

## Supplemental Data

### Population-Based Genome-wide

### Association Studies Reveal Six Loci

### Influencing Plasma Levels of Liver Enzymes

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**Table S1:** Characteristics of the assays used to measure plasma liver enzymes levels in the discovery and replication collections.

Plasma Liver Enzymes	Type of assay <sup>a</sup>	Maximum inter and intra-batch coefficients of variation		
		CoLaus	InCHIANTI	LOLIPOP
ALT	IFCC <sup>b</sup> kinetic method	5.6% – 0.7%	4.4% – 1.6%	3.3% – 9.3%
ALP	IFCC <sup>b</sup> automated enzymatic colorimetric method	3.3% – 0.7%	2.2% – 0.5%	2.4% – 0.9%
GGT	IFCC <sup>b</sup> automated enzymatic colorimetric method C	1.6% – 0.4%	1.3% – 1.5%	3.7% – 0.9%
AST	IFCC <sup>b</sup> kinetic method	3.6% – 1.8%	3.2% – 1.8%	2.3% – 3.1%

<sup>a</sup> Assays were performed with Roche Diagnostics platforms using different protocols.

<sup>b</sup> IFCC indicates International Federation of Clinical Chemistry.

**Table S2:** Associations of 74 SNPs used in the follow up studies with plasma liver enzymes levels in discovery and replication datasets.

SNP <sup>a</sup>	CHR	Position <sup>b</sup>	Nearest gene	Region	Minor Allele <sup>c</sup>	Three discovery collections (n=7,715)		Three replication collections (n=4,704)		Six collections (n=12,419)	
						Pooled beta-coefficient (standard error)	Combined <i>p</i> -value	Pooled beta-coefficient (standard error)	Combined <i>p</i> -value	Pooled beta-coefficient (standard error)	Combined <i>p</i> -value
<b>ALT</b>											
rs9803659	1	163888158	<i>POU2F1</i>	INTERGENIC	C	-0.034(0.008)	7.25E-06	-0.018(0.013)	0.1528	-0.030(0.006)	4.34E-06
rs7645887	3	1364925	<i>CNTN6</i>	INTRONIC	T	-0.044(0.010)	4.09E-06	*	*	*	*
rs11593916	10	101799649	<i>CPN1</i>	INTRONIC	A	-0.036(0.008)	2.17E-06	-0.018(0.013)	0.1626	-0.031(0.007)	1.69E-06
rs11596076	10	101835424	<i>CPN1</i>	UPSTREAM	C	0.040(0.007)	6.80E-08	0.014(0.011)	0.2055	0.033(0.006)	1.87E-07
rs7068215	10	101849860	<i>CPN1</i>	INTERGENIC	G	0.038(0.007)	2.72E-07	0.021(0.012)	0.0955	0.034(0.006)	1.43E-07
rs11597390	10	101851425	<i>CPN1</i>	INTERGENIC	A	-0.044(0.008)	2.94E-08	-0.023(0.013)	0.0787	-0.039(0.007)	1.53E-08
rs2862990	10	101866354	<i>ERLIN1</i>	INTERGENIC	T	0.042(0.008)	2.99E-08	0.021(0.012)	0.0766	0.036(0.006)	2.06E-08
rs7913374	10	101869676	<i>ERLIN1</i>	INTERGENIC	G	0.042(0.008)	2.95E-08	0.021(0.012)	0.0694	0.036(0.006)	1.72E-08
rs11594333	10	101870690	<i>ERLIN1</i>	INTERGENIC	T	0.040(0.007)	8.21E-08	0.021(0.012)	0.0766	0.034(0.006)	4.60E-08
rs2862954	10	101902054	<i>ERLIN1</i>	NON SYNONYMOUS	T	-0.036(0.008)	2.44E-06	-0.030(0.012)	0.0107	-0.034(0.006)	9.24E-08
rs11597086	10	101943695	<i>CHUK</i>	INTRONIC	C	-0.038(0.007)	3.64E-07	-0.030(0.012)	0.0135	-0.036(0.006)	1.83E-08
rs11591741	10	101966491	<i>CHUK</i>	INTRONIC	C	-0.038(0.007)	4.50E-07	-0.029(0.012)	0.0175	-0.035(0.006)	2.97E-08
rs1851134	15	35497700	<i>MEIS2</i>	INTERGENIC	C	0.036(0.008)	7.34E-06	*	*	*	*
rs17542178	15	35499068	<i>MEIS2</i>	INTERGENIC	A	-0.036(0.008)	5.17E-06	*	*	*	*
rs4911389	20	32028702	<i>RALY</i>	INTERGENIC	A	-0.036(0.008)	7.77E-06	-0.003(0.012)	0.7984	-0.026(0.007)	9.50E-05
rs4911146	20	32103708	<i>RALY</i>	INTRONIC	C	-0.037(0.008)	4.90E-06	-0.004(0.012)	0.7613	-0.027(0.007)	6.13E-05
rs2284387	20	32108249	<i>RALY</i>	INTRONIC	G	0.036(0.008)	6.11E-06	*	*	*	*
rs12329791	21	38568505	<i>KCNJ15</i>	INTRONIC	T	0.044(0.009)	3.60E-06	*	*	*	*
rs2836285	21	38578375	<i>KCNJ15</i>	INTRONIC	C	-0.045(0.009)	1.50E-06	-0.005(0.011)	0.6312	-0.029(0.007)	6.26E-05
rs2076211	22	42653979	<i>PNPLA3</i>	INTRONIC	A	-0.065(0.010)	2.45E-11	-0.065(0.012)	1.59E-05	-0.059(0.007)	2.76E-15
rs2281135	22	42657471	<i>PNPLA3</i>	INTRONIC	T	0.065(0.010)	8.21E-12	0.051(0.012)	1.34E-05	0.060(0.007)	8.42E-16
rs2073081	22	42660645	<i>PNPLA3</i>	INTRONIC	C	0.066(0.010)	2.02E-11	0.051(0.012)	5.24E-05	0.060(0.008)	8.30E-15
rs2281298	22	42716135	<i>SAMM50</i>	INTRONIC	A	0.044(0.010)	4.98E-06	0.038(0.012)	0.0017	0.042(0.008)	3.28E-08
rs2143571	22	42716587	<i>SAMM50</i>	INTRONIC	A	0.046(0.009)	9.37E-07	0.038(0.012)	0.0018	0.043(0.007)	7.15E-09

GGT											
rs11129542	3	33077468	<i>GLB1</i>	INTRONIC	T	-0.009(0.002)	9.45E-06	*	*	*	*
rs7953249	12	119866444	<i>C12orf27</i>	INTERGENIC	G	0.007(0.001)	1.44E-08	0.002(0.001)	0.0066	0.004(0.001)	5.05E-08
rs2393791	12	119886676	<i>HNF1A</i>	INTRONIC	G	0.007(0.001)	1.78E-08	0.004(0.001)	0.0022	0.006(0.001)	7.58E-10
rs2259816	12	119898307	<i>HNF1A</i>	SYNONYMOUS	A	0.007(0.001)	3.26E-08	0.003(0.001)	7.00E-05	0.005(0.001)	1.79E-10
rs1169313	12	119905390	<i>C12orf43</i>	INTRONIC	C	-0.007(0.001)	3.18E-08	-0.003(0.001)	7.00E-05	-0.005(0.001)	1.77E-10
rs2258287	12	119917033	<i>C12orf43</i>	UPSTREAM	G	-0.007(0.001)	1.46E-07	-0.002(0.001)	0.009	-0.004(0.001)	2.82E-07
rs5760485	22	23311027	<i>C22orf36</i>	INTRONIC	C	0.006(0.001)	9.38E-06	0.007(0.002)	4.24E-06	0.007(0.001)	2.17E-10
rs4820599	22	23314767	<i>GGT1</i>	INTRONIC	G	0.006(0.001)	3.94E-06	0.008(0.002)	1.75E-06	0.007(0.001)	3.98E-11
ALP											
rs4654947	1	21550354	<i>NBPF3</i>	INTRONIC	C	0.025(0.006)	2.56E-05	0.043(0.016)	0.0069	0.027(0.006)	1.00E-06
rs10799701	1	21566296	<i>NBPF3</i>	INTERGENIC	A	0.031(0.005)	1.88E-10	0.032(0.008)	4.22E-05	0.031(0.004)	3.64E-14
rs1780324	1	21567063	<i>NBPF3</i>	INTERGENIC	T	0.032(0.005)	1.44E-10	0.031(0.007)	1.02E-05	0.031(0.004)	7.03E-15
rs3738097	1	21640122	<i>ALPL</i>	INTRONIC	G	-0.034(0.008)	2.11E-05	-0.045(0.019)	0.0175	-0.035(0.007)	1.29E-06
rs3738095	1	21640301	<i>ALPL</i>	INTRONIC	G	-0.033(0.008)	3.92E-05	-0.045(0.019)	0.0162	-0.034(0.007)	2.34E-06
rs3767145	1	21641108	<i>ALPL</i>	INTRONIC	G	0.033(0.008)	3.92E-05	0.045(0.019)	0.0162	0.035(0.007)	2.29E-06
rs2275369	1	21645750	<i>ALPL</i>	INTRONIC	G	0.035(0.008)	1.24E-05	0.046(0.019)	0.015	0.036(0.007)	6.65E-07
rs829370	1	21678499	<i>RAP1GAP</i>	INTRONIC	C	0.041(0.009)	1.70E-06	0.035(0.012)	0.0049	0.039(0.007)	3.11E-08
rs9295624	6	24547579	<i>GPLD1</i>	INTRONIC	A	0.031(0.006)	1.76E-07	0.031(0.009)	0.0007	0.031(0.005)	4.88E-10
rs9461011	6	24548330	<i>GPLD1</i>	INTRONIC	G	0.033(0.006)	4.42E-08	0.030(0.009)	0.0011	0.032(0.005)	1.88E-10
rs9379660	6	24549614	<i>GPLD1</i>	INTRONIC	C	0.027(0.005)	1.86E-07	0.017(0.007)	0.0124	0.023(0.004)	1.35E-08
rs9467160	6	24549725	<i>GPLD1</i>	INTRONIC	A	0.033(0.006)	2.19E-08	0.035(0.009)	0.0001	0.034(0.005)	1.17E-11
rs9461012	6	24549823	<i>GPLD1</i>	INTRONIC	A	0.034(0.006)	1.36E-08	0.030(0.009)	0.0009	0.033(0.005)	4.98E-11
rs17247566	6	24558383	<i>GPLD1</i>	INTRONIC	T	0.028(0.006)	1.70E-06	0.027(0.008)	0.0016	0.027(0.005)	9.59E-09
rs9467176	6	24572886	<i>GPLD1</i>	INTRONIC	A	-0.033(0.007)	3.57E-06	*	*	*	*
rs6901703	6	24583279	<i>GPLD1</i>	INTRONIC	A	0.034(0.007)	1.57E-06	*	*	*	*
rs2504824	6	40421434	<i>NP_0010017</i>	INTRONIC	A	-0.056(0.011)	2.58E-07	0.002(0.018)	0.9037	-0.040(0.009)	1.33E-05
rs16868911	6	40425447	<i>NP_0010017</i>	INTRONIC	A	0.054(0.011)	6.00E-07	*	*	*	*
rs2477757	6	40429756	<i>NP_0010017</i>	5PRIME_UTR	T	0.052(0.011)	1.55E-06	*	*	*	*
rs6558648	8	2277246	<i>MYOM2</i>	INTERGENIC	G	0.022(0.005)	7.89E-06	0.005(0.009)	0.5471	0.018(0.004)	2.68E-05
rs6981064	8	2277300	<i>MYOM2</i>	INTERGENIC	A	0.022(0.005)	7.39E-06	0.005(0.009)	0.5471	0.018(0.004)	2.51E-05
rs897445	8	2283162	<i>MYOM2</i>	INTERGENIC	A	0.025(0.005)	9.33E-07	0.002(0.008)	0.776	0.018(0.004)	1.52E-05

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rs10866938	8	2310221	MYOM2	INTERGENIC	T	0.024(0.005)	4.41E-06	0.001(0.008)	0.9482	0.017(0.004)	8.76E-05
rs8176720	9	133162427	ABO	SYNONYMOUS	G	0.031(0.005)	1.41E-08	0.031(0.008)	7.00E-05	0.031(0.004)	4.29E-12
rs641959	9	133163253	ABO	INTRONIC	G	0.035(0.006)	6.83E-10	0.024(0.008)	0.0044	0.031(0.005)	2.05E-11
rs514708	9	133163297	ABO	INTRONIC	T	0.035(0.006)	6.15E-10	0.024(0.008)	0.0044	0.031(0.005)	1.85E-11
rs672316	9	133167679	ABO	INTRONIC	C	0.032(0.006)	1.40E-08	0.023(0.008)	0.0057	0.029(0.005)	4.42E-10
rs657152	9	133168819	ABO	INTRONIC	T	-0.057(0.005)	4.56E-29	-0.029(0.007)	4.85E-05	-0.047(0.004)	1.73E-30
rs474279	9	133169171	ABO	INTRONIC	T	0.030(0.006)	3.39E-07	0.023(0.008)	0.0057	0.028(0.005)	8.29E-09
rs8176681	9	133169308	ABO	INTRONIC	G	0.035(0.005)	3.68E-12	*	*	*	*
rs552148	9	133183035	ABO	UPSTREAM	T	0.032(0.006)	3.06E-08	0.022(0.008)	0.0076	0.029(0.005)	1.24E-09
rs652600	9	133340571	ADAMTS13	INTRONIC	C	-0.027(0.006)	1.11E-06	-0.011(0.011)	0.2873	-0.024(0.005)	1.59E-06
rs4962153	9	133353308	ADAMTS13	INTRONIC	A	-0.059(0.007)	2.17E-18	-0.064(0.019)	0.0009	-0.060(0.006)	8.19E-21
rs3124765	9	133358211	C9orf7	SYNONYMOUS	A	0.063(0.007)	7.65E-19	*	*	*	*
rs10761739	10	64732014	JMJD1C	INTRONIC	C	0.023(0.005)	5.48E-06	0.024(0.008)	0.0013	0.023(0.004)	2.69E-08
rs10761741	10	64736192	JMJD1C	INTRONIC	A	-0.022(0.005)	9.06E-06	-0.024(0.008)	0.0014	-0.023(0.004)	4.70E-08
rs10740118	10	64771213	JMJD1C	INTRONIC	C	0.022(0.005)	7.82E-06	0.024(0.007)	0.0012	0.023(0.004)	3.53E-08
rs12355784	10	64791571	JMJD1C	INTRONIC	A	0.026(0.005)	4.68E-07	0.025(0.007)	0.0003	0.025(0.004)	5.02E-10
rs3999089	10	64873814	JMJD1C	INTRONIC	C	-0.024(0.005)	1.28E-06	-0.023(0.007)	0.0005	-0.024(0.004)	2.55E-09
rs10761779	10	64944933	REEP3	INTERGENIC	G	0.025(0.005)	3.86E-07	0.024(0.007)	0.0004	0.025(0.004)	6.89E-10
rs281408	19	53925218	RASIP1	INTRONIC	A	0.027(0.005)	7.12E-08	0.004(0.007)	0.6266	0.020(0.004)	2.05E-06
rs12975781	19	53941510	IZUMO1	5PRIME_UTR	T	-0.029(0.005)	7.50E-09	*	*	*	*

<sup>a</sup> Position and minor allele are of NCBI Build 35

<sup>b</sup> Minor allele corresponds to forward strand

<sup>c</sup> MAF: Minor allele frequency. It is based on CoLaus stud

\* Empty cells indicate those SNPs were removed from follow up meta analysis, due to either lack of imputation, low quality of imputation or inconsistent direction of effects.

**Table S3:** List of 32 SNPs associated with plasma liver enzymes levels with genome-wide significance in combined analysis of discovery and replication datasets

SNP <sup>a</sup>	CHR	Position <sup>b</sup>	Nearest gene	Region	Minor Allele <sup>c</sup>	MAF <sup>b</sup>	Three discovery collections (n=7,715)		Three replication collections (n=4,704)		Six collections (n=12,419)	
							Pooled beta-coefficient (standard error)	Combined <i>p</i> -value	Pooled beta-coefficient (standard error)	Combined <i>p</i> -value	Pooled beta-coefficient (standard error)	Combined <i>p</i> -value
<b>ALT</b>												
rs11597390	10	101851425	<i>CPN1</i>	INTERGENIC	A	0.36	-0.044(0.008)	2.9 × 10 <sup>-8</sup>	-0.023(0.013)	0.08	-0.039(0.007)	1.5 × 10 <sup>-8</sup>
rs2862990	10	101866354	<i>ERLIN1</i>	INTERGENIC	T	0.42	0.042(0.008)	3.0 × 10 <sup>-8</sup>	0.021(0.011)	0.08	0.036(0.006)	2.1 × 10 <sup>-8</sup>
rs7913374	10	101869676	<i>ERLIN1</i>	INTERGENIC	G	0.41	0.042(0.008)	3.0 × 10 <sup>-8</sup>	0.021(0.012)	0.07	0.036(0.006)	1.7 × 10 <sup>-8</sup>
rs11594333	10	101870690	<i>ERLIN1</i>	INTERGENIC	T	0.43	0.040(0.007)	8.2 × 10 <sup>-8</sup>	0.021(0.012)	0.08	0.034(0.006)	4.6 × 10 <sup>-8</sup>
rs11597086	10	101943695	<i>CHUK</i>	INTRONIC	C	0.43	-0.038(0.007)	3.6 × 10 <sup>-7</sup>	-0.030(0.012)	0.01	-0.036(0.006)	1.8 × 10 <sup>-8</sup>
rs11591741	10	101966491	<i>CHUK</i>	INTRONIC	C	0.43	-0.038(0.007)	4.5 × 10 <sup>-7</sup>	-0.029(0.012)	0.02	-0.035(0.006)	3.0 × 10 <sup>-8</sup>
rs2076211	22	42653979	<i>PNPLA3</i>	INTRONIC	A	0.18	-0.065(0.010)	2.5 × 10 <sup>-11</sup>	-0.065(0.010)	1.6 × 10 <sup>-5</sup>	-0.059(0.007)	2.8 × 10 <sup>-15</sup>
rs2281135	22	42657471	<i>PNPLA3</i>	INTRONIC	T	0.18	0.065(0.010)	8.2 × 10 <sup>-12</sup>	0.051(0.012)	1.3 × 10 <sup>-5</sup>	0.060(0.007)	8.4 × 10 <sup>-16</sup>
rs2073081	22	42660645	<i>PNPLA3</i>	INTRONIC	C	0.18	0.066(0.010)	2.0 × 10 <sup>-11</sup>	0.051(0.012)	5.2 × 10 <sup>-5</sup>	0.060(0.008)	8.3 × 10 <sup>-15</sup>
rs2143571	22	42716587	<i>SAMM50</i>	INTRONIC	A	0.19	0.046(0.009)	9.4 × 10 <sup>-7</sup>	0.038(0.012)	1.8 × 10 <sup>-3</sup>	0.043(0.007)	7.2 × 10 <sup>-9</sup>
<b>GGT</b>												
rs7953249	12	119866444	<i>C12orf27</i>	INTERGENIC	G	0.43	0.007(0.001)	1.4 × 10 <sup>-8</sup>	0.002(0.001)	0.007	0.004(0.001)	5.1 × 10 <sup>-8</sup>
rs2393791	12	119886676	<i>HNF1A</i>	INTRONIC	G	0.40	0.007(0.001)	1.8 × 10 <sup>-8</sup>	0.004(0.001)	0.002	0.006(0.001)	7.6 × 10 <sup>-10</sup>
rs2259816	12	119898307	<i>HNF1A</i>	SYNONYMOUS	A	0.37	0.007(0.001)	3.3 × 10 <sup>-8</sup>	0.003(0.001)	7.0 × 10 <sup>-5</sup>	0.005(0.001)	1.8 × 10 <sup>-10</sup>
rs1169313	12	119905390	<i>HNF1A-C12orf43</i>	INTRONIC	C	0.38	-0.007(0.001)	3.2 × 10 <sup>-8</sup>	-0.003(0.001)	7.0 × 10 <sup>-5</sup>	-0.005(0.001)	1.8 × 10 <sup>-10</sup>
rs5760485	22	23311027	<i>C22orf36</i>	INTRONIC	C	0.31	0.006(0.001)	9.4 × 10 <sup>-6</sup>	0.007(0.002)	4.2 × 10 <sup>-6</sup>	0.007(0.001)	2.2 × 10 <sup>-10</sup>
rs4820599	22	23314767	<i>GGT1</i>	INTRONIC	G	0.31	0.006(0.001)	3.9 × 10 <sup>-6</sup>	0.008(0.002)	1.8 × 10 <sup>-6</sup>	0.007(0.001)	4.0 × 10 <sup>-11</sup>
<b>ALP</b>												
rs10799701	1	21566296	<i>NBPF3-ALPL</i>	INTERGENIC	A	0.43	0.031(0.005)	1.9 × 10 <sup>-10</sup>	0.032(0.008)	4.2 × 10 <sup>-5</sup>	0.031(0.004)	3.6 × 10 <sup>-14</sup>
rs1780324	1	21567063	<i>NBPF3-ALPL</i>	INTERGENIC	T	0.43	0.032(0.005)	1.4 × 10 <sup>-10</sup>	0.031(0.007)	1.0 × 10 <sup>-5</sup>	0.031(0.004)	7.0 × 10 <sup>-15</sup>
rs9295624	6	24547579	<i>GPLD1</i>	INTRONIC	A	0.23	0.031(0.006)	1.8 × 10 <sup>-7</sup>	0.031(0.009)	7.2 × 10 <sup>-4</sup>	0.031(0.005)	4.9 × 10 <sup>-10</sup>

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rs9461011	6	24548330	<i>GPLD1</i>	INTRONIC	G	0.23	0.033(0.006)	$4.4 \times 10^{-8}$	0.030(0.009)	0.001	0.032(0.005)	$1.9 \times 10^{-10}$
rs9467160	6	24549725	<i>GPLD1</i>	INTRONIC	A	0.24	0.033(0.006)	$2.2 \times 10^{-8}$	0.035(0.009)	$1.3 \times 10^{-4}$	0.034(0.005)	$1.2 \times 10^{-11}$
rs9461012	6	24549823	<i>GPLD1</i>	INTRONIC	A	0.23	0.034(0.006)	$1.4 \times 10^{-8}$	0.030(0.009)	$8.6 \times 10^{-4}$	0.033(0.005)	$5.0 \times 10^{-11}$
rs17247566	6	24558383	<i>GPLD1</i>	INTRONIC	T	0.25	0.028(0.006)	$1.7 \times 10^{-6}$	0.027(0.008)	0.002	0.027(0.005)	$9.6 \times 10^{-9}$
rs8176720	9	133162427	<i>ABO</i>	SYNONYMOUS	G	0.32	0.031(0.005)	$1.4 \times 10^{-8}$	0.031(0.008)	$7.0 \times 10^{-5}$	0.031(0.004)	$4.3 \times 10^{-12}$
rs641959	9	133163253	<i>ABO</i>	INTRONIC	G	0.26	0.035(0.006)	$6.8 \times 10^{-10}$	0.024(0.008)	0.004	0.031(0.005)	$2.1 \times 10^{-11}$
rs514708	9	133163297	<i>ABO</i>	INTRONIC	T	0.26	0.035(0.006)	$6.2 \times 10^{-10}$	0.024(0.008)	0.004	0.031(0.005)	$1.9 \times 10^{-11}$
rs672316	9	133167679	<i>ABO</i>	INTRONIC	C	0.27	0.032(0.006)	$1.4 \times 10^{-8}$	0.023(0.008)	0.006	0.029(0.005)	$4.4 \times 10^{-10}$
rs657152	9	133168819	<i>ABO</i>	INTRONIC	T	0.39	-0.057(0.005)	$4.6 \times 10^{-29}$	-0.029(0.007)	$4.9 \times 10^{-5}$	-0.047(0.004)	$1.7 \times 10^{-30}$
rs474279	9	133169171	<i>ABO</i>	INTRONIC	T	0.24	0.030(0.006)	$3.4 \times 10^{-7}$	0.023(0.008)	0.006	0.028(0.005)	$8.3 \times 10^{-9}$
rs552148	9	133183035	<i>ABO</i>	UPSTREAM	T	0.24	0.032(0.006)	$3.1 \times 10^{-8}$	0.022(0.008)	0.008	0.029(0.005)	$1.2 \times 10^{-9}$
rs12355784	10	64791571	<i>JMJD1C</i>	INTRONIC	A	0.48	0.026(0.005)	$4.7 \times 10^{-7}$	0.025(0.007)	$2.7 \times 10^{-4}$	0.025(0.004)	$5.0 \times 10^{-10}$
rs10761779	10	64944933	<i>REEP3</i>	INTERGENIC	G	0.49	0.025(0.005)	$3.9 \times 10^{-7}$	0.024(0.007)	$4.5 \times 10^{-4}$	0.025(0.004)	$6.9 \times 10^{-10}$

<sup>a</sup> Position and minor allele are of NCBI Build 35

<sup>b</sup> Minor allele corresponds to forward strand

<sup>c</sup> MAF: Minor allele frequency. It is based on CoLaus study

**Table S4:** Minor allele frequency, proportion of variance and heterogeneity for 32 SNPs associated with plasma liver enzymes levels across discovery and replication datasets.

SNP	CHR	Nearest gene	Minor Allele	Proportion of Variance for the trait	p-val for heterogeneity	MAF					
						Discovery Sets			Replication Sets		
						ALT	CoLaus	LOLIPOP	InCHIANTI	Indian Asian (Illumina)	Indian Asian (Perlegen)
rs11597390	10	<i>CPN1</i>	A	0.3	0.748	0.38	0.36	0.41	0.15	0.17	0.37
rs2862990	10	<i>ERLIN1</i>	T	0.3	0.723	0.42	0.40	0.46	0.23	0.23	0.40
rs7913374	10	<i>ERLIN1</i>	G	0.3	0.771	0.41	0.39	0.46	0.23	0.23	0.40
rs11594333	10	<i>ERLIN1</i>	T	0.3	0.791	0.43	0.41	0.46	0.23	0.23	0.40
rs11597086	10	<i>CHUK</i>	C	0.2	0.821	0.43	0.42	0.44	0.17	0.17	0.37
rs11591741	10	<i>CHUK</i>	C	0.2	0.732	0.43	0.42	0.46	0.16	0.17	0.44
rs2076211	22	<i>PNPLA3</i>	A	0.4	0.273	0.18	0.14	0.18	0.20	0.21	0.37
rs2281135	22	<i>PNPLA3</i>	T	0.4	0.392	0.18	0.15	0.19	0.21	0.21	0.19
rs2073081	22	<i>PNPLA3</i>	C	0.4	0.449	0.18	0.15	0.19	0.21	0.21	0.18
rs2143571	22	<i>SAMM50</i>	A	0.2	0.341	0.19	0.18	0.20	0.19	0.24	0.19
GGT						CoLaus	LOLIPOP	InCHIANTI	Indian Asian (Illumina)	Indian Asian (Perlegen)	Caucasian (Perlegen)
rs7953249	12	<i>C12orf27</i>	G	0.6	0.003	0.43	0.41	0.47	0.55	0.49	0.41
rs2393791	12	<i>HNF1A</i>	G	0.6	0.146	0.40	0.38	0.45	0.51	0.48	0.38
rs2259816	12	<i>HNF1A</i>	A	0.4	0.014	0.37	0.36	0.42	0.50	0.45	0.36
rs1169313	12	<i>HNF1A-C12orf43</i>	C	0.4	0.014	0.38	0.36	0.42	0.49	0.55	0.36
rs5760485	22	<i>C22orf36</i>	C	0.4	0.197	0.31	0.30	0.30	0.36	0.29	0.32
rs4820599	22	<i>GGT1</i>	G	0.4	0.266	0.31	0.30	0.30	0.36	0.29	0.32
ALP						CoLaus	LOLIPOP	InCHIANTI	Indian Asian (Illumina)	Indian Asian (Perlegen)	Caucasian (Perlegen)
rs10799701	1	<i>NBPF3-ALPL</i>	A	0.6	0.766	0.43	0.46	0.45	0.49	0.45	0.46
rs1780324	1	<i>NBPF3-ALPL</i>	T	0.6	0.789	0.43	0.46	0.45	0.48	0.43	0.46
rs9295624	6	<i>GPLD1</i>	A	0.4	0.341	0.23	0.26	0.18	0.18	0.18	0.25
rs9461011	6	<i>GPLD1</i>	G	0.4	0.355	0.23	0.26	0.18	0.18	0.18	0.25
rs9467160	6	<i>GPLD1</i>	A	0.5	0.580	0.24	0.28	0.19	0.20	0.21	0.27
rs9461012	6	<i>GPLD1</i>	A	0.4	0.342	0.23	0.26	0.18	0.18	0.18	0.25
rs17247566	6	<i>GPLD1</i>	T	0.3	0.620	0.25	0.29	0.20	0.21	0.20	0.28
rs8176720	9	<i>ABO</i>	G	0.5	0.859	0.32	0.33	0.33	0.49	0.44	0.32
rs641959	9	<i>ABO</i>	G	0.5	0.888	0.26	0.27	0.26	0.23	0.23	0.26
rs514708	9	<i>ABO</i>	T	0.5	0.898	0.26	0.27	0.26	0.23	0.23	0.26
rs672316	9	<i>ABO</i>	C	0.4	0.958	0.27	0.28	0.26	0.22	0.22	0.25
rs657152	9	<i>ABO</i>	T	2.0	0.010	0.39	0.34	0.38	0.50	0.42	0.36
rs474279	9	<i>ABO</i>	T	0.3	0.938	0.24	0.25	0.23	0.21	0.22	0.23
rs552148	9	<i>ABO</i>	T	0.4	0.900	0.24	0.25	0.24	0.21	0.21	0.23
rs12355784	10	<i>JMJD1C</i>	A	0.4	0.575	0.48	0.44	0.47	0.52	0.54	0.49
rs10761779	10	<i>REEP3</i>	G	0.4	0.700	0.49	0.47	0.48	0.52	0.54	0.49

**Figure S1.** Genomic context plot (using WGAviewer<sup>41</sup>, Hapmap build36) for ALT signal at *CPN1-CHUK* region on chromosome 10 identified through genotyping and imputation from meta-analysis of three discovery datasets. Panel **A**: Ideogram of chromosome 10; Panel **B**:  $-\log_{10} p$ -values for imputed SNPs. SNPs with  $p$ -value  $\leq 1 \times 10^{-8}$  are in red; Panel **C**:  $-\log_{10} p$ -values for Affymetrix genotyped SNPs; Panel **D**: Known genes track in the region. Panel **E**: LD plot in CEU.

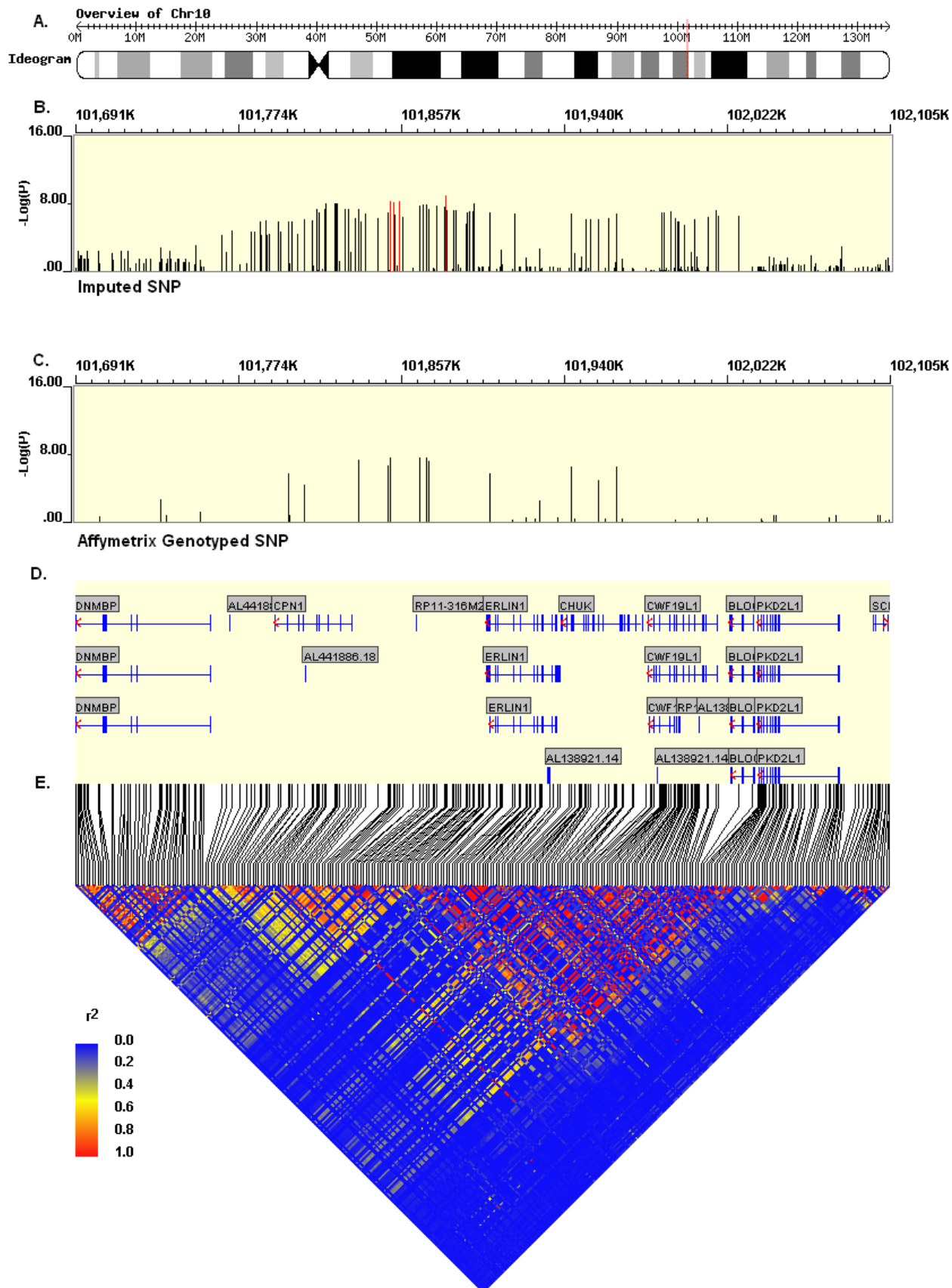
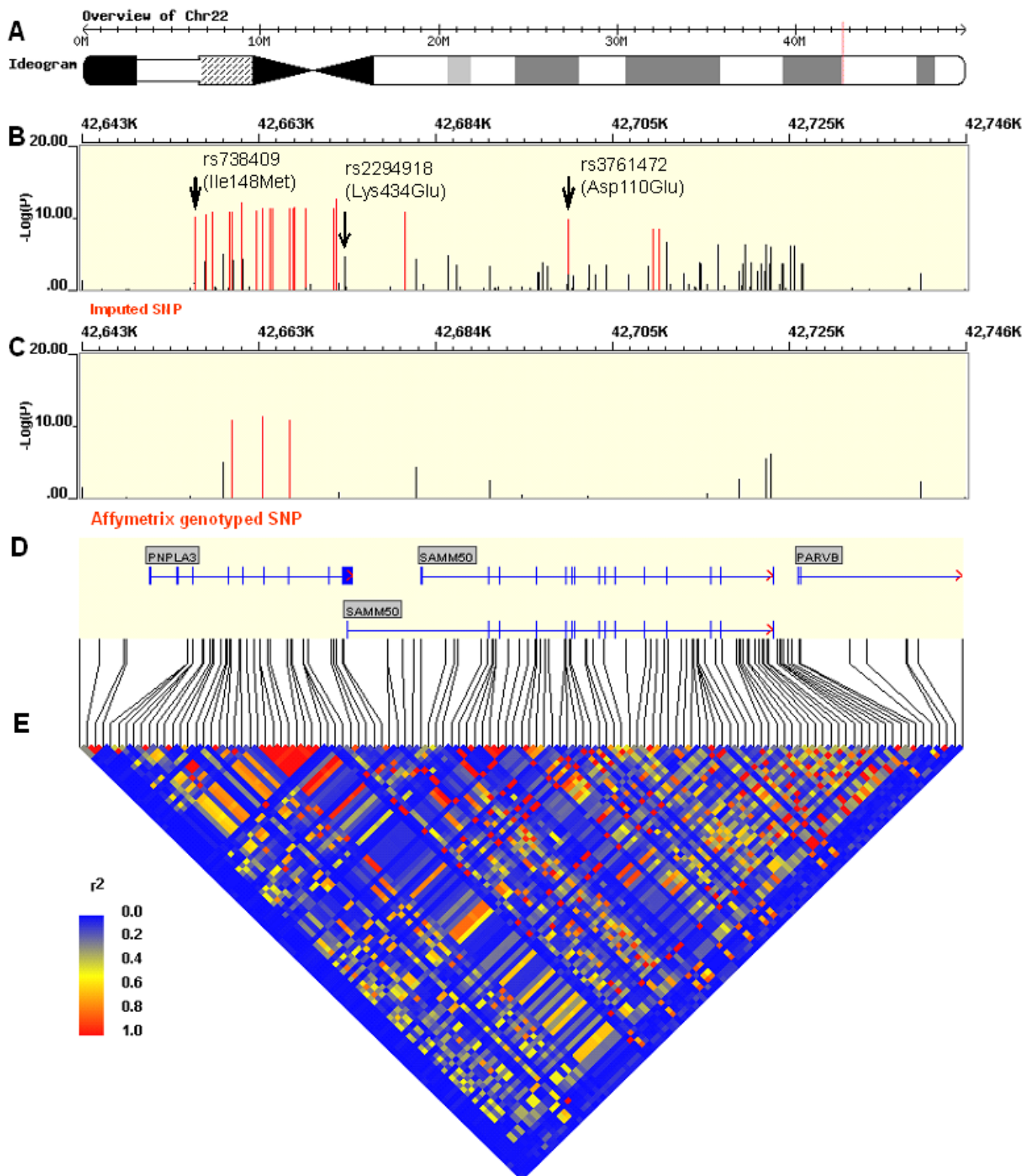




Figure S2. ALT signal region at *PNPLA3-SAMM50* on chromosome 22.



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 Figure S3. GGT1 signal region at *GGT1* on chromosome 22.

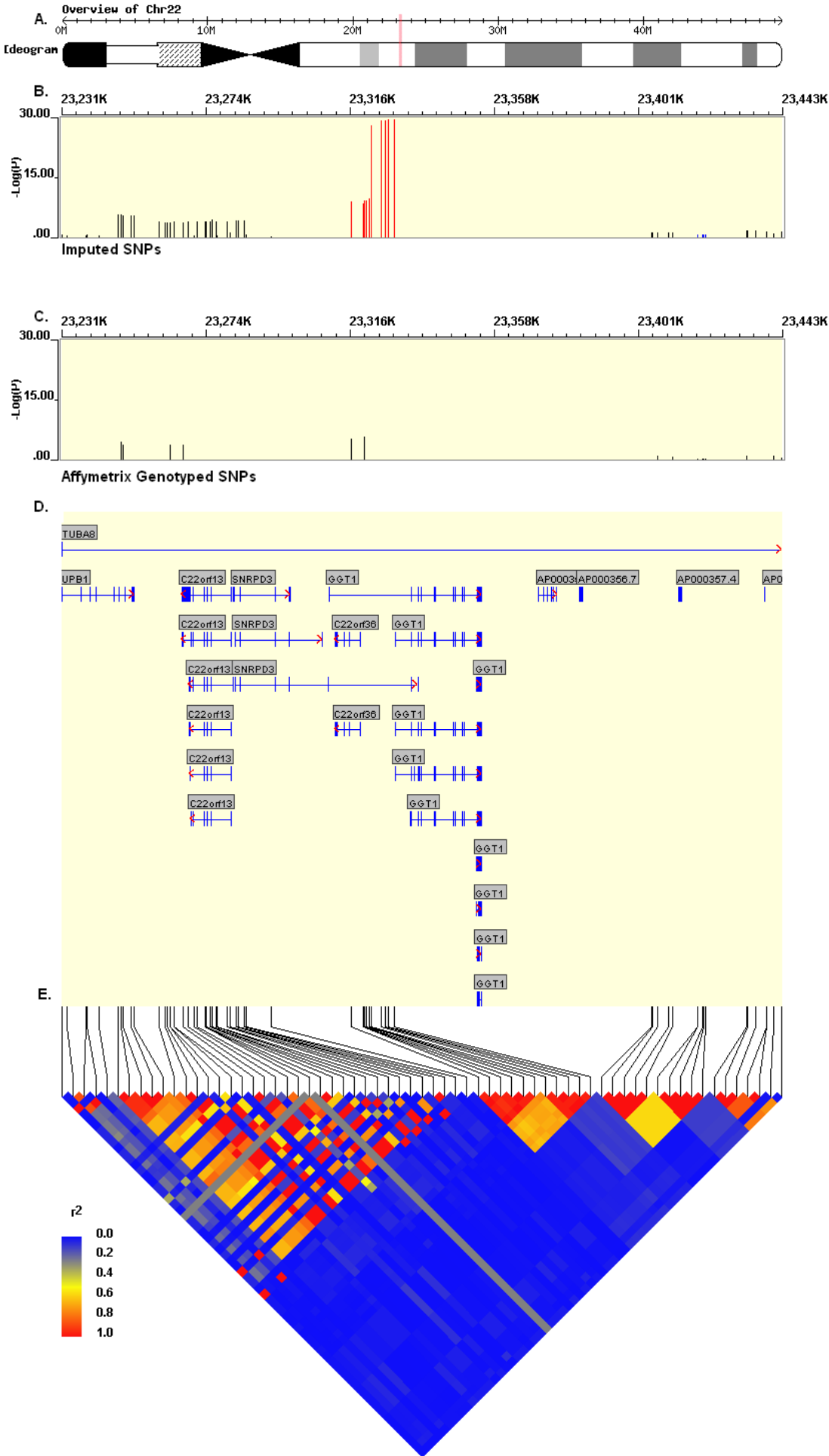


Figure S4. GGT signal region at *HNF1A* on chromosome 12.

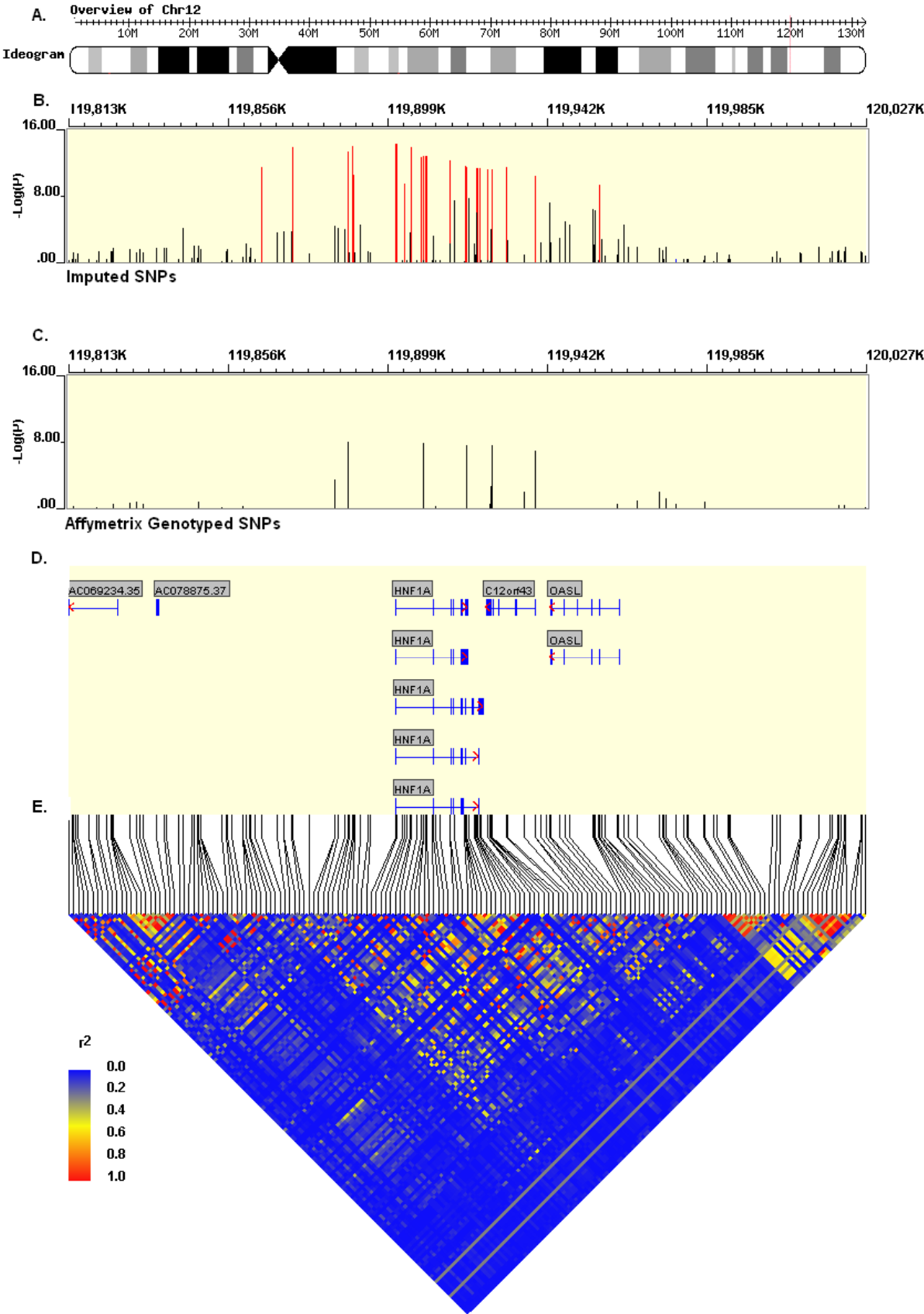


Figure S5. ALP signal region at *ABO* on chromosome 9.

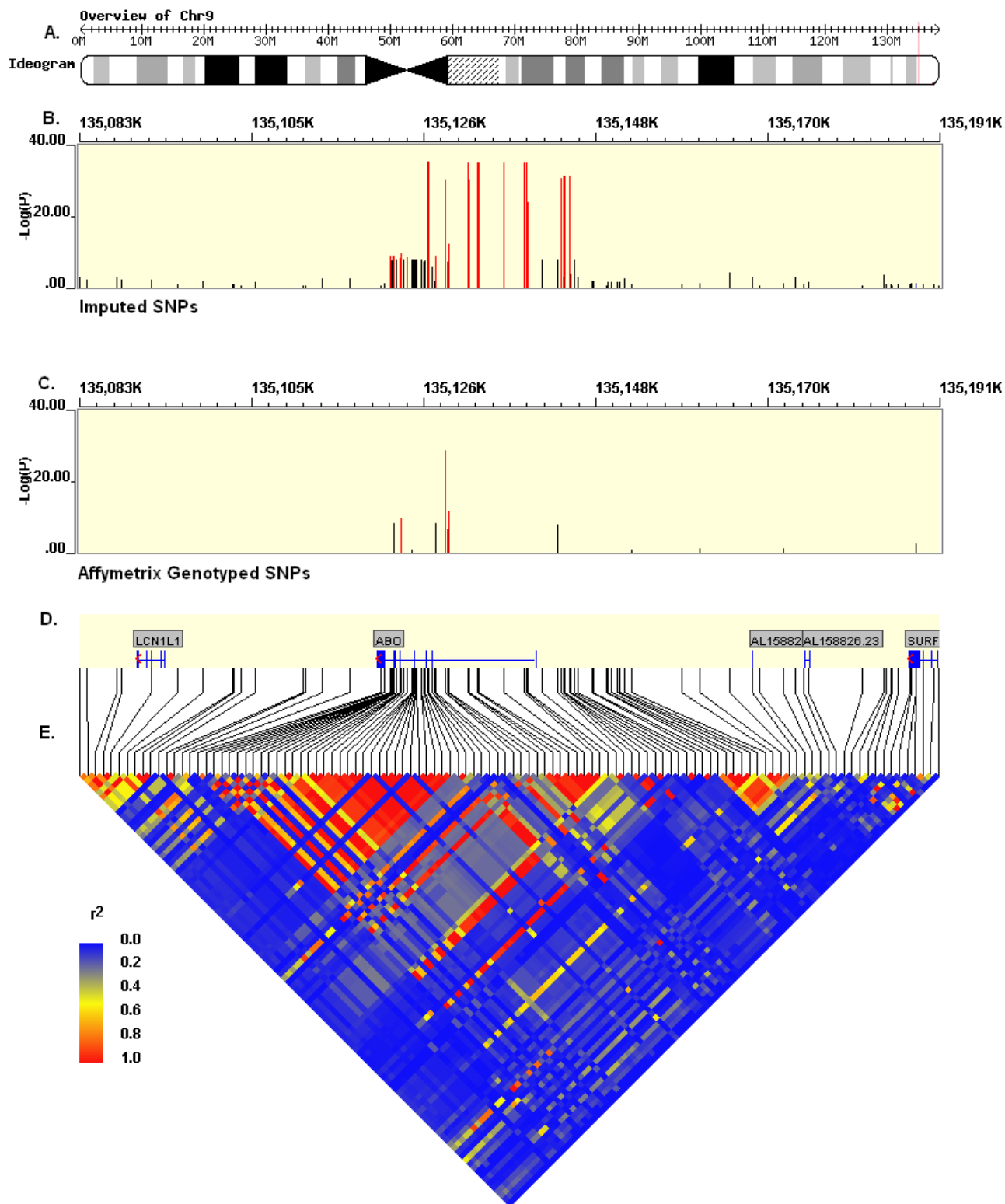


Figure S6. ALP signal at *NBPF3-ALPL* region on chromosome 1.

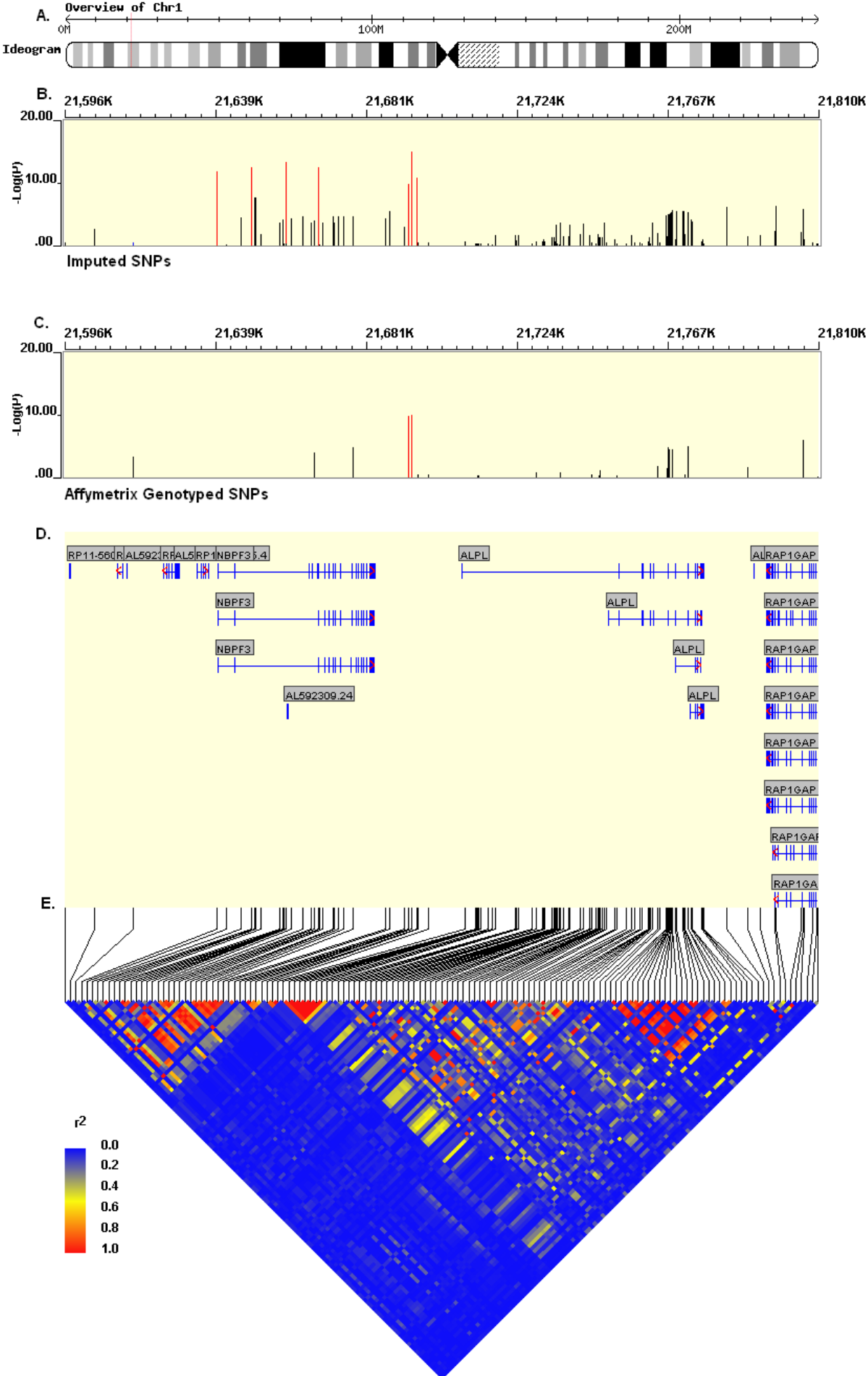




Figure S7. ALP signal at *GPLD1* region on chromosome 6.

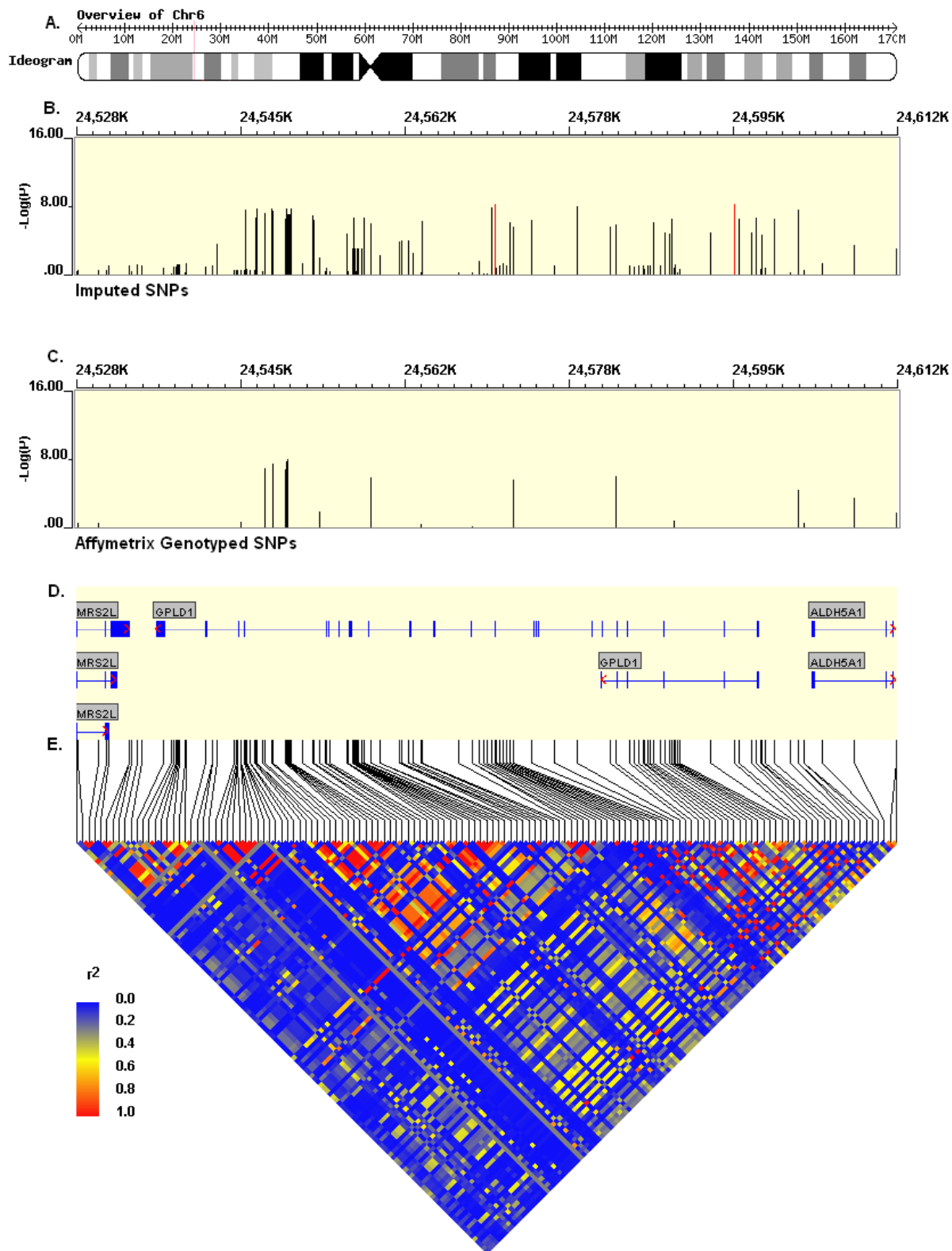
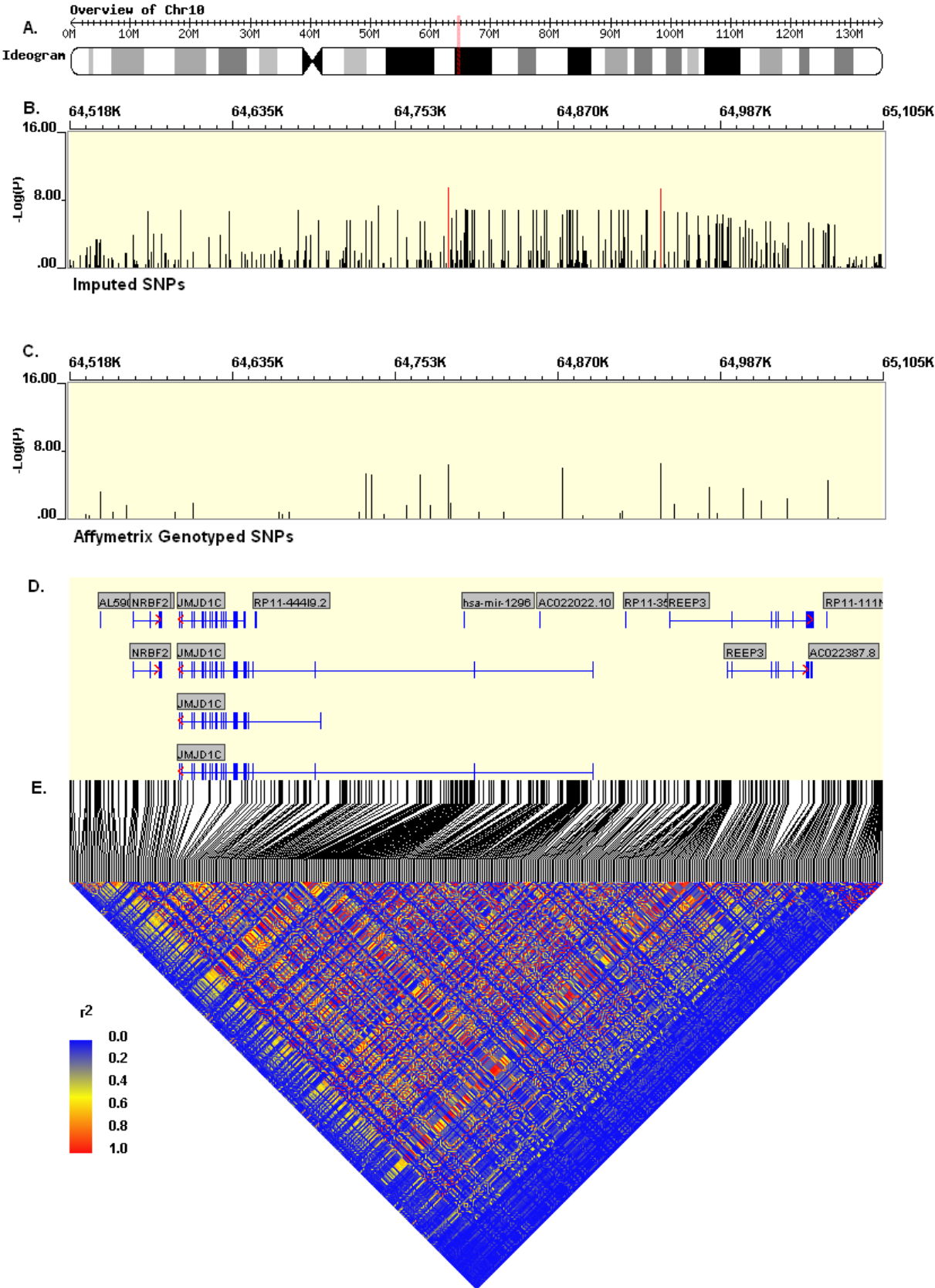
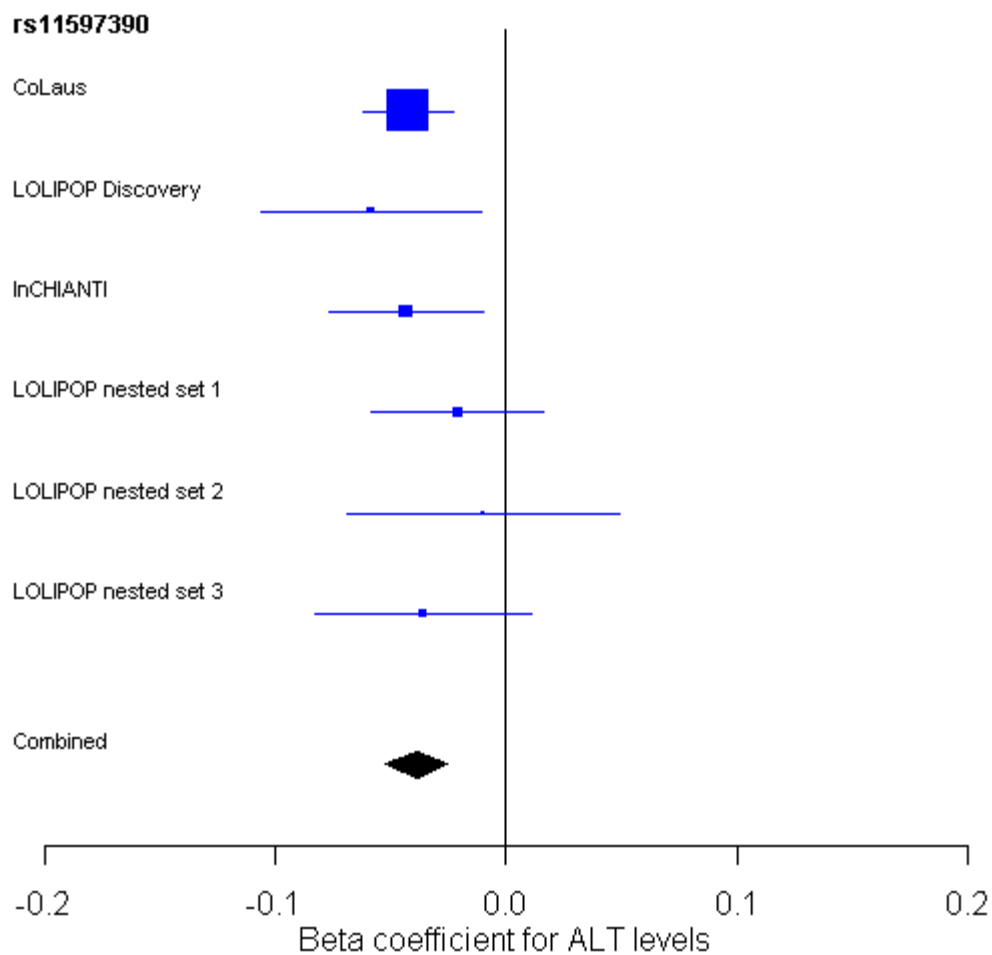


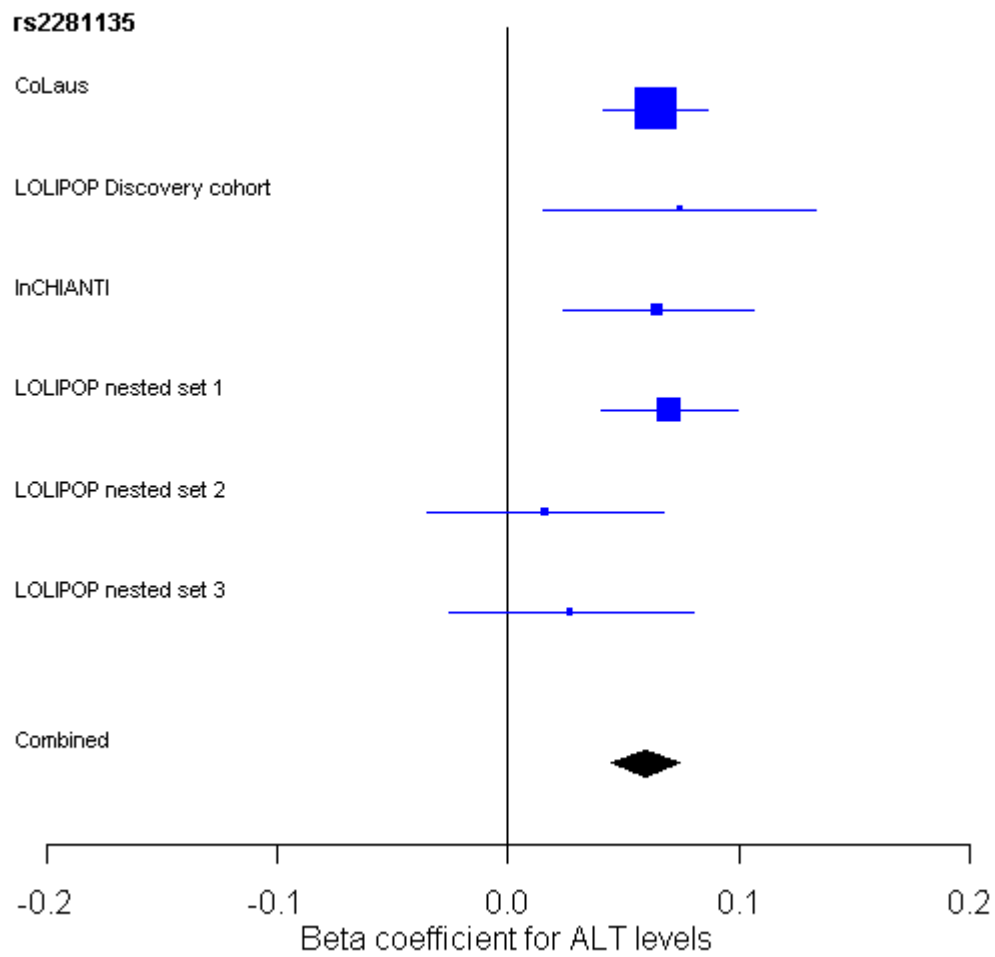
Figure S8. ALP signal at *JMJD1C-REEP3* on chromosome 10.





**Figure S9. Association between rs11597390 and plasma ALT levels.** For individual studies  $\beta$ -coefficients are depicted by blue boxes and spanned by 95% CI. Diamond represents combined  $\beta$ -coefficient and the width of the diamond delineate its 95% CI.





**Figure S10. Association between rs2281135 and plasma ALT levels.**

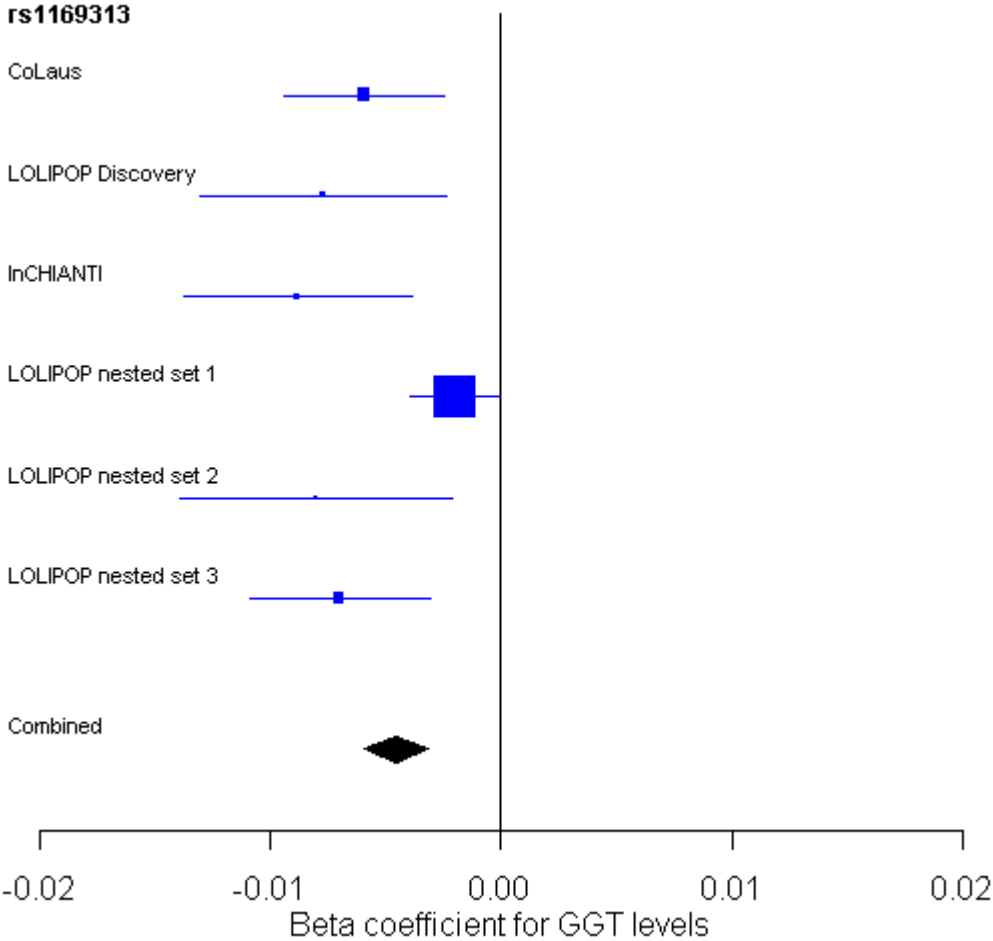
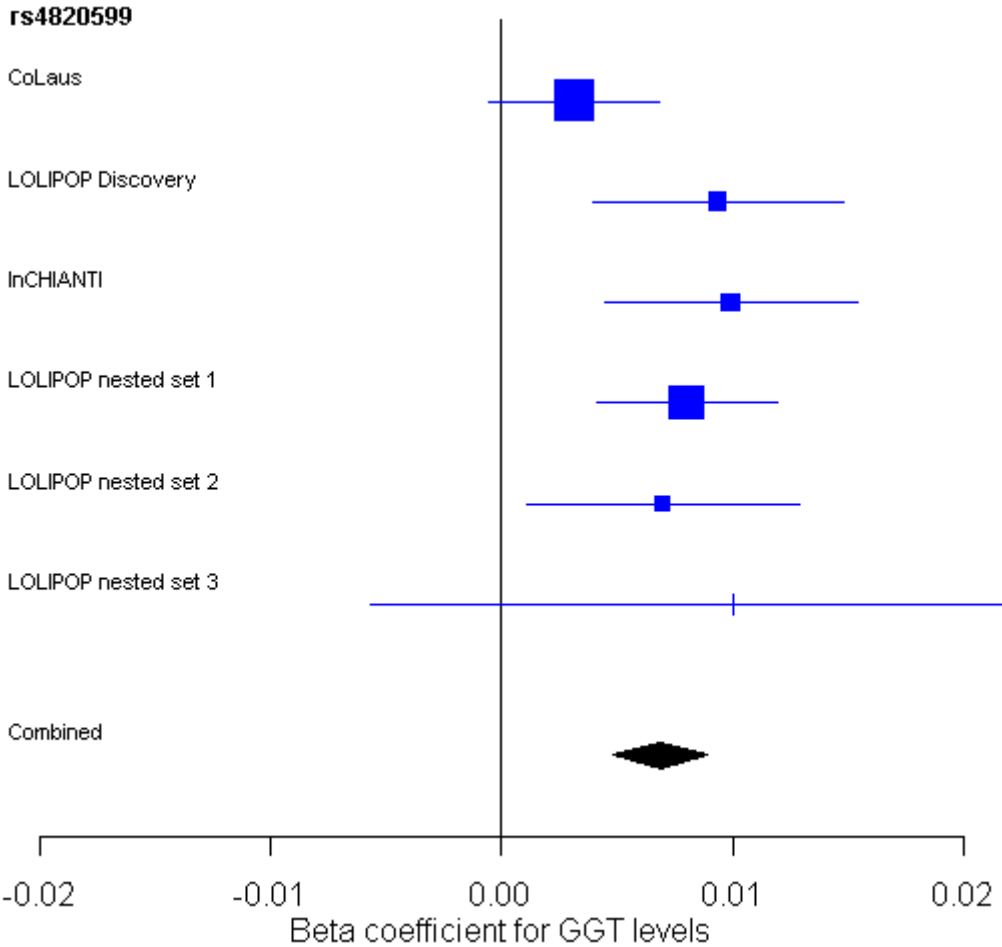
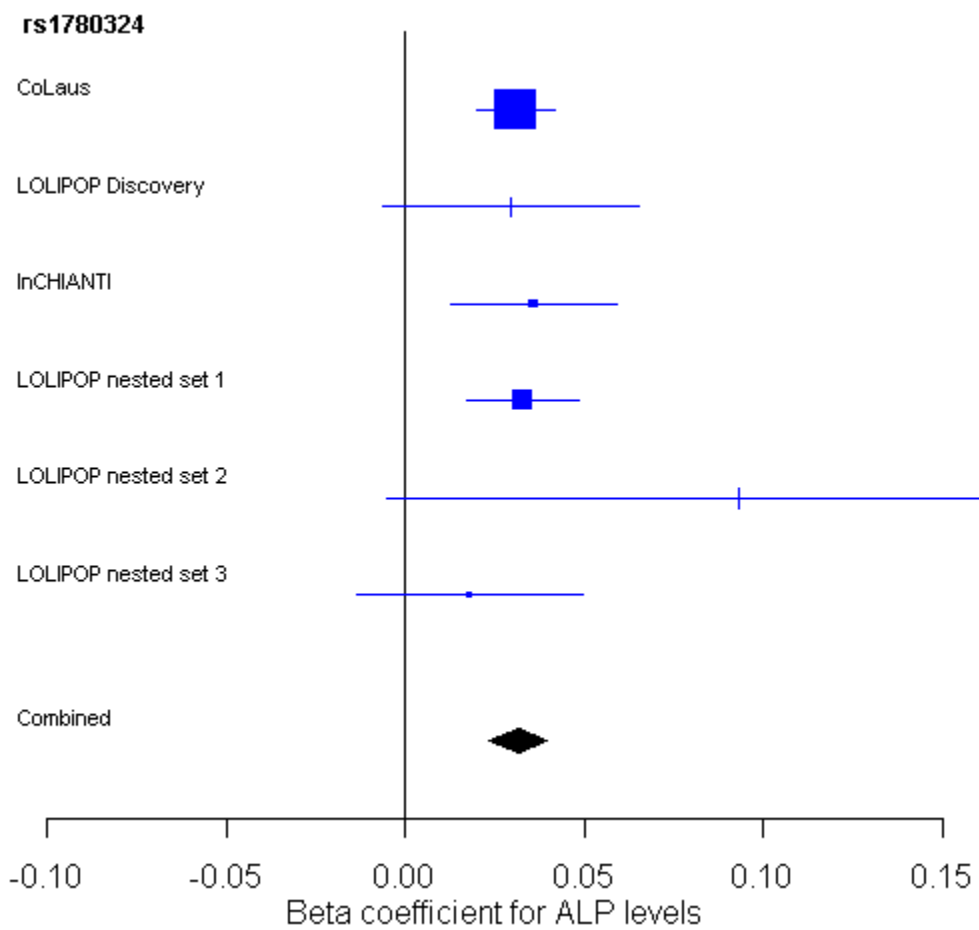


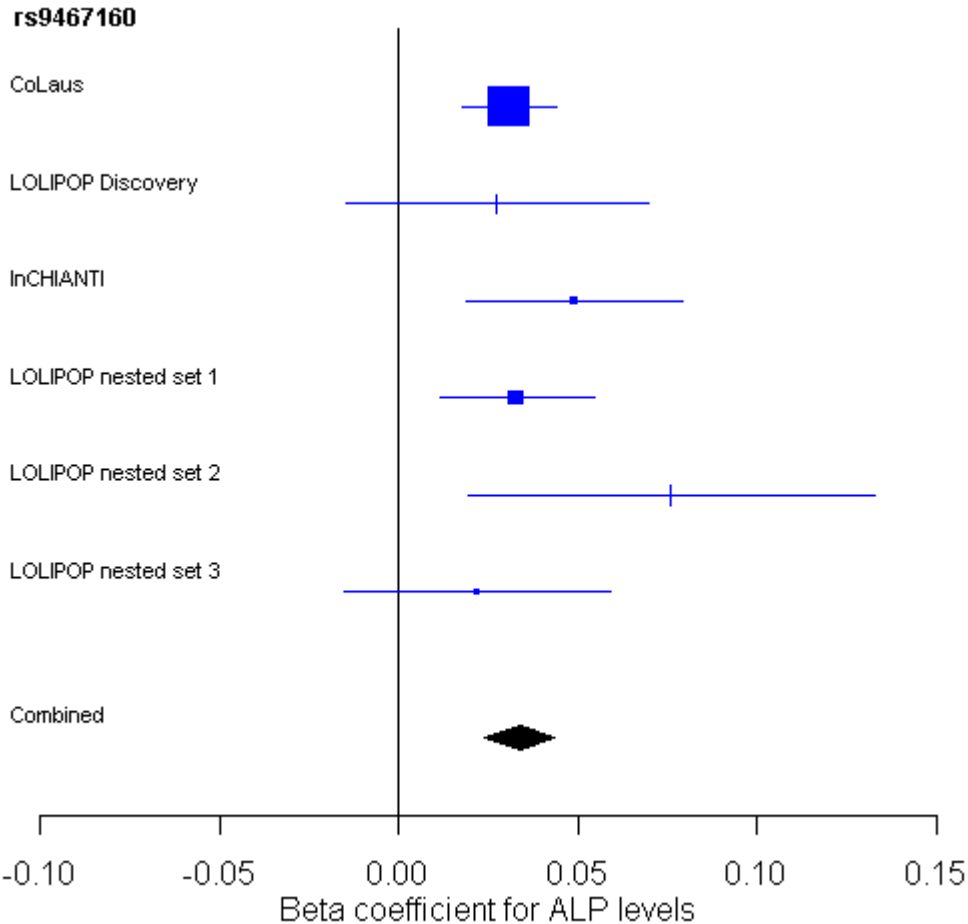
Figure S11. Association between rs1169313 and plasma GGT levels.



**Figure S12. Association between rs4820599 and plasma GGT levels.**



**Figure S13. Association between rs1780324 and plasma ALP levels.**



**Figure S14. Association between rs9467160 and plasma ALP levels.**

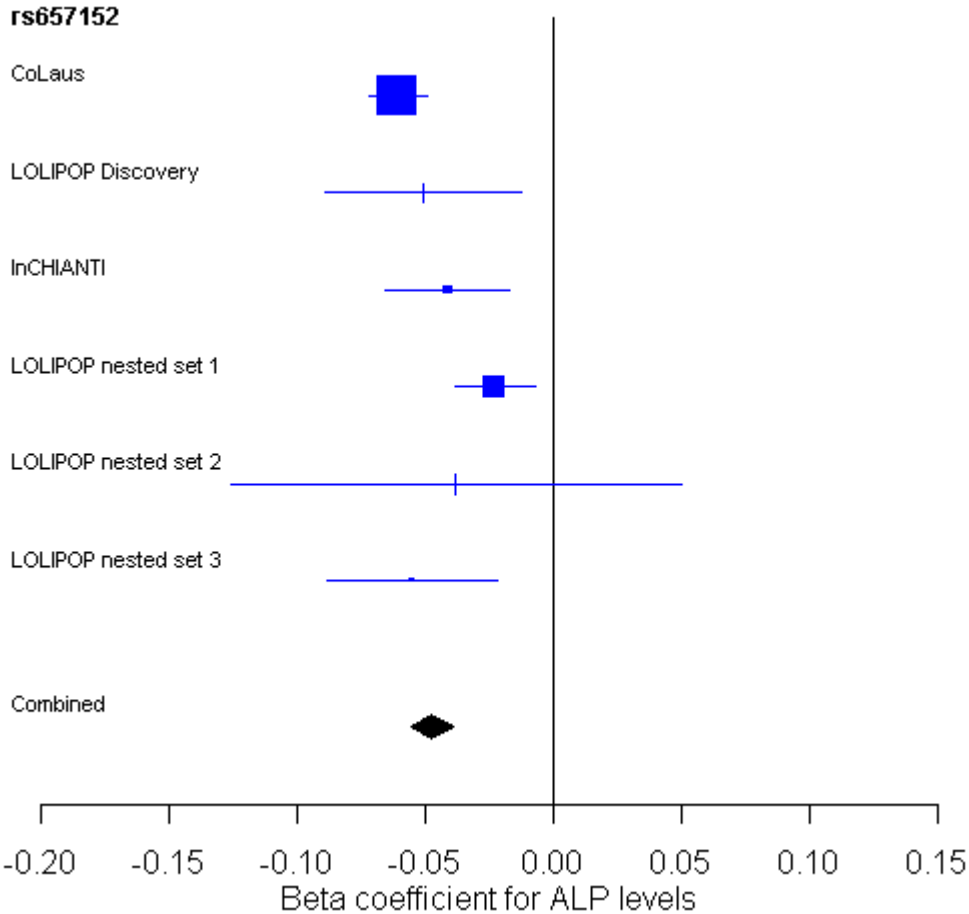
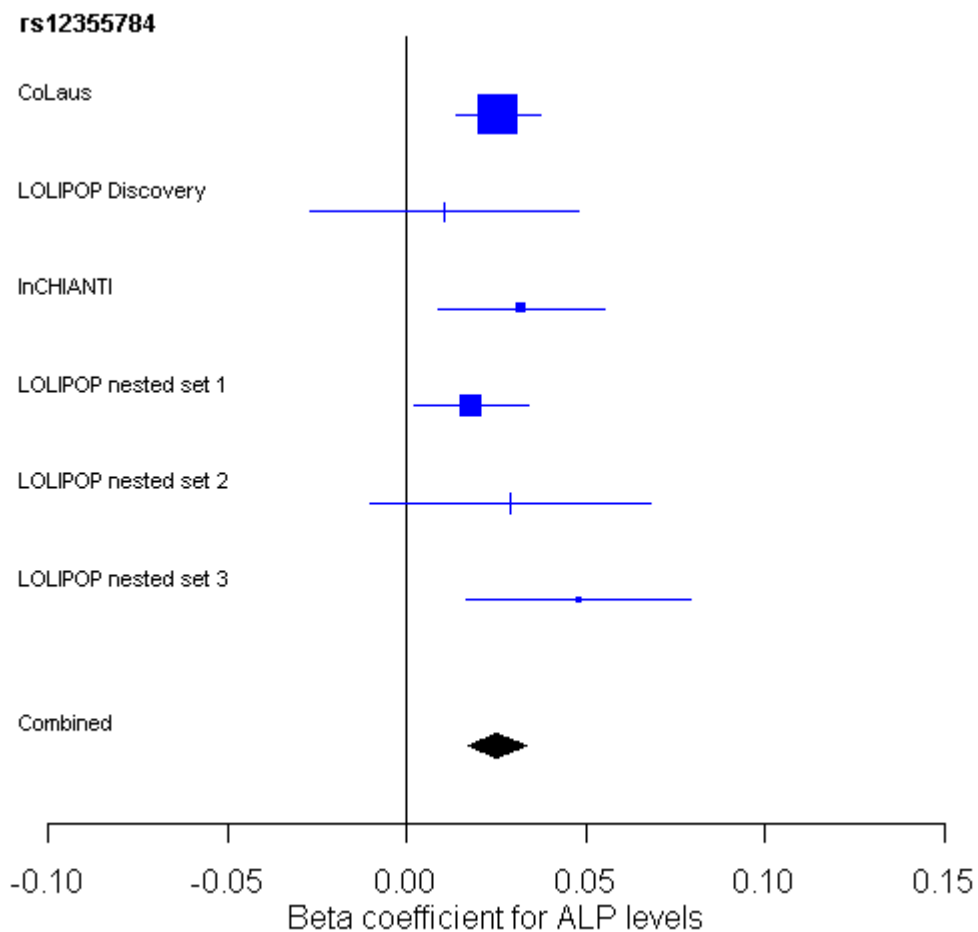


Figure S15. Association between rs657152 and plasma ALP levels.



**Figure S16. Association between rs12355784 and plasma ALP levels.**

Supplemental Reference

41. Ge, D., Zhang, K., Need, A. C., Martin, O., Fellay, J., Urban, T. J., Telenti, A., and Goldstein, D. B. (2008) WGAViewer: software for genomic annotation of whole genome association studies. *Genome Res.* 18:640-643