

Supplementary Material

Table 1: Top-ranked SNPs from GWAS association with NODAT ($p \leq 10^{-5}$)

SNP	Gene	Location	OR	95%CI	p
rs7533125	<i>DNAJC16</i>	1:15883744	4.6	2.4 - 8.6	3.4×10^{-6}
rs2020902	<i>CASP9</i>	1:15834360	4.0	2.2 - 7.2	4.5×10^{-6}
rs3212574	<i>ITGA2</i>	5:52366779	4.1	2.2 - 7.8	1.1×10^{-5}
rs2861484	<i>CELA2B</i>	1:15812665	4.2	2.2 - 8.1	1.3×10^{-5}
rs2265477	<i>SHPRH</i>	6:146212338	4.4	2.2 - 8.7	2.8×10^{-5}
rs11580170	<i>AGMAT</i>	1:15909744	3.7	2.0 - 6.8	2.9×10^{-5}
rs17657199	<i>NDST1</i>	5:149950246	8.8	3.2 - 24.8	3.3×10^{-5}
rs1783606	<i>SHANK2</i>	11:70576651	4.4	2.2 - 8.9	4.1×10^{-5}
rs6903252	<i>intergenic</i>	6:145922777	4.4	2.2 - 8.8	4.4×10^{-5}
rs1871184	<i>ITGA1</i>	5:52234323	4.3	2.1 - 8.7	4.4×10^{-5}
rs198372	<i>NPPA</i>	1:11909514	3.9	2.0 - 7.6	5.0×10^{-5}
rs2240747	<i>ZNRF4</i>	19:5456930	4.7	2.2 - 9.8	5.1×10^{-5}
rs4394754	<i>INPP5A</i>	10:134343062	3.6	1.9 - 6.8	5.2×10^{-5}
rs1836882	<i>NOX4</i>	11:89232161	4.3	2.1 - 8.6	5.3×10^{-5}
rs341497	<i>DIAPH3</i>	13:60429001	6.5	2.6 - 16.1	5.4×10^{-5}
rs10117679	<i>GRIN3A</i>	9:104378479	8.1	2.9 - 22.3	5.6×10^{-5}
rs16936667	<i>PRDM14</i>	8:70975726	4.3	2.1 - 8.6	5.9×10^{-5}
rs10899444	<i>SHANK2</i>	11:70606500	4.1	2.0 - 8.0	6.2×10^{-5}
rs2265917	<i>SHPRH</i>	6:146212285	3.9	2.0 - 7.6	6.3×10^{-5}
rs2265919	<i>SHPRH</i>	6:146221753	3.9	2.0 - 7.6	6.3×10^{-5}
rs1370602	<i>NCKAP5</i>	2:133688972	4.0	2.0 - 7.9	6.7×10^{-5}
rs10484821	<i>ATP5F1P6</i>	6:139868910	4.0	2.0 - 7.9	7.3×10^{-5}
rs17722392	<i>KIDINS220</i>	2:8940154	6.2	2.5 - 15.4	8.1×10^{-5}
rs1016429	<i>GRIN3A</i>	9:104402364	5.6	2.4 - 13.3	8.2×10^{-5}
rs6793265	<i>ITPR1</i>	3:4735533	4.2	2.0 - 8.7	9.1×10^{-5}
rs7145618	<i>PPP2R5C</i>	14:102329098	5.8	2.4 - 13.9	9.5×10^{-5}

Table 2: GWAS results for SNPs previously reported to be associated with NODAT

SNP	Proxy SNP	r^2	OR	95% CI	p
rs8192678	NA	NA	1.8	1.0 - 3.3	0.04
rs1169288	rs2650000	0.922	1.7	0.9 - 3.0	0.09
rs1799854	NA	NA	1.6	0.9 - 2.8	0.1
rs1494558	NA	NA	0.6	0.3 - 1.2	0.2
rs2172749	rs1494558	1	0.6	0.3 - 1.2	0.2
rs7903146	NA	NA	1.5	0.8 - 2.7	0.2
rs5219	NA	NA	0.7	0.4 - 1.3	0.2
rs1124053	rs3759614	0.81	1.5	0.8 - 2.9	0.3
rs2069763	rs4505848	1	0.7	0.3 - 1.4	0.3
rs2280789	rs2306630	1	0.5	0.2 - 1.8	0.3
rs13266634	NA	NA	1.4	0.7 - 2.5	0.3
rs1025689	rs7627178	1	1.3	0.7 - 2.4	0.3
rs2430561	rs2069727	1	1.3	0.7 - 2.3	0.4
rs4819554	rs2041629	0.954	1.3	0.7 - 2.5	0.4
rs12255372	NA	NA	1.3	0.7 - 2.4	0.4
rs1043261	NA	NA	0.7	0.2 - 2.3	0.5
rs2144908	rs4812829	1	0.8	0.3 - 1.9	0.6
rs2069762	rs6835946	0.951	1.2	0.7 - 2.0	0.6
rs1801282	rs6802898	1	0.8	0.3 - 2.0	0.6
rs1044498	rs6926970	1	1.1	0.5 - 2.4	0.7
rs2340721	rs905594	0.925	1.1	0.6 - 2.0	0.8
rs3817655	rs2291299	1	0.9	0.4 - 2.0	0.8
rs2107538	rs2251660	0.858	1.1	0.5 - 2.5	0.8
rs2070874	rs2243290	1	0.9	0.4 - 2.2	0.8
rs1800795	rs1554606	0.868	0.9	0.5 - 1.7	0.8
rs1800961	NA	NA	-	0	1.0

Table 3: Association results for *de novo* genotyped SNPs with NODAT in the original discovery cohort and in the new cases from the second stage genotyping cohort

This table displays the odds ratios and p values for SNPs previously reported to be associated with NODAT and newly identified associations from the discovery GWAS in the cohort typed as part of the GWAS ($OR_{\text{discovery}}$ and $p_{\text{discovery}}$) and in the new cases genotyped in the second stage genotyping (OR_{new} and p_{new}). The overall odds ratios and p values from the second stage genotyping are recorded in Table 4. The failure of the p values to reach statistical significance in the new cases during second stage genotyping reflects the much smaller number of samples typed.

SNP	Gene	Location	$OR_{\text{discovery}}$	$p_{\text{discovery}}$	OR_{new}	p_{new}
rs10484821	<i>ATP5F1P6</i>	6:139868910	4.394	1.87×10^{-5}	2.986	0.000188
rs7533125	<i>DNAJC16</i>	1:15883744	3.944	3.12×10^{-6}	1.289	0.3682
rs2861484	<i>CELA2B</i>	1:15812665	3.735	6.52×10^{-6}	1.37	0.2797
rs11580170	<i>AGMAT</i>	1:15909744	3.288	3.53×10^{-5}	1.426	0.1783
rs2020902	<i>CASP9</i>	1:15834360	3.596	6.63×10^{-6}	1.151	0.6567
rs1836882	<i>NOX4</i>	11:89232161	4.108	0.000115	1.817	0.117
rs198372	<i>NPPA</i>	1:11909514	3.95	3.87×10^{-5}	1.366	0.3878
rs4394754	<i>INPP5A</i>	10:134343062	3.325	4.03×10^{-5}	1.144	0.6188
rs7145618	<i>PPP2R5C</i>	14:102329098	4.699	0.000185	1.176	0.7448
rs17722392	<i>KIDINS220</i>	2:8940154	5.397	0.000127	0.8648	0.8174
rs2265919	<i>SHPRH</i>	6:146221753	4.171	3.06×10^{-5}	1.052	0.8584
rs1783606	<i>SHANK2</i>	11:70576651	4.355	2.74×10^{-5}	0.7621	0.5452
rs2265477	<i>SHPRH</i>	6:146212338	4.233	3.33×10^{-5}	0.9246	0.7738
rs2069763*	<i>IL-2</i>	4:123377482	0.6453	0.2203	0.3988	0.01062
rs6903252	<i>Intergenic</i>	6:145922777	4.123	6.16×10^{-5}	0.9258	0.7766
rs2265917	<i>SHPRH</i>	6:146212285	3.666	9.73×10^{-5}	1.003	0.9905
rs10899444	<i>SHANK2</i>	11:70606500	4.279	3.50×10^{-5}	0.6258	0.3343
rs16936667	<i>PRDM14</i>	8:70975726	3.15	0.000606	0.9153	0.8542
rs341497	<i>DIAPH3</i>	13:60429001	4.556	0.000196	1.435	0.4422
rs1016429	<i>GRIN3A</i>	9:104402364	4.644	0.000121	0.7479	0.6309
rs10117679	<i>GRIN3A</i>	9:104378479	6.138	9.15×10^{-5}	1.006	0.993
rs1871184	<i>ITGA1</i>	5:52234323	2.84	0.000764	1.058	0.8777
rs3212574	<i>ITGA2</i>	5:52366779	3.345	4.97×10^{-5}	0.9083	0.7667
rs2240747	<i>ZNRF4</i>	19:5456930	2.98	0.001381	1.23	0.5472

rs6793265	<i>ITPR1</i>	3:4735533	3.62	0.000321	0.755	0.5355
rs2070874*	<i>IL-4</i>	5:132009710	0.6676	0.4028	0.4972	0.143
rs17657199	<i>NDST1</i>	5:149950246	3.777	0.006313	N/A	0.9967
rs2069762*	<i>IL-2</i>	4:123377980	1.337	0.3174	1.418	0.1674
rs7903146*	<i>TCF7L2</i>	10:114758349	1.3	0.4097	1.331	0.2887
rs1043261*	<i>IL-17RB</i>	3:53899276	0.4964	0.3419	0.5659	0.3498
rs2280789*	<i>CCL5</i>	17:34207003	0.5451	0.3133	0.8338	0.679
rs2172749*	<i>IL-7R</i>	5:35855264	0.671	0.2401	0.9203	0.7624
rs1494558*	<i>IL-7R</i>	5:35861068	0.6747	0.2487	0.9281	0.7868
rs1800795*	<i>IL-6</i>	7:22766645	1.092	0.7636	1.248	0.3803
rs12255372*	<i>TCF7L2</i>	10:114808902	1.344	0.3307	1.118	0.6824
rs5219*	<i>KCNJ11</i>	11:17409572	0.6043	0.1403	1.253	0.3902
rs2107538*	<i>CCL5</i>	17:34207780	0.7982	0.5864	0.7686	0.4778
rs1801282*	<i>PPARG</i>	3:12393125	0.7297	0.5144	0.9024	0.7936
rs3817655*	<i>CCL5</i>	17:34199641	0.8007	0.5916	0.7711	0.4831
rs1799854	<i>ABCC8</i>	11:17448704	1.475	0.1899	0.9902	0.9695
rs4819554*	<i>IL-17RA</i>	22:17565035	1.222	0.5391	0.5795	0.1248
rs1169288*	<i>HNF1A</i>	12:121416650	1.511	0.1829	0.8952	0.704
rs2340721*	<i>ATF6</i>	1:161849385	1.274	0.4272	1.226	0.4549
rs1025689*	<i>IL-17RB</i>	3:53883722	1.423	0.2569	0.9165	0.7621
rs1124053*	<i>IL-17E</i>	14:22914819	1.266	0.4435	0.9479	0.8514
rs2144908*	<i>HNF4A</i>	20:42985717	1.004	0.9927	0.7388	0.5759
rs8192678*	<i>PPARGC1A</i>	4:23815662	1.428	0.2349	0.5731	0.0643
rs13266634*	<i>SLC30A8</i>	8:118184783	1.245	0.4851	1.026	0.9367
rs1044498*	<i>ENPP1</i>	6:132172368	1.049	0.9078	0.9768	0.9486
rs1800961*	<i>HNF4A</i>	20:43042364	N/A	0.9966	N/A	0.9965

N/A - no minor alleles present in NODAT cases

* - SNPs previously reported to be associated with NODAT

Table 4: Information on SNPs failing second stage genotyping

[illegible]

Table 5: Top ranked (p <0.005) gene enrichment sets

Function	Type	Enrichment Score	Enrichment p-value
receptor complex	cellular component	10.7	0.00002
basal part of cell	cellular component	10.5	0.00003
postsynaptic density	cellular component	8.8	0.0002
intrinsic apoptotic signaling pathway	biological process	8.2	0.0003
ionotropic glutamate receptor complex	cellular component	7.9	0.0004
integrin complex	cellular component	7.9	0.0004
positive regulation of neuron apoptotic process	biological process	7.1	0.0009
protein serine/threonine phosphatase complex	cellular component	7.1	0.0009
positive regulation of neuron death	biological process	7.0	0.0009
collagen binding	molecular function	6.9	0.001
intrinsic apoptotic signaling pathway in response to DNA damage	biological process	6.9	0.001
regulation of apoptotic process	biological process	6.7	0.001
regulation of programmed cell death	biological process	6.7	0.001
apoptotic signaling pathway	biological process	6.6	0.001
regulation of execution phase of apoptosis	biological process	6.6	0.001
regulation of cell death	biological process	6.5	0.001
cellular response to growth factor stimulus	biological process	6.5	0.002
response to growth factor stimulus	biological process	6.4	0.002
positive regulation of catalytic activity	biological process	6.3	0.002
positive regulation of protein phosphorylation	biological process	6.0	0.002
neurotrophin TRK receptor signaling pathway	biological process	6.0	0.002
neurotrophin signaling pathway	biological process	6.0	0.002
cellular response to radiation	biological process	6.0	0.002
integrin-mediated signaling pathway	biological process	5.9	0.003
positive regulation of phosphorylation	biological process	5.9	0.003
homeostatic process	biological process	5.9	0.003
spermidine biosynthetic process	biological process	5.8	0.003
putrescine biosynthetic process	biological process	5.8	0.003
oxygen sensor activity	molecular function	5.8	0.003
apoptosome	cellular component	5.8	0.003

PH domain binding	molecular function	5.8	0.003
inositol-1,3,4,5-tetrakisphosphate 5-phosphatase activity	molecular function	5.8	0.003
platelet dense tubular network	cellular component	5.8	0.003
starch binding	molecular function	5.8	0.003
cell-matrix adhesion	biological process	5.8	0.003
macromolecular complex	cellular component	5.8	0.003
cellular homeostasis	biological process	5.7	0.003
tissue homeostasis	biological process	5.7	0.003
GKAP/Homer scaffold activity	molecular function	5.5	0.004
inositol-1,4,5-trisphosphate 5-phosphatase activity	molecular function	5.5	0.004
inositol 1,4,5-trisphosphate-sensitive calcium-release channel activity	molecular function	5.5	0.004
calcineurin complex	cellular component	5.5	0.004
positive regulation of phosphorus metabolic process	biological process	5.5	0.004
positive regulation of phosphate metabolic process	biological process	5.5	0.004
positive regulation of molecular function	biological process	5.5	0.004
amino acid binding	molecular function	5.4	0.004
signal transduction in response to DNA damage	biological process	5.4	0.004

Regional association plots highlighting the genomic context and local significance values for all SNPs selected for second stage genotyping, Initially the SNPs identified from the GWAS and secondly, those previously reported to be associated with NODAT. Each circle represents a SNP; with proximal SNPs to the index SNP color coded according to linkage disequilibrium based on HapMap Phase II CEU reference data (Plotted SNPs). Known functional SNPs are indicated with symbols other than filled circles. Blue lines indicate the recombination rate (cM/Mb).

(i) SNPs associated with NODAT ($p < 10^{-5}$) from GWAS

Figure 1: rs198372

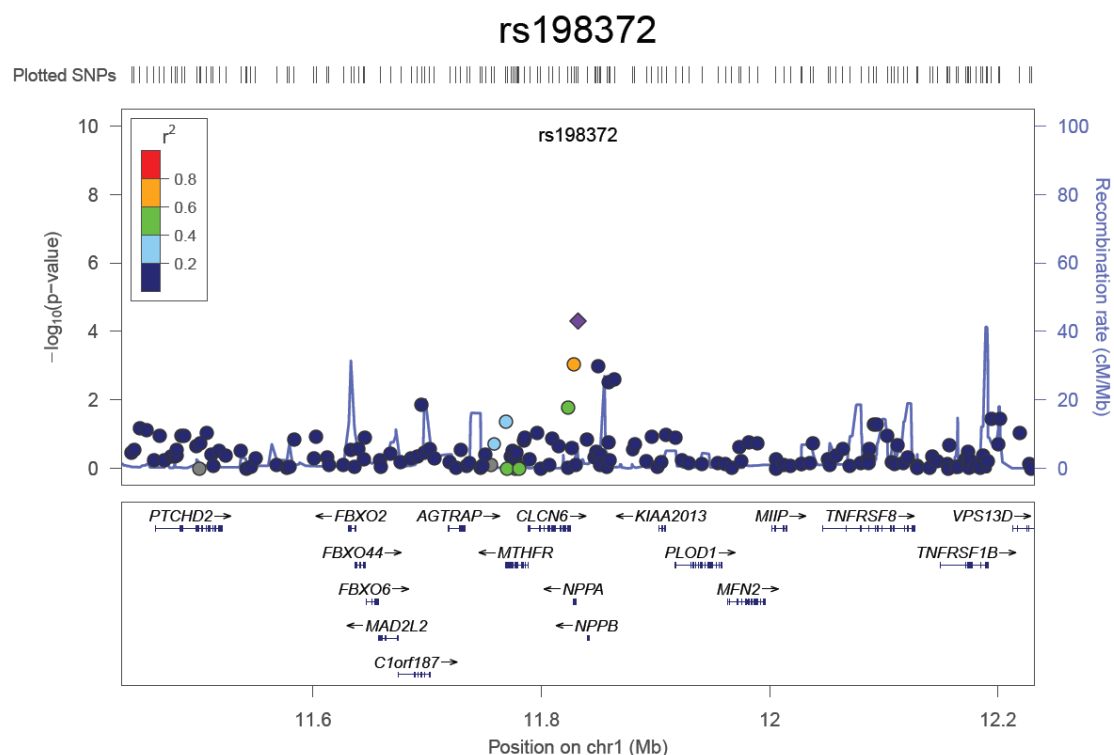


Figure 2: rs341497

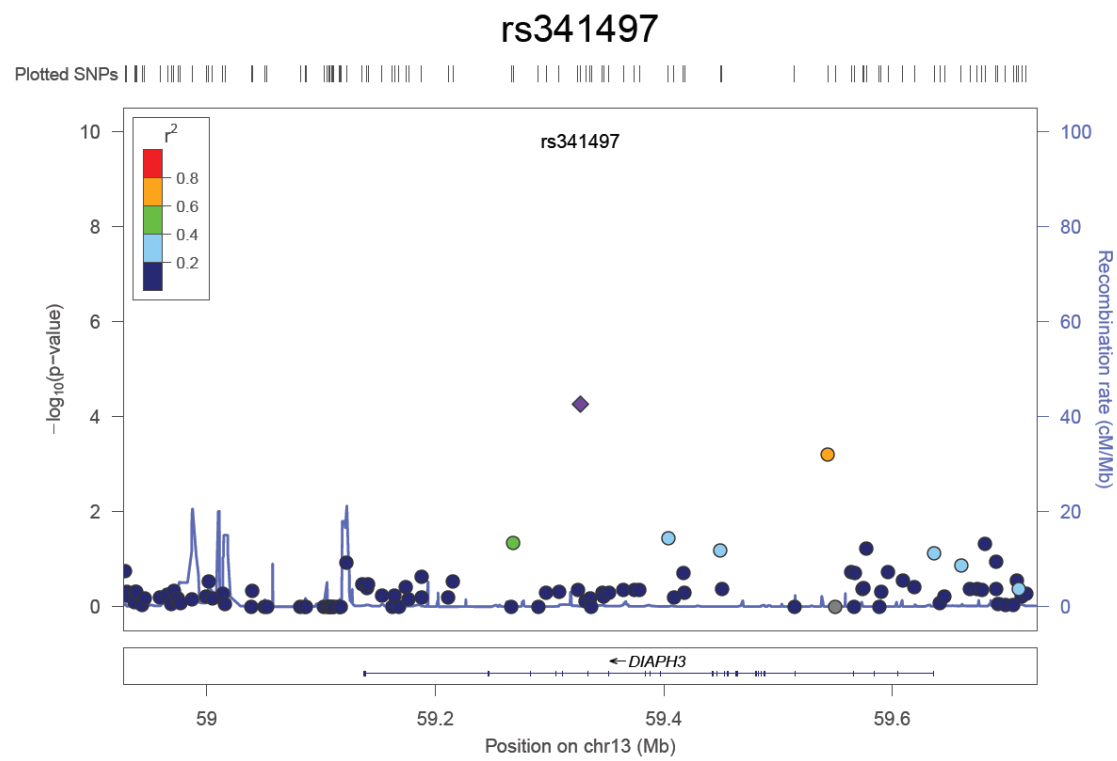


Figure 3: rs1016429

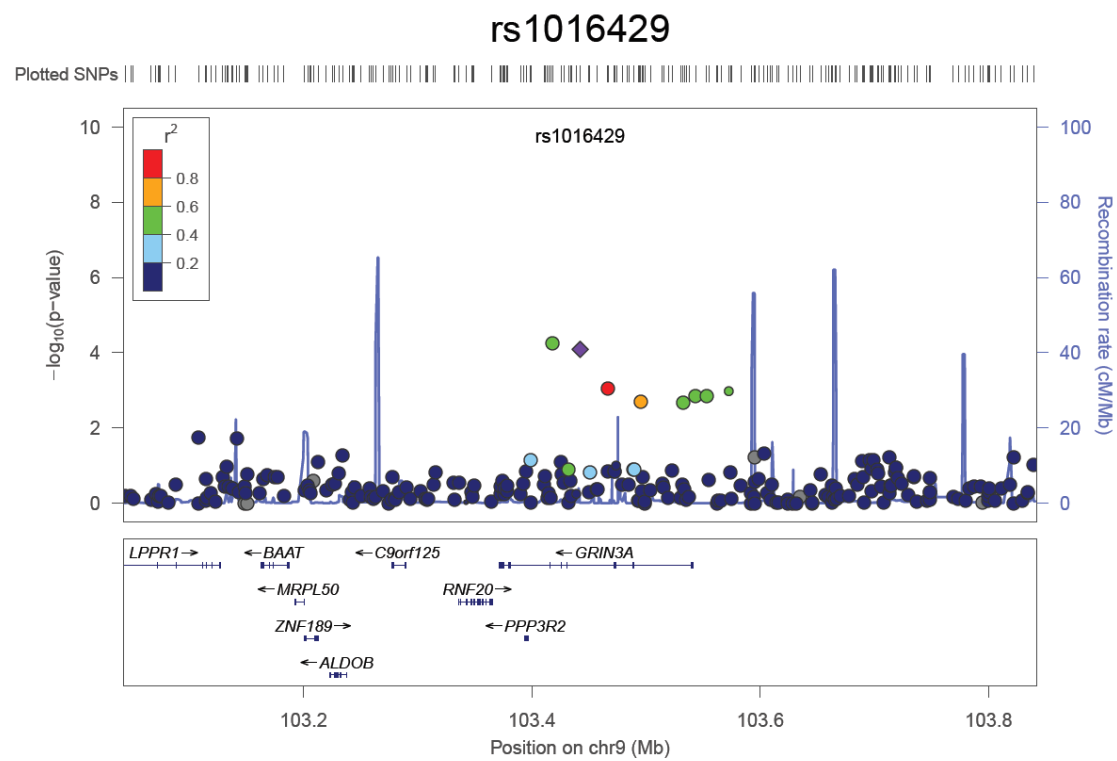


Figure 4: rs1370602

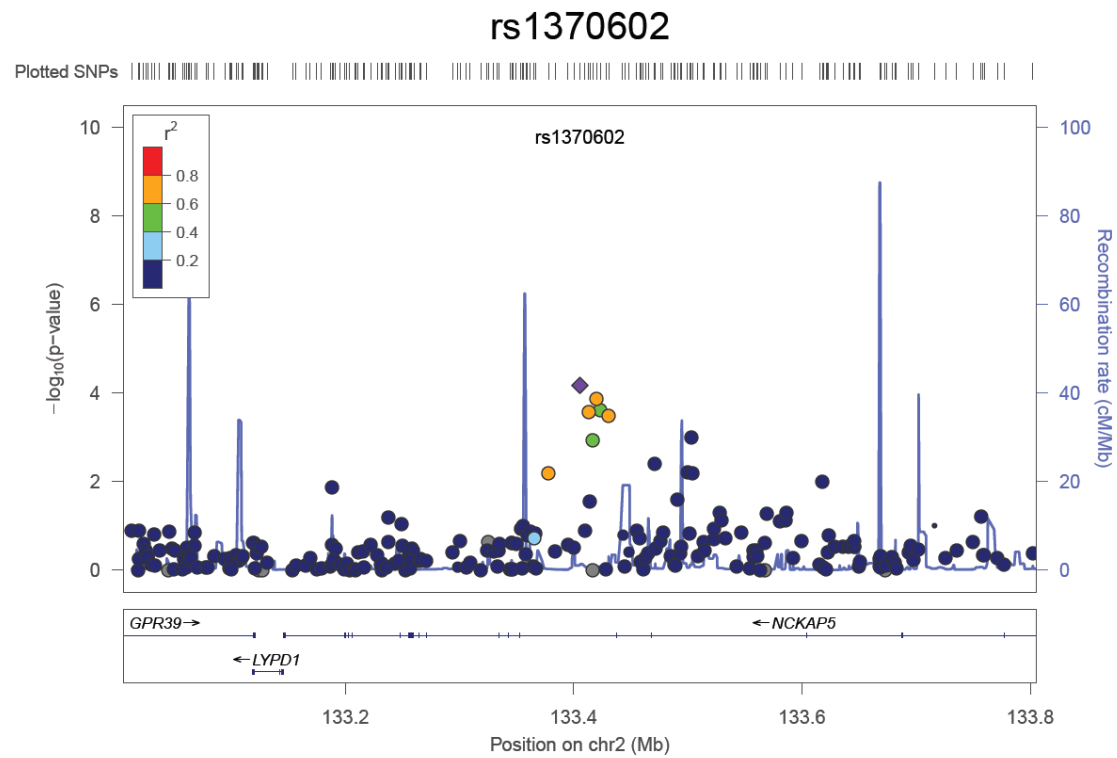


Figure 5: rs1783606

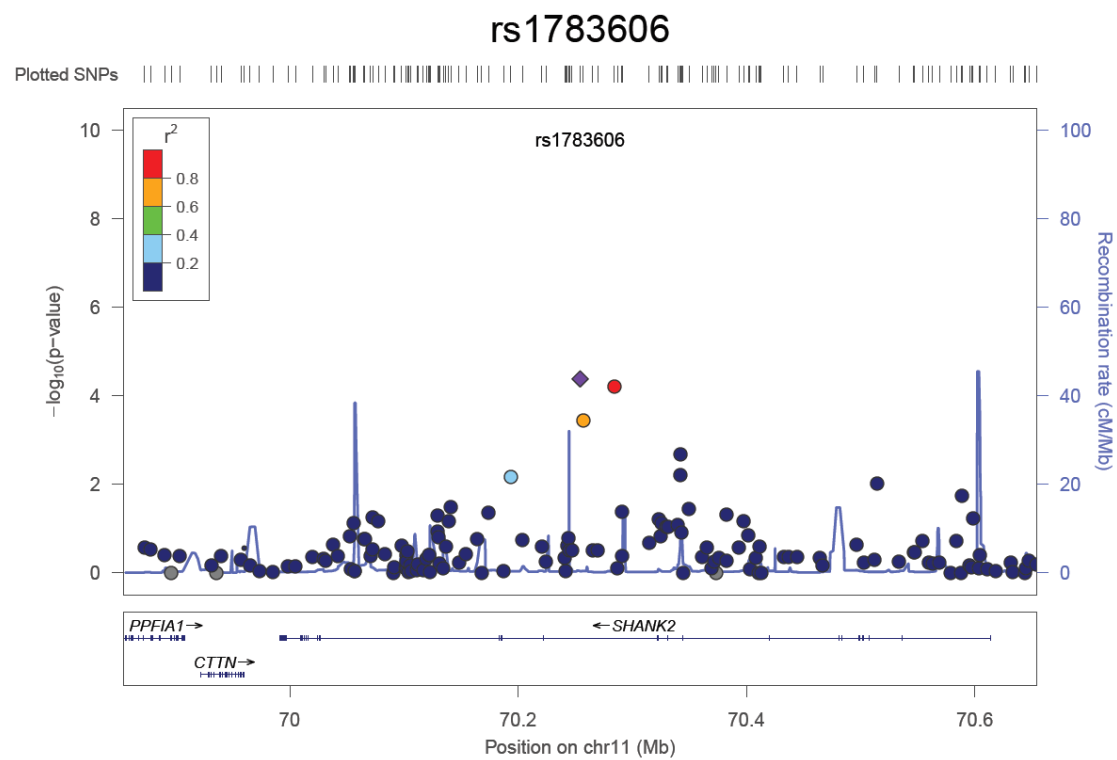


Figure 6: rs1836882

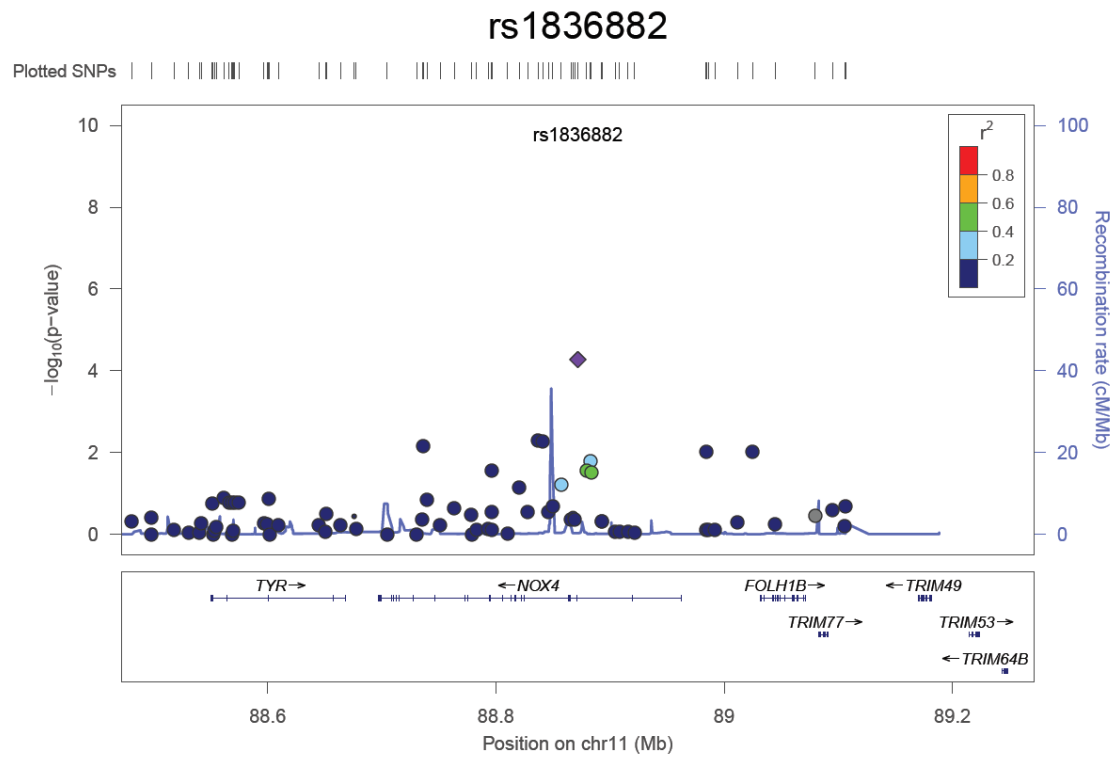


Figure 7: rs1871184

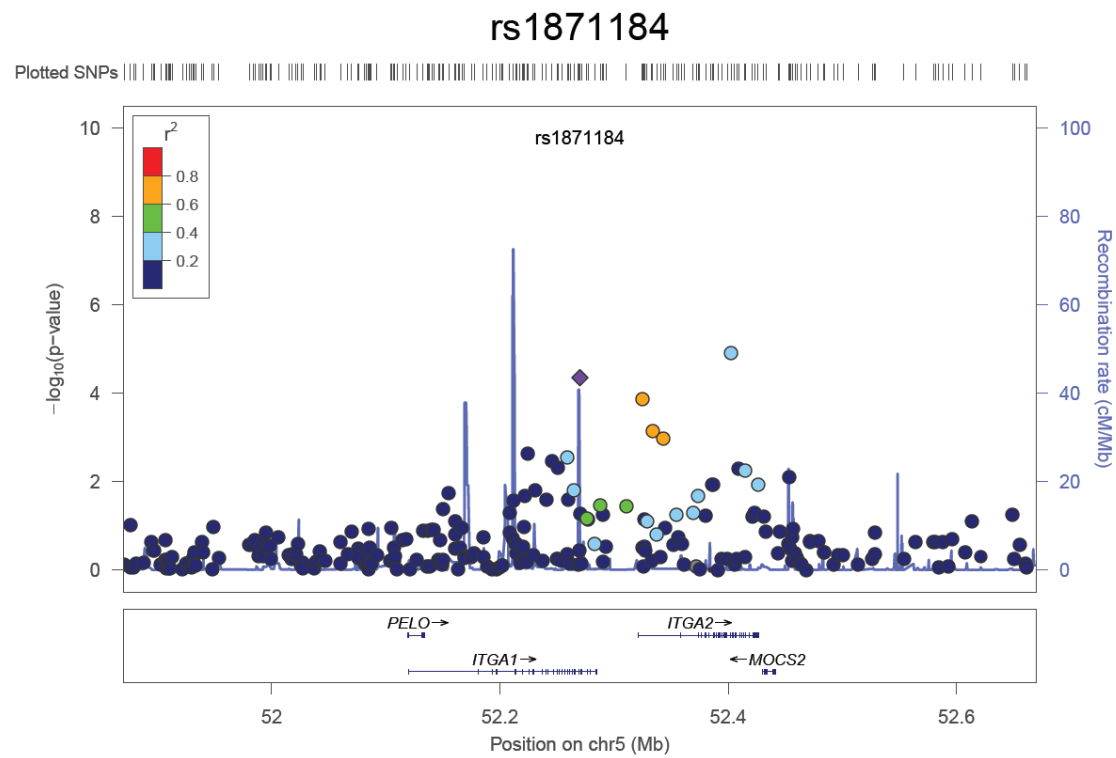


Figure 8: rs2020902

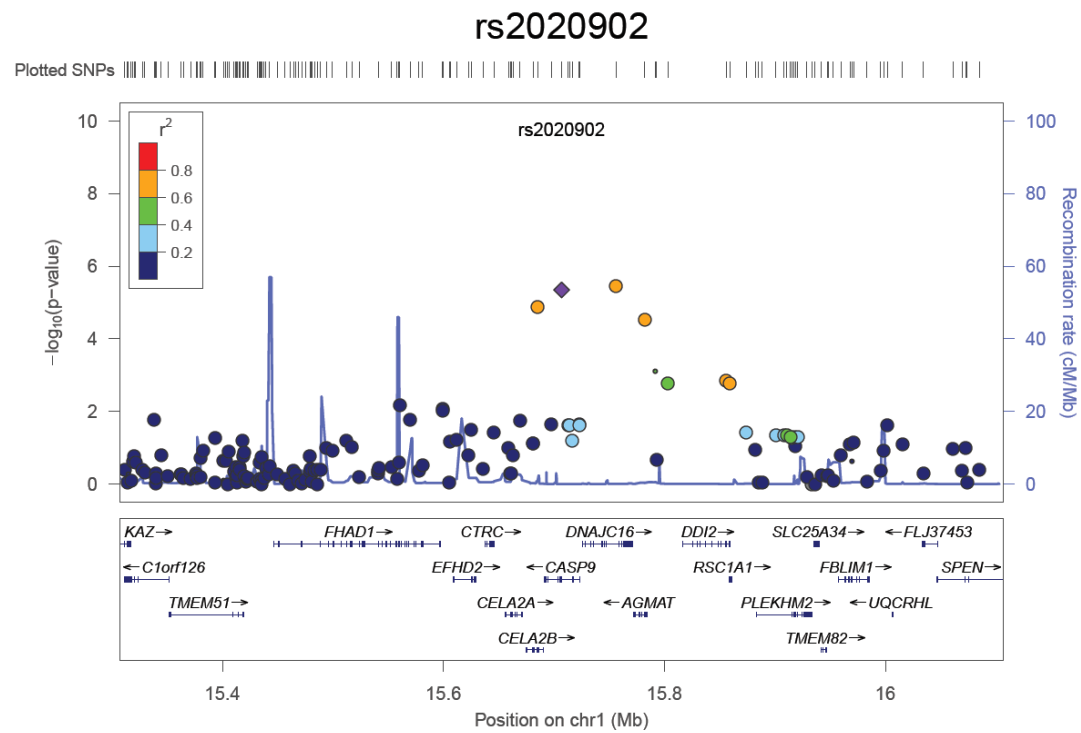
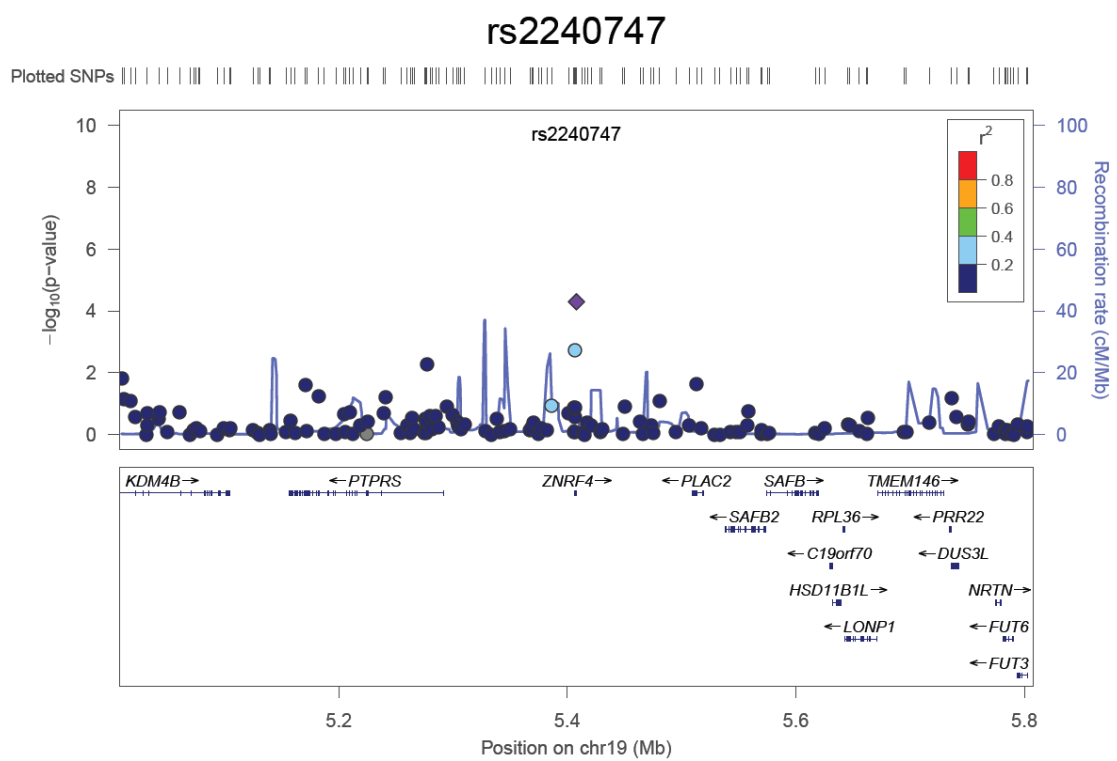


Figure 9: rs2240747



rs2265917

Plotted SNPs

$-\log_{10}(p\text{-value})$

rs2265917

r^2

Recombination rate (cM/Mb)

←EPM2A←FBXO30←SHPRHGRM1→

Position on chr6 (Mb)

Figure 12: rs2861484

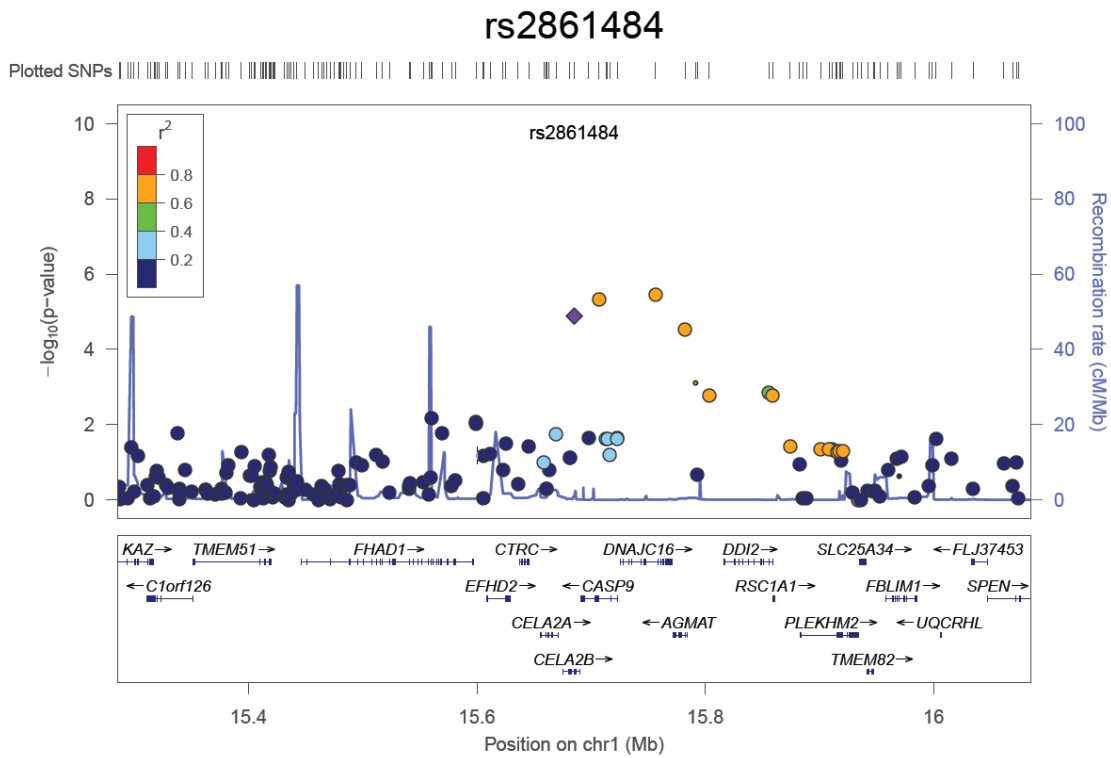


Figure 13: rs3212574

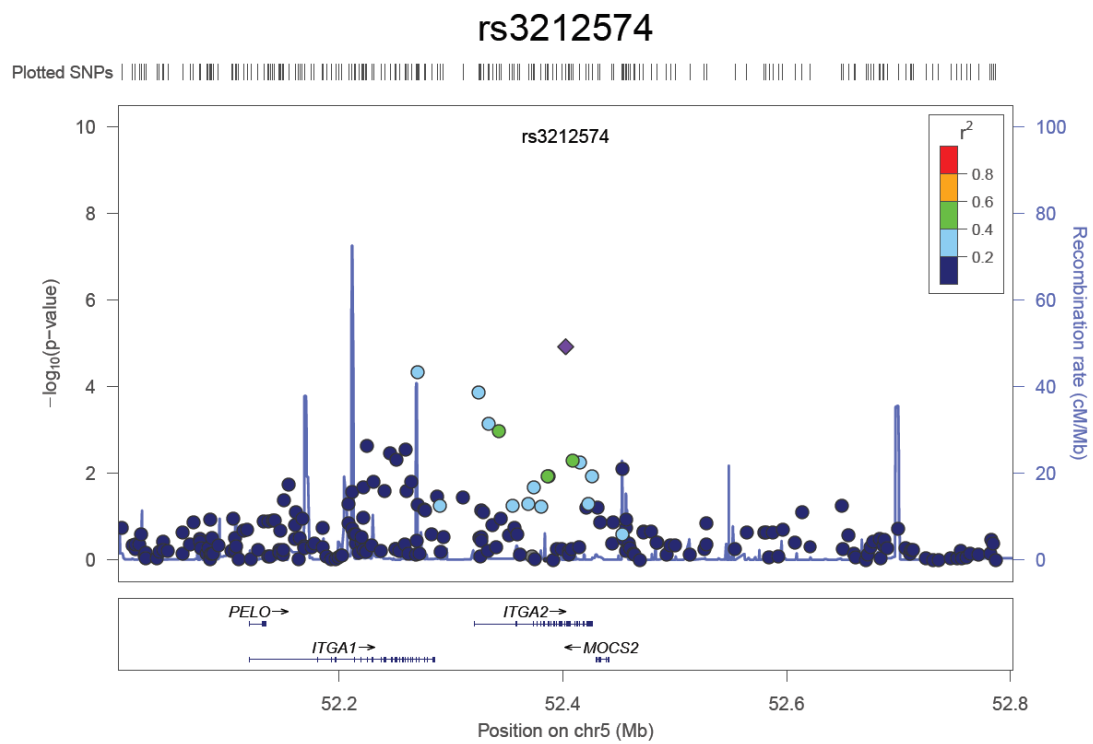


Figure 14: rs4394754

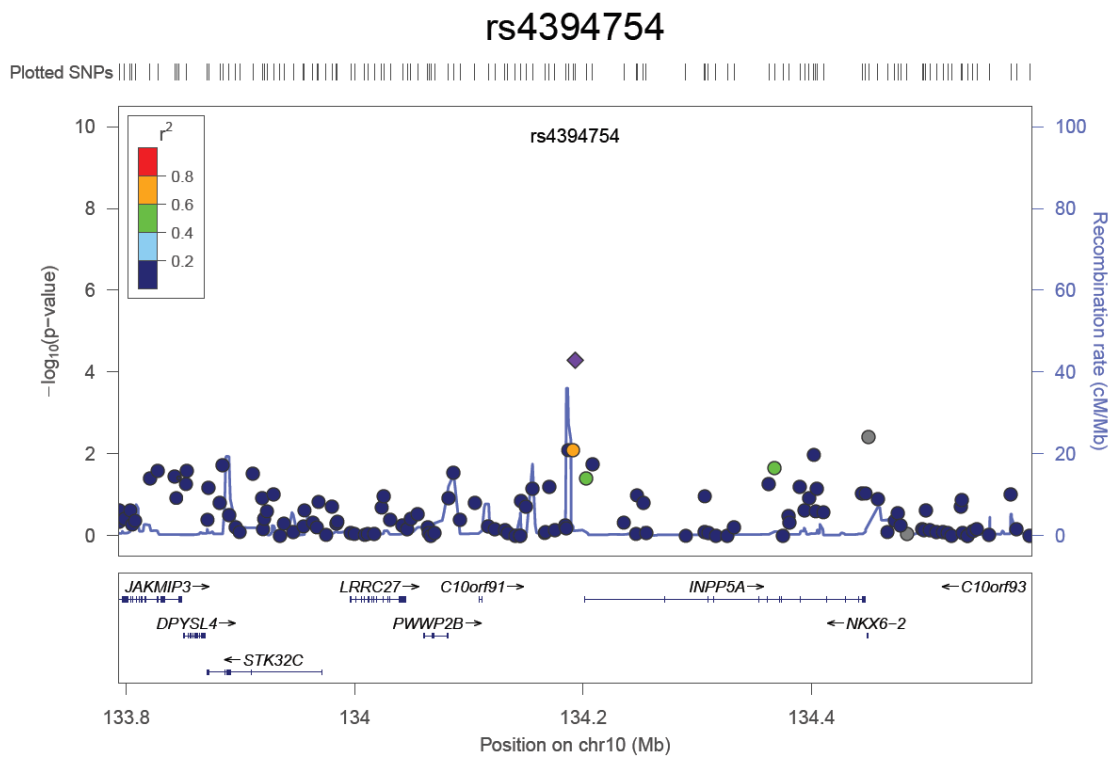


Figure 15: rs6793265

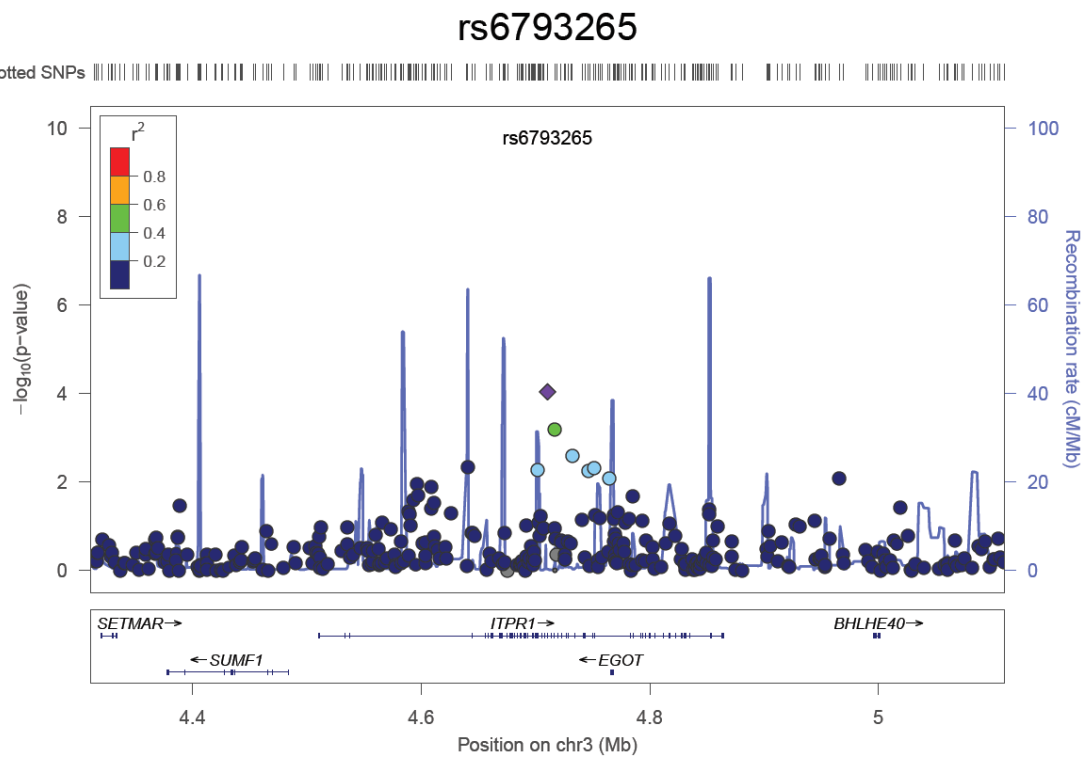


Figure 16: rs6903252

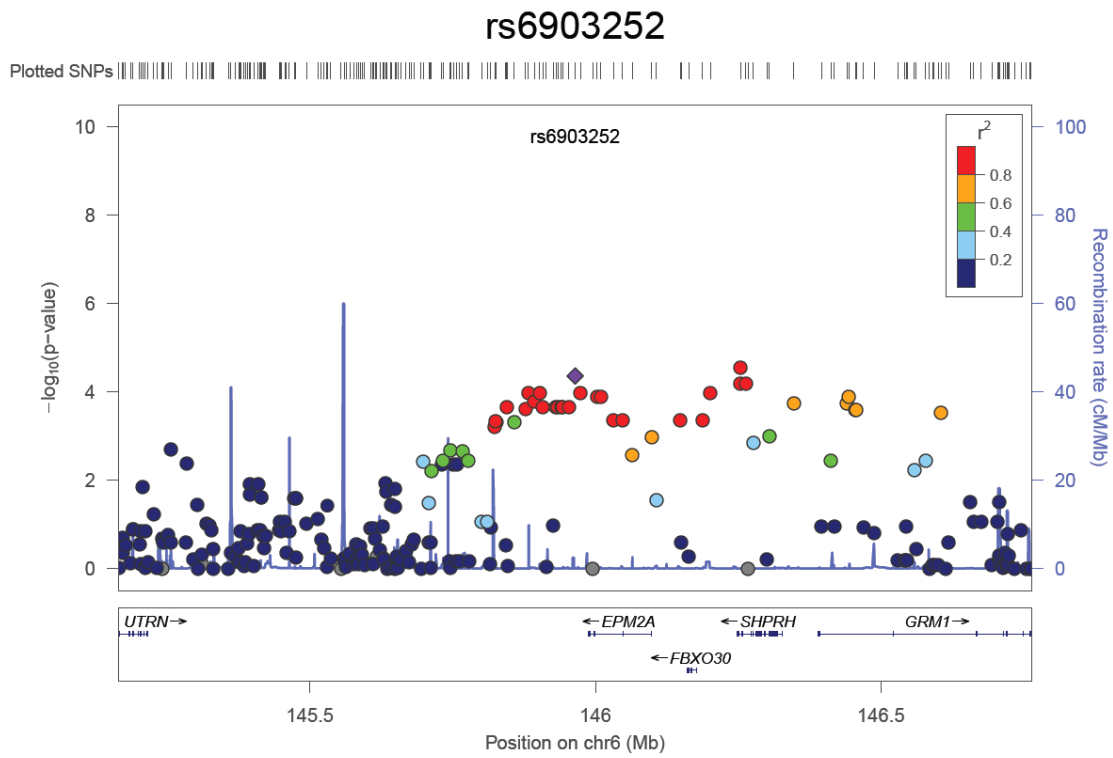


Figure 17: rs7145618

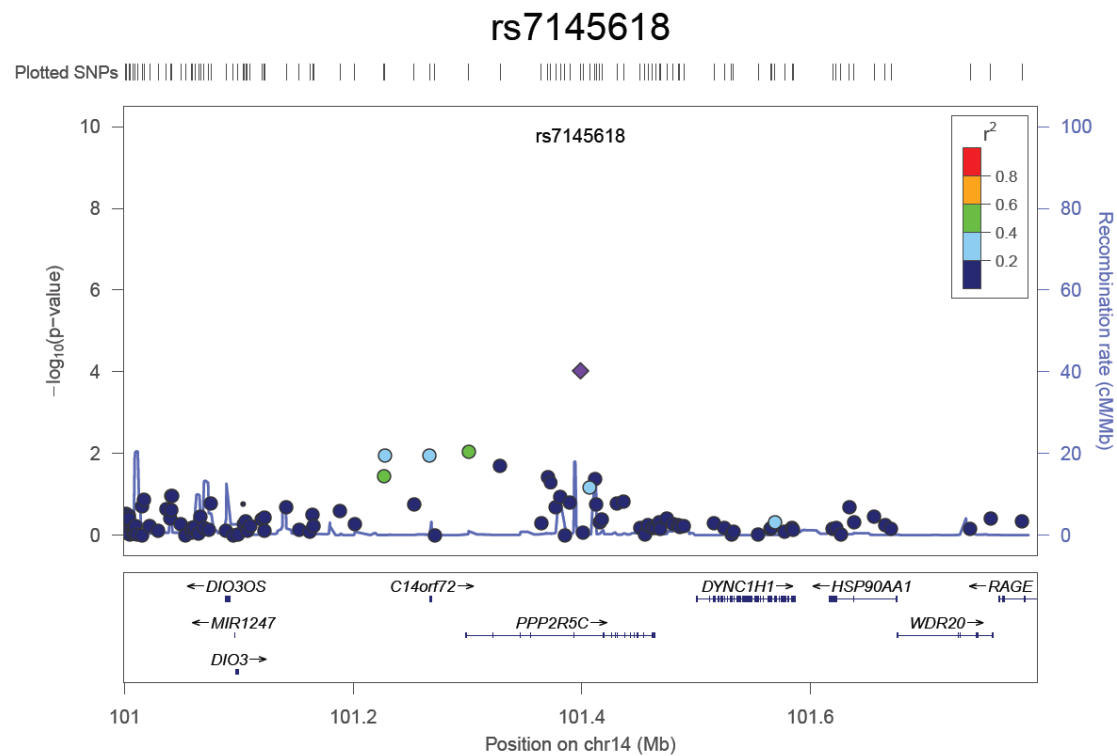


Figure 18: rs10117679

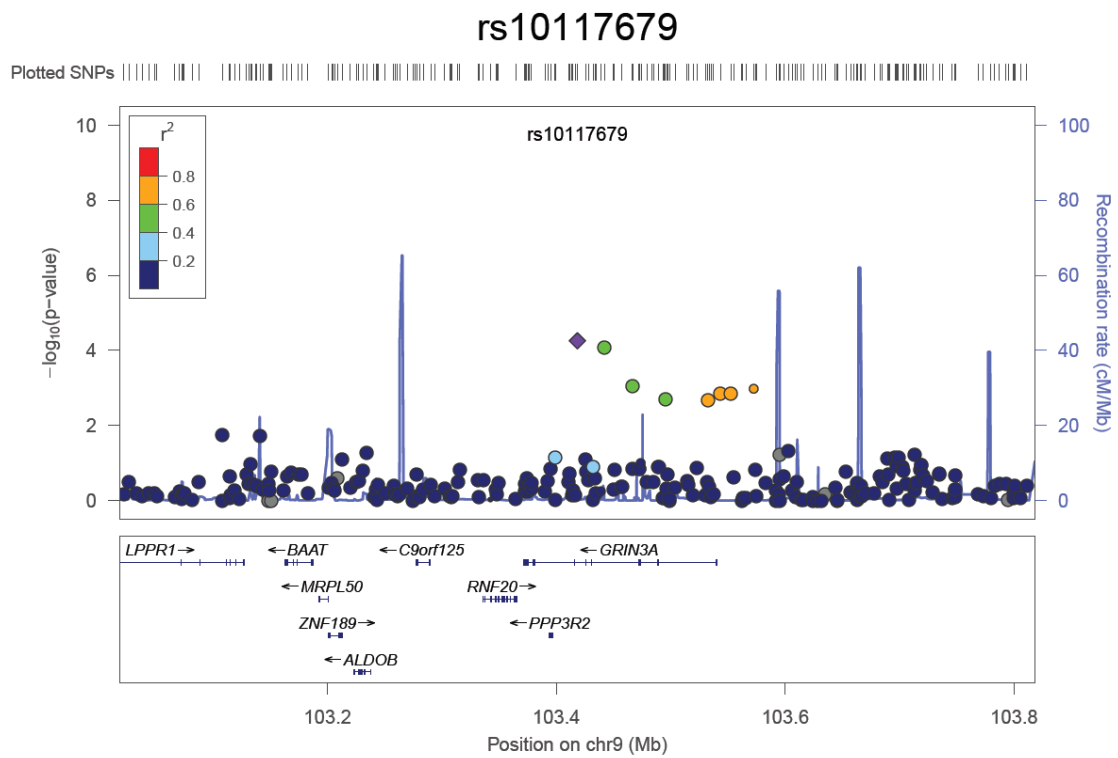


Figure 19: rs104848

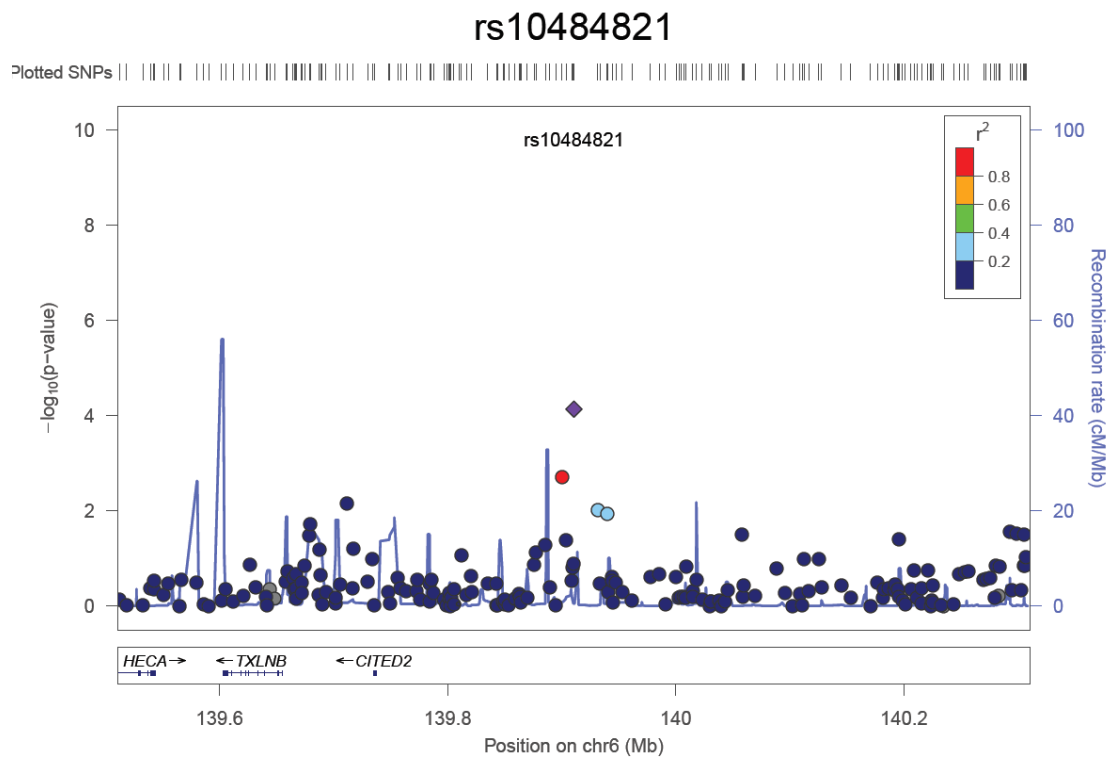


Figure 20: rs10899444

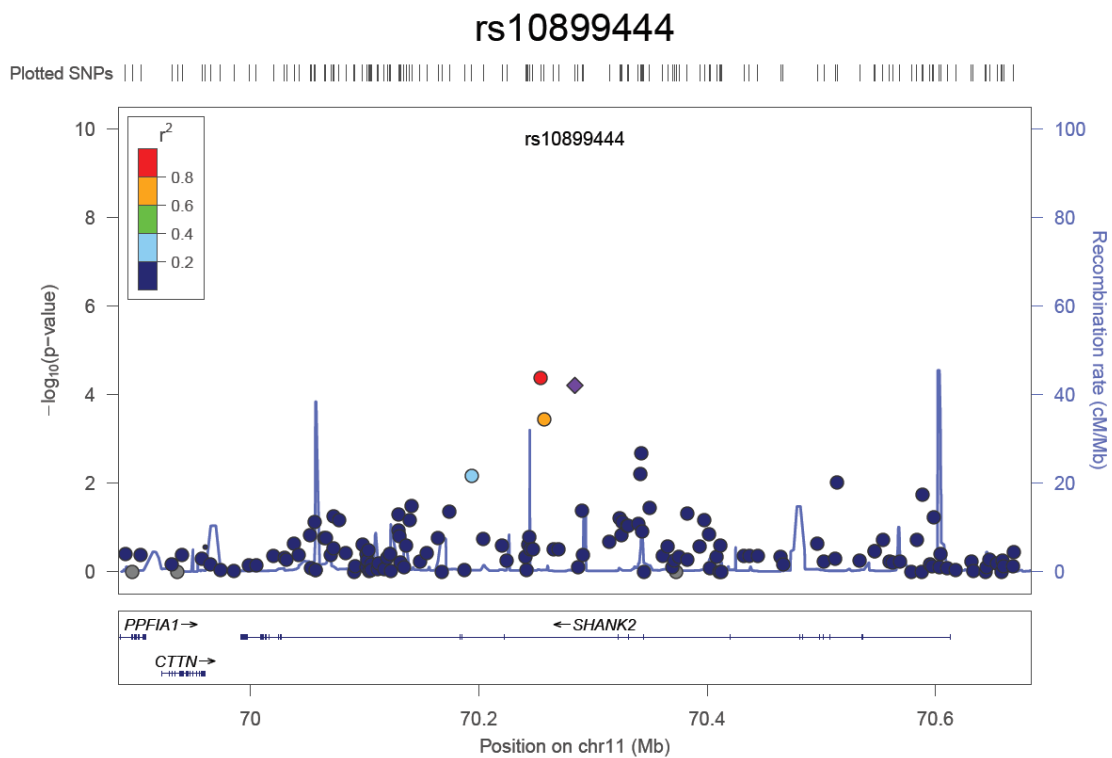


Figure 21: rs11580170

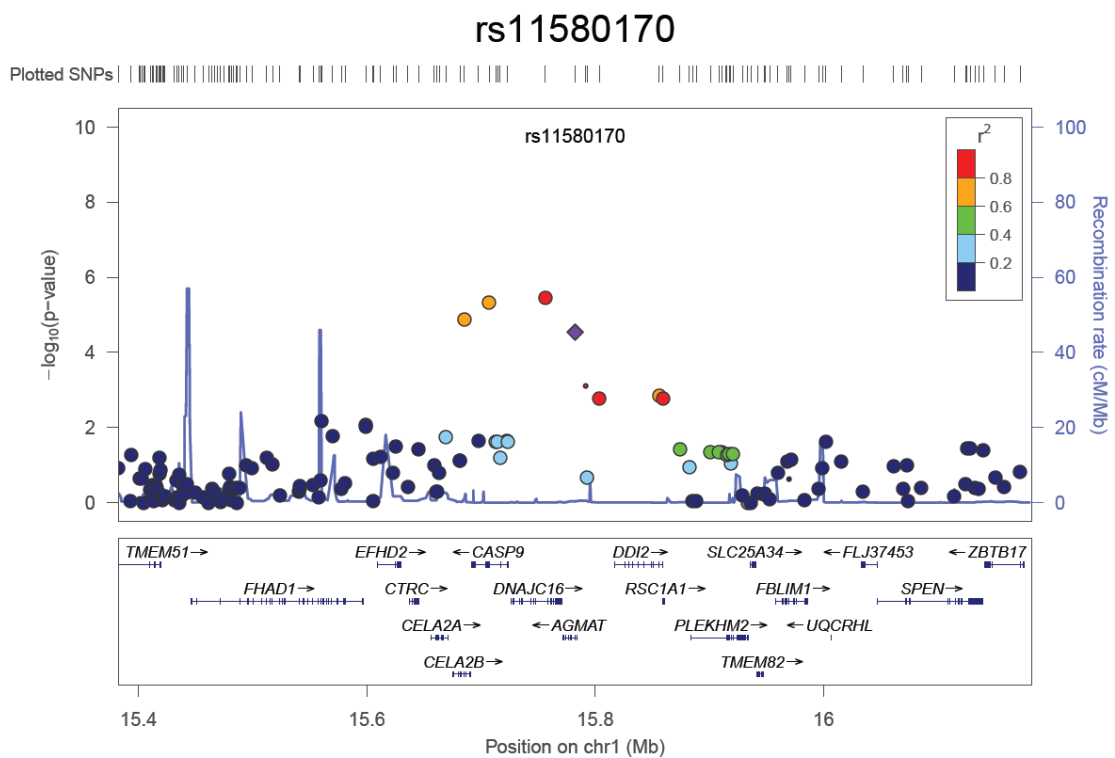


Figure 22: rs16936667

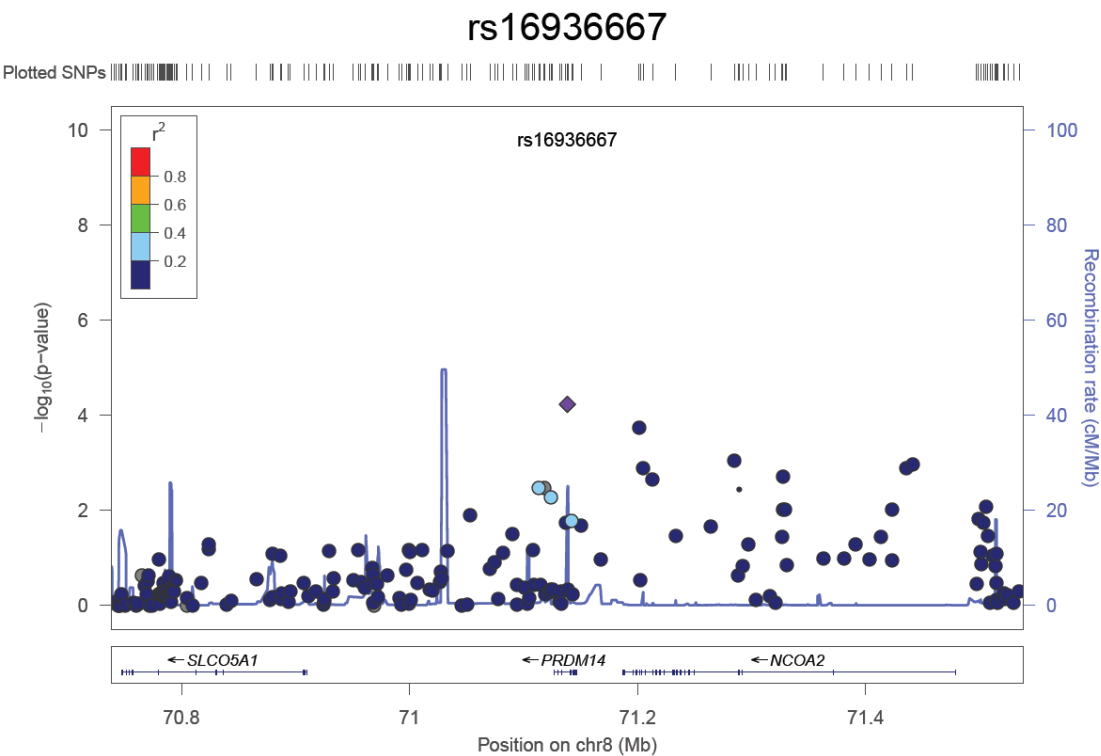


Figure 23: rs17657199

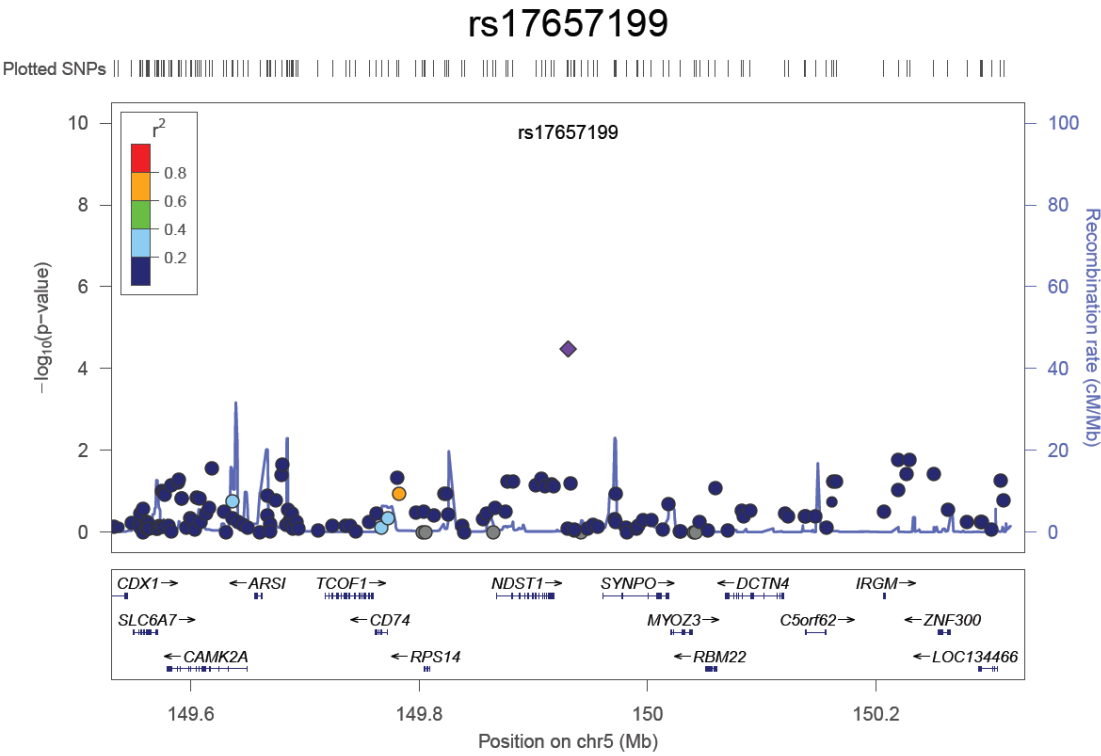
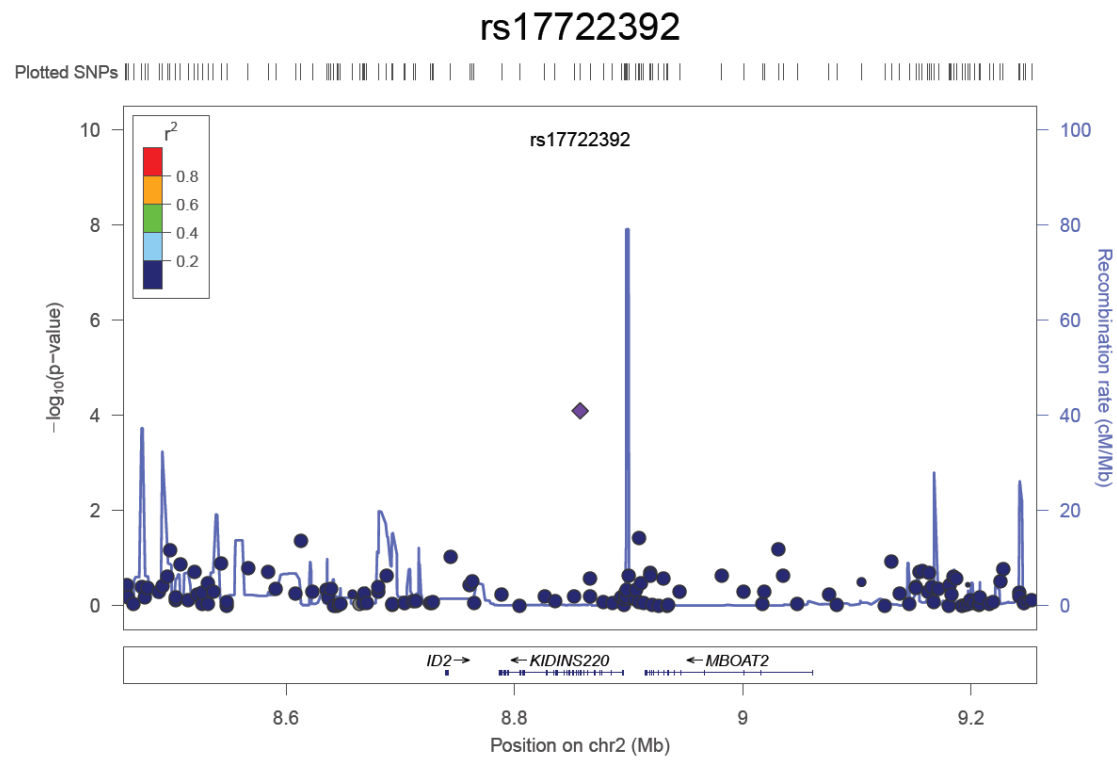


Figure 24: rs17722392



(ii) SNPs previously reported to be associated with NODAT

Figure 25: rs5219

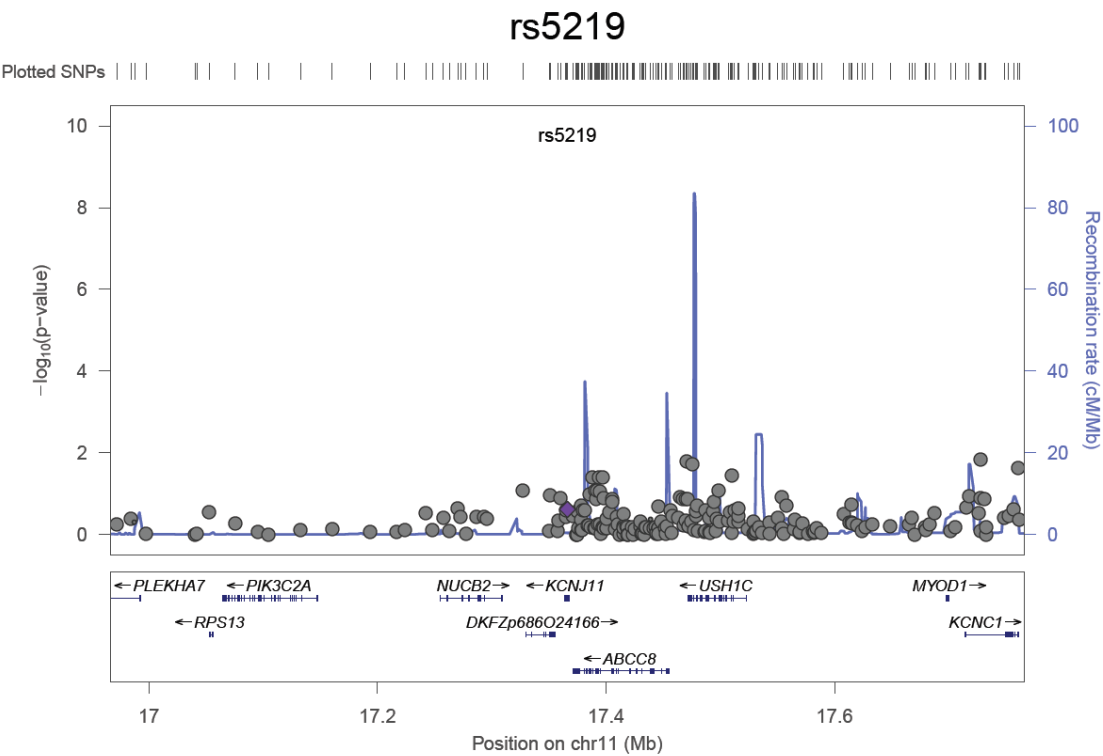


Figure 26: rs1025689 (proxy rs7627178)

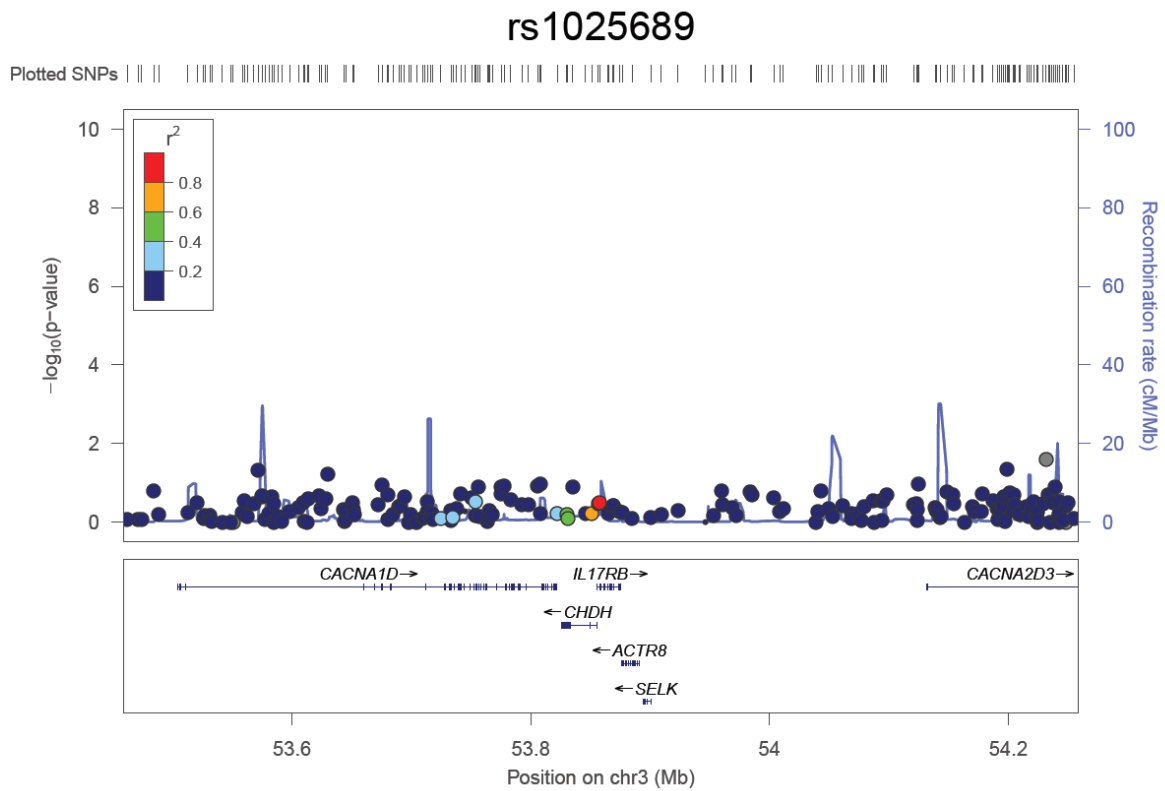


Figure 27: rs1043261

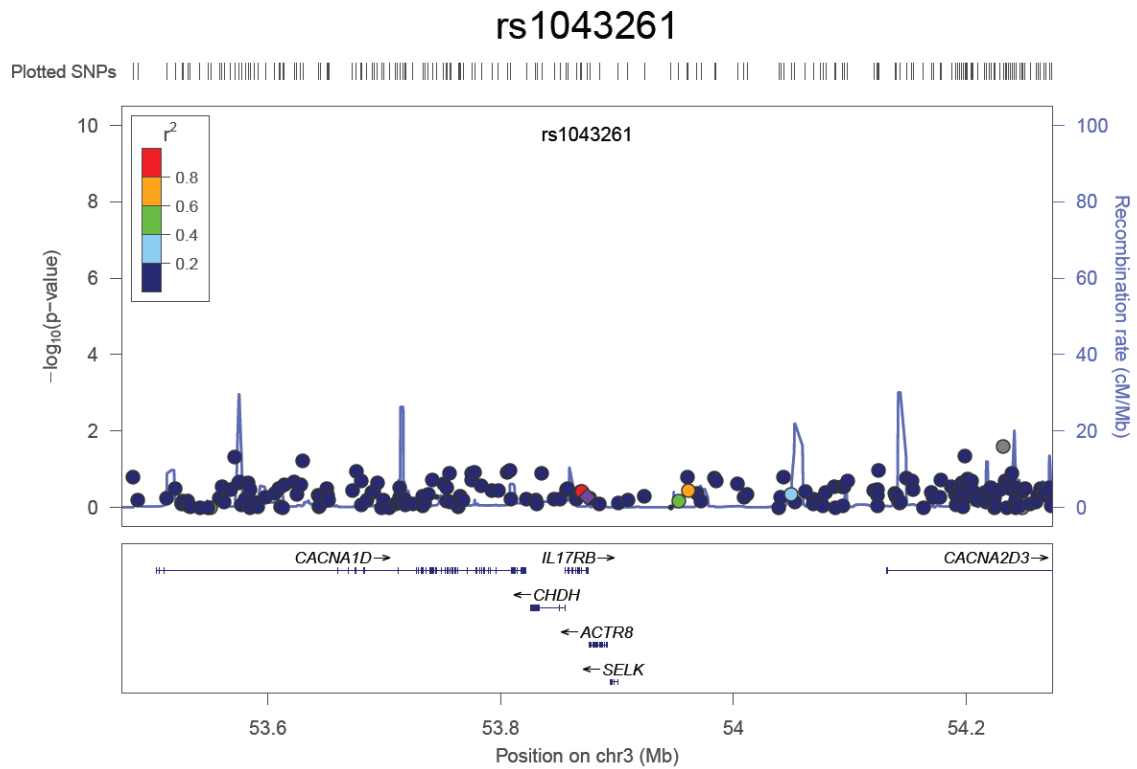


Figure 28: rs1044498 (proxy rs6926970)

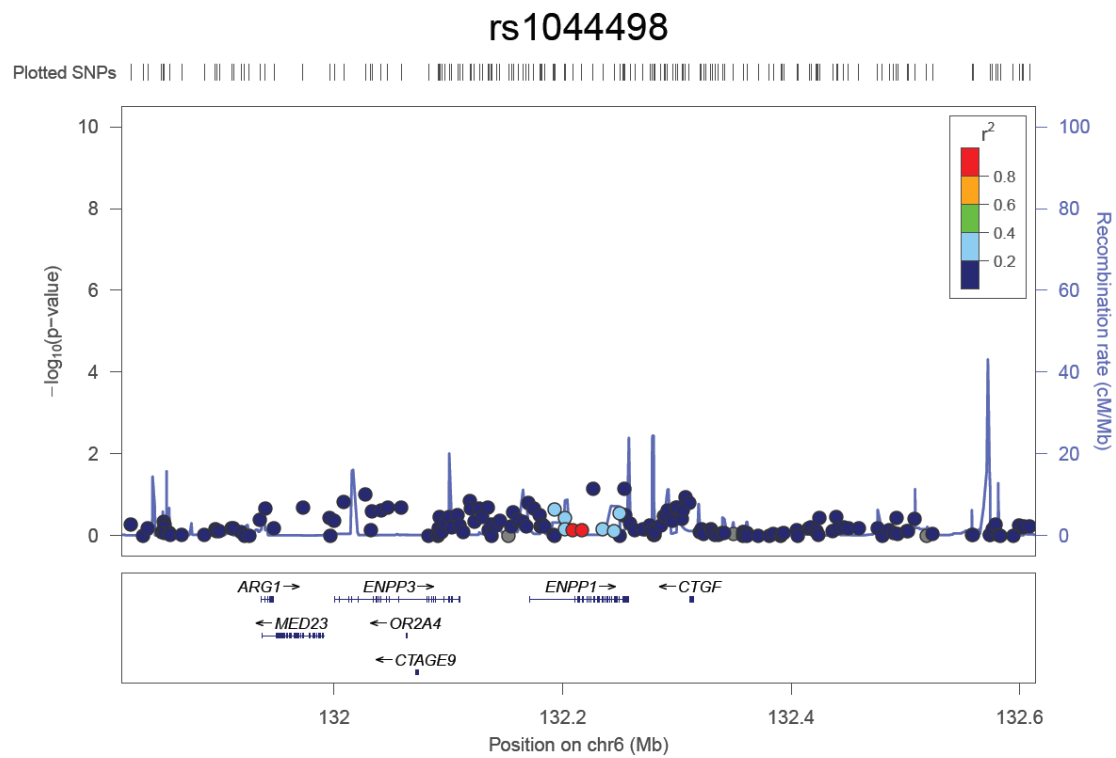


Figure 29: rs1124053 (proxy rs3759614)

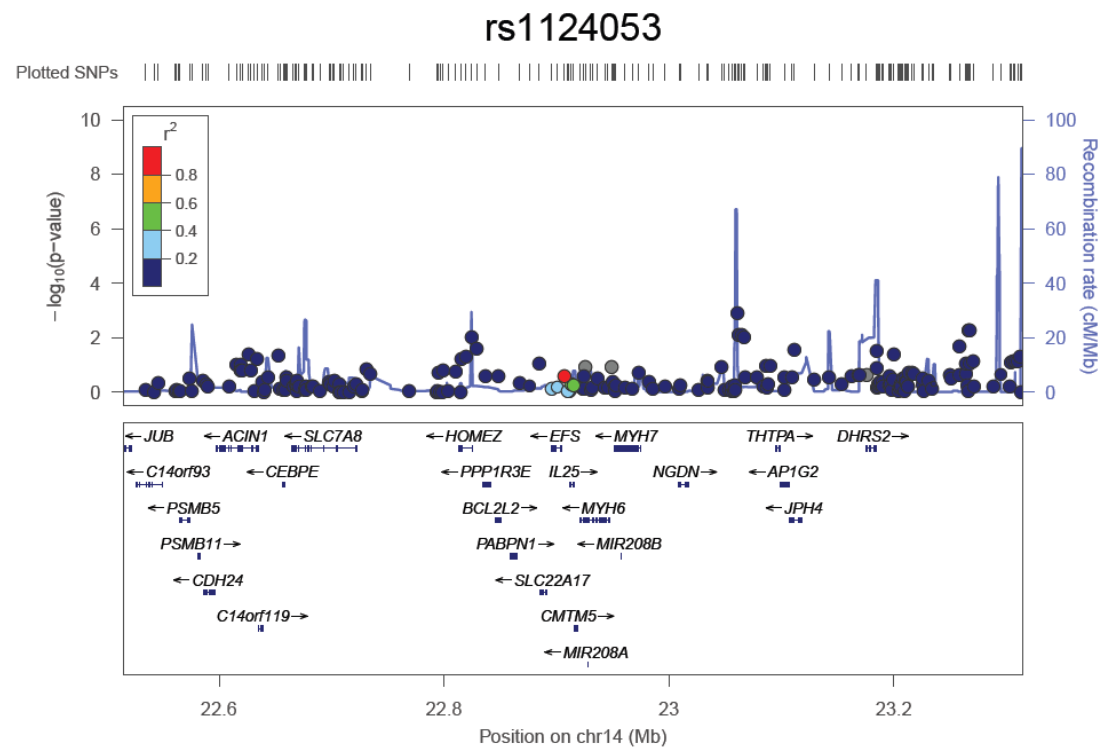


Figure 30: rs1169288 (proxy rs2650000)

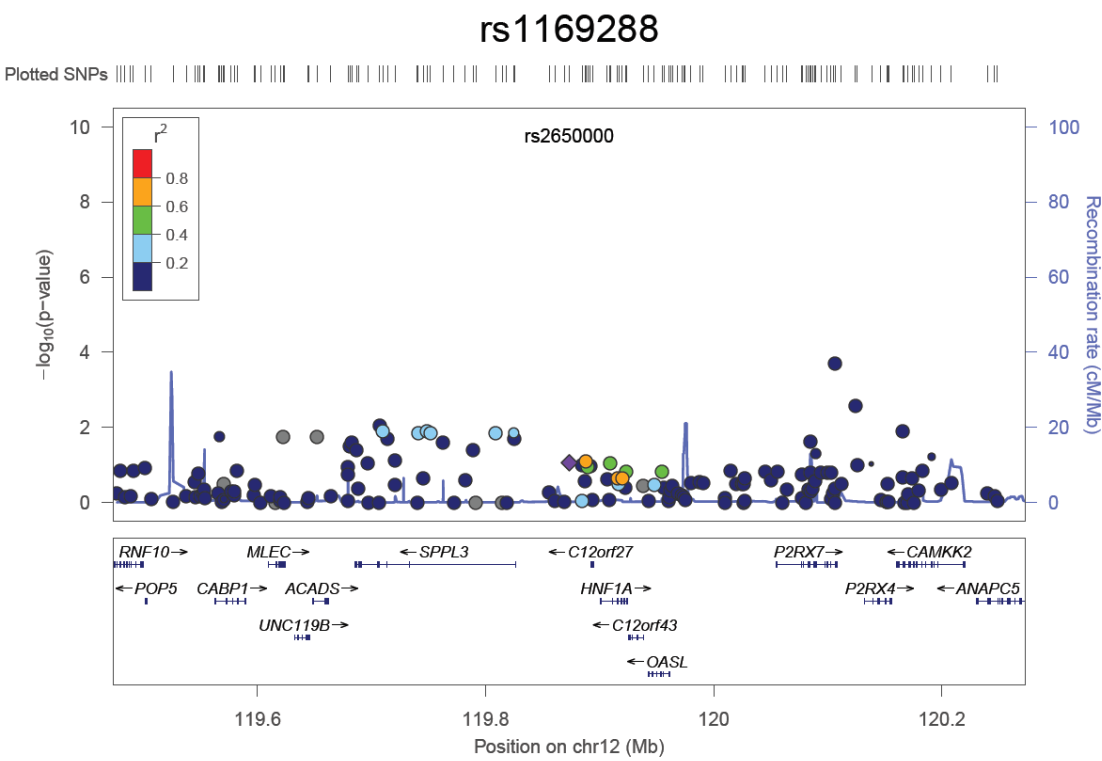


Figure 31: rs1494558

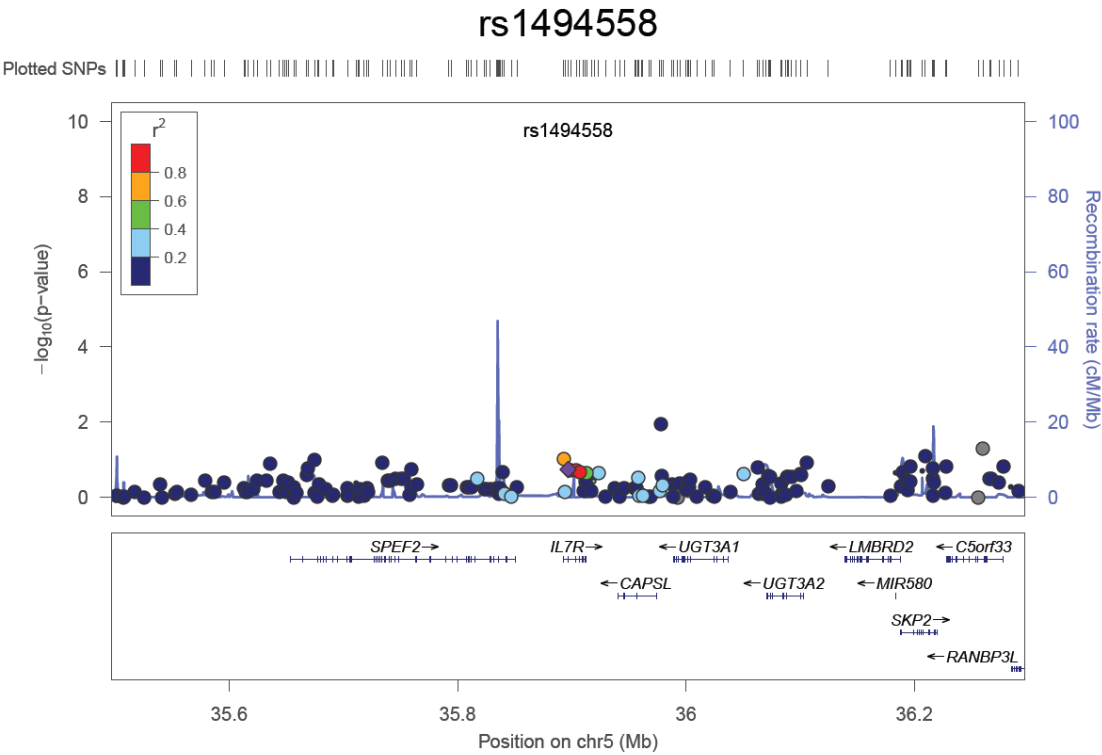


Figure 32: rs1799854

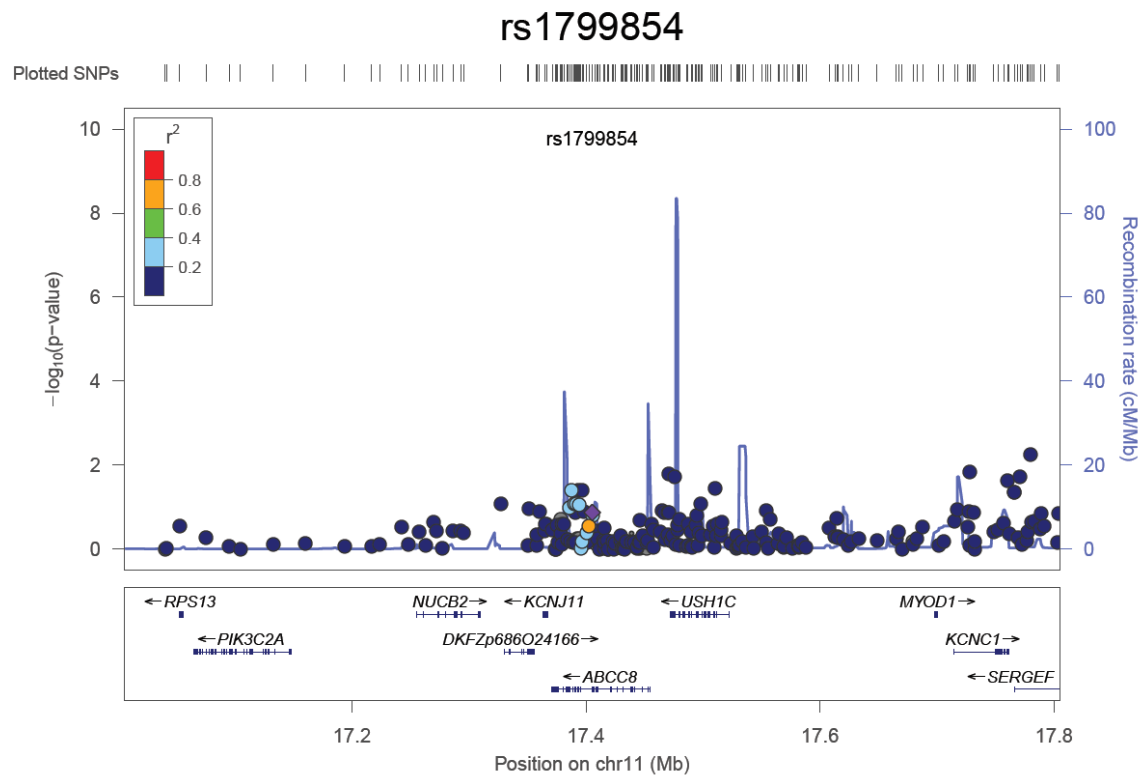


Figure 33: rs1800795 (proxy rs1554606)

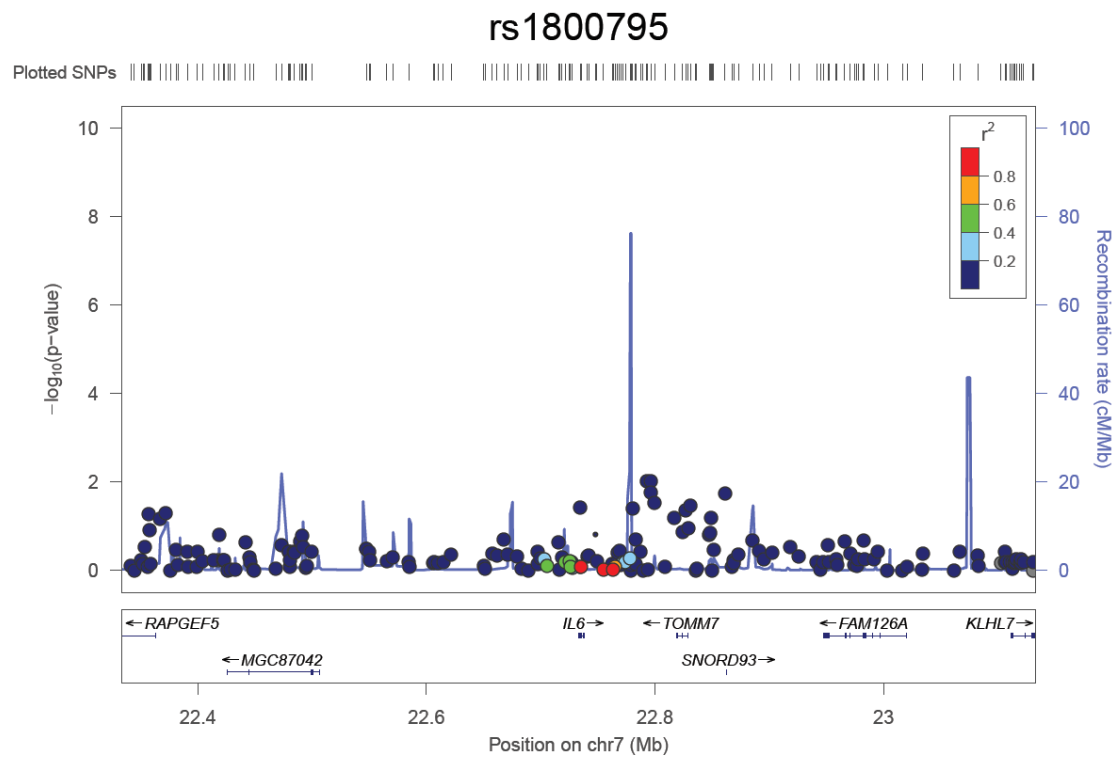


Figure 34: rs1800961

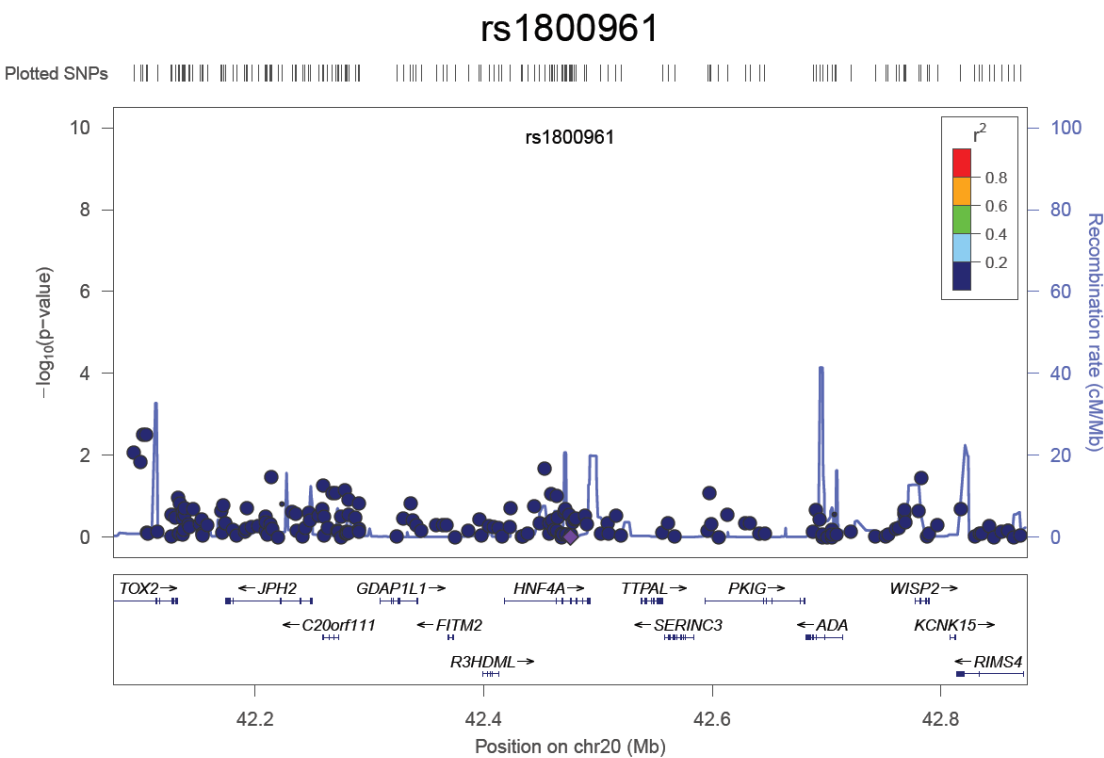


Figure 35: rs1801282 (proxy rs6802898)

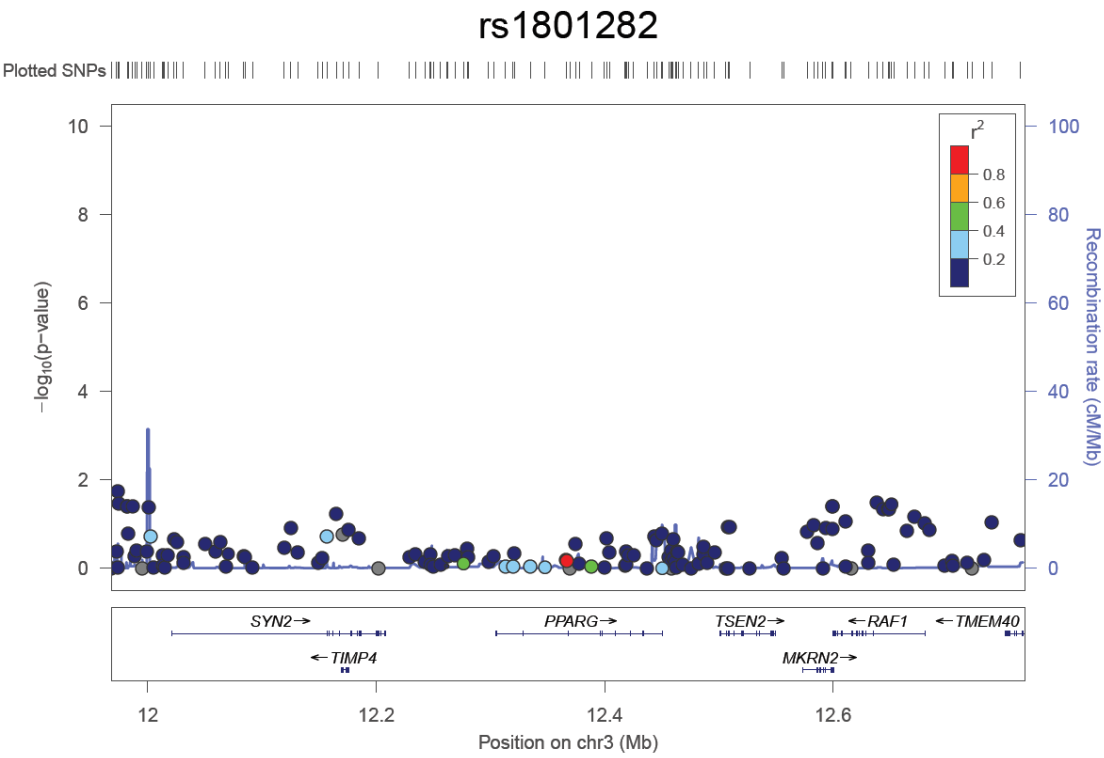


Figure 36: rs2069762 (proxy rs6835946)

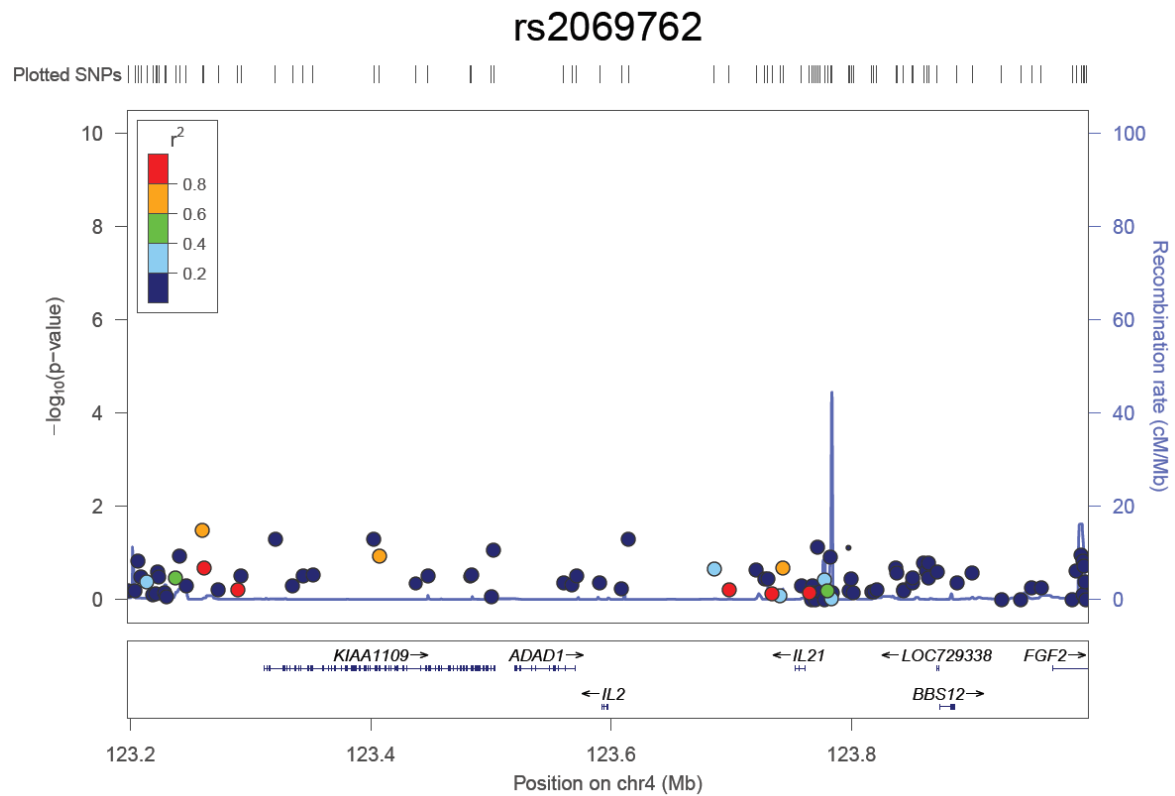


Figure 37: rs2069763 (proxy rs4505848)

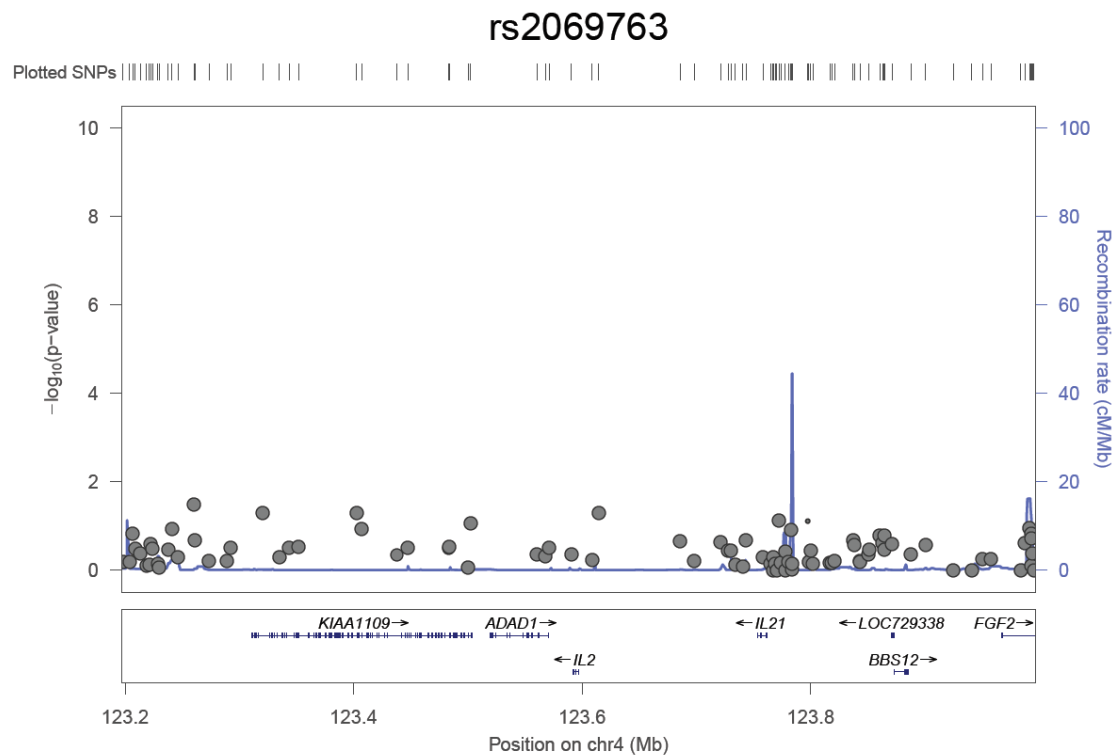


Figure 38: rs2070874 (proxy rs2243290)

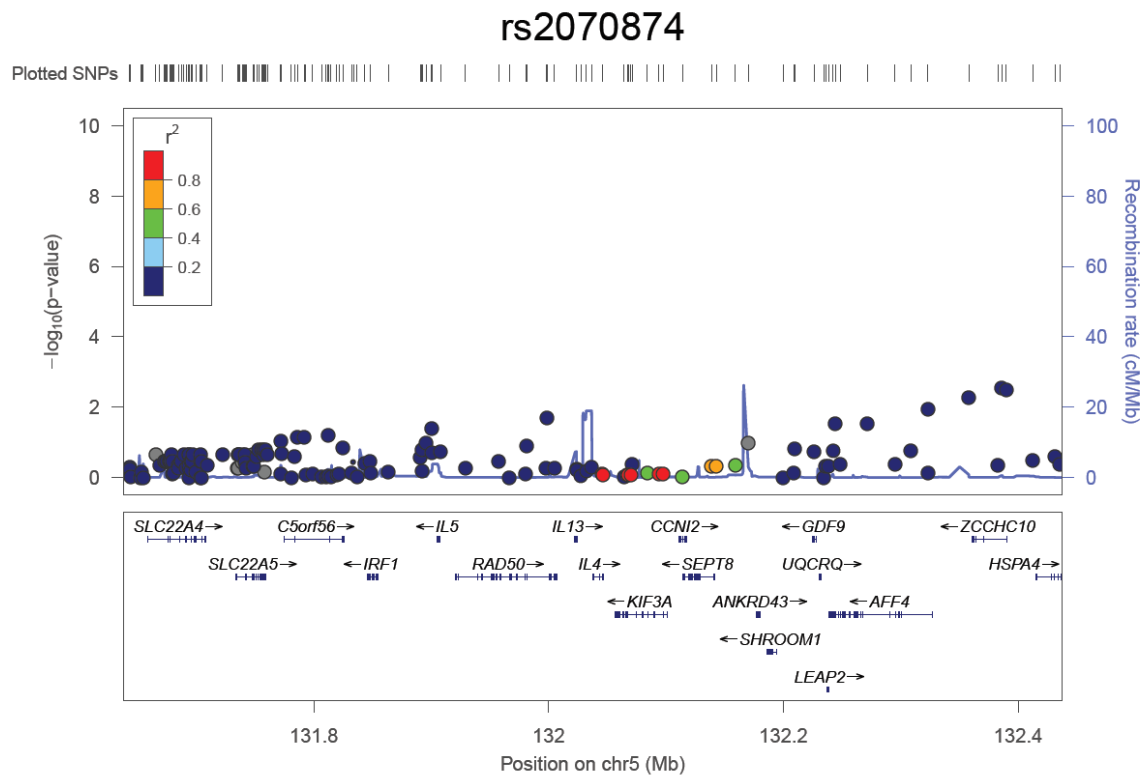


Figure 39: rs2107538 (proxy rs2251660)

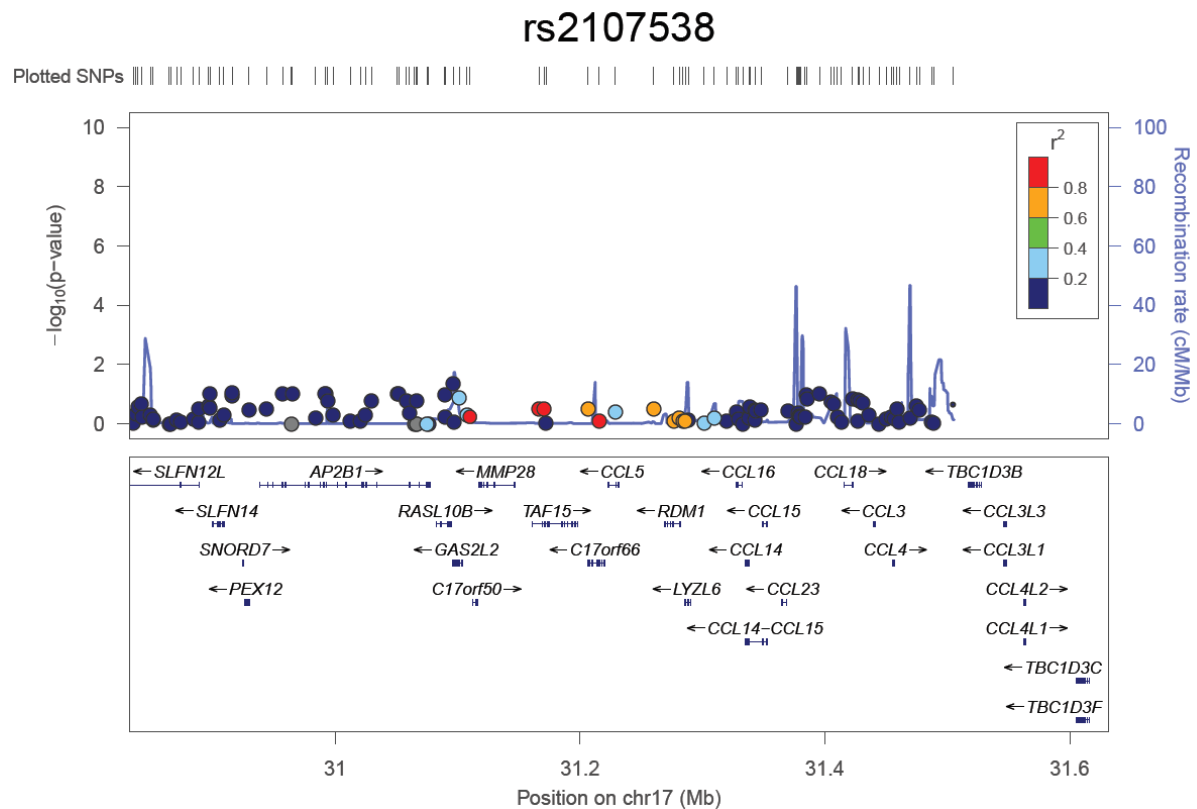


Figure 40: rs2144908 (proxy rs4812829)

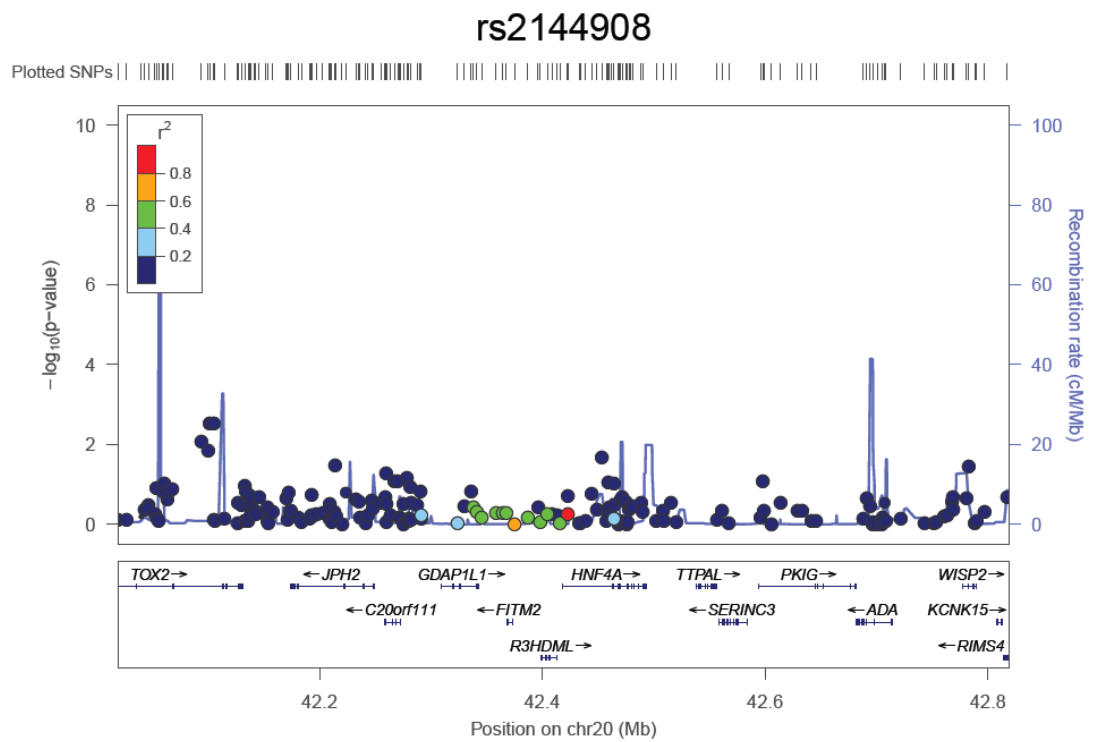


Figure 41: rs2172749 (proxy rs1494558)

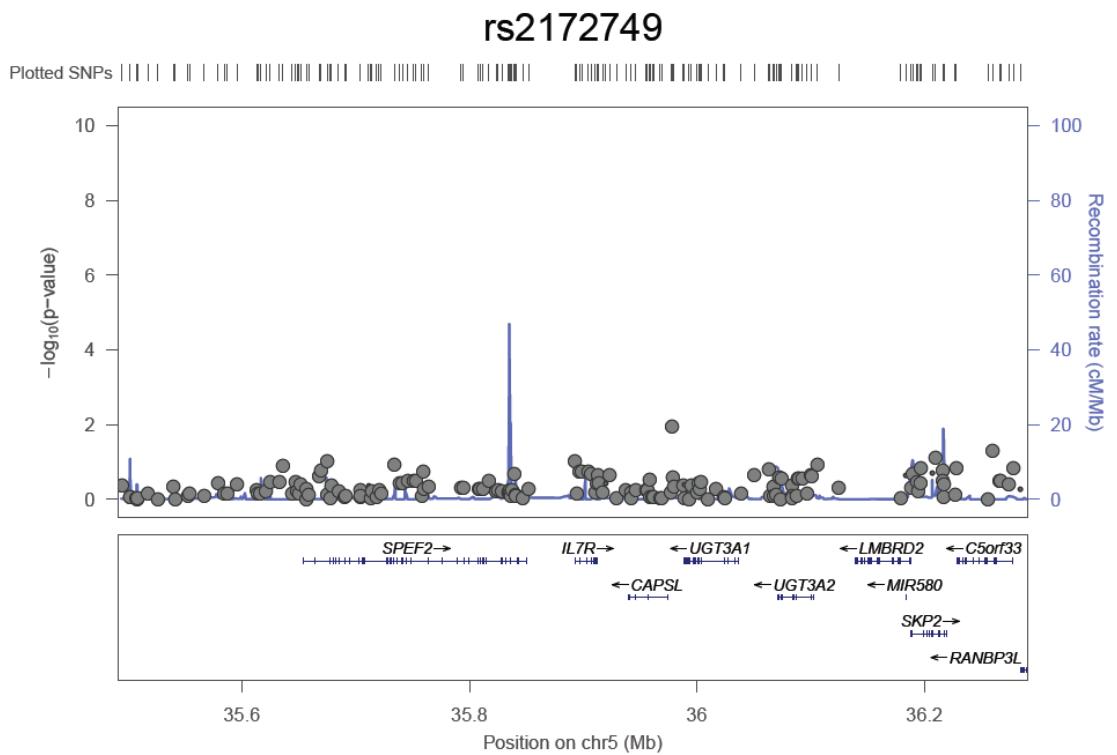


Figure 42: rs2280789 (proxy rs2306630)

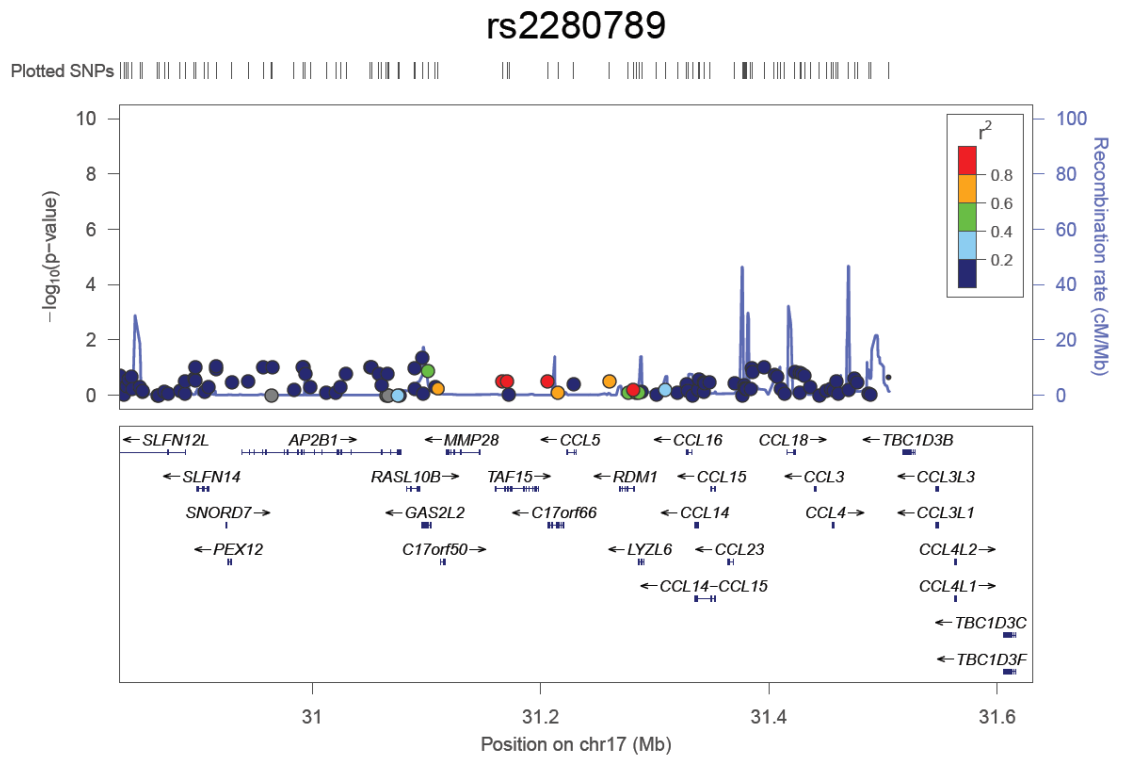


Figure 43: rs2340721 (proxy rs905594)

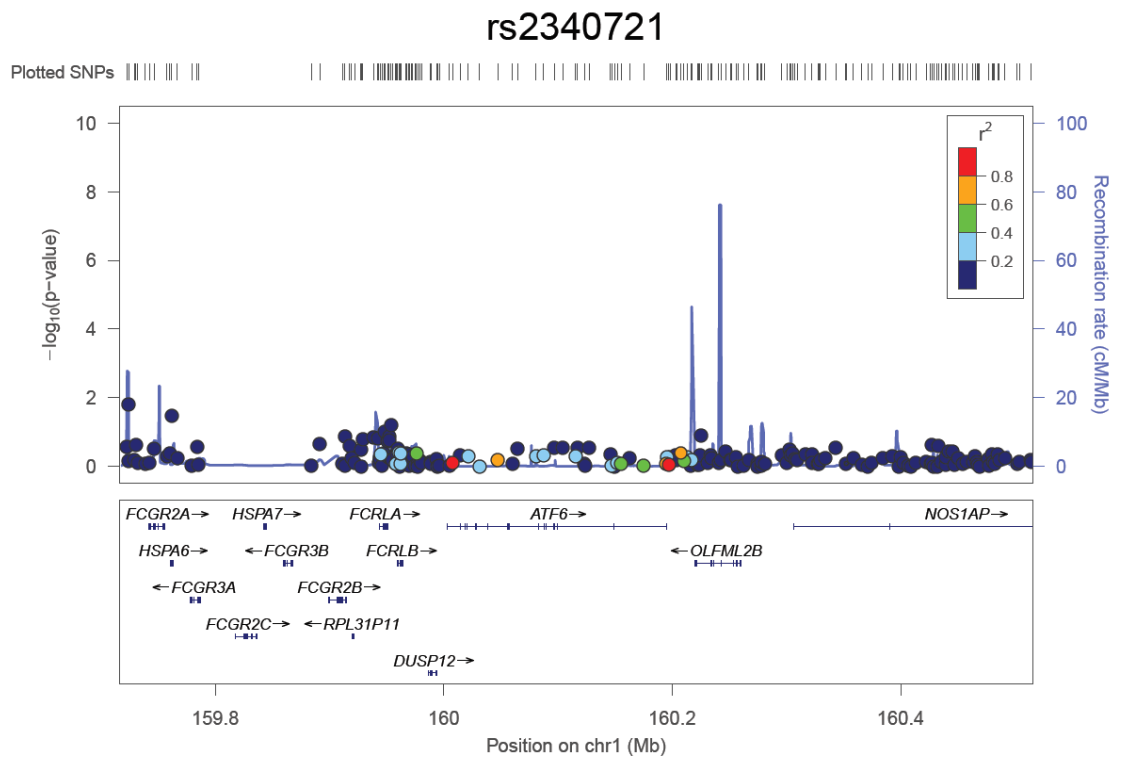


Figure 44: rs2430561 (proxy rs2069727)

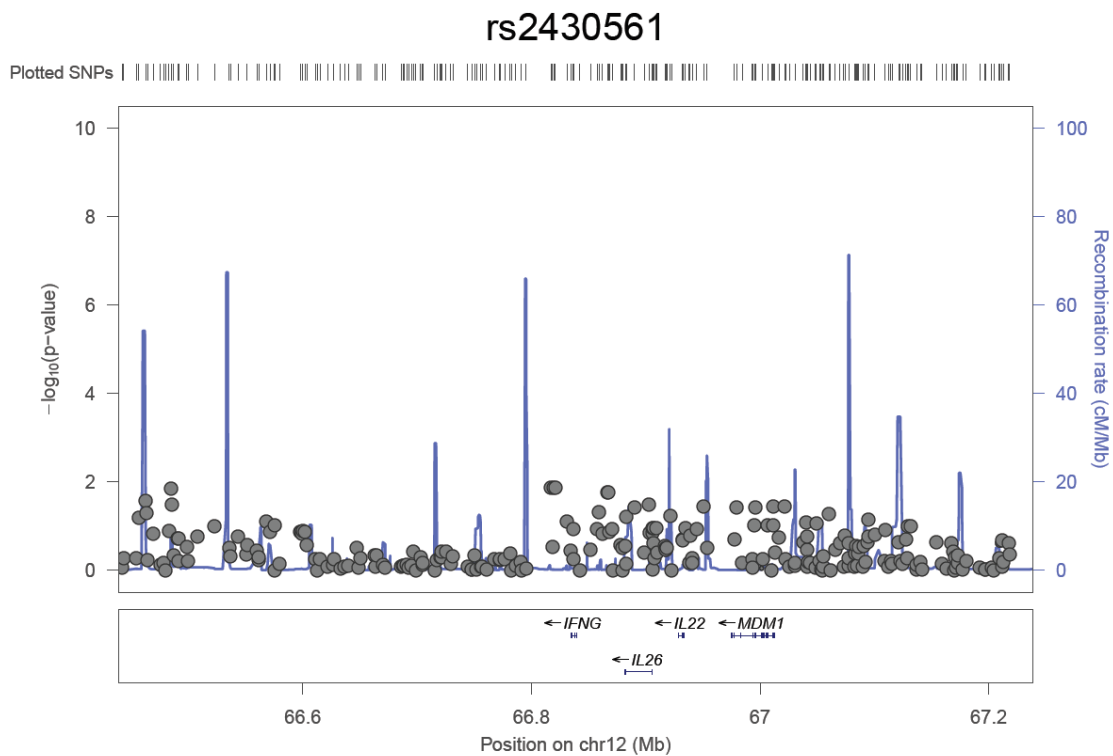


Figure 45: rs3817655 (proxy rs2291299)

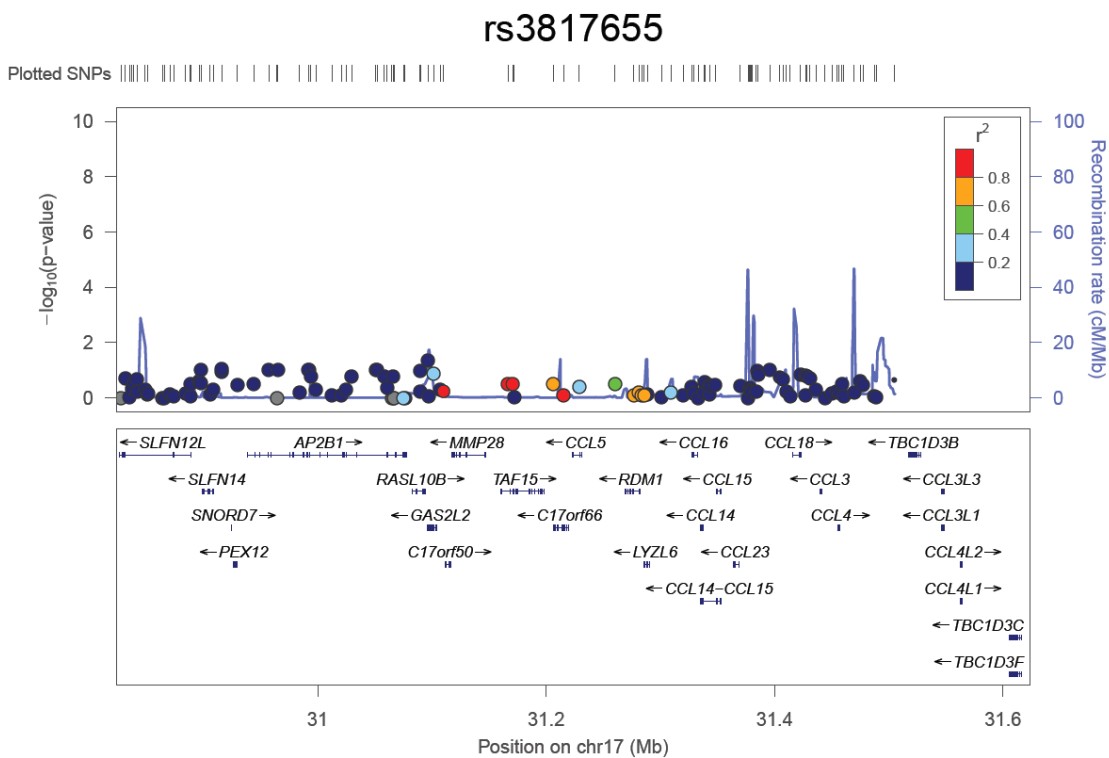


Figure 46: rs4819554 (proxy rs2041629)

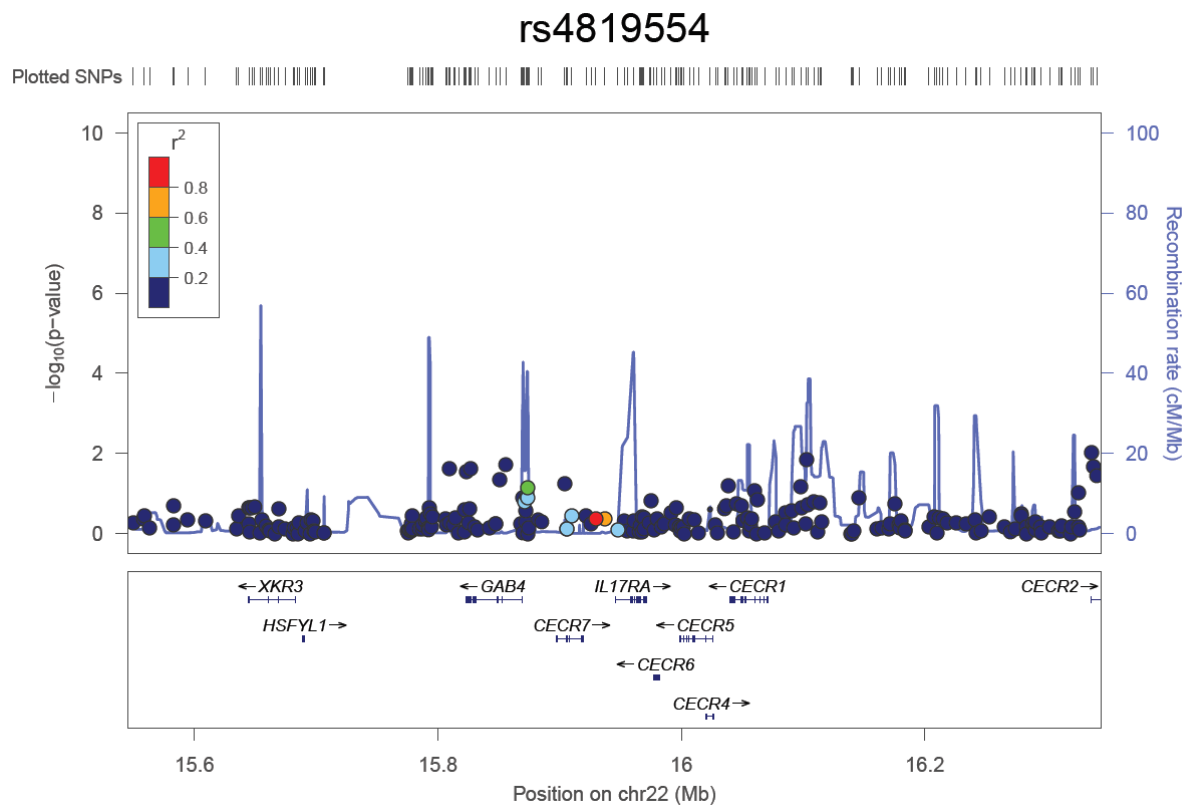


Figure 47: rs7903146

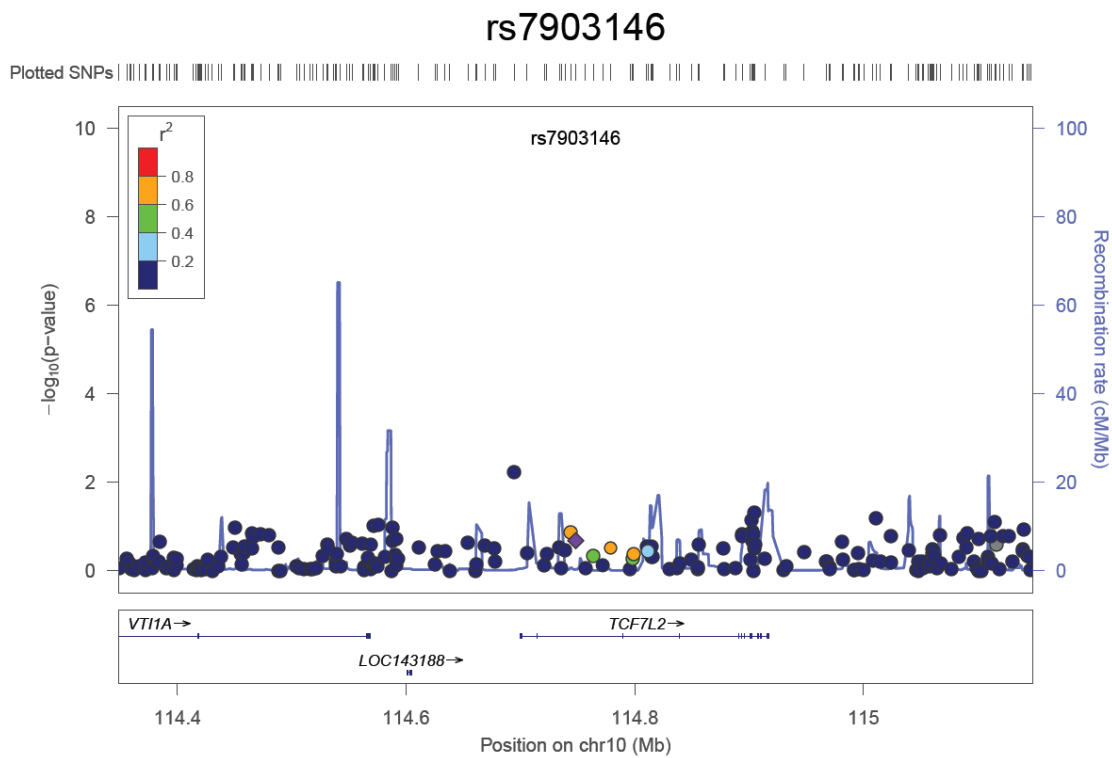


Figure 48: rs8192678

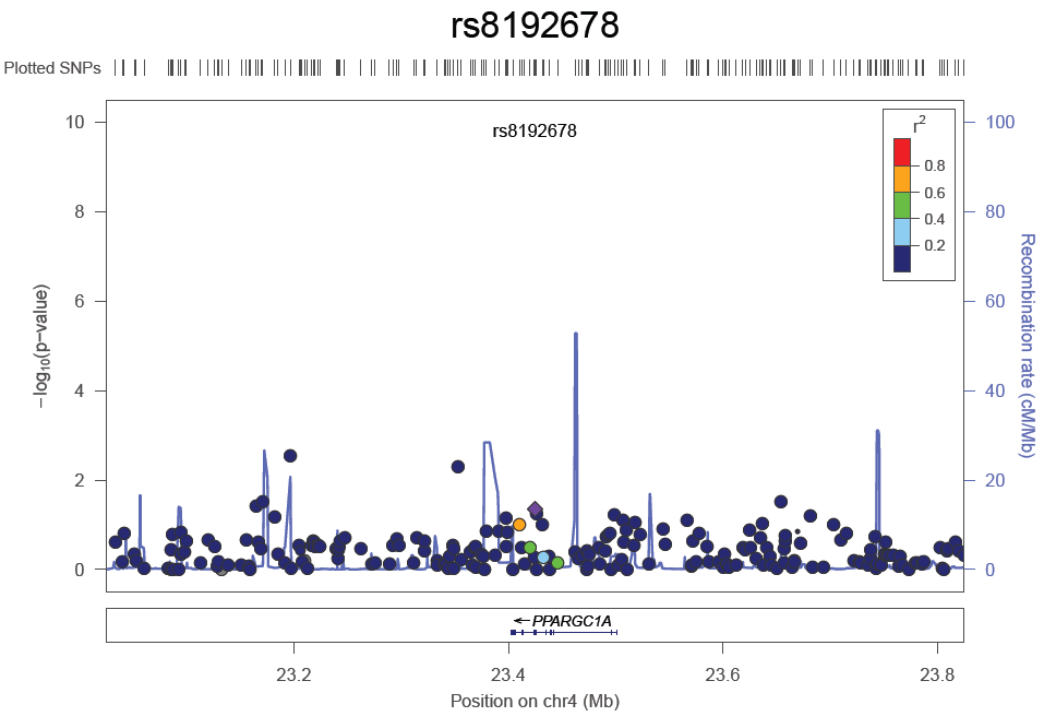


Figure 49:

rs12255372

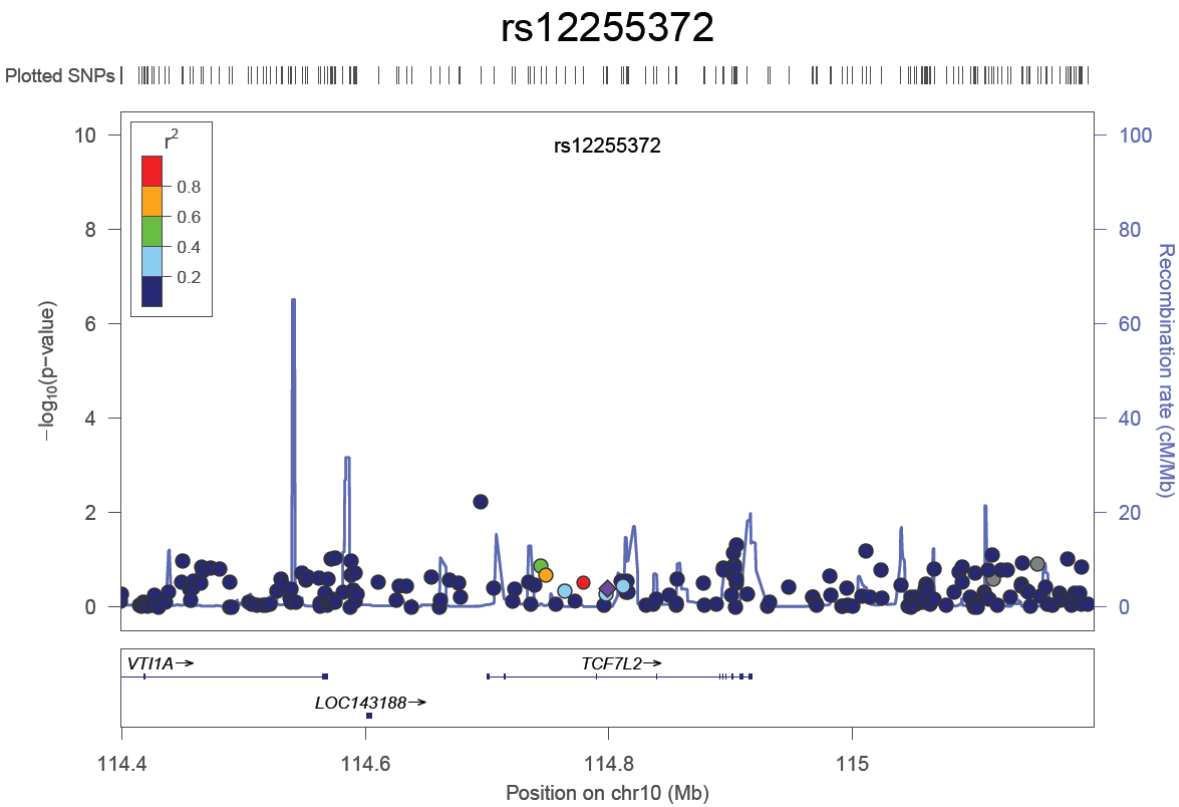
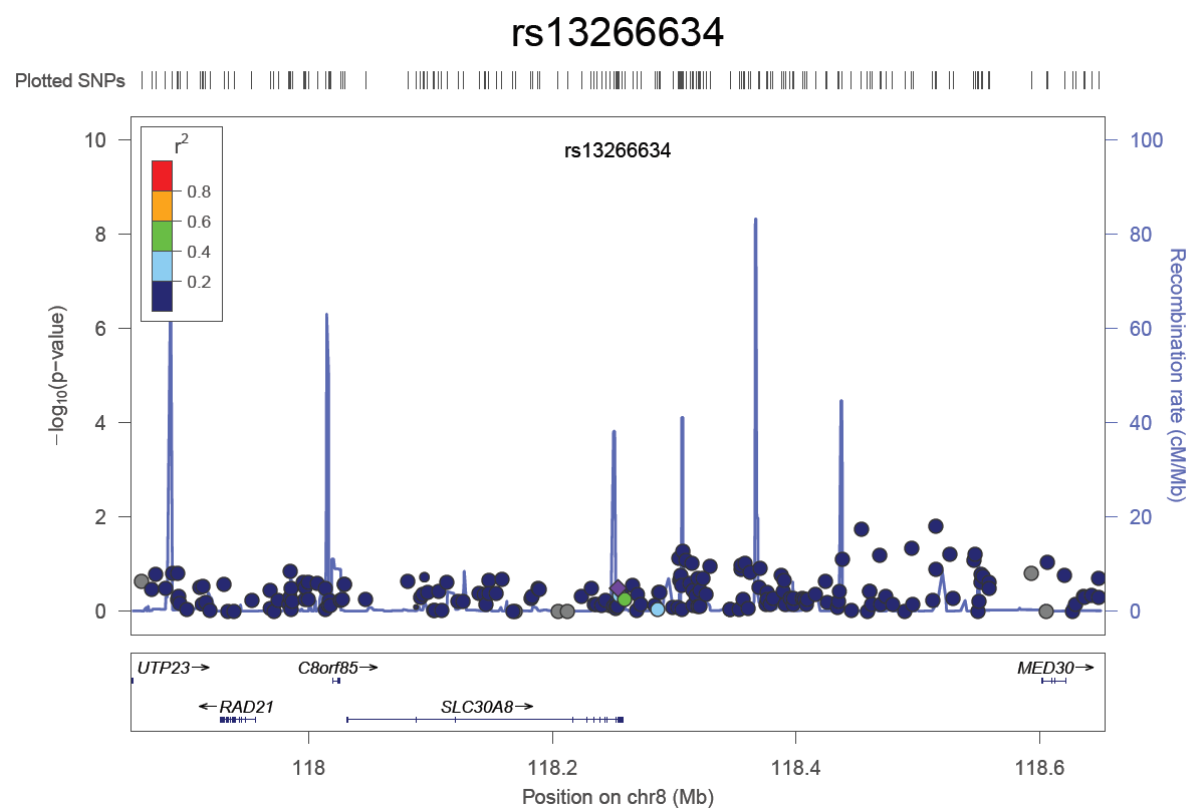


Figure 50: rs13266634



Cluster plots for SNPs from second stage genotyping

Figure 51: rs5219

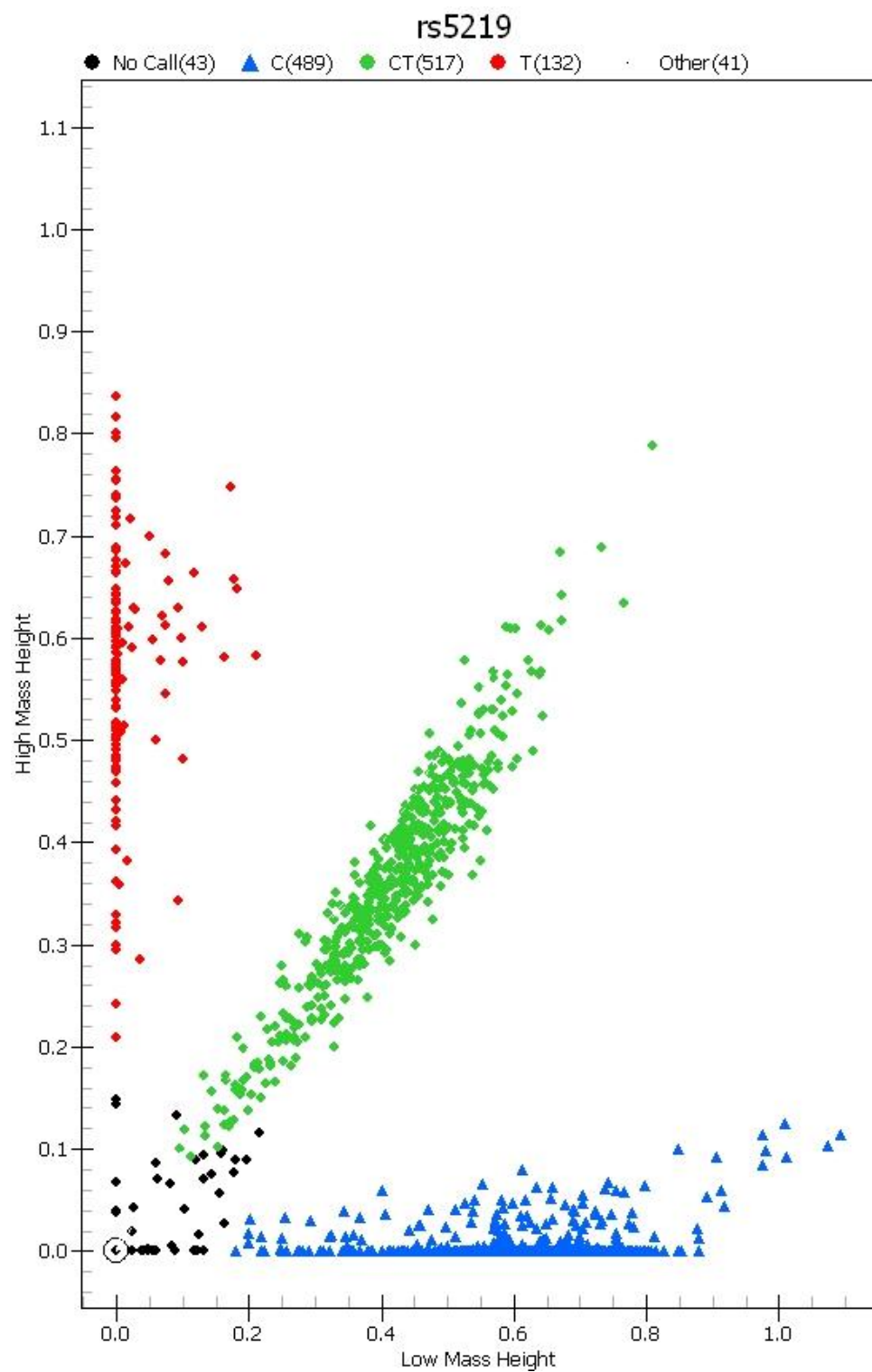


Figure 52: rs198372

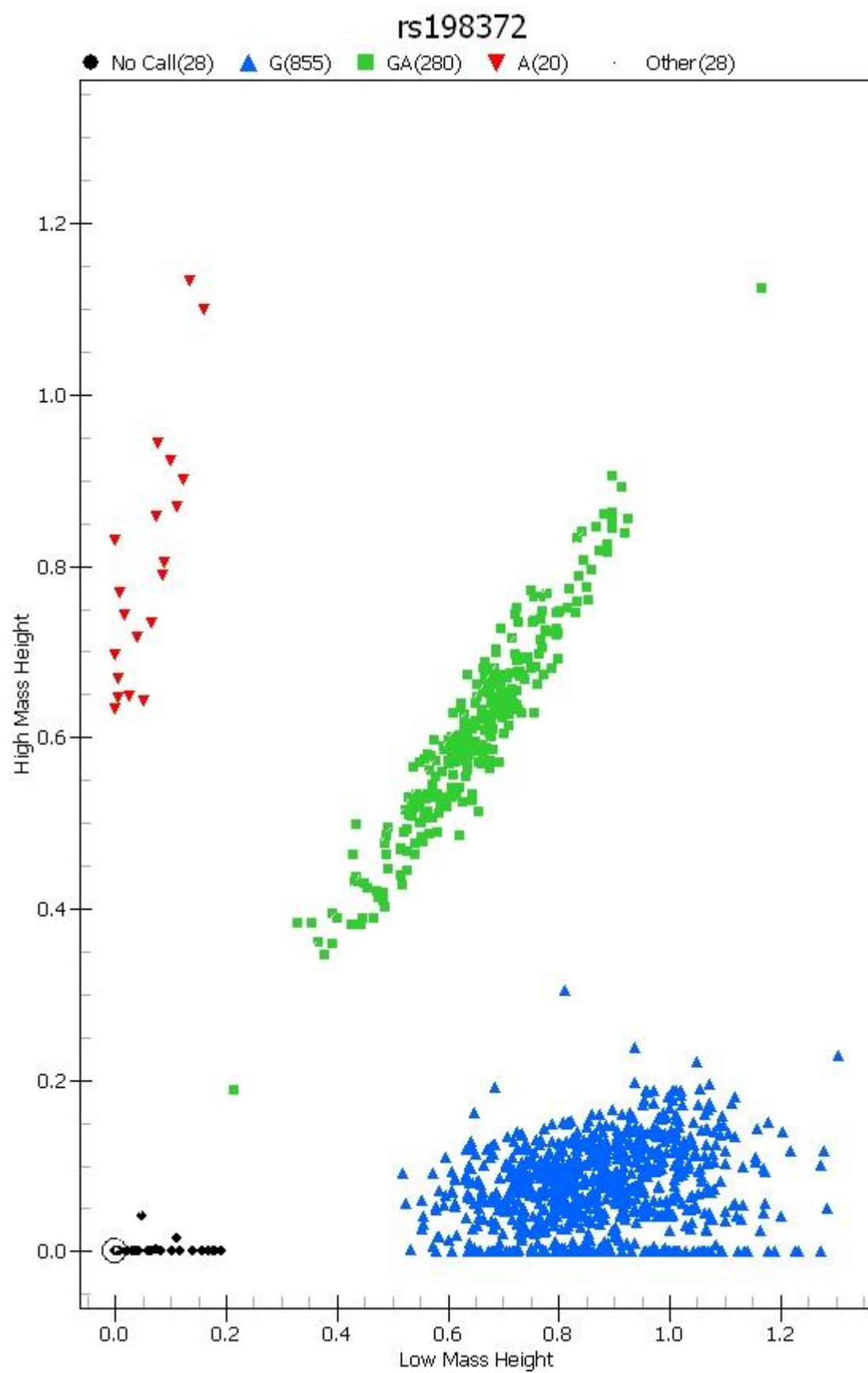


Figure 53: rs341497

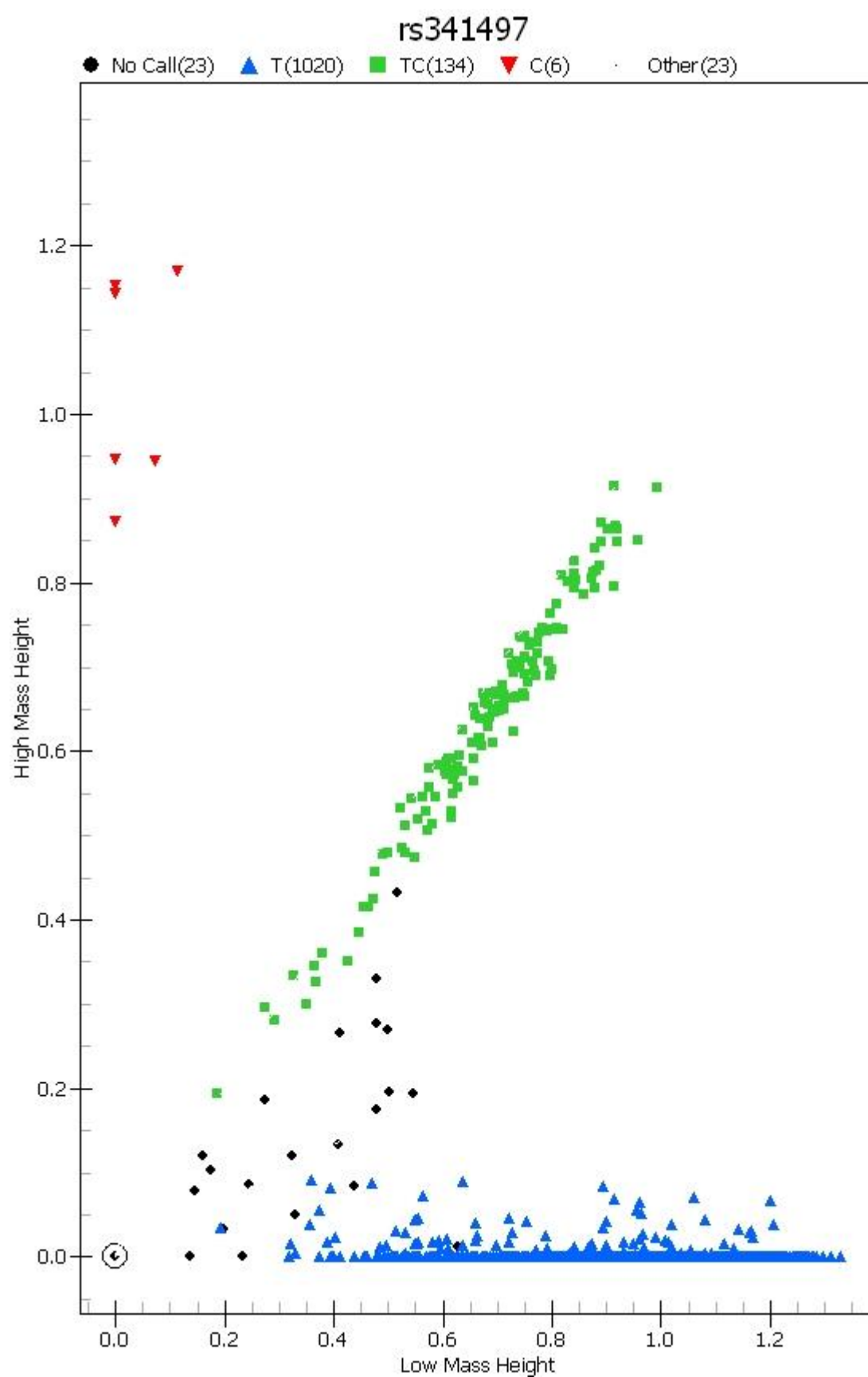


Figure 54: rs1016429

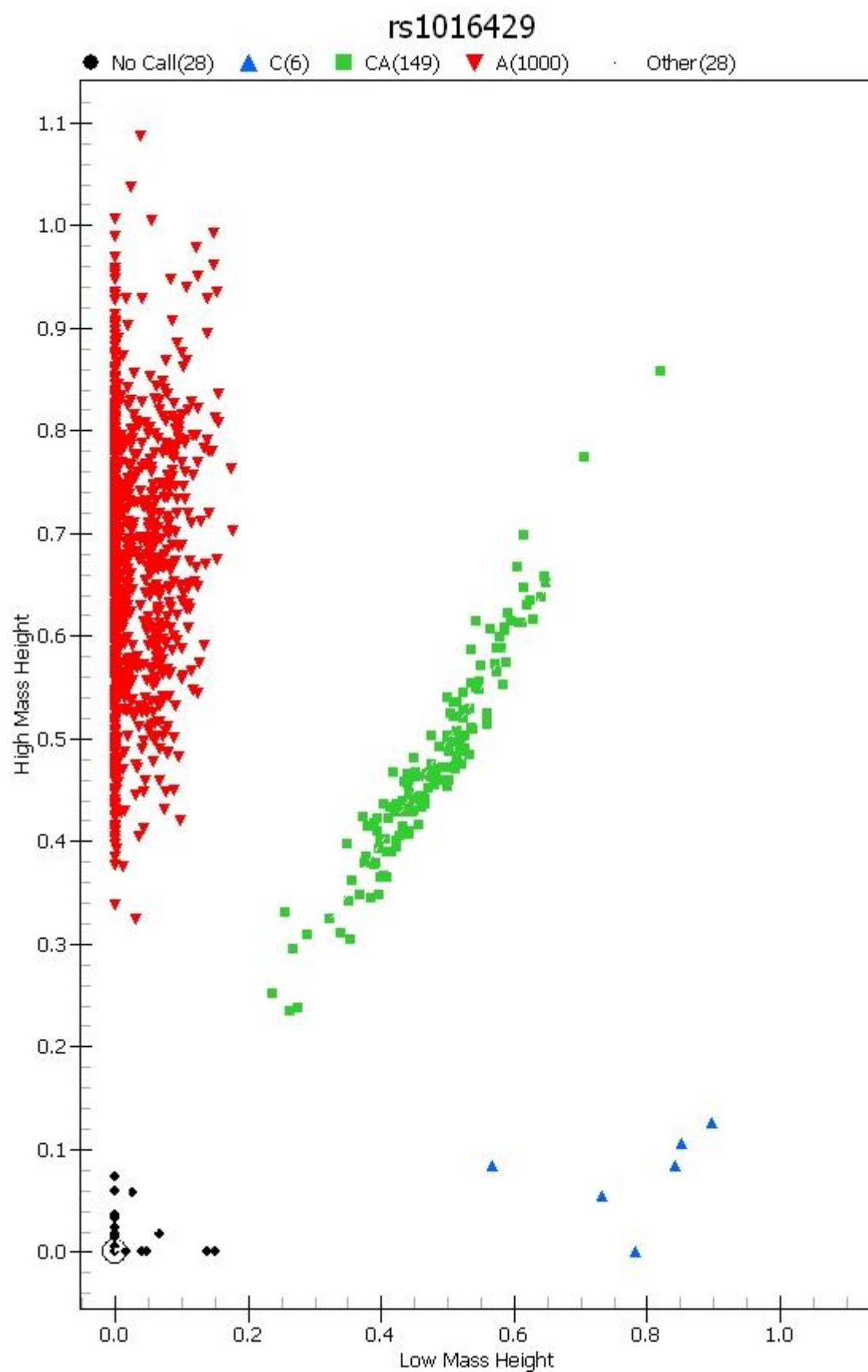


Figure 55: rs1025689

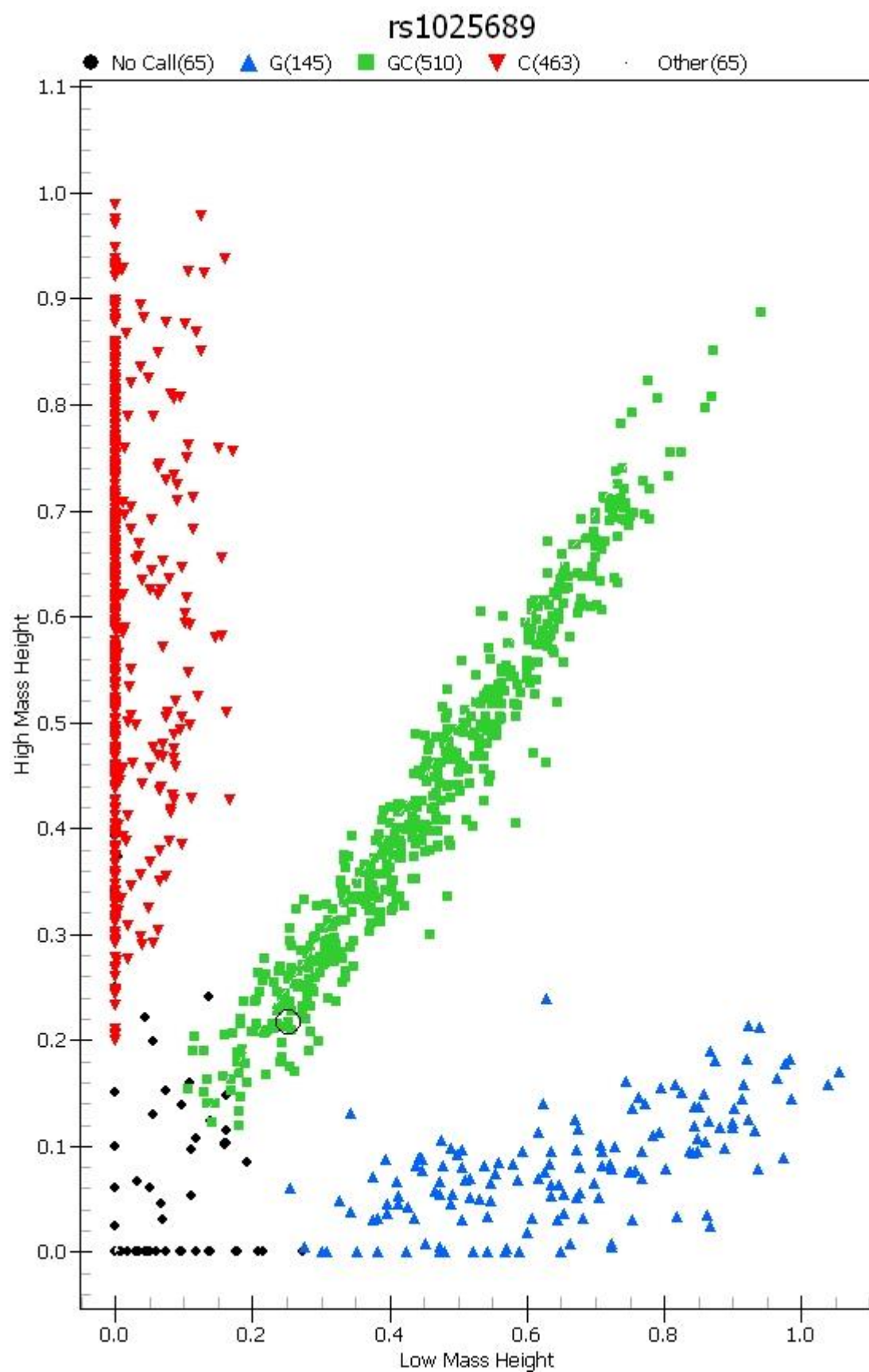


Figure 56: rs1043261

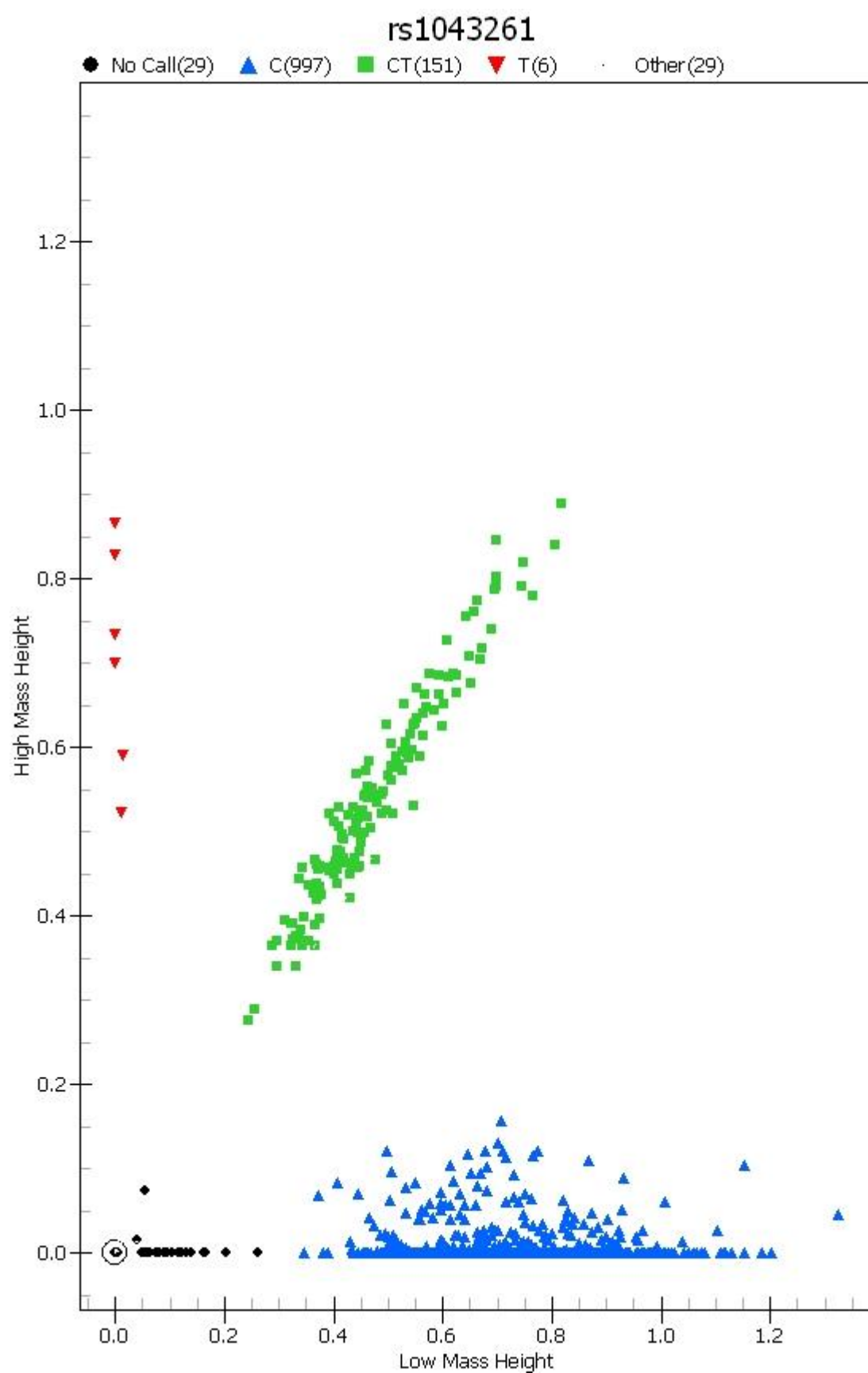


Figure 57: rs1044498

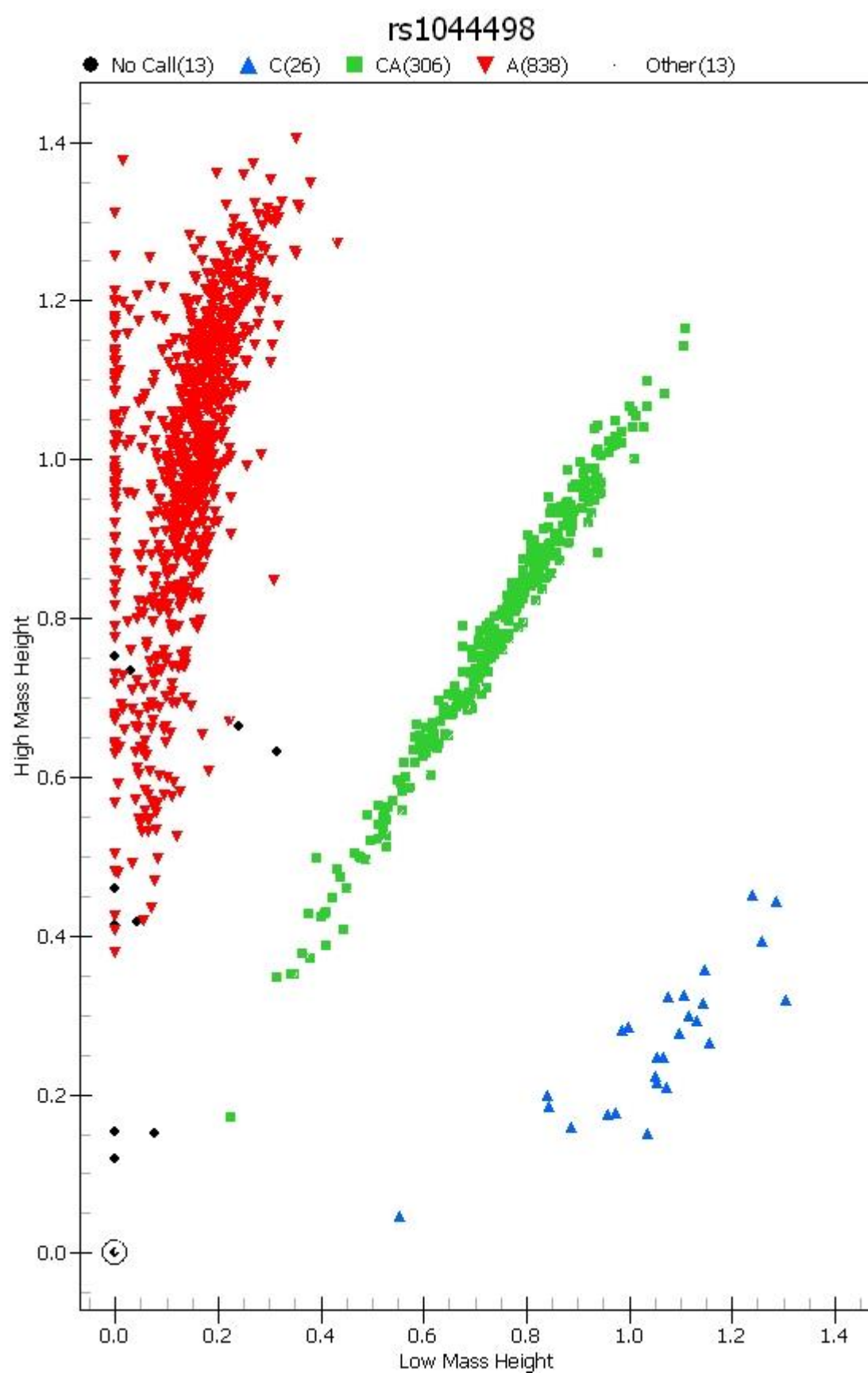


Figure 58: rs1124053

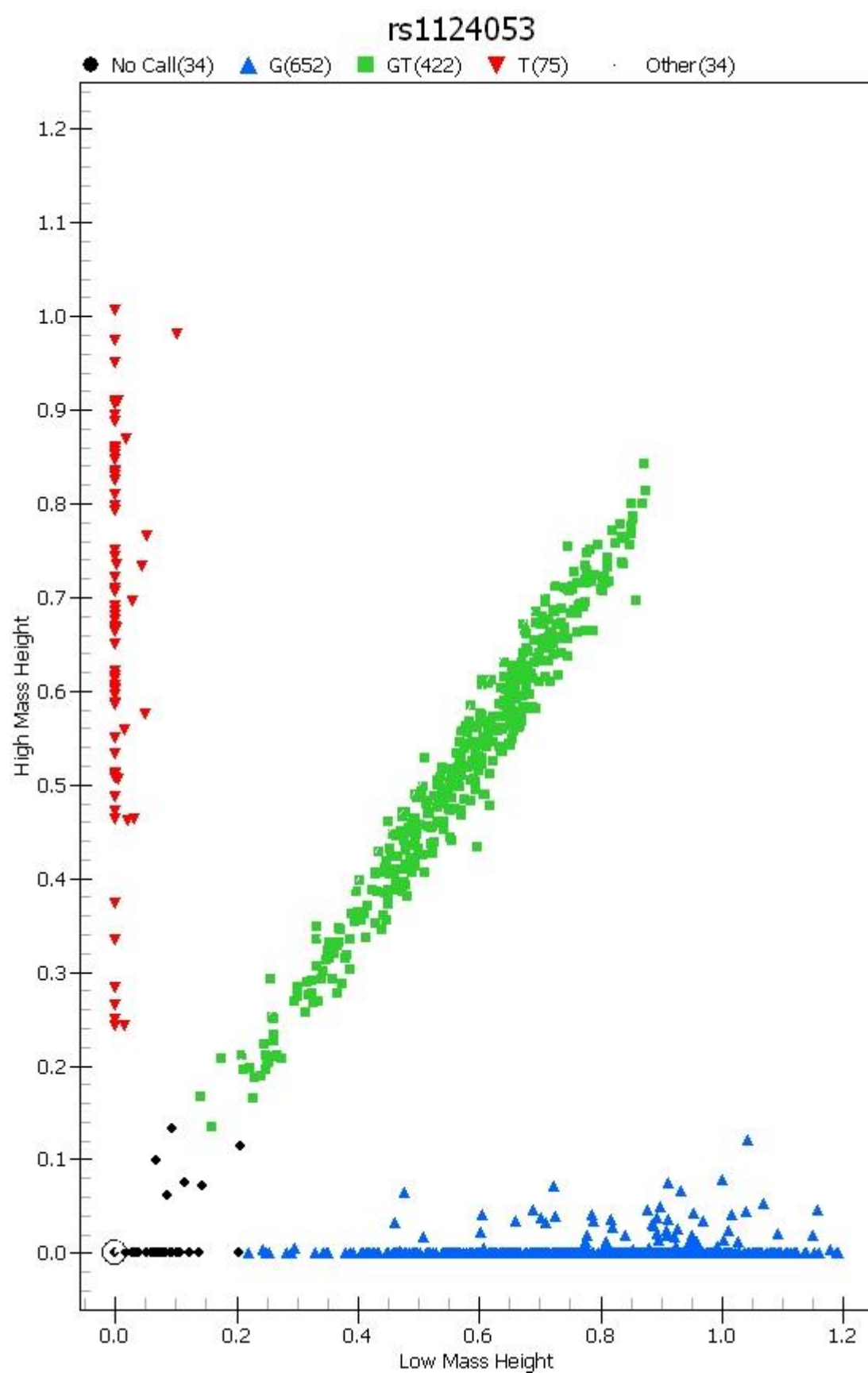


Figure 59: rs1169288

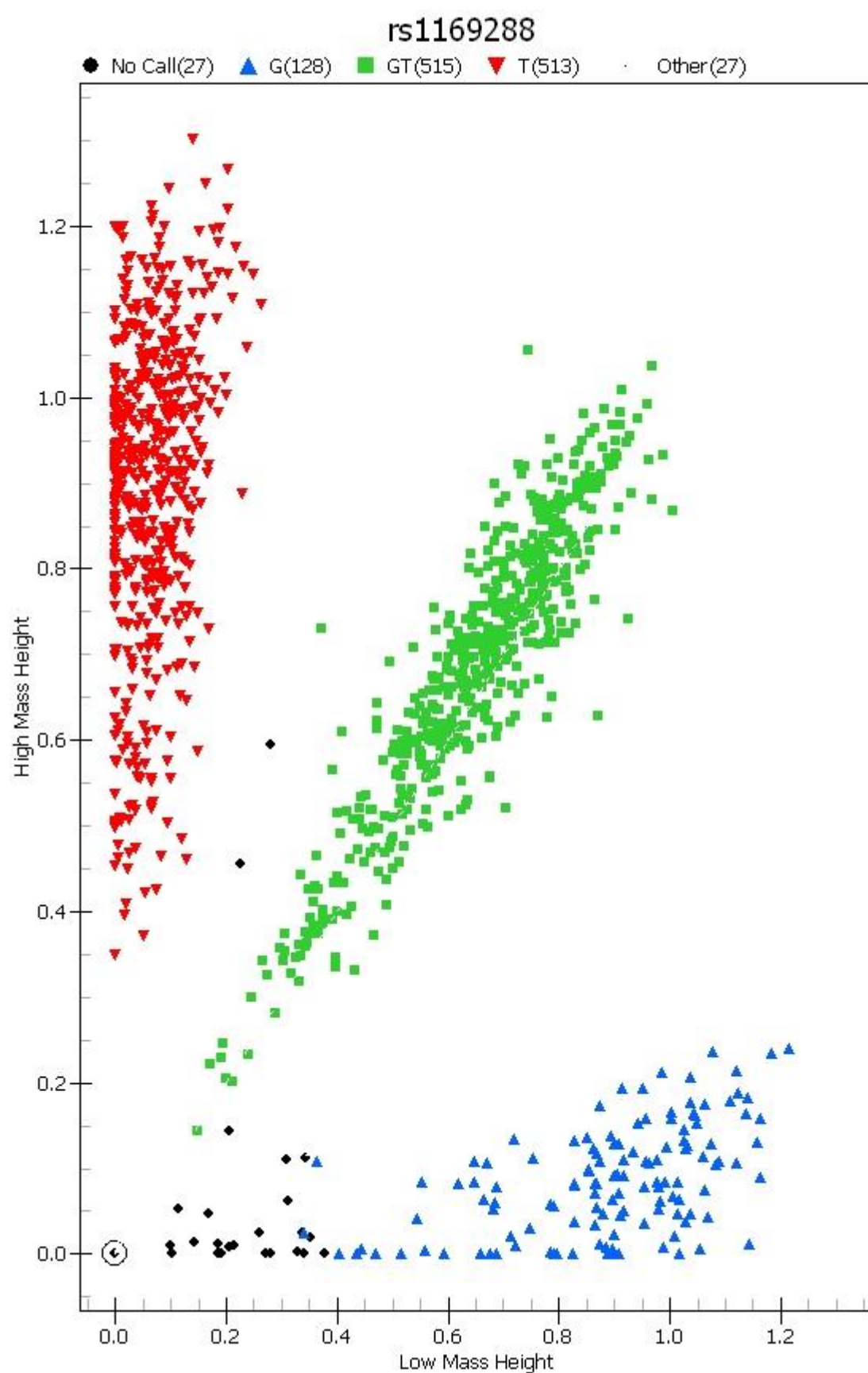


Figure 60:

rs1494558

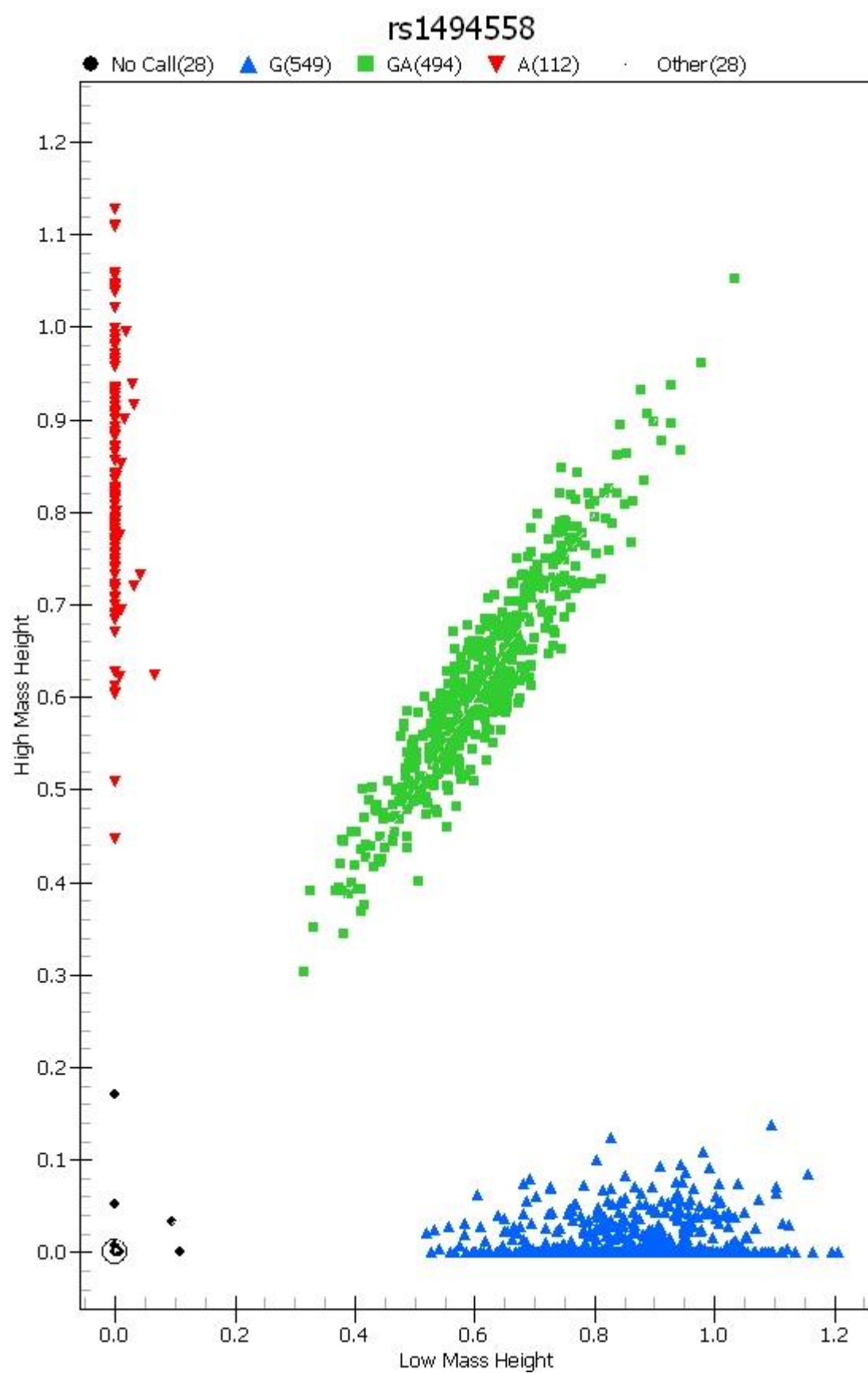


Figure 61:

rs1783606

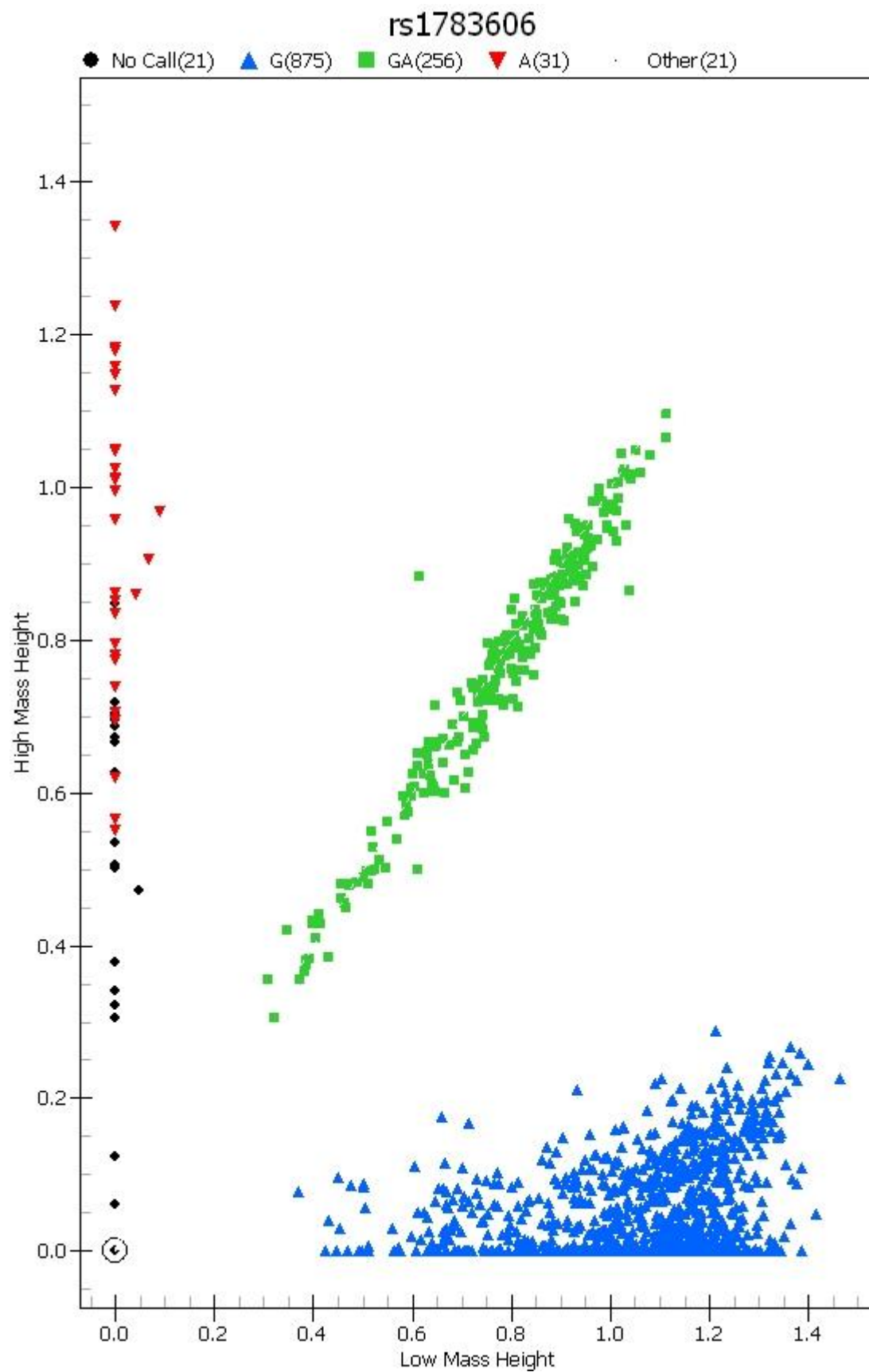


Figure 62:

rs1799854

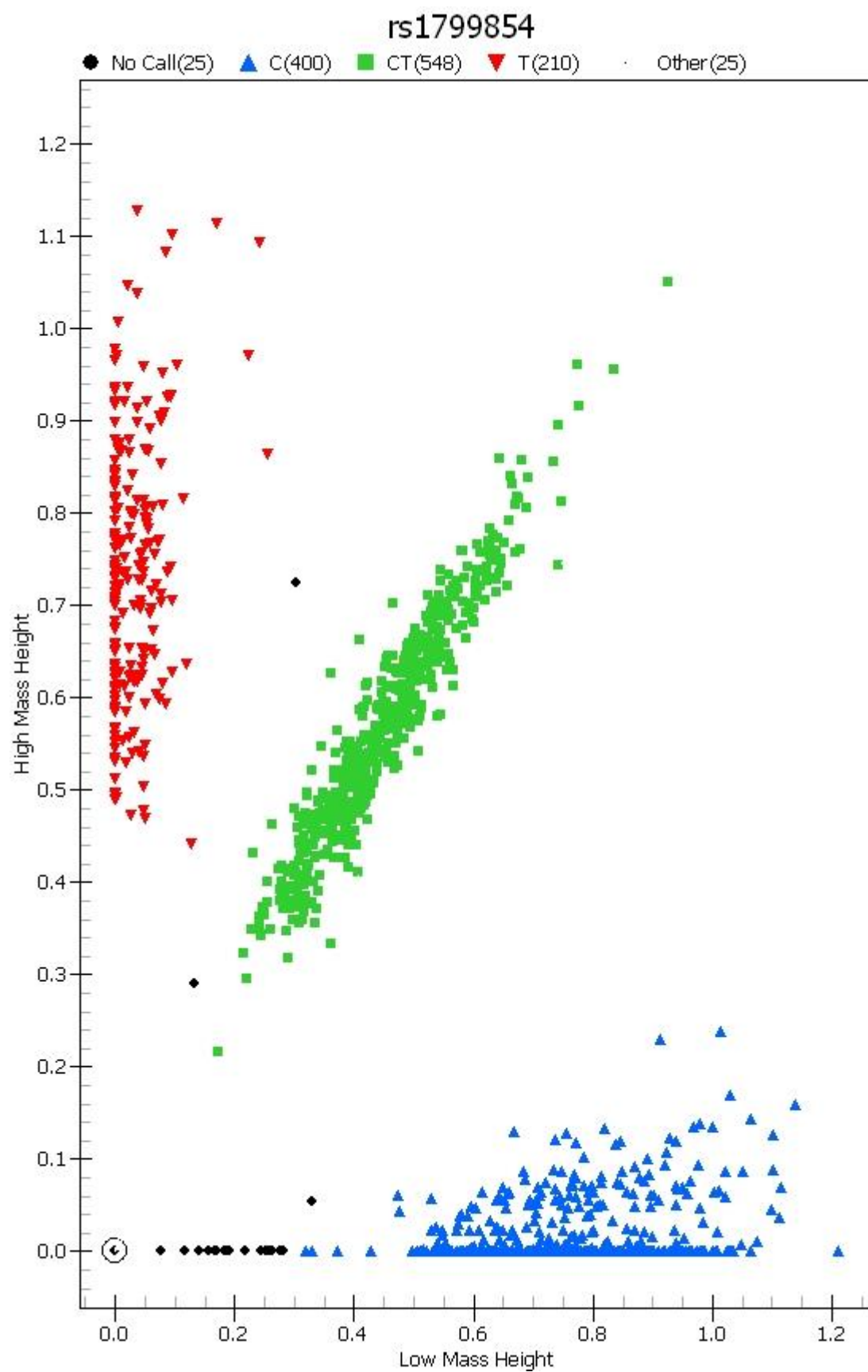


Figure 63: rs1800795

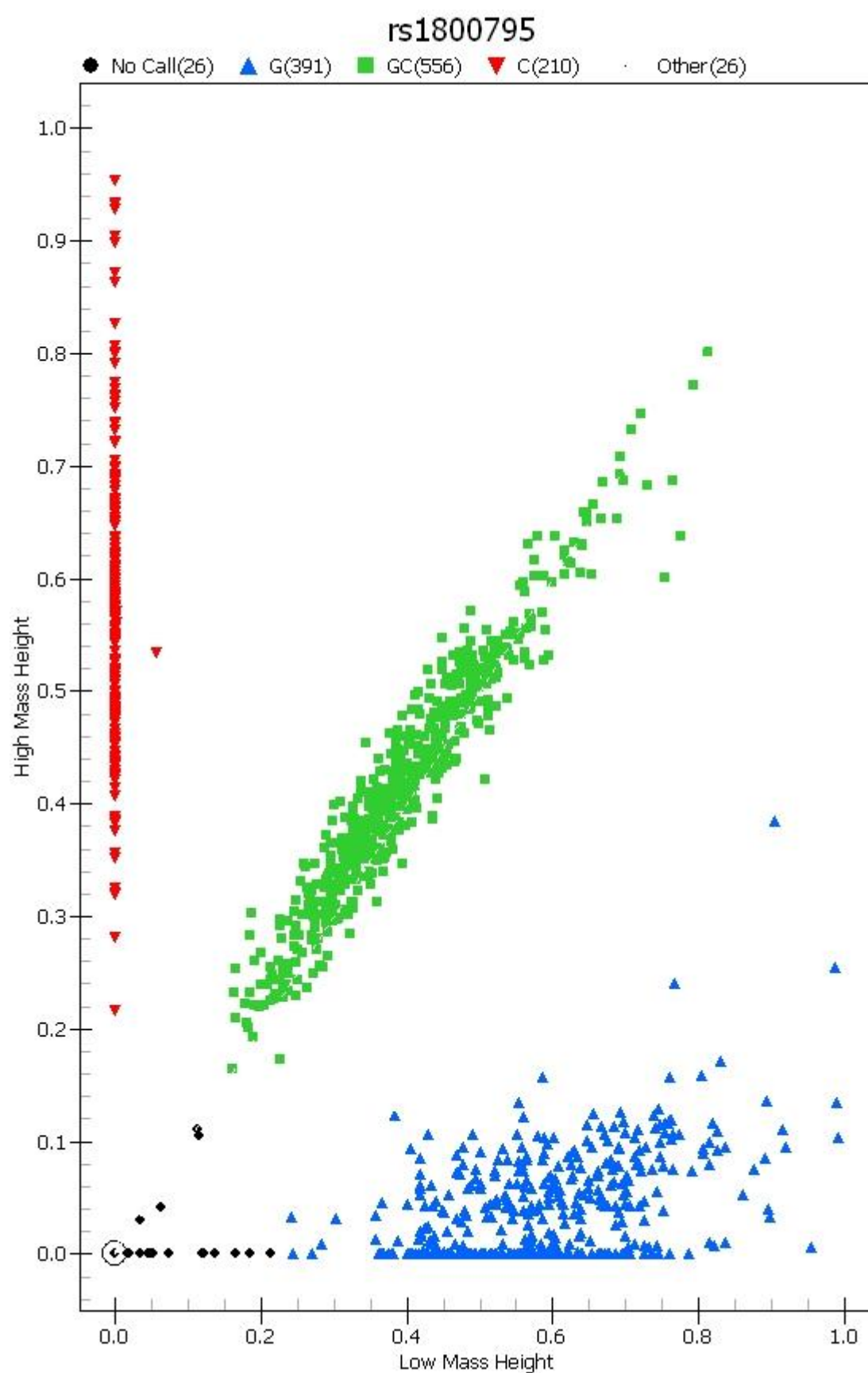


Figure 64: rs1800961 (Taqman)

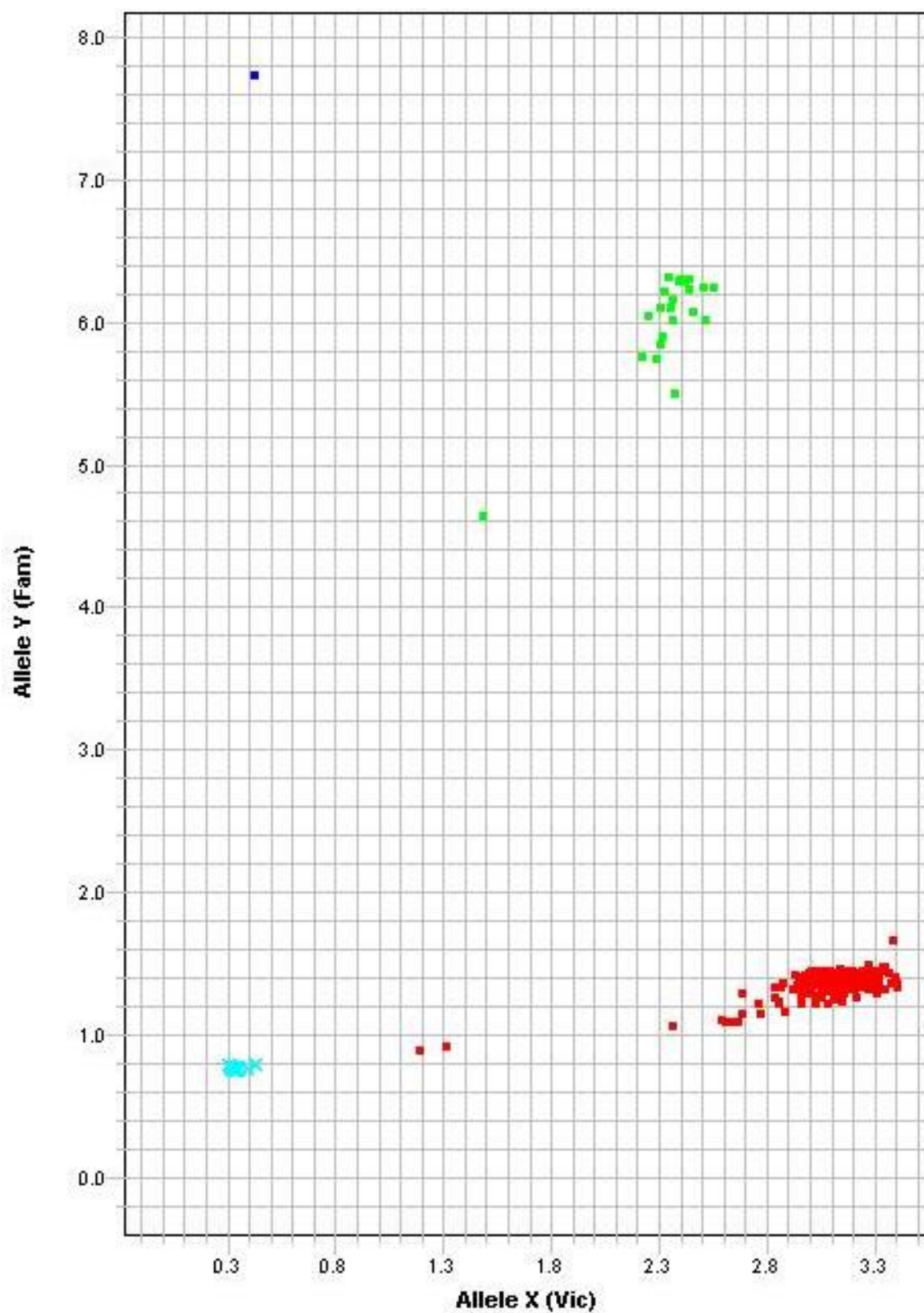


Figure 65: rs1801282

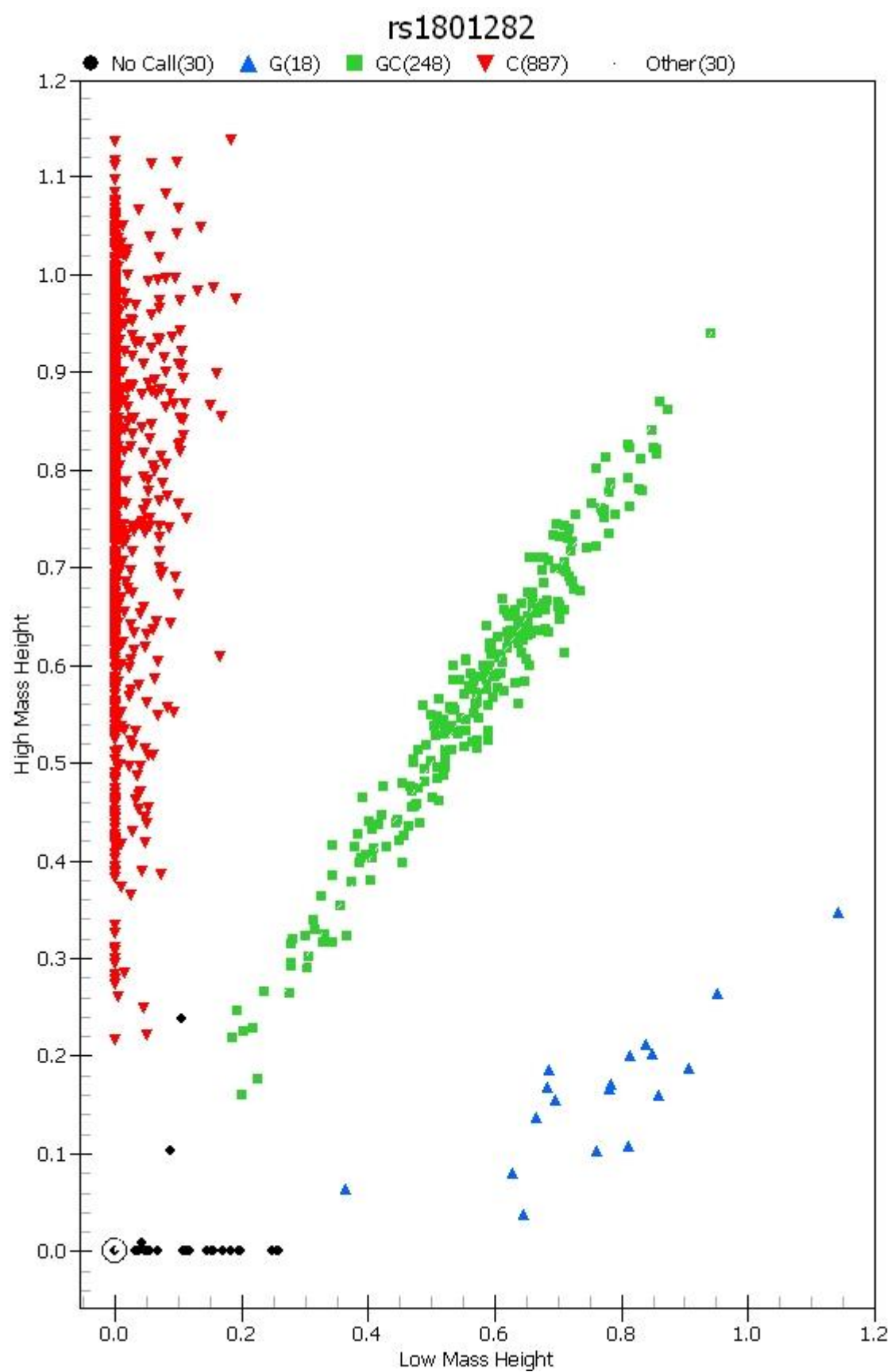


Figure 66:

rs1836882

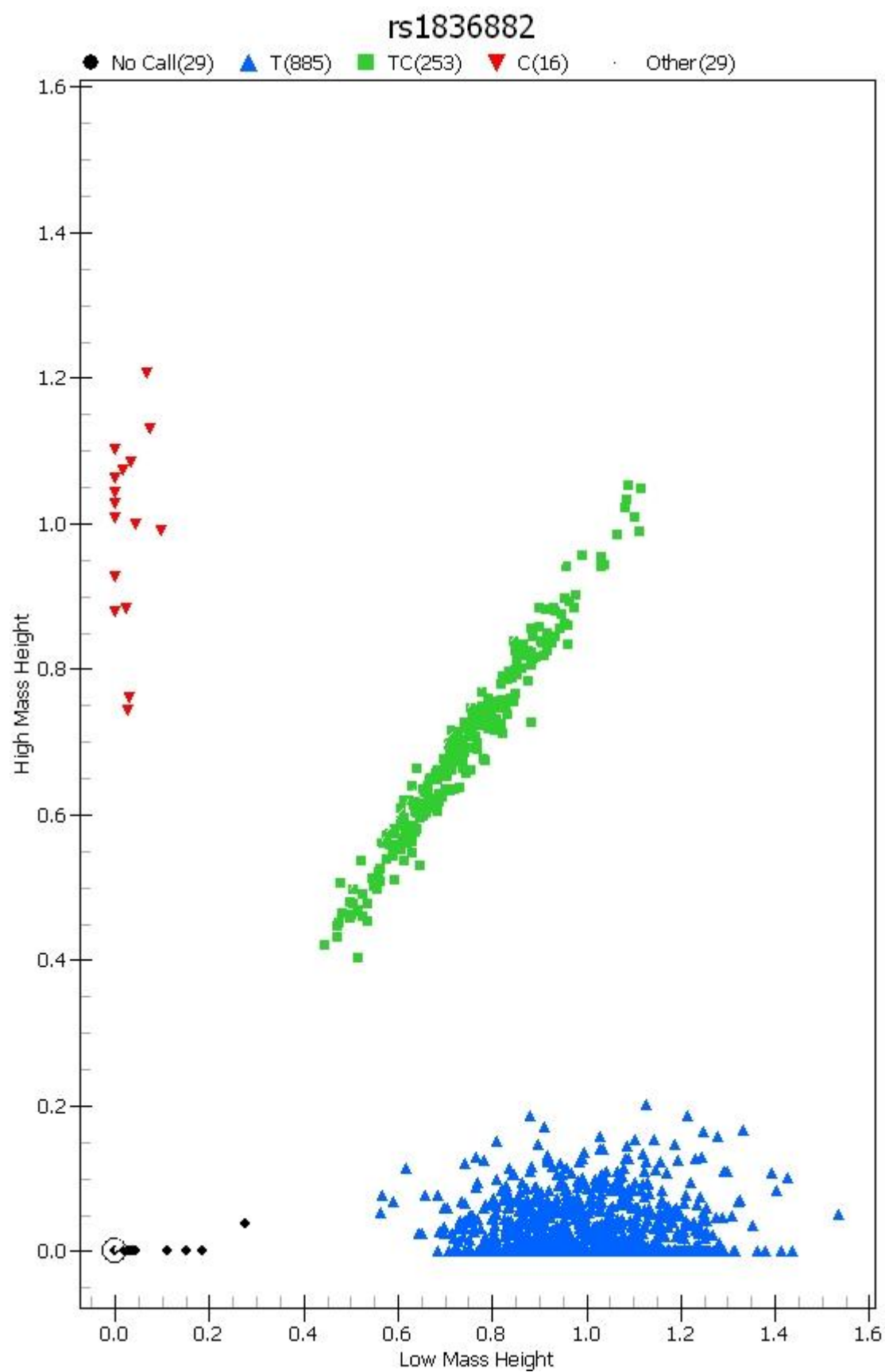


Figure 67: rs1871184

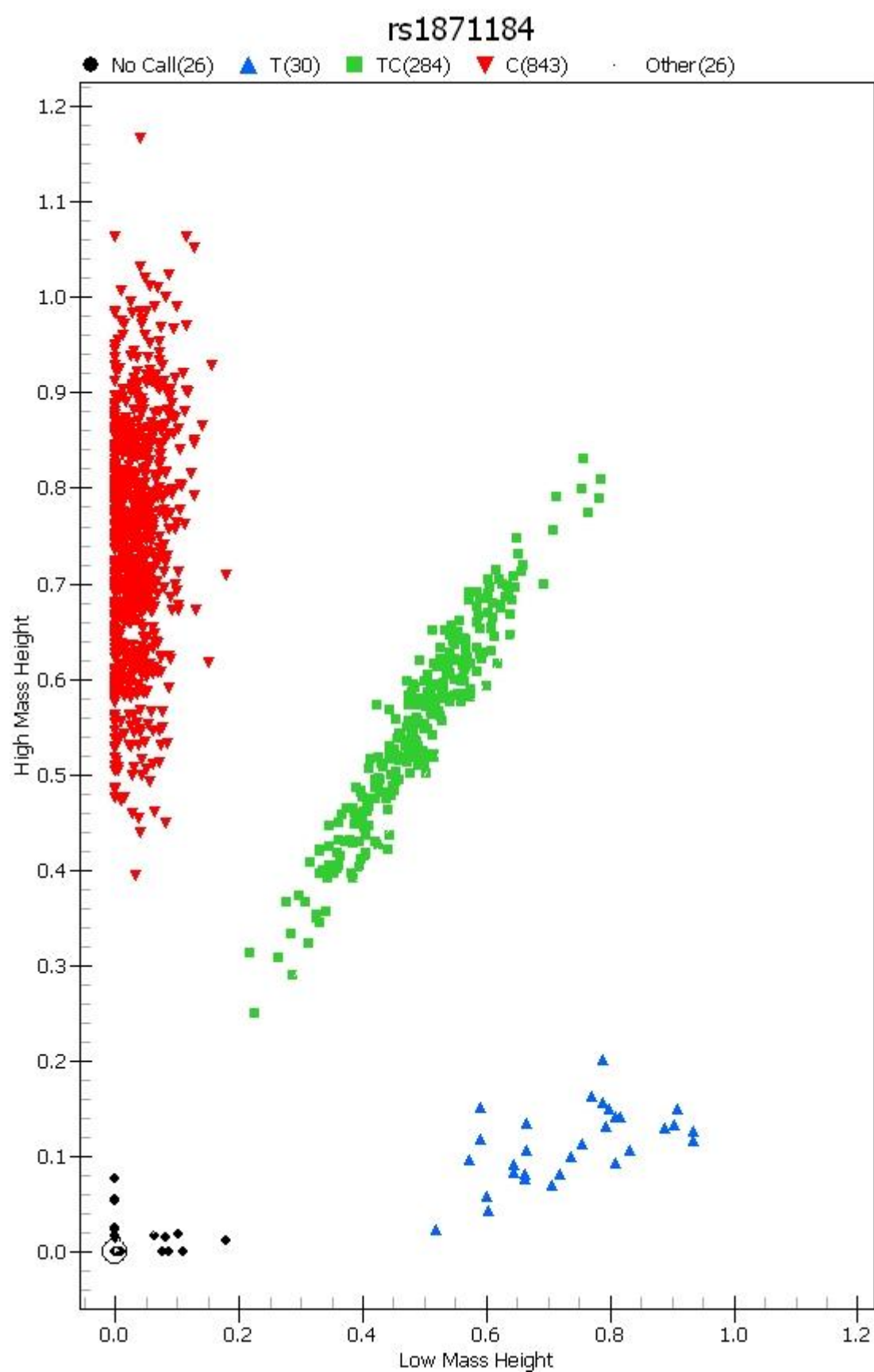


Figure 68: rs2020902

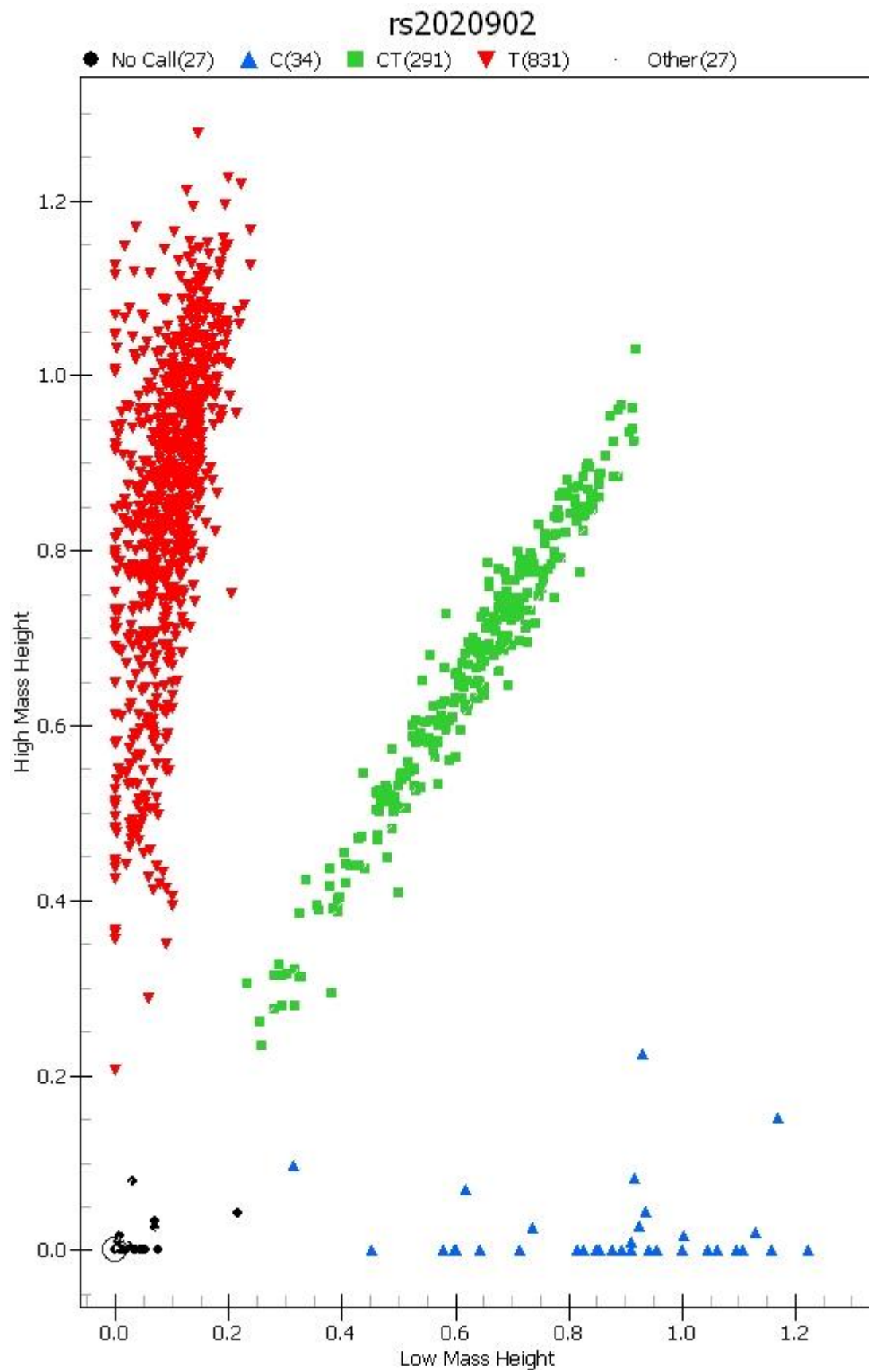


Figure 69: rs2069762 (Taqman)

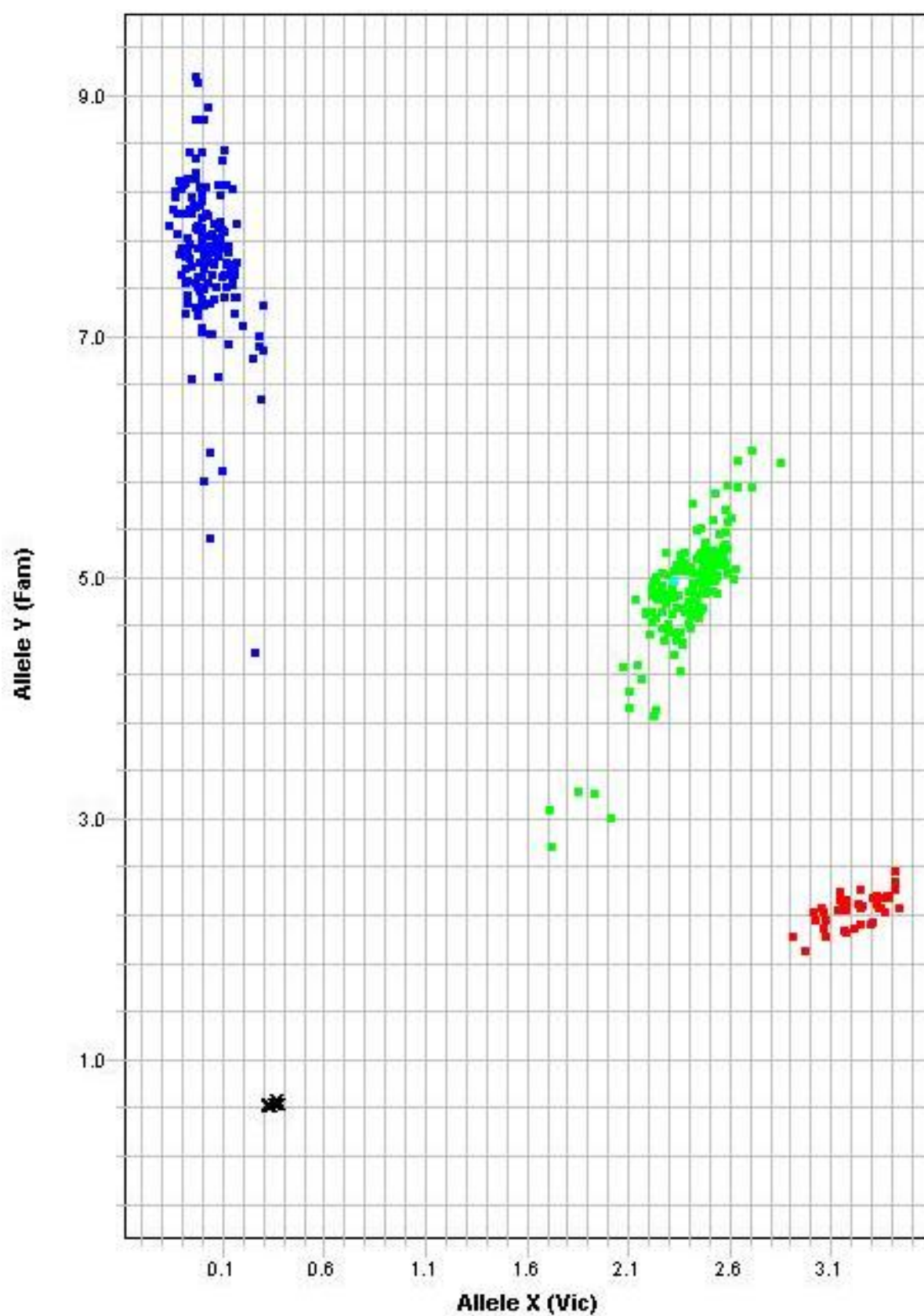


Figure 70: rs2069763 (Taqman)

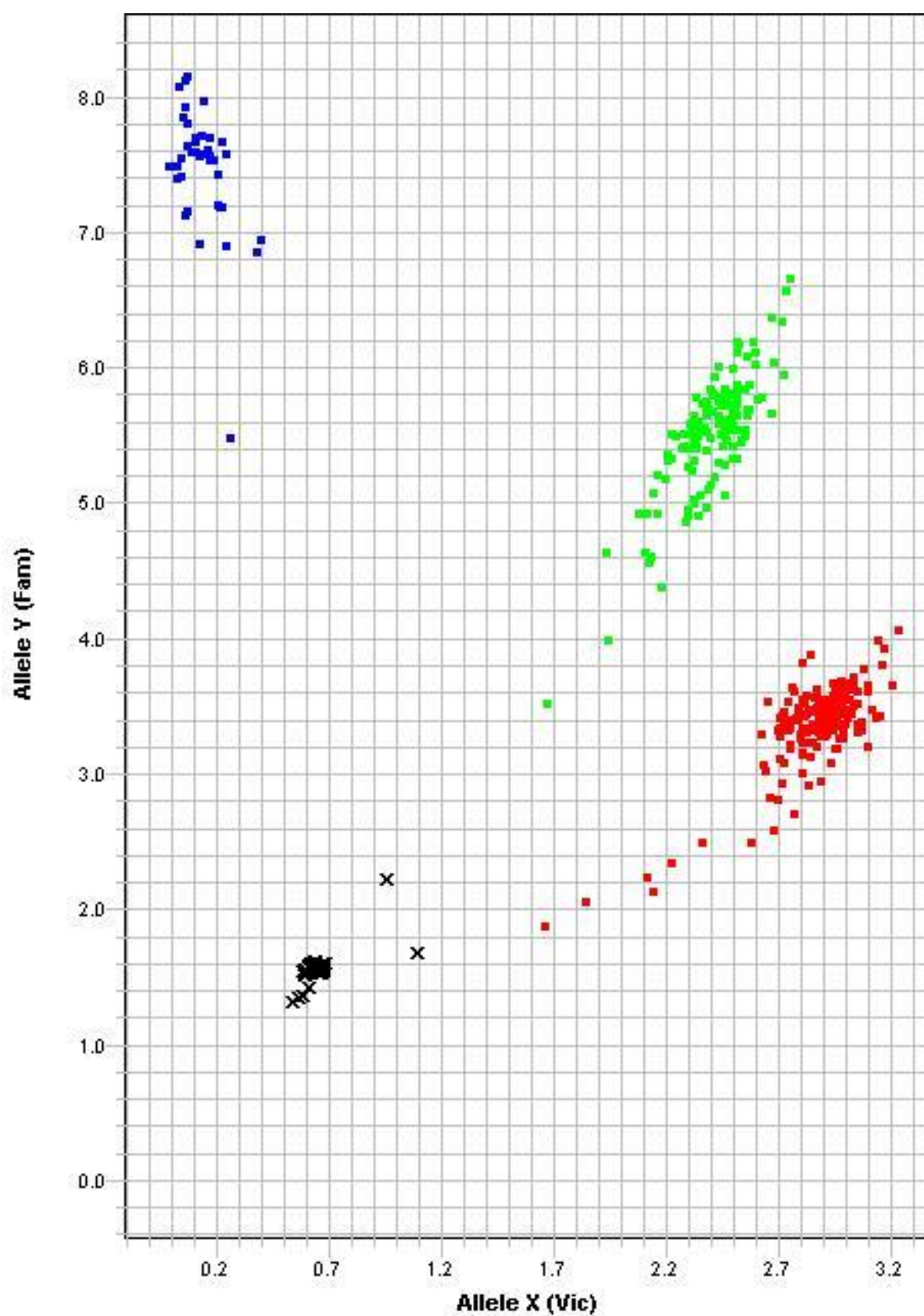


Figure 71: rs2070874

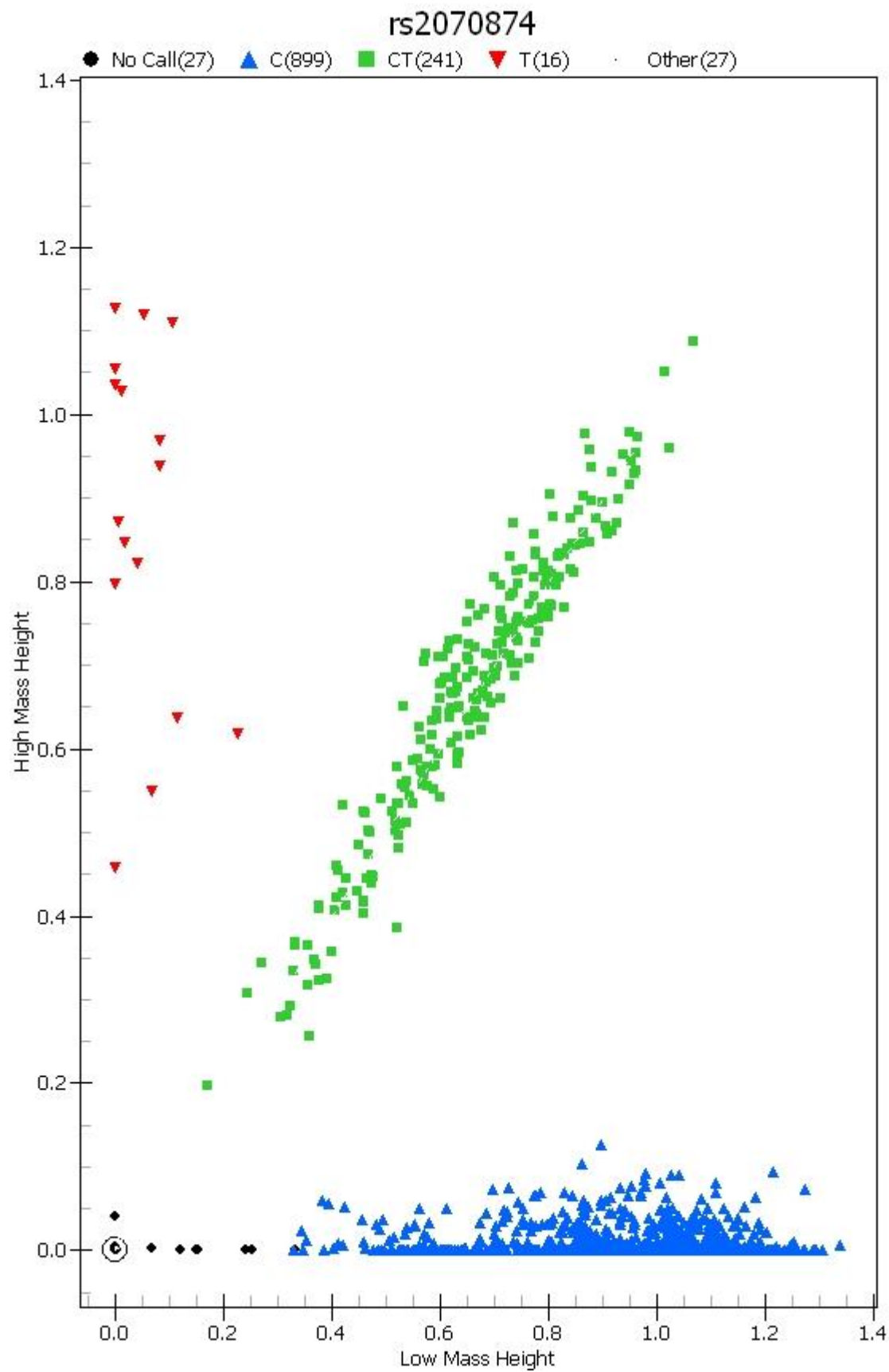


Figure 72: rs2107538

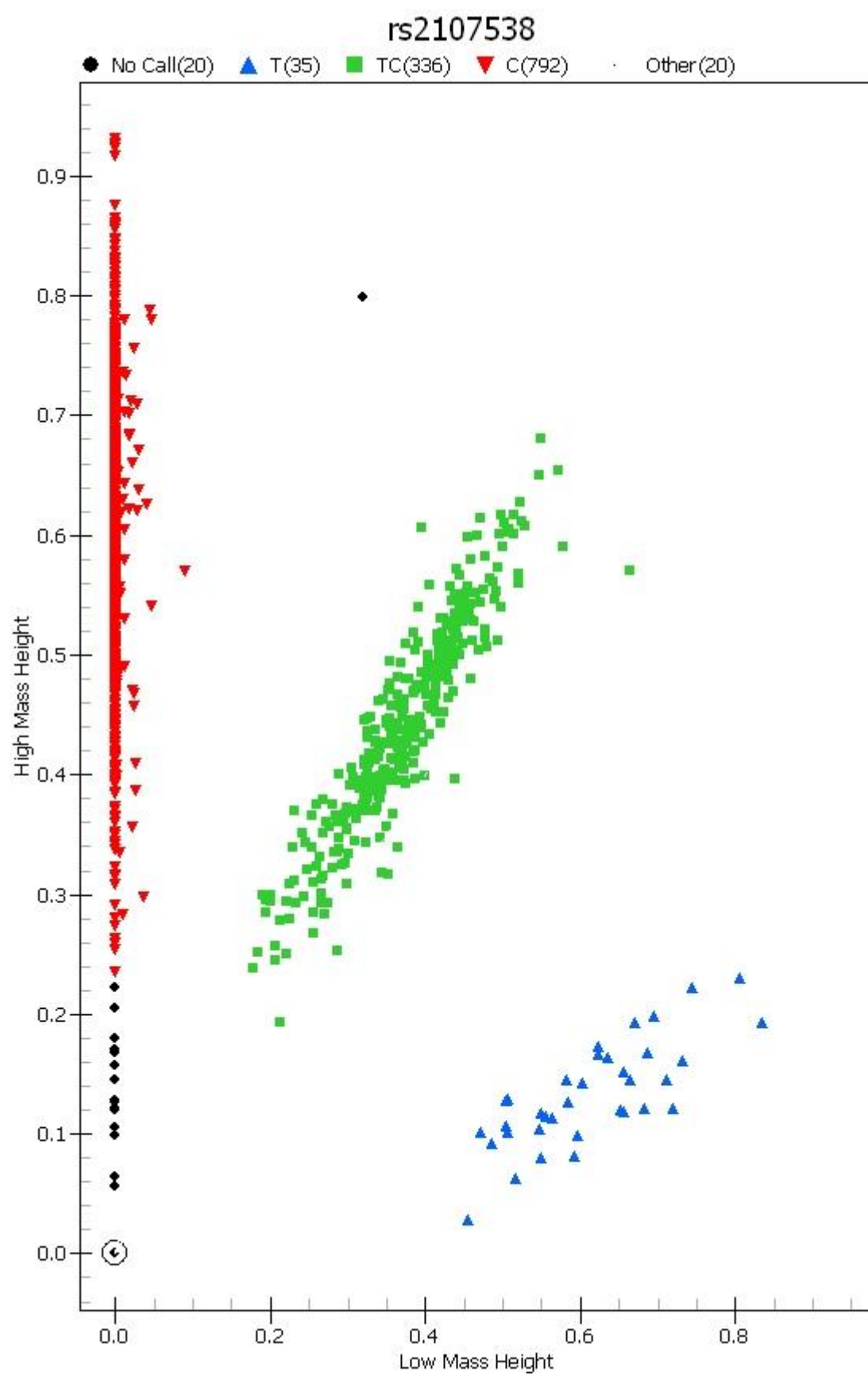


Figure 73: rs2144908

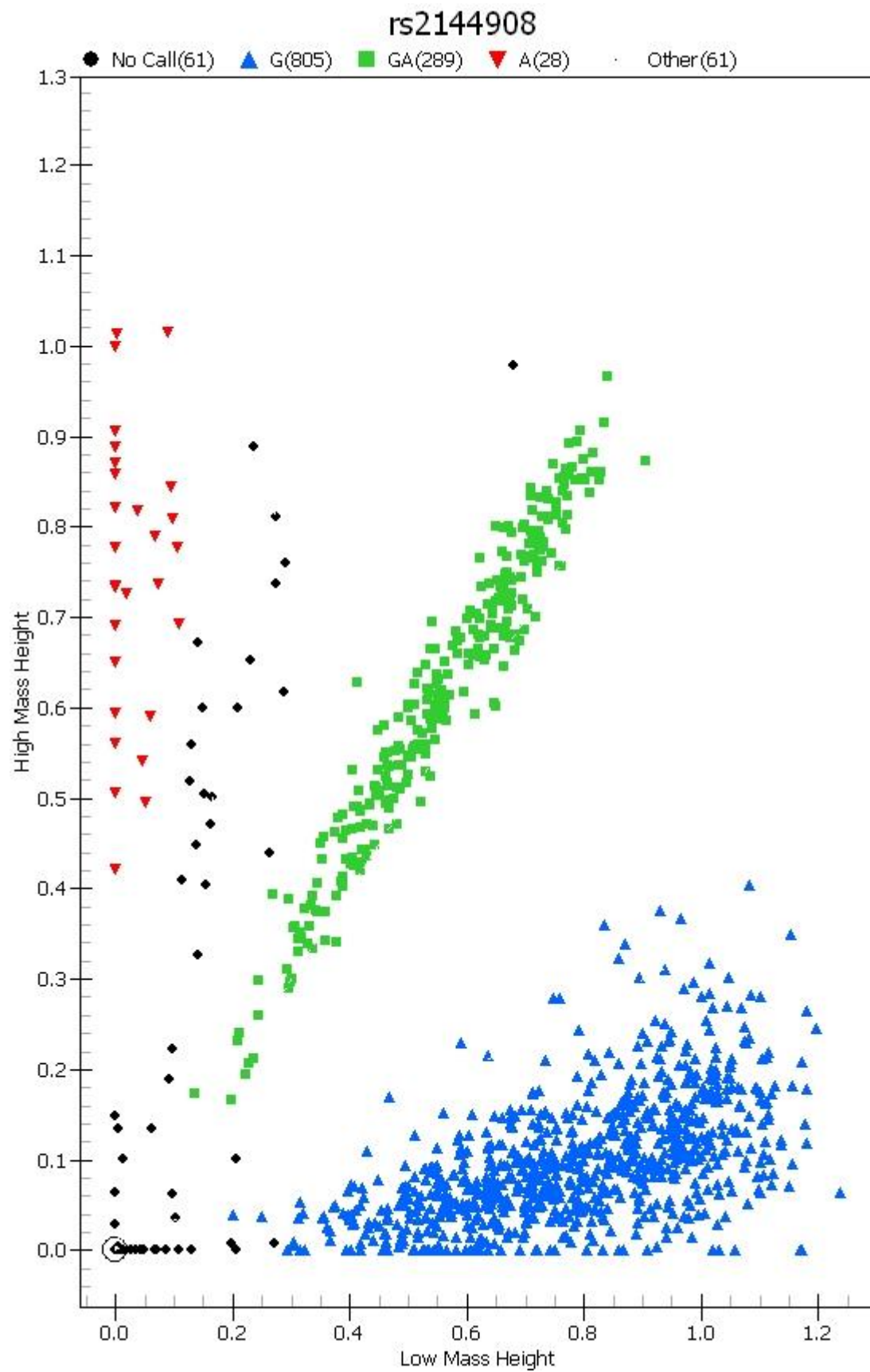


Figure 74: rs2172749

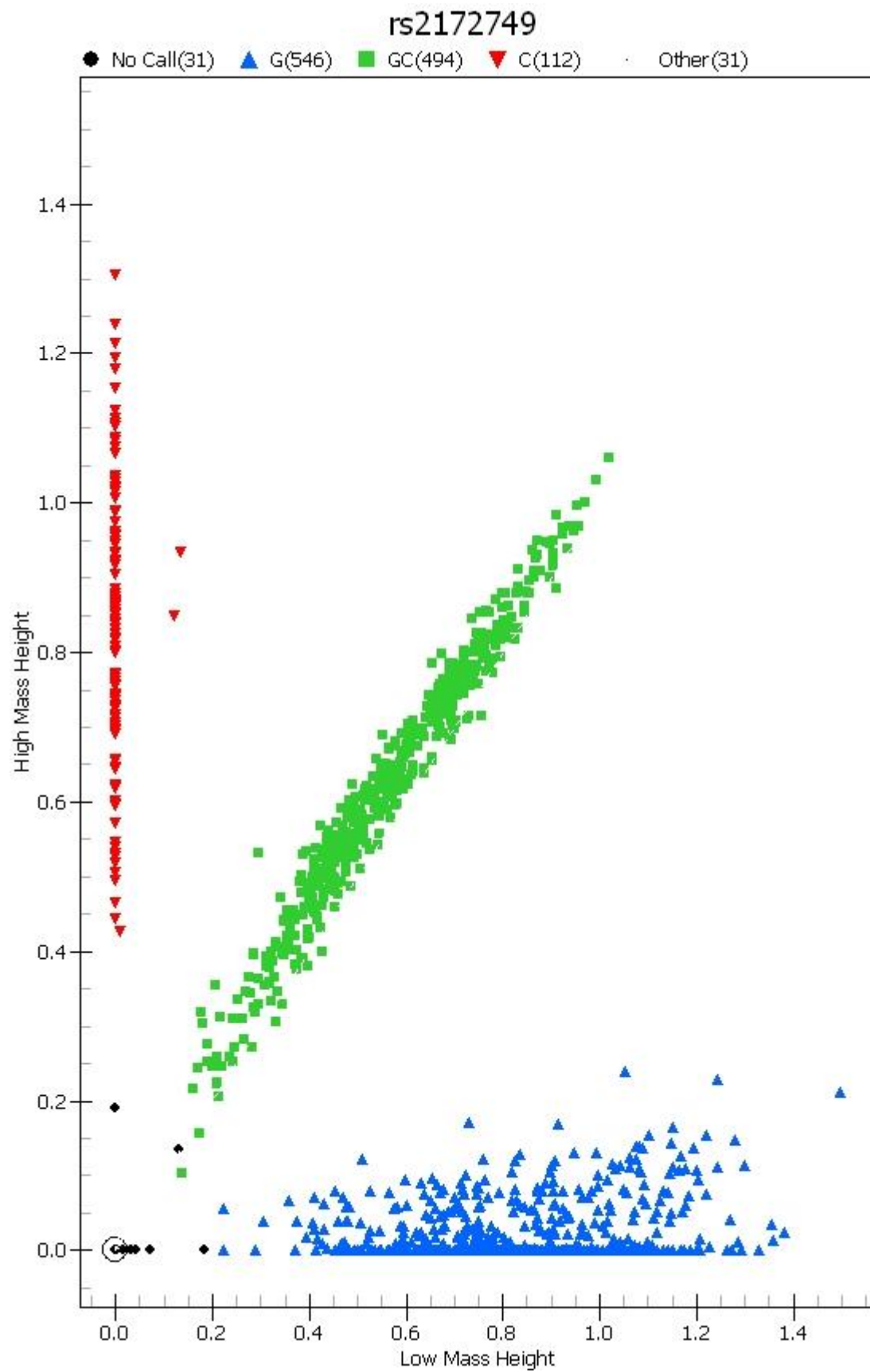


Figure 75: rs2240747

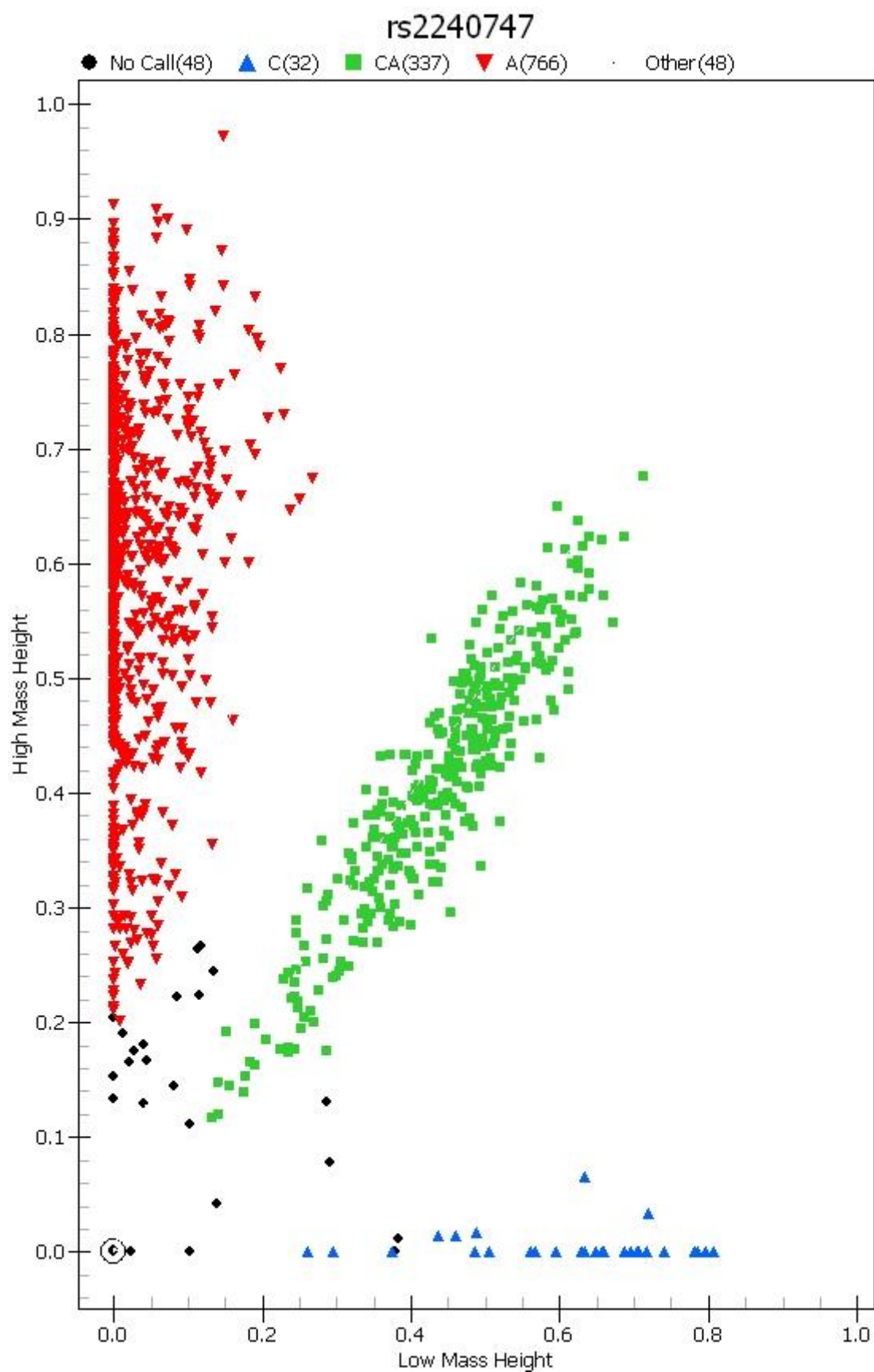


Figure 76: rs2265477

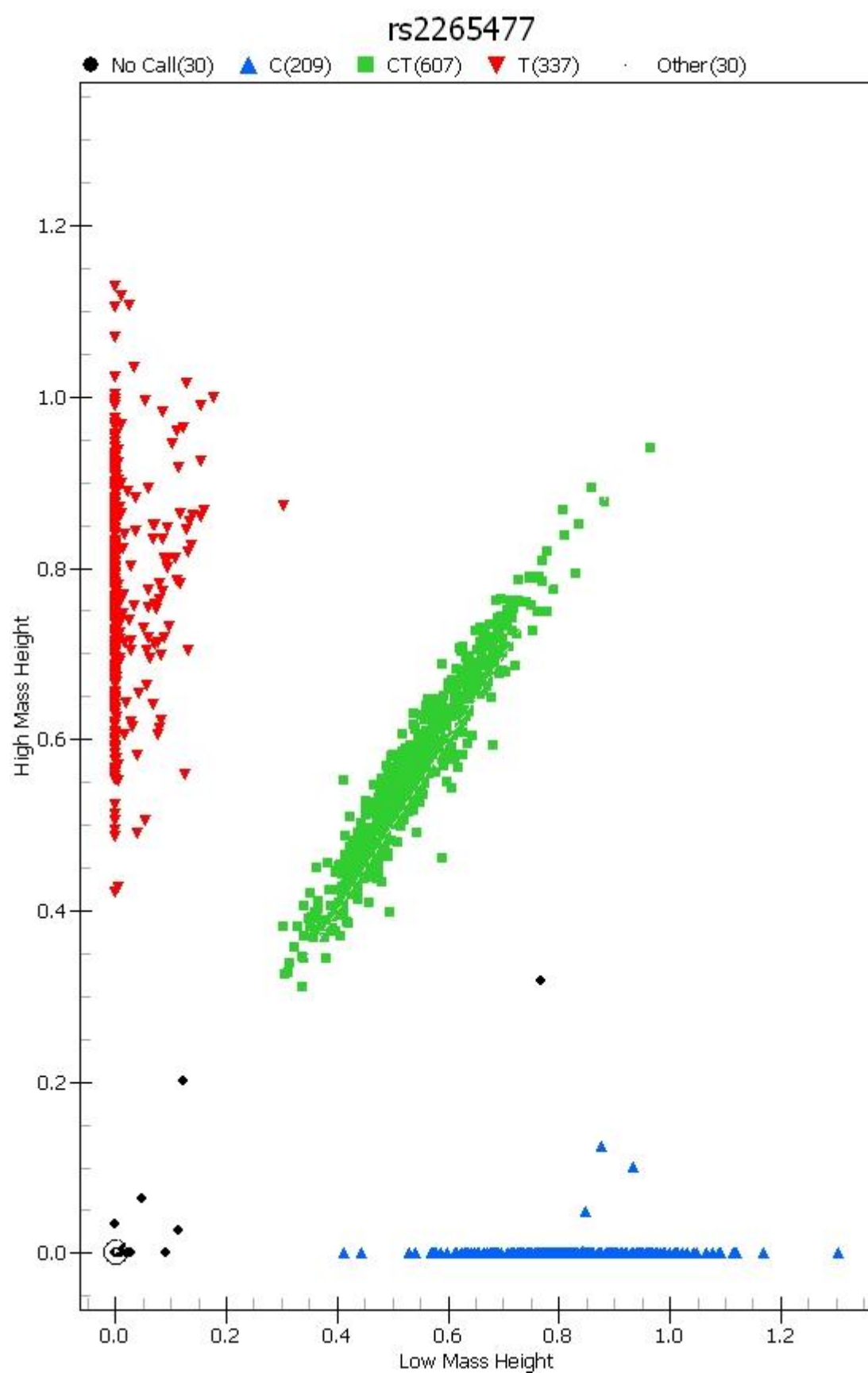


Figure 77: rs2265917 (Taqman)

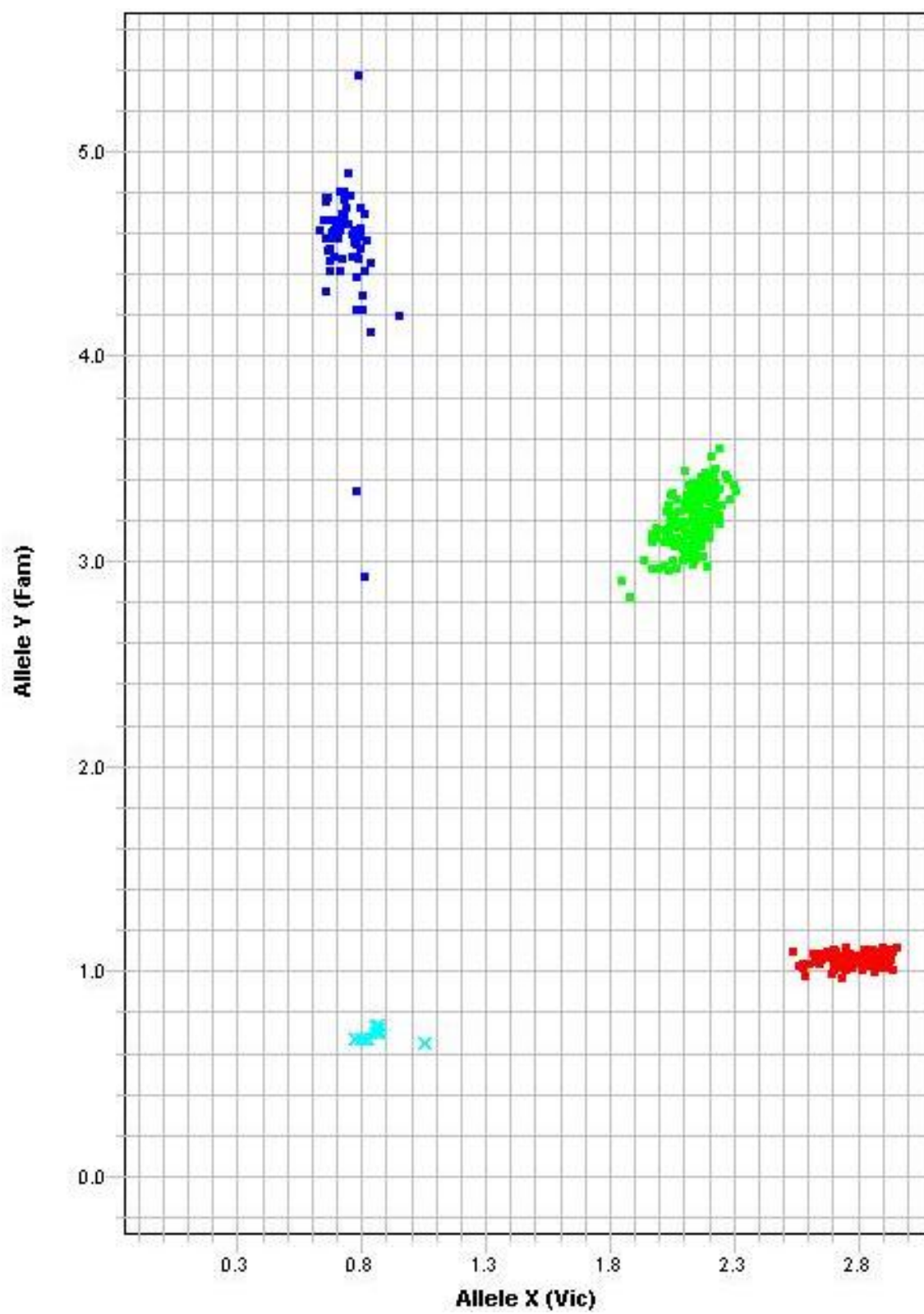


Figure 78: rs2265919

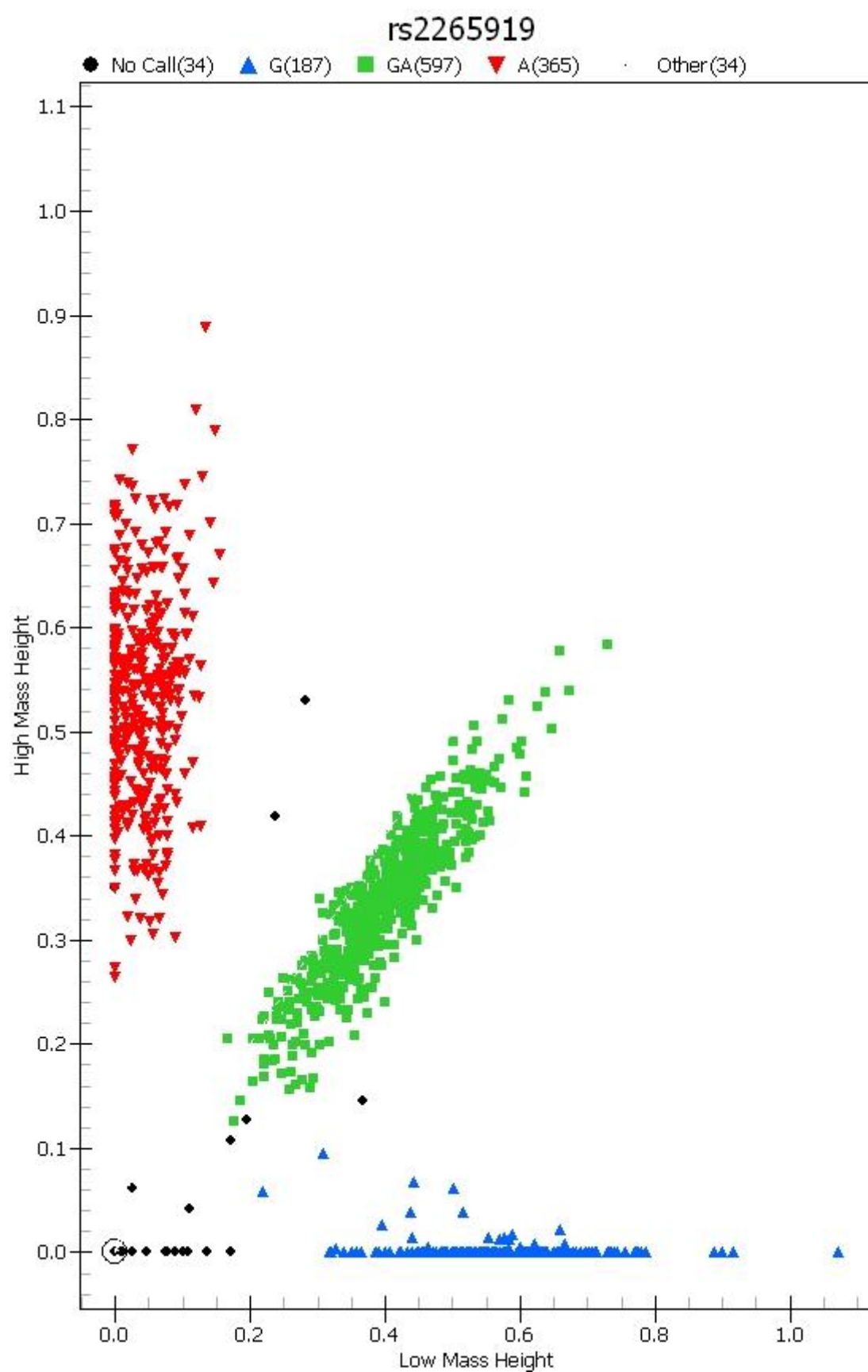


Figure 79: rs2280789

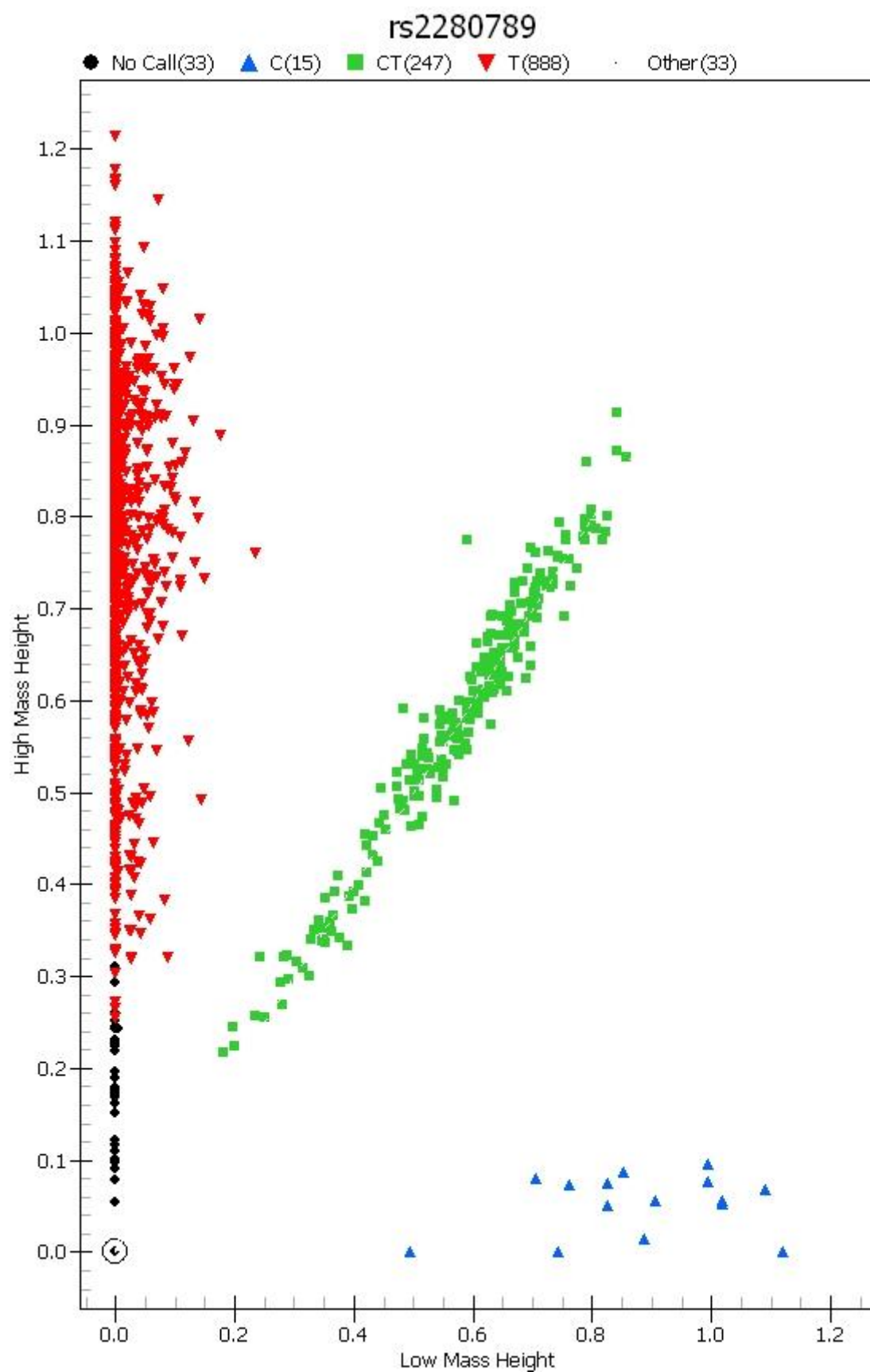


Figure 80: rs2340721

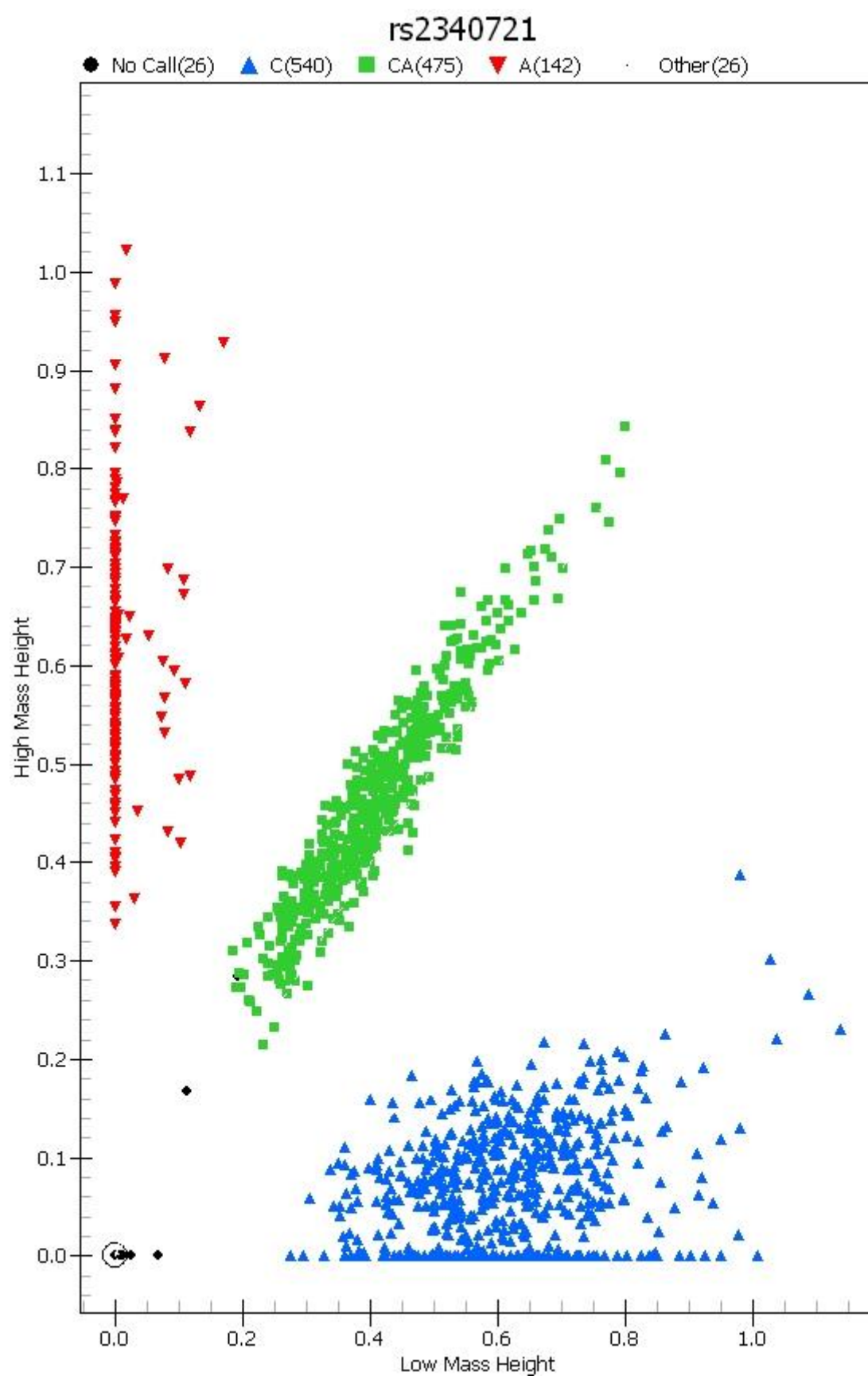


Figure 81: rs2861484

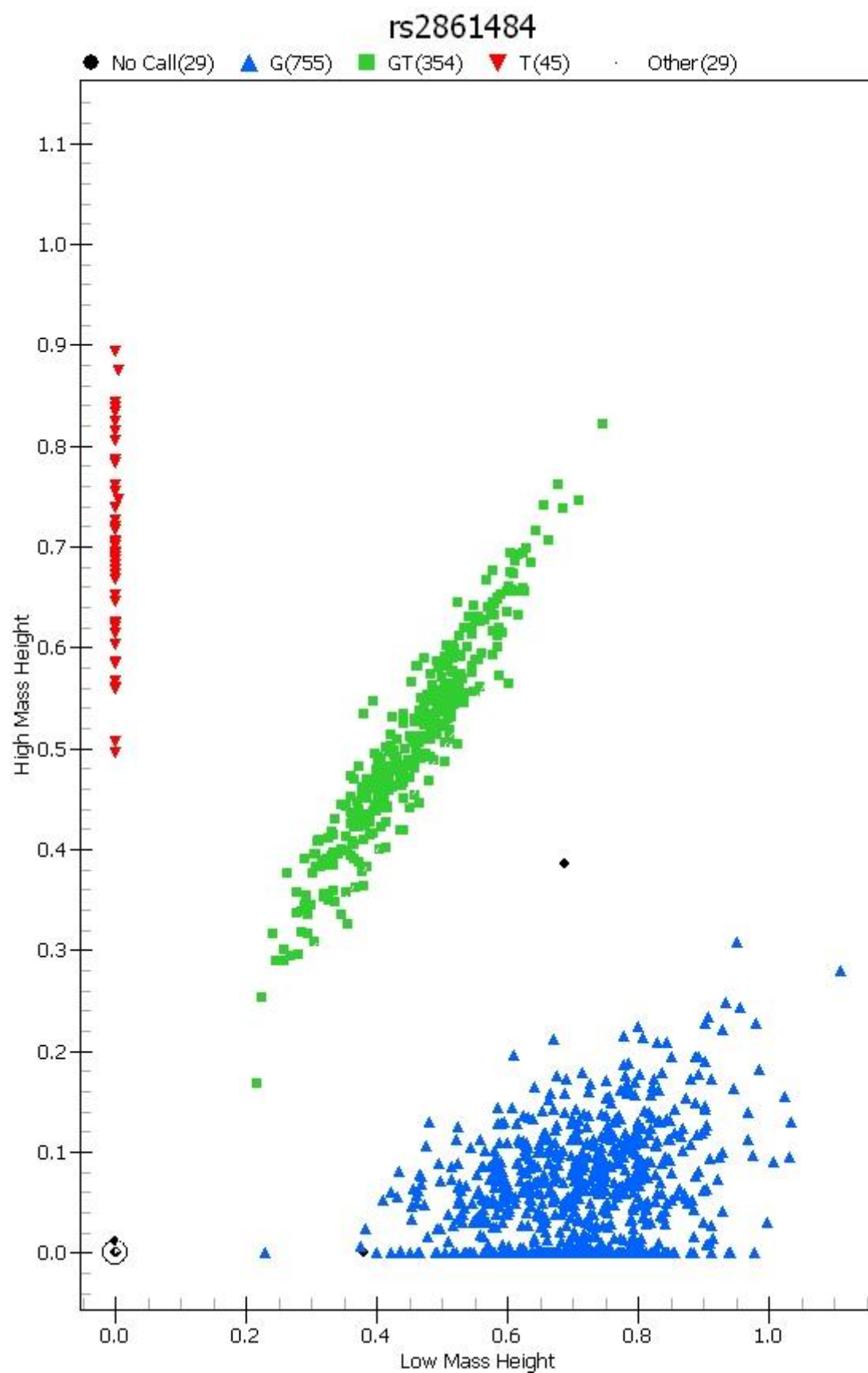


Figure 82: rs3212574

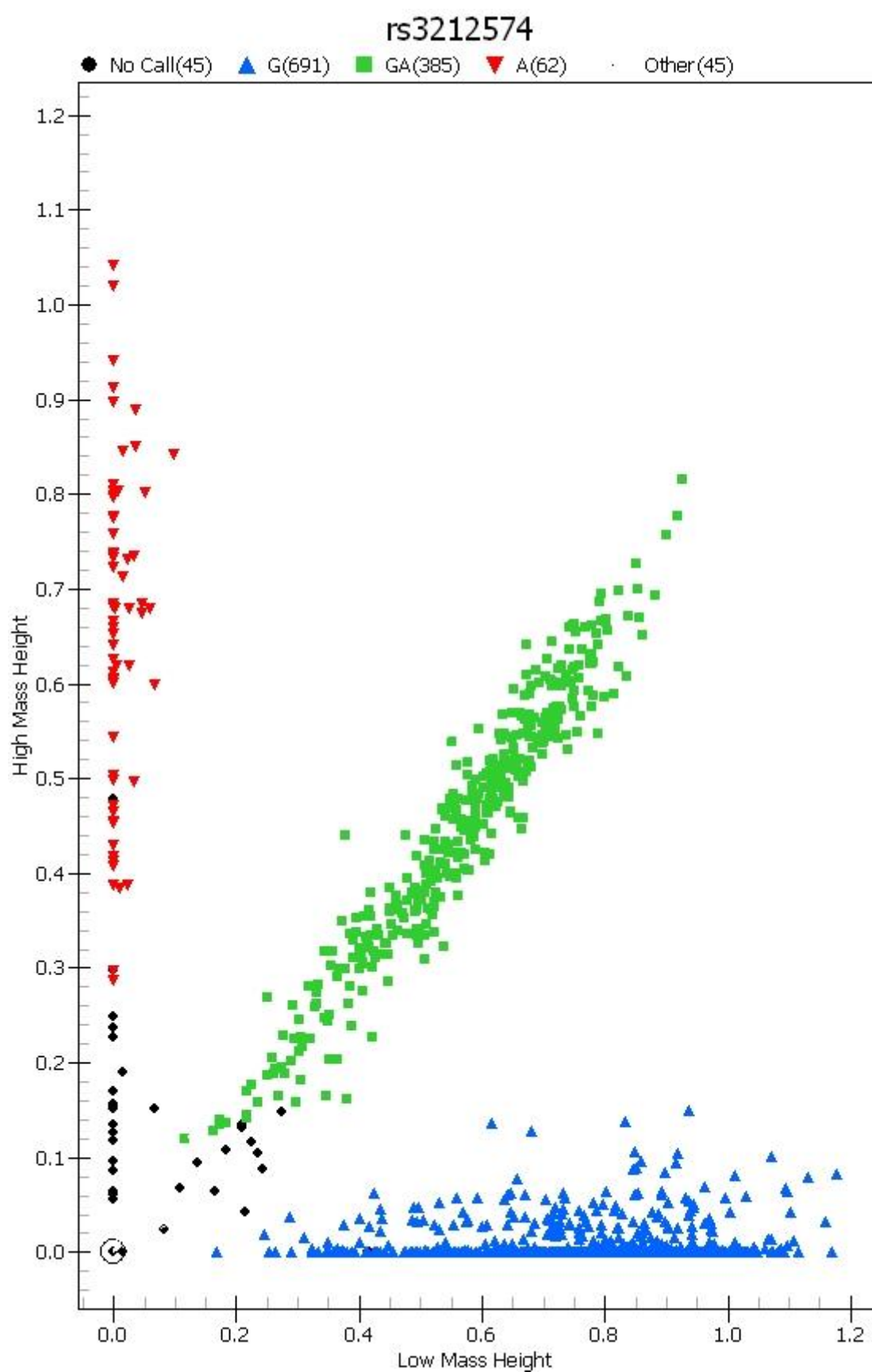


Figure 83: rs3817655

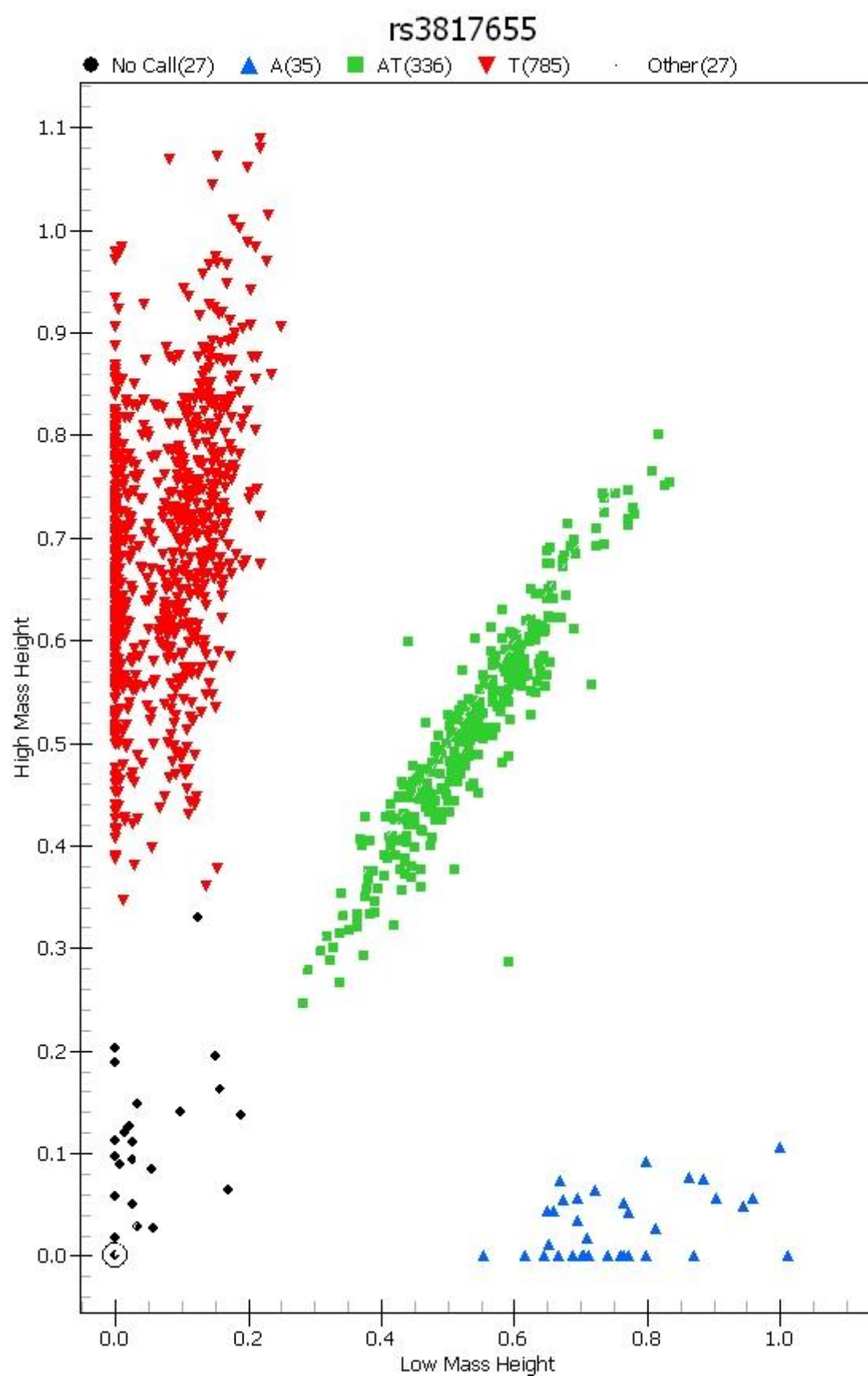


Figure 84: rs4394754

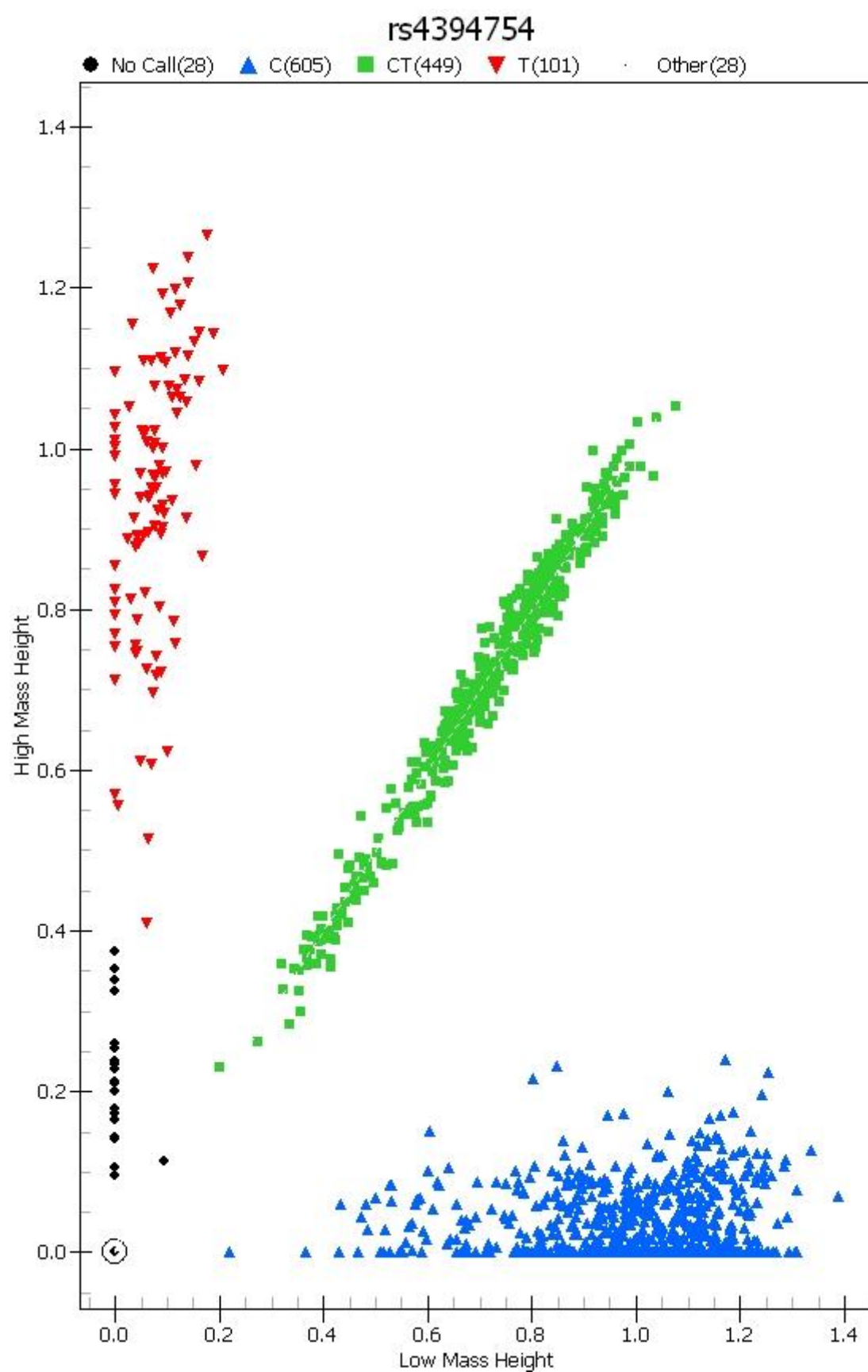


Figure 85: rs4819554

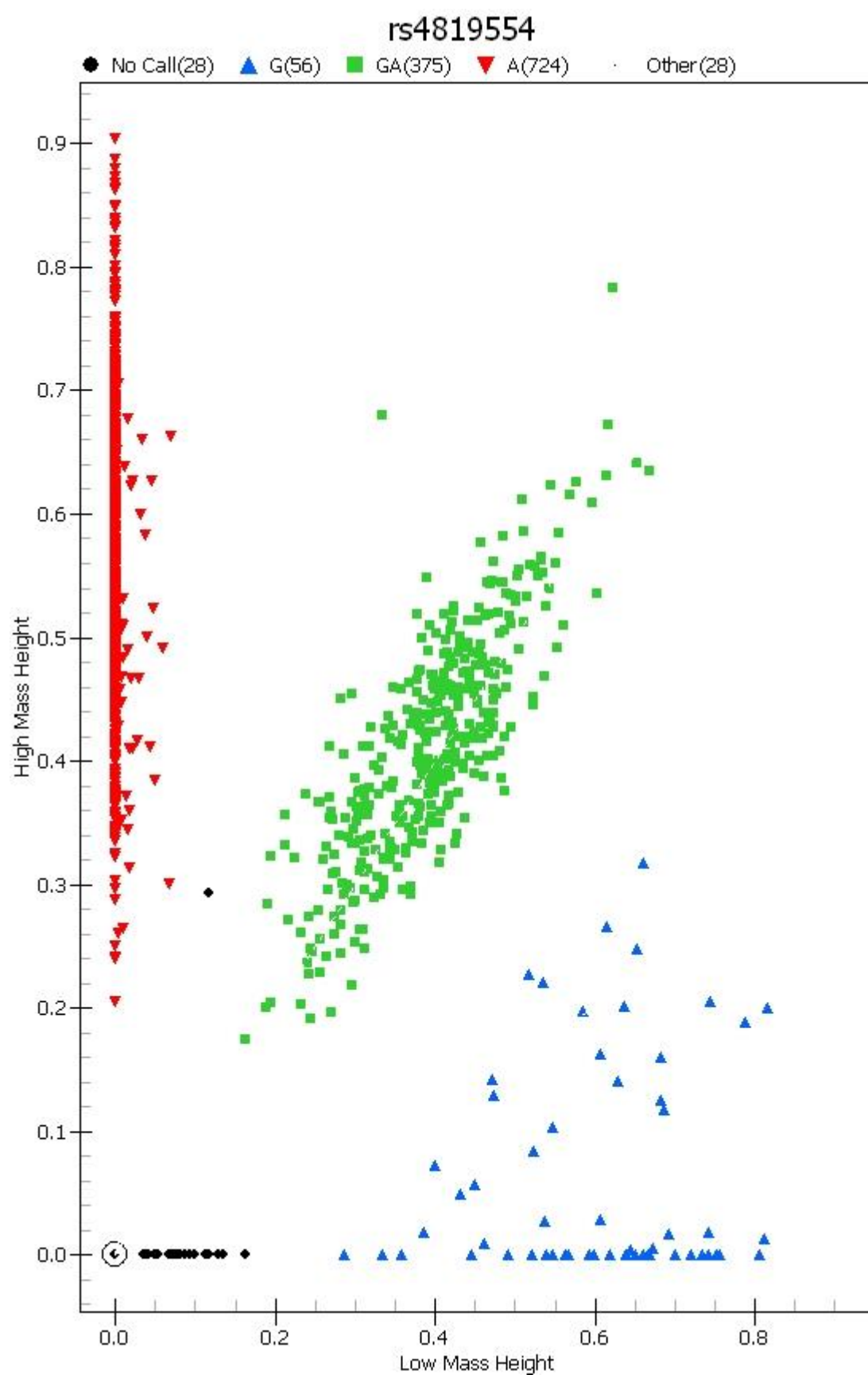


Figure 86: rs6793265

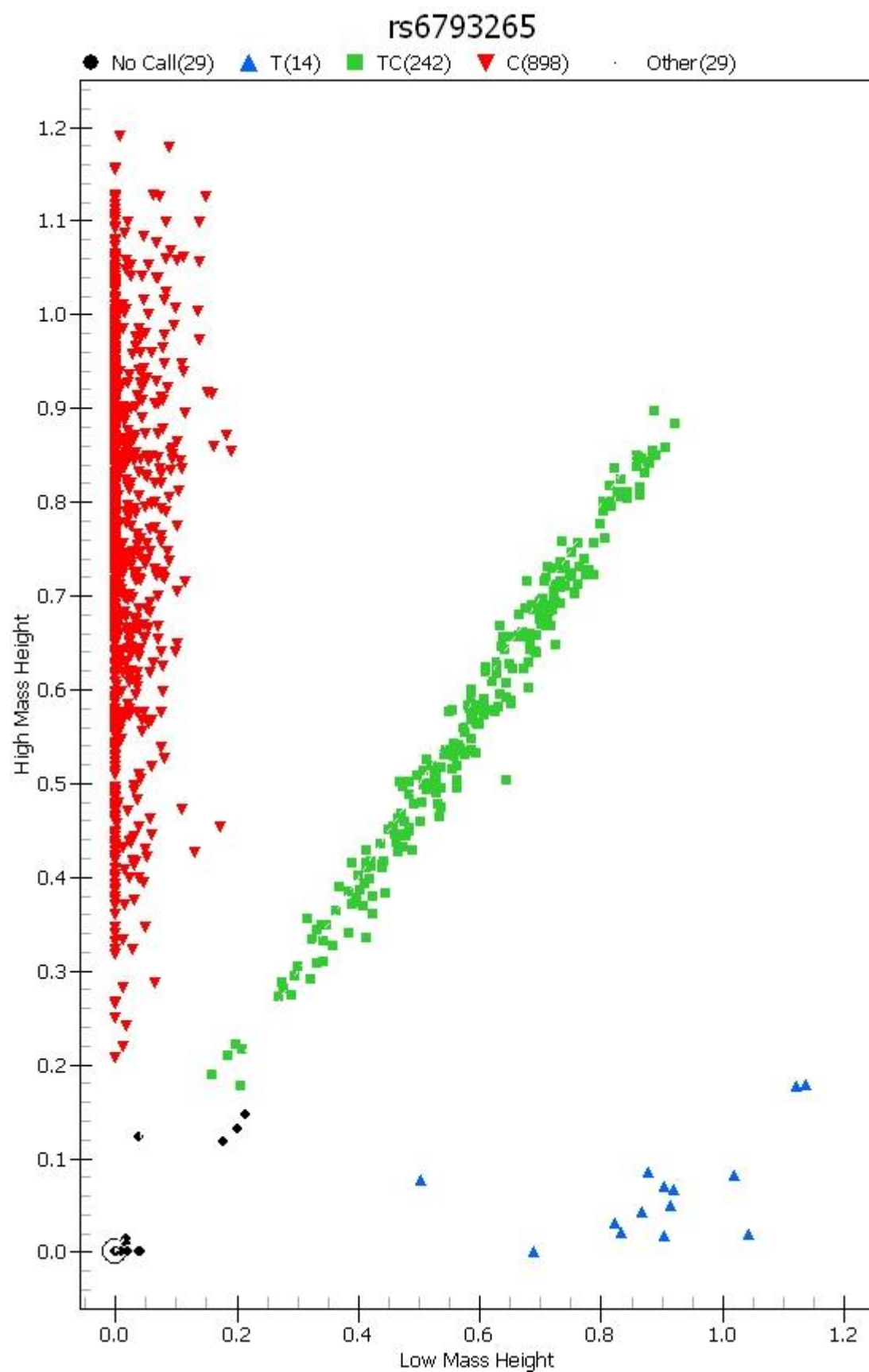


Figure 87: rs6903252

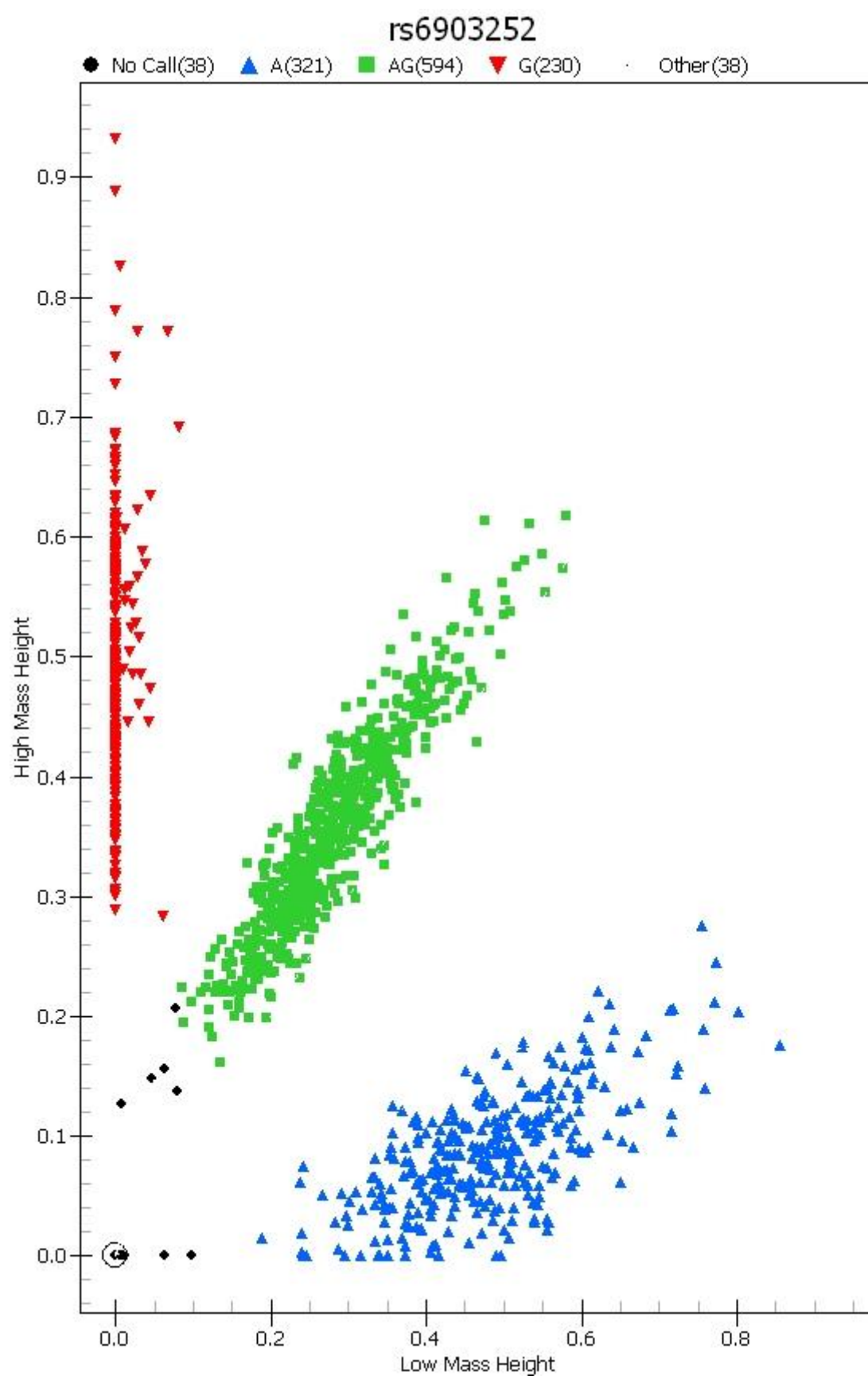


Figure 88: rs7145618

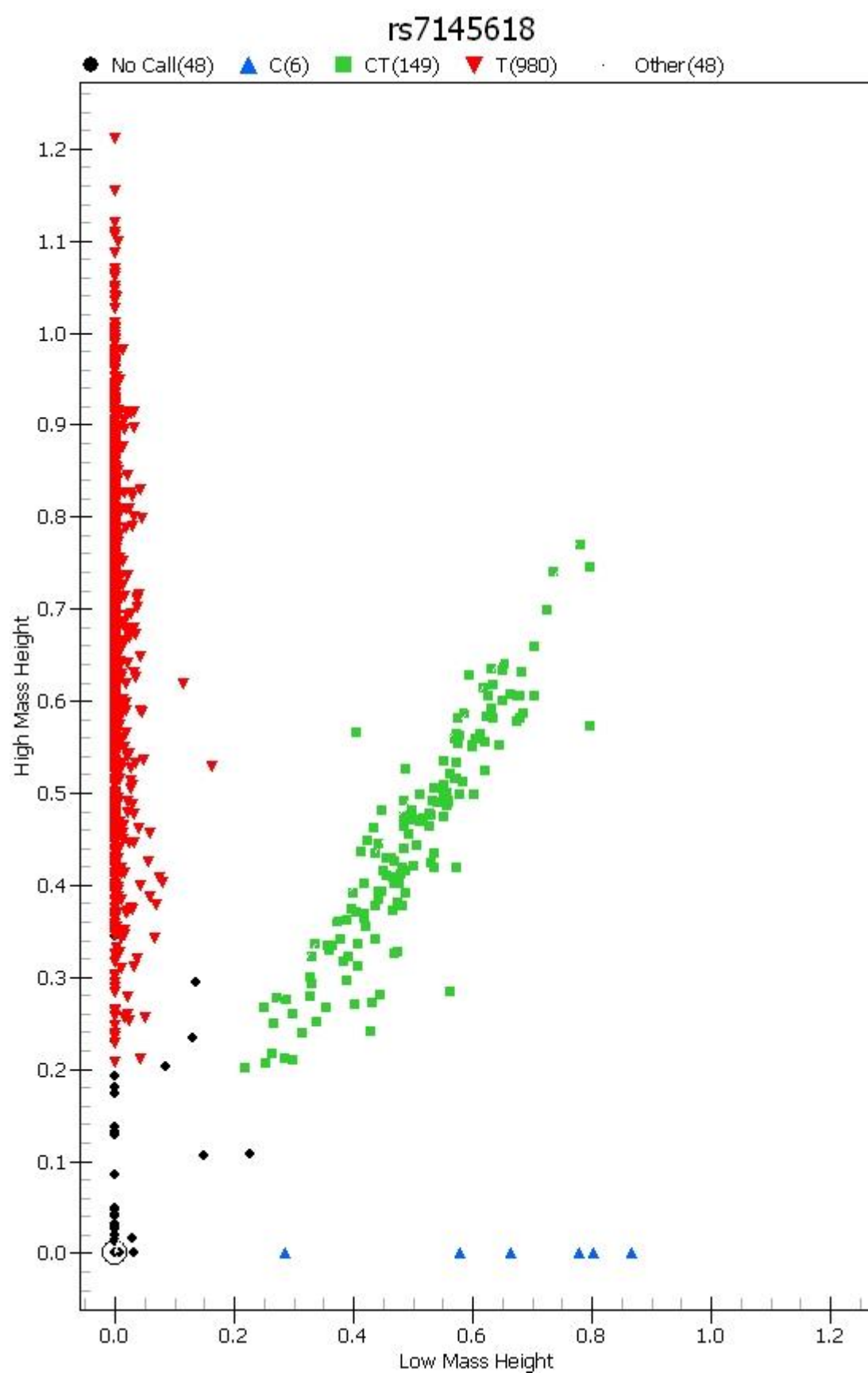


Figure 89: rs7533125

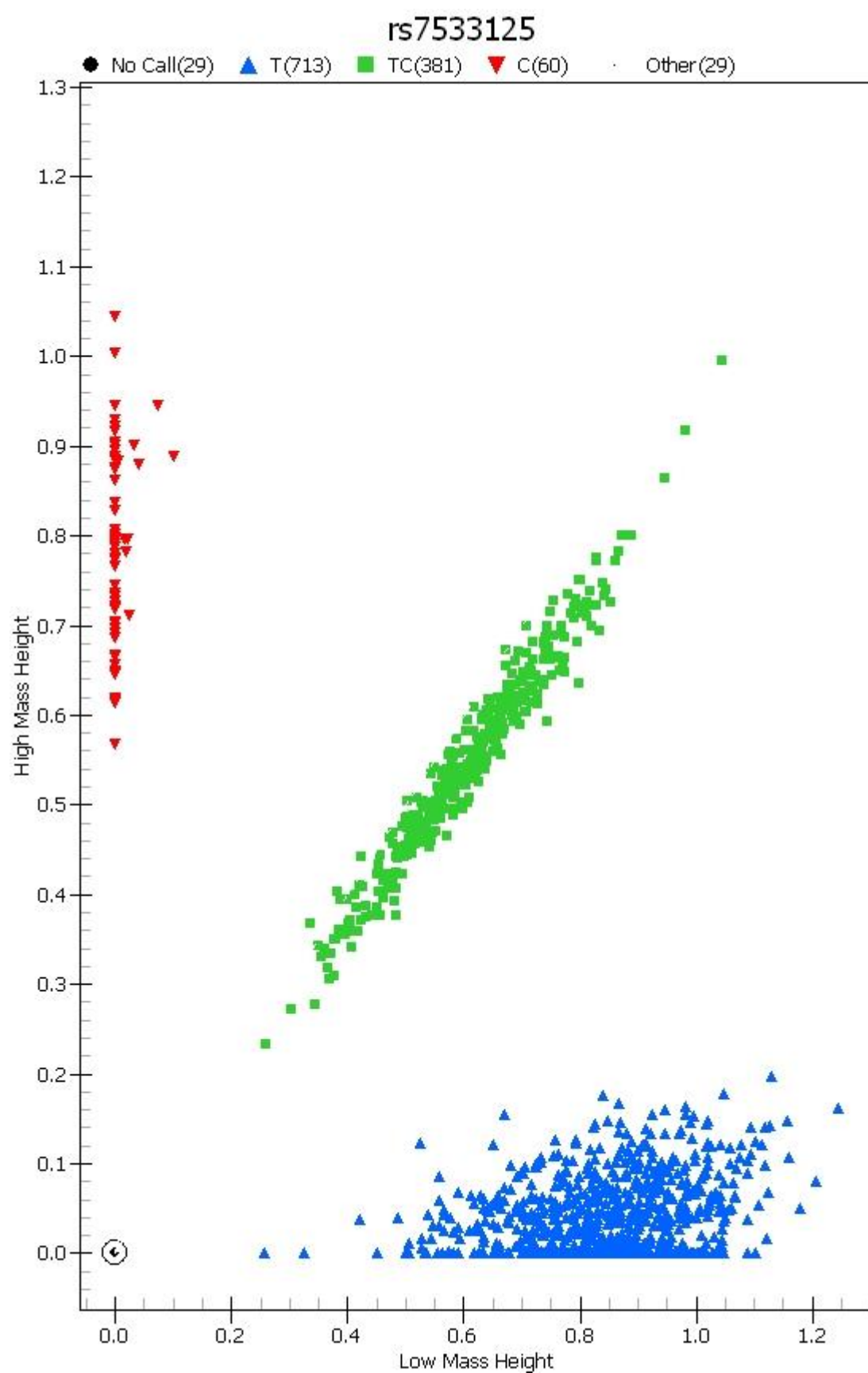


Figure 90: rs7903146 (Taqman)

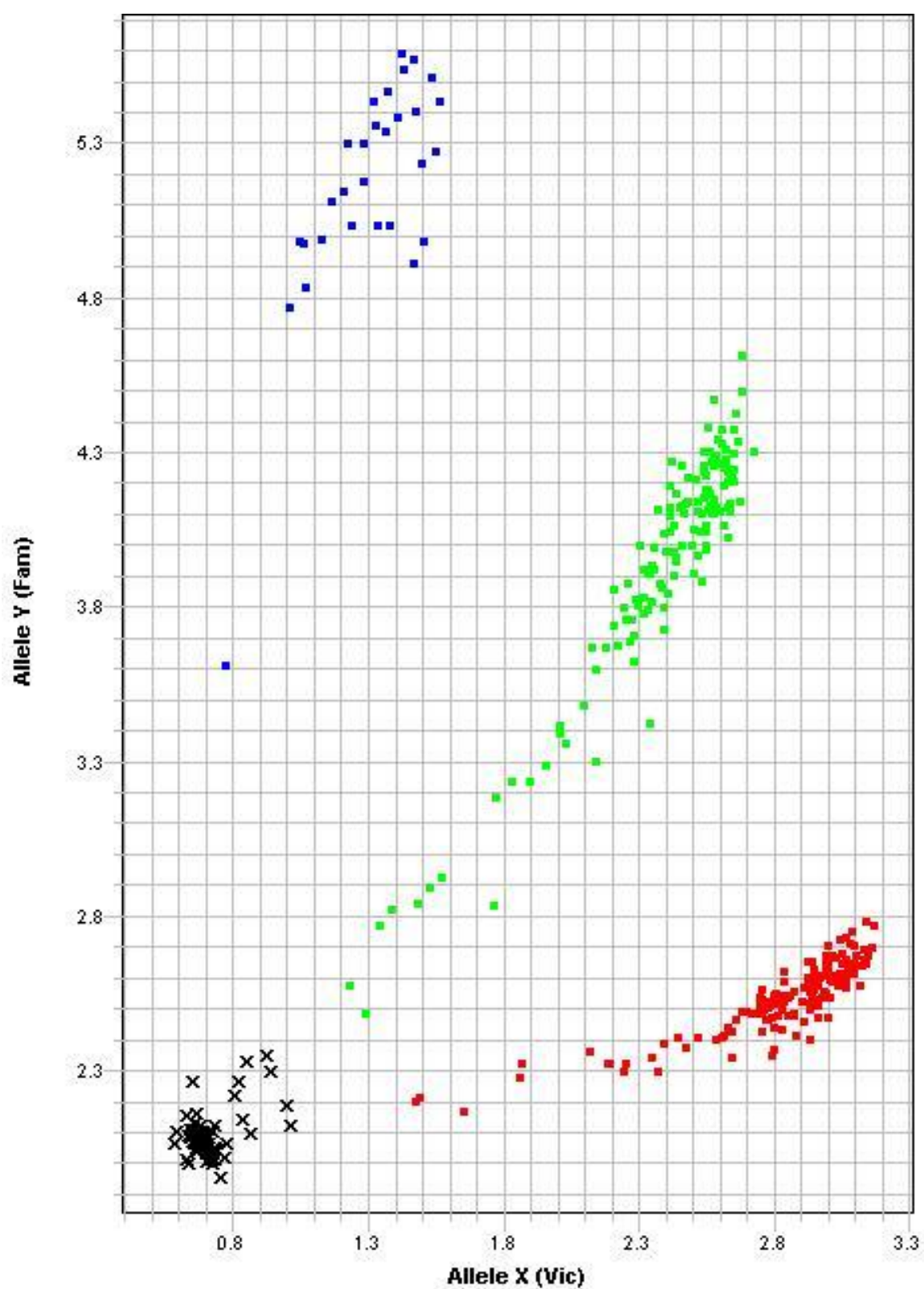


Figure 91: rs8192678

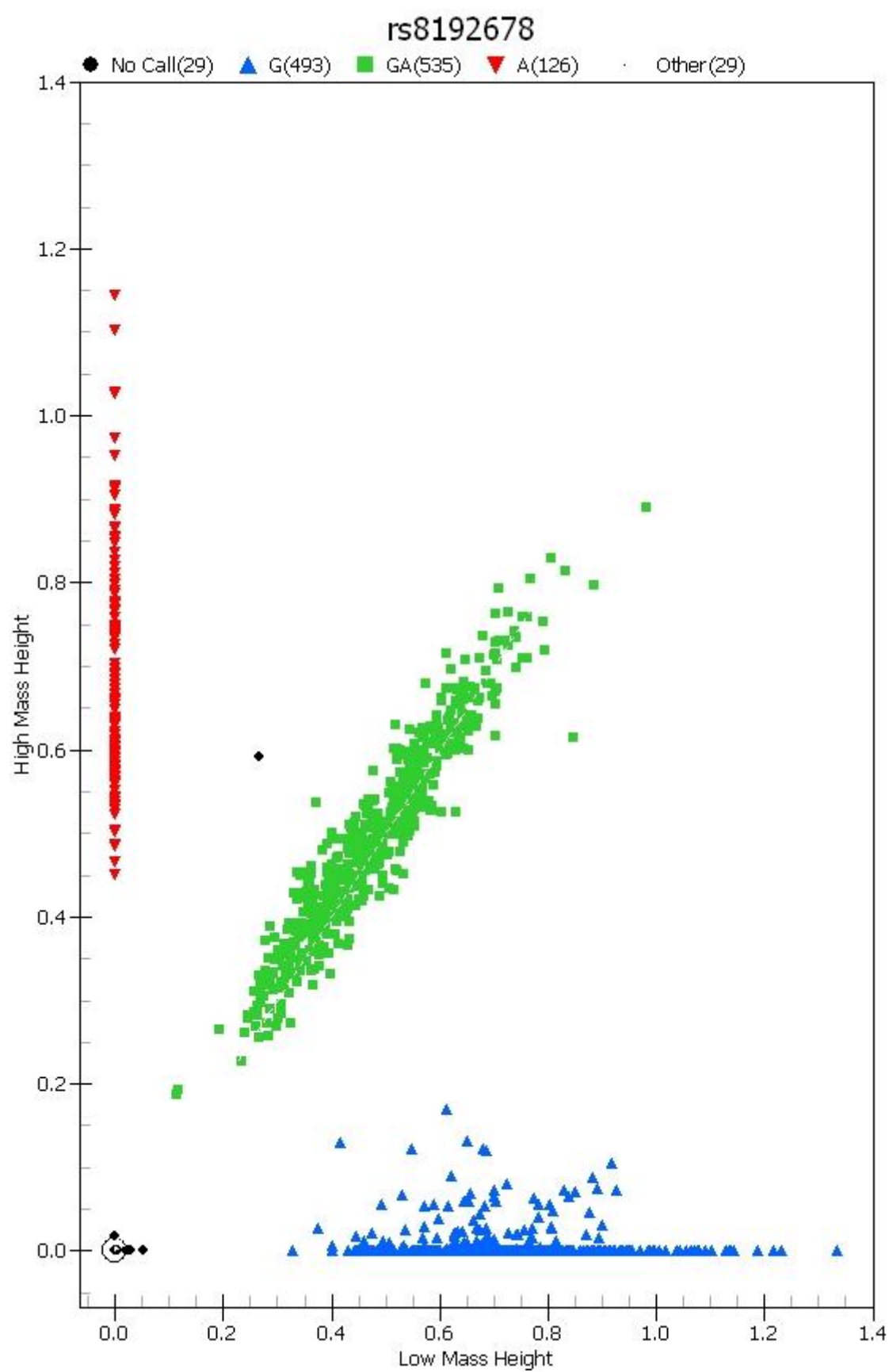


Figure 92: rs10117679

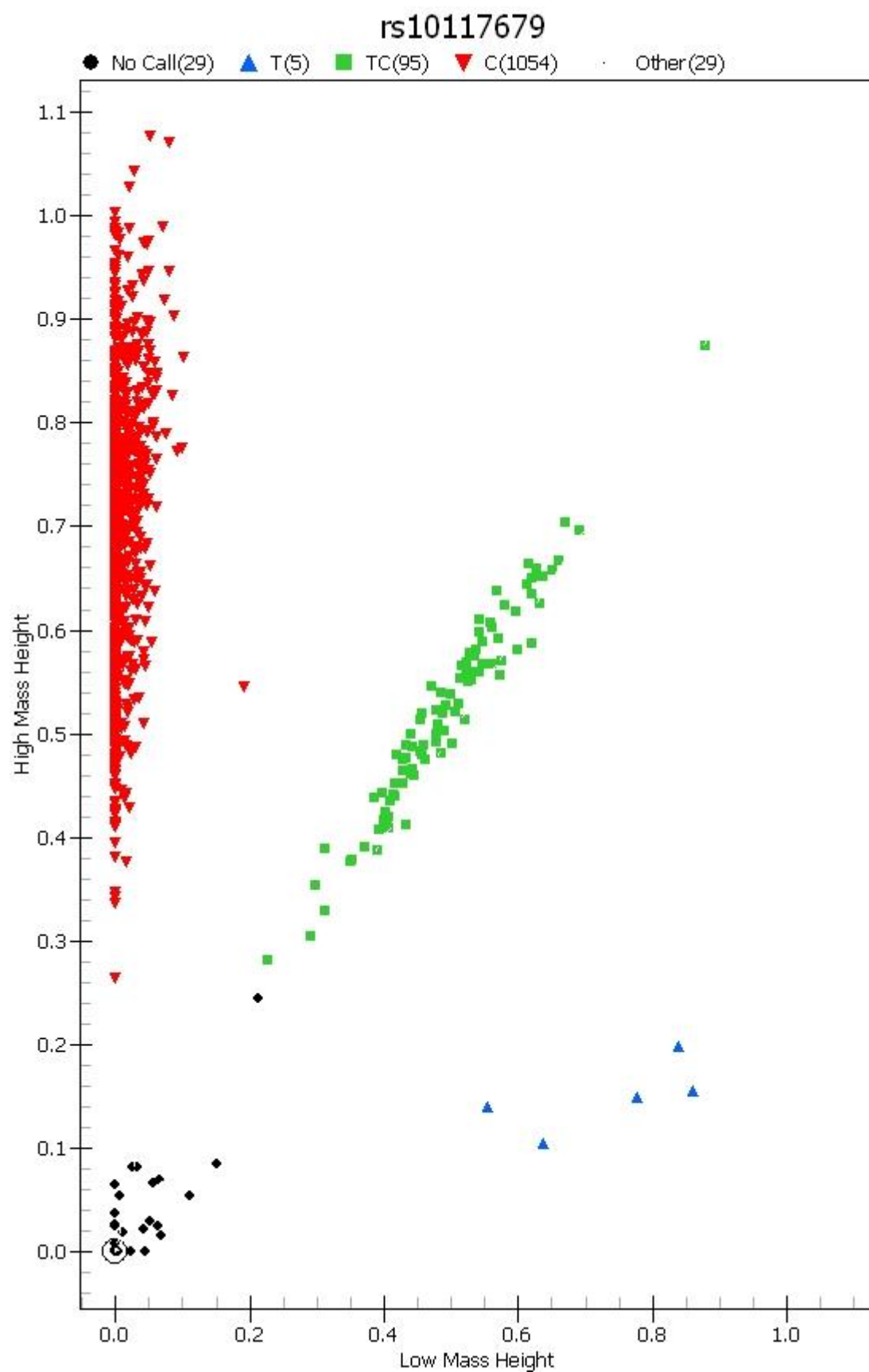


Figure 93: rs10484821

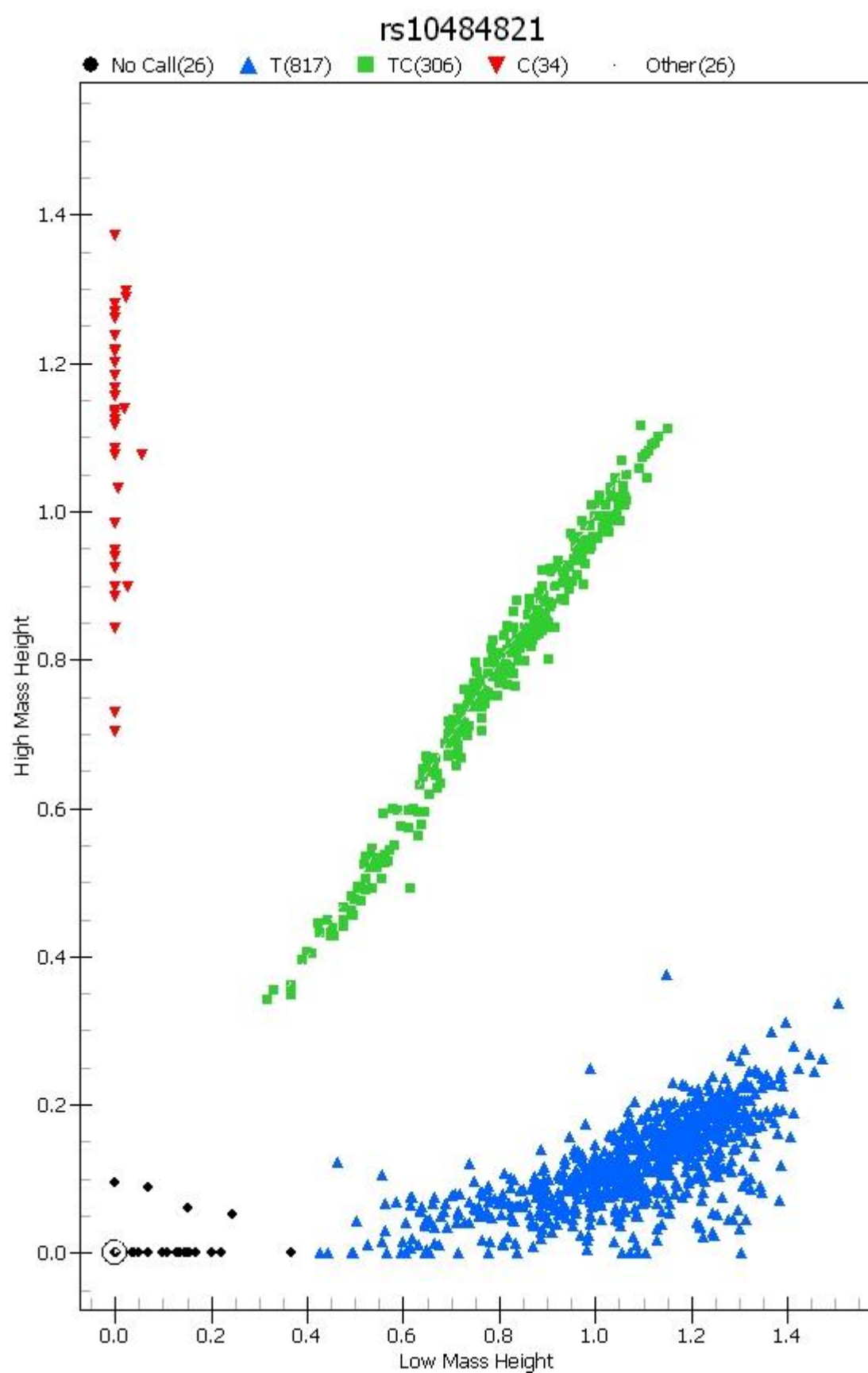


Figure 94: rs10899444

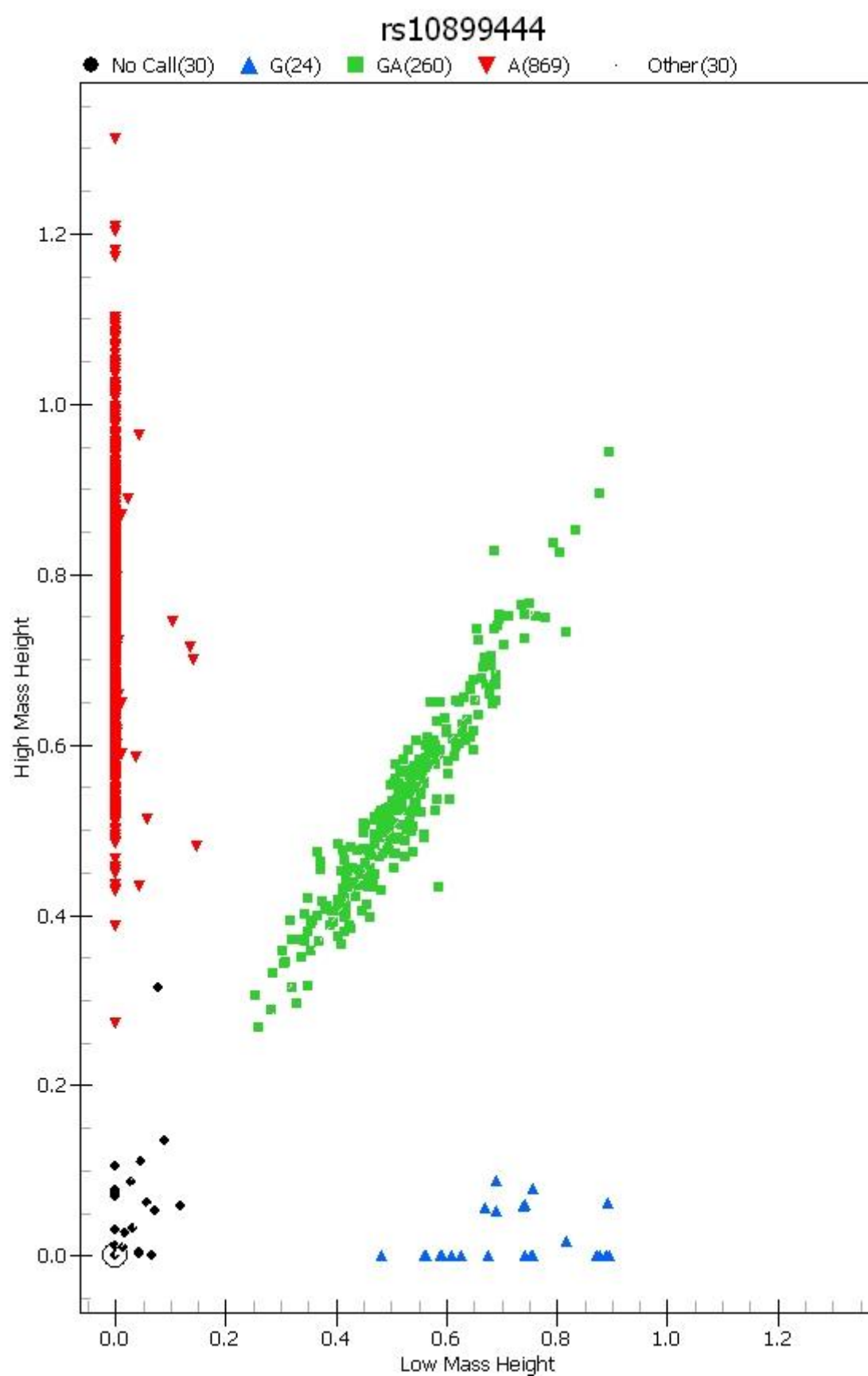


Figure 95: rs11580170

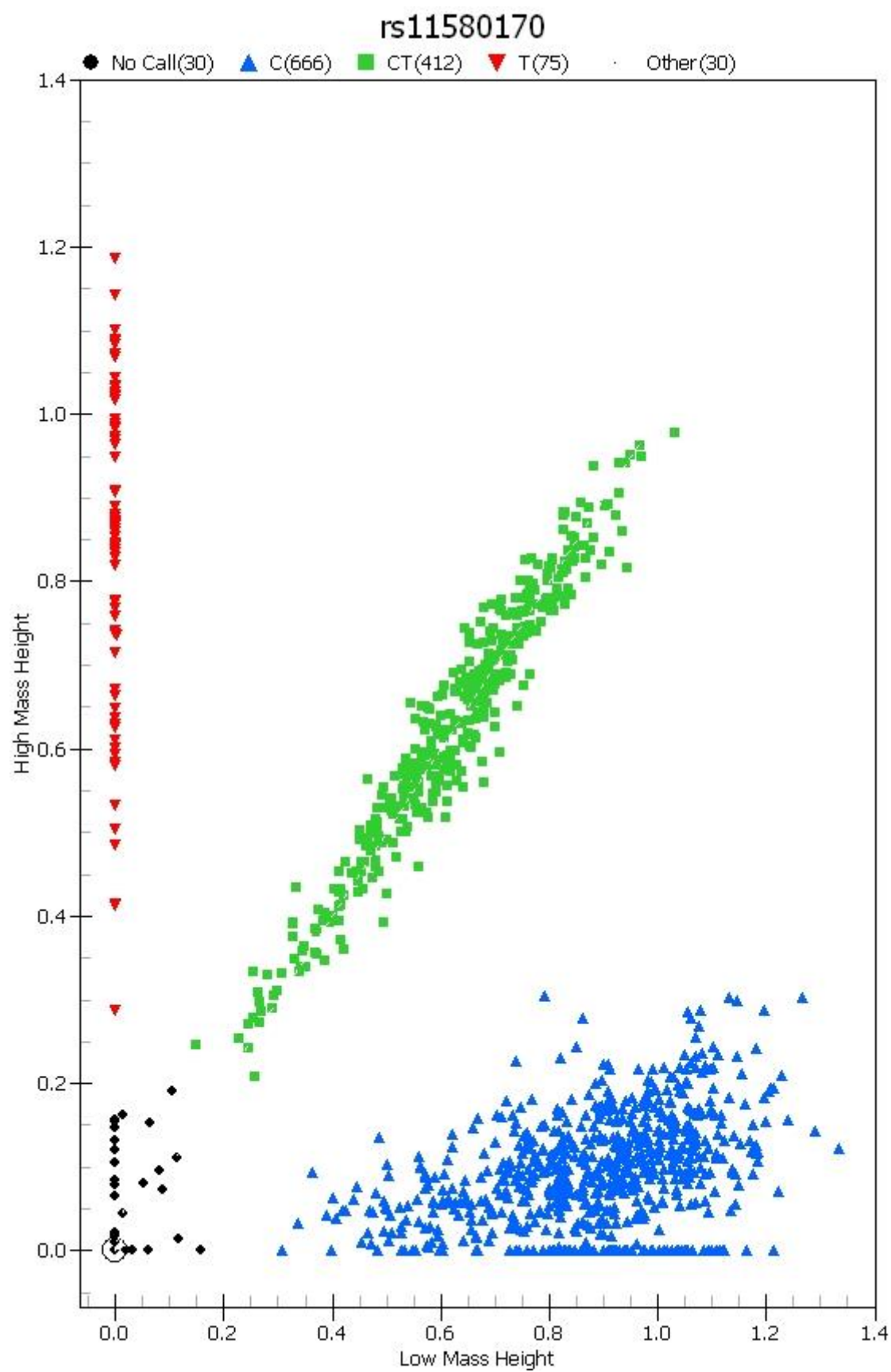


Figure 96: rs12255372

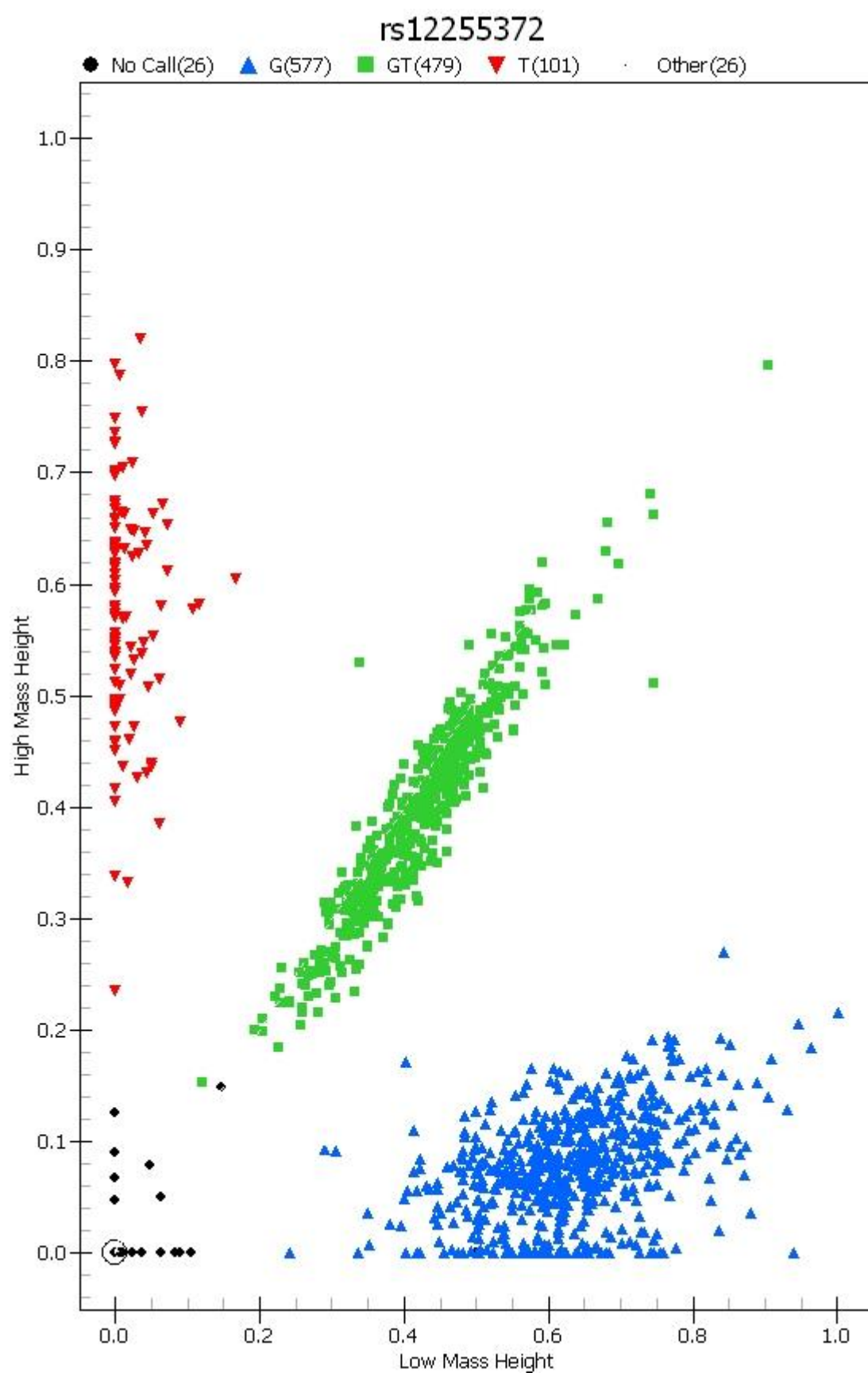


Figure 97: rs13266634

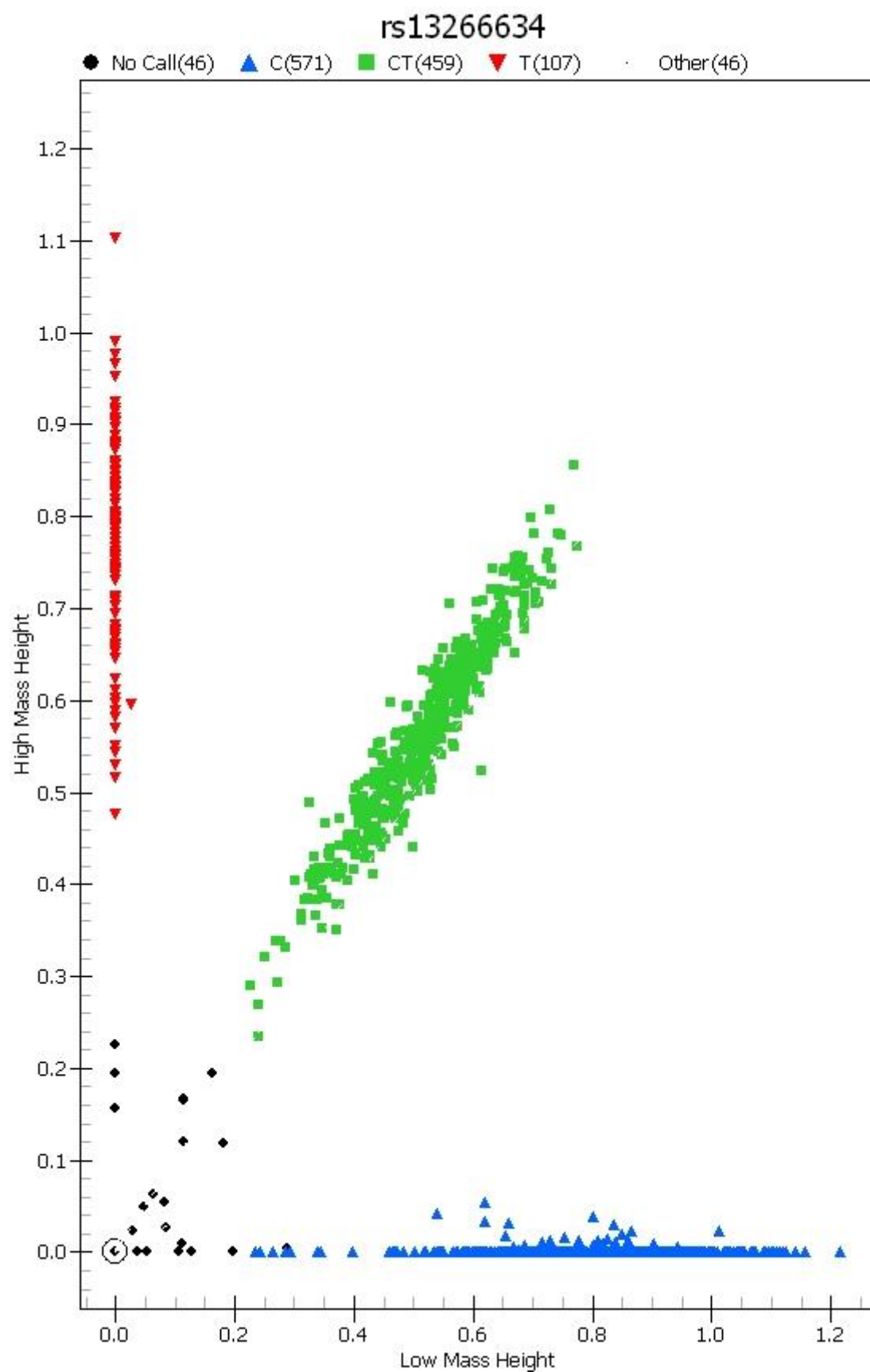


Figure 98: rs16936667

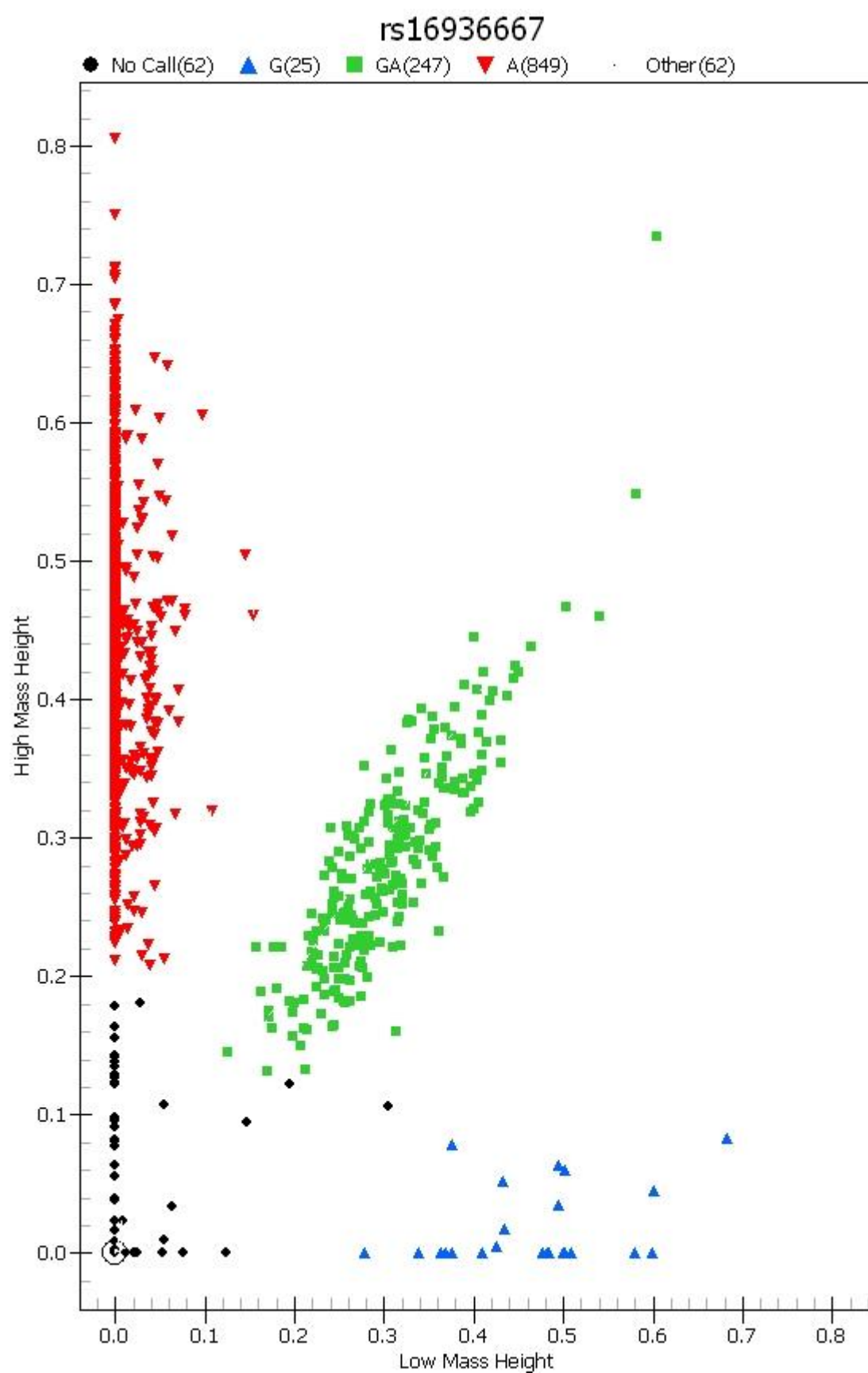


Figure 99: rs17657199

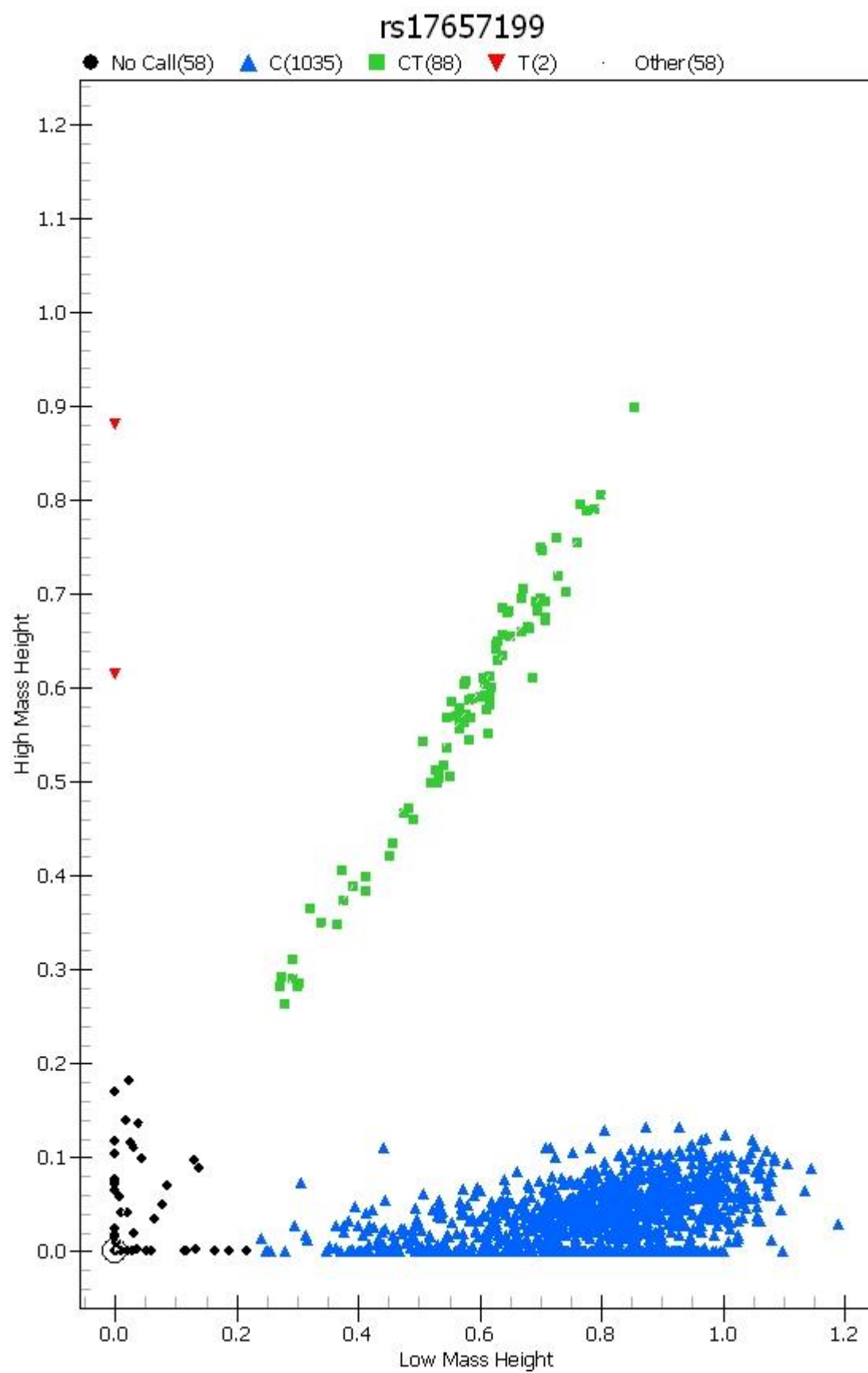


Figure 100: rs17722392

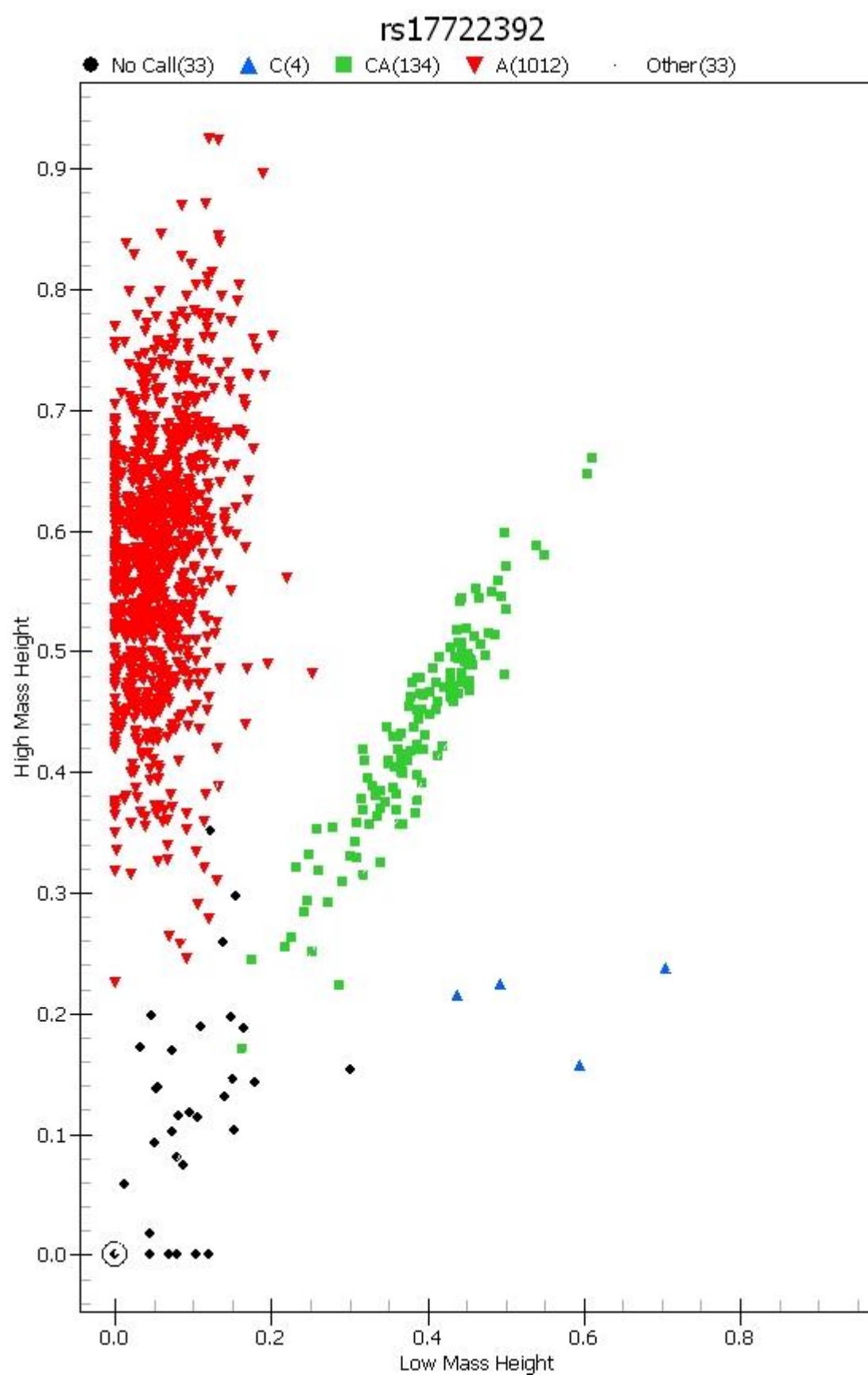


Figure 101: Results of gene set enrichment performed using Fisher's exact test, restricting gene sets to those with two or more genes included and analysing genes according to the hg19 genome build

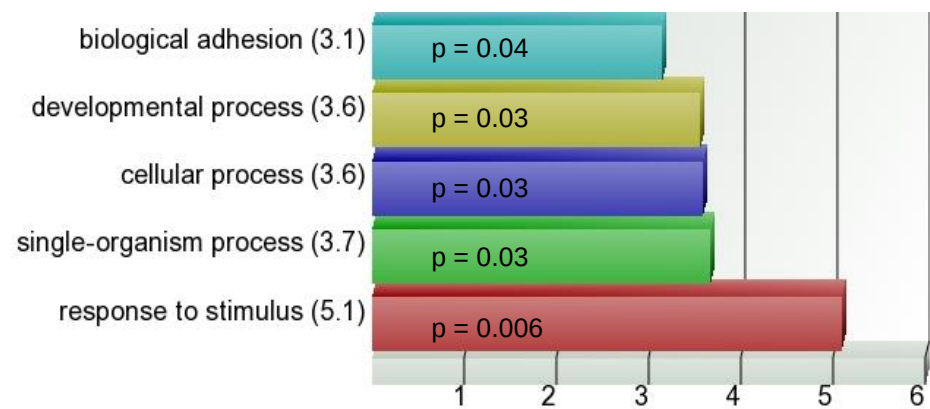


Figure 102: The P13K-AKT signaling pathway with coloured boxes identifying top ranked genes and pathways in the NODAT GWAS

