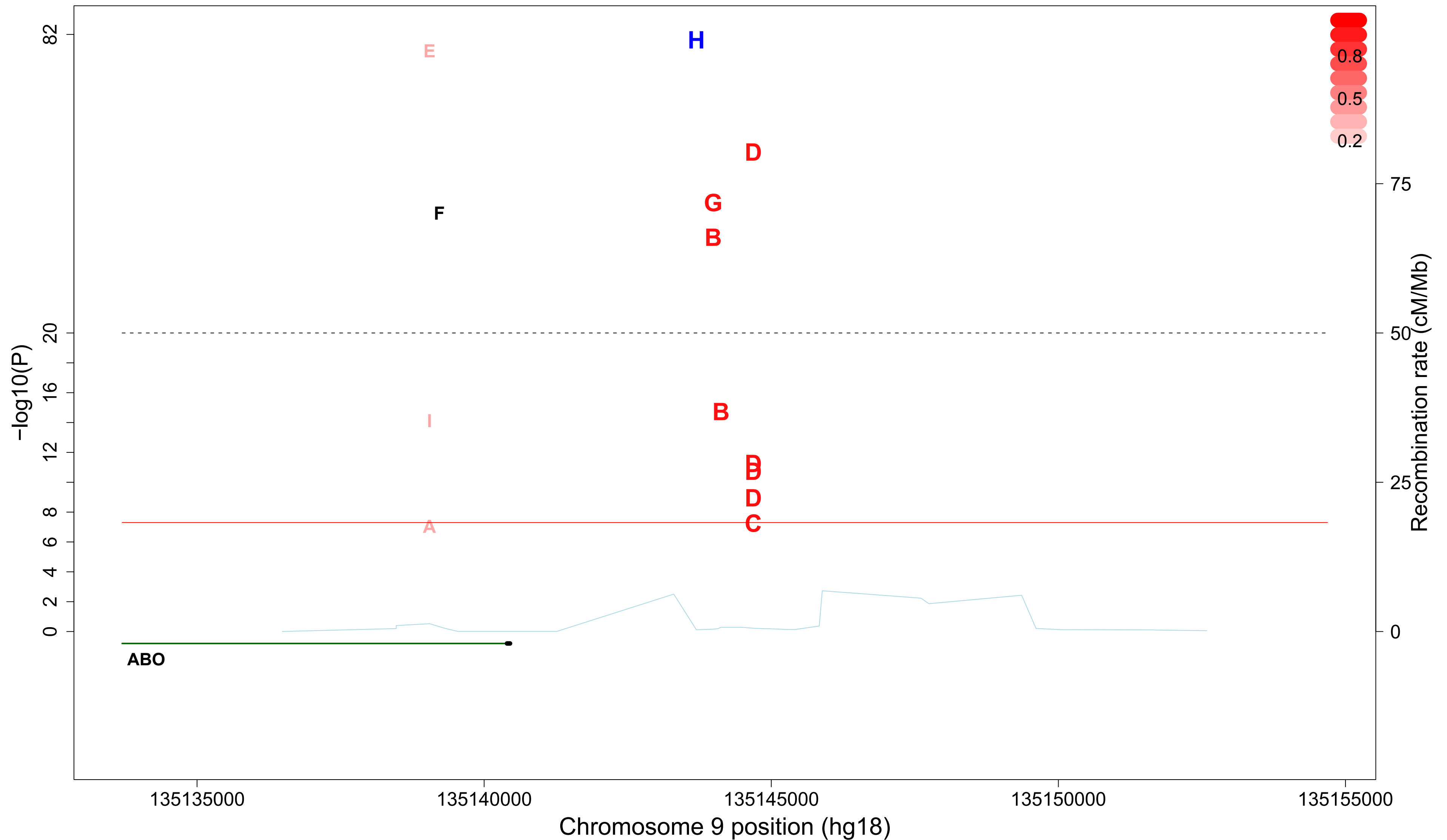


A. Aulchenko(19060911)(Triglycerides)  
 B. Chambers(18454146)(Waist\_circumference)  
 C. Dupuis(20081858)(Fasting\_glucose)  
 D. Dupuis(20081858)(Fasting\_insulin)  
 E. Johansen(20657596)(Hypertriglyceridemia)  
 F. Kamatani(20139978)(Hematological\_traits)

G. Kathiresan(18193044)(Triglycerides)  
 H. Kathiresan(19060906)(Triglycerides)  
 I. Kolz(19503597)(Serum\_uric\_acid)  
 J. Kottgen(20383146)(Chronic\_kidney\_disease)  
 K. O'Seaghdha(20705733)(Serum\_calcium)  
 L. Ridker(18439548)(C-reactive\_protein)

M. Sabatti(19060910)(Other\_metabolic\_traits)  
 N. Saxena(20081857)(glucose\_challenge)  
 O. Wallace(18179892)(LDL\_cholesterol)  
 P. Waterworth(20864672)(Triglycerides)  
 Q. Willer(18193043)(Triglycerides)  
 R. Yang(20884846)(Serum\_urate)

Figure S6. Pleiotropy Index: 9; driver SNP (in blue): rs651007; passenger LD threshold: 0.8



A. Amundadottir(19648918)(Pancreatic\_cancer)  
B. Barbalic(20167578)(adhesion\_molecules)  
C. Chung(20066004)(Angiotensin\_enzyme)

D. Kamatani(20139978)(Hematological\_traits)  
E. Melzer(18464913)(Protein\_QTL)  
F. Pare(18604267)(Soluble\_ICAM-1)

G. Paterson(19729612)(E-selectin)  
H. Qi(20147318)(Plasma\_E-selectin\_levels)  
I. Tregouet(19278955)(Venous\_thromboembolism)

**Figure S7.** Simulated distribution of Pleiotropy Index for 9 traits with pair-wise correlation coefficient ranging from 0 to 0.5. The LD matrix of the *SH2B3* region is used, and 100 million simulations are run.

