

## ONLINE METHODS

**Phenotype harmonization and selection.** We spent substantial effort harmonizing the smoking phenotypes across studies. Briefly, first, we created the Phenotype Working Group (PWG) to address these crucial issues. Second, we obtained English versions of the exact smoking-related questions, responses and summary data from each study. These were entered into a master database and examined for completeness, outliers and distributions of all smoking variables. Third, we produced a list of candidate smoking phenotypes available from each study. Fourth, as has been recommended<sup>25</sup>, we calculated heritabilities and intercorrelations between the candidate smoking variables using data from the Swedish Twin Registry<sup>26,27</sup> and the Finnish Twin Cohort Study<sup>28,29</sup>, two population-based twin registries containing extensive smoking data. Finally, the PWG integrated all these data to derive the operational phenotypes to be used in the meta-analyses.

The central criteria were that a candidate phenotype had to (i) be exactly or nearly exactly assessed in nearly all studies, (ii) have distributional properties similar across studies and conducive to meta-analyses (for example, sufficiently prevalent to allow reasonable statistical power), (iii) have reasonable heritability so that genetic analysis was suitable and (iv) have face validity to senior researchers in the field.

These analyses yielded unexpected results. For example, the Fagerström Test for Nicotine Dependence is commonly used in the field, as either a continuous or dichotomized variable. However, item-level twin analyses showed it to be a composite measure of some items with high heritability (for example, CPD) but some items with heritability near zero and with important common environmental effects (unpublished data).

We examined three elements of smoking behavior: smoking initiation, smoking heaviness and smoking cessation. Smoking initiation was assessed in two ways: by contrasting individuals who reported having ever versus never smoked regularly, and age of smoking initiation.

**Ever versus never regular smokers.** Regular smokers were defined as those who reported having smoked  $\geq 100$  cigarettes during their lifetime and never regular smokers were defined as those who reported having smoked between 0 and 99 cigarettes during their lifetime. This definition is consistent with the Centers for Disease Control classification of “ever smoker”<sup>30</sup>.

**Age of smoking initiation.** Age of smoking initiation was the reported age the participant started smoking cigarettes. Some studies collected the age at which the participant first tried smoking, whereas others collected the age the participant began smoking regularly. As both variables (age first tried and age began smoking regularly) were available in the Swedish Twin Registry, we calculated the univariate heritabilities for each variable and the genetic correlation between them. We studied only females due to the confounding effects of prevalent smokeless tobacco (‘snus’) use in Swedish males<sup>31</sup>. The heritabilities for the two variables were similar and the genetic correlation was 0.97, which suggested a great deal of overlap in the genetic contributors to each trait and supported the idea of using either value in a general assessment of age of smoking initiation in the meta-analysis.

**Cigarettes per day.** Smoking quantity was assessed as the CPD value. Some studies collected the average CPD, whereas other studies collected the maximum CPD. Longitudinal data from the Finnish Twin Cohort Study revealed a high correlation ( $>0.71$ ) between these variables over time and supported the idea of using either value in a general assessment of CPD in the meta-analysis.

**Smoking cessation.** Smoking cessation contrasted former versus current smokers, where current smokers reported that they smoked at the time of the interview and former smokers had quit smoking at least 1 year before the interview. As relapse to smoking is highest within the first year of quitting smoking, smokers who had quit smoking for less than 1 year at interview were excluded from the analysis. Descriptive characteristics of the 16 studies participating in the TAG Consortium are presented in **Table 1**.

**Genotyping and imputation.** The 16 TAG studies performed their own genotyping, quality control and imputation (**Supplementary Tables 2 and 3**). Studies ranged in size from  $n = 585$  to  $n = 22,037$  and were genotyped on six different

GWAS platforms. Each study applied its own set of quality control filters, which were comparable among studies. Each study excluded SNPs with a call rate  $<89\%$ ,  $<1\%$  minor allele frequency or departure from Hardy-Weinberg equilibrium. Subjects were excluded for non-European ancestry using PLINK multidimensional scaling<sup>32</sup>, STRUCTURE<sup>33</sup> or EigenSoft principal component analysis<sup>34</sup>. In addition, subjects were excluded for  $<90\%$  call rate, excess autosomal heterozygosity, mismatch between reported and genetically determined sex or first- or second-degree relatedness. Genotype imputation<sup>5</sup> was used to harmonize genotyping across different studies, as well as to infer genotypes for SNPs that were not genotyped directly on the platforms but that were genotyped on the HapMap-2 CEU samples<sup>32</sup>. SNP imputation was performed using either MACH<sup>35</sup>, IMPUTE<sup>36</sup> or BAMBAM10 v0.99<sup>37</sup> and resulted in a common set of  $\sim 2.5$  million SNPs after removal of SNPs with minor allele frequency  $<1\%$  or poor imputation performance (**Supplementary Table 3**). Imputed allele dosages for each SNP (that is, the number of copies of the minor allele) were tested for association with each smoking phenotype using an additive model.

**Study-specific GWAS analysis.** Each study conducted uniform cross-sectional analyses for each smoking phenotype using an additive genetic model. Linear regression was used for quantitative traits (CPD and age of smoking initiation), and logistic regression was used for discrete traits (ever versus never smokers and former versus current smokers). Age of smoking initiation was transformed using the natural logarithm owing to heavy tails and non-normality. The dependent variables were the smoking phenotypes and the independent variables were the imputed allele dosage for a SNP plus an indicator variable for whether a subject was classified as a case in the primary study. If the primary study was case-control in design and the phenotype being studied was known to be associated with smoking, we adjusted for case status to reduce potential confounding<sup>38</sup>. Individual study results were corrected for residual inflation of the test statistic using genomic control<sup>39</sup>.

Due to the known differences in the prevalences of the smoking phenotypes between the two sexes<sup>40</sup>, all TAG Consortium analyses were run separately for males and females. We then tested whether associations between  $\sim 2.5$  million SNPs and each smoking phenotype differed by sex by meta-analyzing males and females separately and performing a  $t$ -test of their parameter estimates for each SNP using a significance threshold of  $P < 5 \times 10^{-8}$  (ref. 41).

**Meta-analysis of GWAS results.** We performed fixed-effect meta-analysis for each smoking phenotype by computing pooled inverse-variance-weighted  $\beta$  coefficients, standard errors and  $z$ -scores for each SNP<sup>6</sup>. Fixed effects analyses were chosen because they are regarded as the most efficient method for discovery in the GWAS setting<sup>7,8</sup>. Meta-analyses were performed using METAL (see URLs). Heterogeneity across studies was investigated using the  $I^2$  statistic<sup>9</sup>. We used a significance threshold of  $P < 5 \times 10^{-8}$  (refs. 10,11).

**In silico follow-up of top regions.** To validate potential associations identified in the TAG Consortium analyses, we partnered with two other smoking GWAS consortia and conducted a reciprocal exchange of the 15 most significant genetic regions for each smoking phenotype in each study<sup>12,13</sup>. Regions were defined by SNPs with  $P$  values  $<10^{-4}$  that clustered together ( $r^2 > 0.5$  and/or locations  $<50$  kb apart). The ENGAGE Smoking GWAS Consortium consisted of 34,762 individuals and the Ox-GSK Smoking GWAS Consortium consisted of 34,226 individuals, making the final sample size across the three consortia  $n = 143,023$ . Studies that participated in multiple consortia were only represented once in the final analyses.

**URLs.** Genetic Computing Cluster, <http://www.geneticcluster.org/>; METAL, <http://www.sph.umich.edu/csg/abecasis/metal/>.

25. Pomerleau, O.F. *et al.* Genetic research on complex behaviors: an examination of attempts to identify genes for smoking. *Nicotine Tob. Res.* **9**, 883–901 (2007).

26. Lichtenstein, P. *et al.* The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies. *J. Intern. Med.* **252**, 184–205 (2002).

27. Furberg, H., Lichtenstein, P., Pedersen, N.L., Bulik, C. & Sullivan, P.F. Cigarettes and oral snuff use in Sweden: prevalence and transitions. *Addiction*. **10**, 1509–1515 (2006).

28. Kaprio, J., Pulkkinen, L. & Rose, R.J. Genetic and environmental factors in health-related behaviors: studies on Finnish twins and twin families. *Twin Res.* **5**, 366–371 (2002).
29. Kaprio, J. & Koskenvuo, M. Genetic and environmental factors in complex diseases: the older Finnish Twin Cohort. *Twin Res.* **5**, 358–365 (2002).
30. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 2007. *MMWR Morb. Mortal. Wkly. Rep.* **57**, 1221–1226 (2008); erratum **57**, 1281 (2008).
31. Furberg, H., Lichtenstein, P., Pedersen, N.L., Bulik, C. & Sullivan, P.F. Cigarettes and oral snuff use in Sweden: Prevalence and transitions. *Addiction* **101**, 1509–1515 (2006).
32. Frazer, K.A. *et al.* A second generation human haplotype map of over 3.1 million SNPs. *Nature* **449**, 851–861 (2007).
33. Pritchard, J.K., Stephens, M. & Donnelly, P. Inference of population structure using multilocus genotype data. *Genetics* **155**, 945–959 (2000).
34. Price, A.L. *et al.* Principal components analysis corrects for stratification in genome-wide association studies. *Nat. Genet.* **38**, 904–909 (2006).
35. Li, Y., Ding, J. & Abecasis, G.R. MACH 1.0: rapid haplotype reconstruction and missing genotype inference. *Am. J. Hum. Genet.* **S79**, 2290 (2006).
36. Marchini, J., Howie, B., Myers, S., McVean, G. & Donnelly, P. A new multipoint method for genome-wide association studies by imputation of genotypes. *Nat. Genet.* **39**, 906–913 (2007).
37. Servin, B. & Stephens, M. Imputation-based analysis of association studies: candidate regions and quantitative traits. *PLoS Genet.* **3**, e114 (2007).
38. Lin, D.Y. & Zeng, D. Proper analysis of secondary phenotype data in case-control association studies. *Genet. Epidemiol.* **33**, 256–265 (2009).
39. Devlin, B. & Roeder, K. Genomic control for association studies. *Biometrics* **55**, 997–1004 (1999).
40. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 2006. *MMWR CDC Surveill. Summ.* **56**, 1157–1161 (2007).
41. Dudbridge, F. & Gusnanto, A. Estimation of significance thresholds for genomewide association scans. *Genet. Epidemiol.* **32**, 227–234 (2008).

Type of file: table

Label: 3

Filename: TAGSuppMatTable6.xls

**Supplementary Table 6. Association testing for CPD on chromosome 15, conditional or**

SNP	Position	Coded Allele	Noncoded Allele	r <sup>2</sup> to rs1051730	Conditioned	P- Unconditioned	Gene
					value	P-	
rs1051730	76,681,394	G	A	1	-	8.00X10 <sup>-33</sup>	CHRNA3
rs684513	76,645,455	G	C	0.139	6.3X10 <sup>-09</sup>	5.87X10 <sup>-25</sup>	CHRNA5
rs9788682	76,589,641	G	A	0.167	1.06X10 <sup>-08</sup>	2.44X10 <sup>-23</sup>	LOC123688
rs7163730	76,601,736	G	A	0.175	1.22X10 <sup>-08</sup>	2.21X10 <sup>-24</sup>	LOC123688
rs7164594	76,590,112	T	C	0.175	1.25X10 <sup>-08</sup>	3.1X10 <sup>-24</sup>	LOC123688
rs667282	76,650,527	T	C	0.129	1.26X10 <sup>-08</sup>	3.65X10 <sup>-24</sup>	CHRNA5
rs4461039	76,604,502	T	A	0.169	1.29X10 <sup>-08</sup>	2.59X10 <sup>-24</sup>	LOC123688
rs2036534	76,614,003	T	C	0.175	1.38X10 <sup>-08</sup>	1.49X10 <sup>-23</sup>	LOC123688
rs7177514	76,694,461	G	C	0.175	1.43X10 <sup>-08</sup>	3.95X10 <sup>-25</sup>	CHRNA3
rs8042059	76,694,914	C	A	0.175	1.49X10 <sup>-08</sup>	4.57X10 <sup>-25</sup>	CHRNA3
rs3813570	76,619,887	T	C	0.126	1.53X10 <sup>-08</sup>	1.24X10 <sup>-23</sup>	PSMA4
rs11637630	76,686,774	G	A	0.178	1.59X10 <sup>-08</sup>	3.95X10 <sup>-25</sup>	CHRNA3
rs637137	76,661,031	T	A	0.115	1.66X10 <sup>-08</sup>	5.32X10 <sup>-24</sup>	CHRNA5
rs6495308	76,694,711	T	C	0.178	1.74X10 <sup>-08</sup>	4.69X10 <sup>-25</sup>	CHRNA3
rs938682	76,683,602	G	A	0.175	1.76X10 <sup>-08</sup>	1.76X10 <sup>-24</sup>	CHRNA3
rs12910984	76,678,682	G	A	0.151	2.07X10 <sup>-08</sup>	1.84X10 <sup>-24</sup>	CHRNA3
rs3743078	76,681,814	G	C	0.169	2.25X10 <sup>-08</sup>	4.22X10 <sup>-25</sup>	CHRNA3
rs8042374	76,695,087	G	A	0.175	2.85X10 <sup>-08</sup>	2.38X10 <sup>-24</sup>	CHRNA3
rs2869030	76,498,858	T	G	0.061	3.7X10 <sup>-08</sup>	3.52X10 <sup>-12</sup>	
rs4887069	76,696,125	G	A	0.127	7.46X10 <sup>-08</sup>	6.52X10 <sup>-23</sup>	CHRNA3
rs6495309	76,702,300	T	C	0.167	7.48X10 <sup>-08</sup>	4.51X10 <sup>-23</sup>	
rs12440014	76,713,781	G	C	0.161	8.57X10 <sup>-08</sup>	6.02X10 <sup>-24</sup>	CHRNB4
rs4887053	76,499,754	C	A	0.15	1.09X10 <sup>-07</sup>	3.71X10 <sup>-19</sup>	
rs2869032	76,501,616	T	C	0.15	1.14X10 <sup>-07</sup>	3.78X10 <sup>-19</sup>	
rs2869045	76,505,954	T	C	0.15	1.15X10 <sup>-07</sup>	3.95X10 <sup>-19</sup>	
rs5019044	76,583,337	T	A	0.15	1.47X10 <sup>-07</sup>	4.22X10 <sup>-20</sup>	
rs11072766	76,558,601	T	C	0.158	3.78X10 <sup>-07</sup>	1.47X10 <sup>-18</sup>	IREB2
rs2938674	76,544,968	C	A	0.158	4.42X10 <sup>-07</sup>	2.06X10 <sup>-18</sup>	IREB2
rs2568483	76,539,398	G	A	0.158	4.52X10 <sup>-07</sup>	2.31X10 <sup>-18</sup>	IREB2
rs2568488	76,523,648	T	A	0.158	4.62X10 <sup>-07</sup>	2.66X10 <sup>-18</sup>	IREB2
rs2656073	76,529,331	T	G	0.158	4.91X10 <sup>-07</sup>	3.07X10 <sup>-18</sup>	IREB2
rs2656069	76,532,762	T	C	0.158	5.18X10 <sup>-07</sup>	6.05X10 <sup>-18</sup>	IREB2
rs2656071	76,532,398	T	A	0.158	5.23X10 <sup>-07</sup>	3.08X10 <sup>-18</sup>	IREB2
rs924840	76,518,863	T	A	0.167	1.11X10 <sup>-06</sup>	3.54X10 <sup>-18</sup>	IREB2
rs2938671	76,519,809	G	A	0.167	1.14X10 <sup>-06</sup>	3.7X10 <sup>-18</sup>	IREB2
rs2958719	76,530,084	G	A	0.089	3.98X10 <sup>-06</sup>	9.62X10 <sup>-16</sup>	IREB2
rs12441088	76,715,319	T	G	0.172	4.21X10 <sup>-06</sup>	7.6X10 <sup>-22</sup>	CHRNB4
rs12443170	76,694,791	G	A	0.041	5.97X10 <sup>-06</sup>	7.34X10 <sup>-18</sup>	CHRNA3
rs11636605	76,715,933	G	A	0.094	1.37X10 <sup>-05</sup>	8.58X10 <sup>-16</sup>	CHRNB4
rs11072768	76,716,533	T	G	0.102	1.44X10 <sup>-05</sup>	2.18X10 <sup>-15</sup>	CHRNB4
rs12441998	76,716,427	G	A	0.111	1.54X10 <sup>-05</sup>	2.45X10 <sup>-15</sup>	CHRNB4
rs1316971	76,717,565	G	A	0.108	1.54X10 <sup>-05</sup>	3.37X10 <sup>-15</sup>	CHRNB4
rs569207	76,660,174	T	C	0.126	2.35X10 <sup>-05</sup>	6.35X10 <sup>-06</sup>	CHRNA5
rs11072774	76,739,752	T	C	0.096	3.88X10 <sup>-05</sup>	1.99X10 <sup>-12</sup>	
rs9920506	76,718,112	G	A	0.078	3.98X10 <sup>-05</sup>	7.08X10 <sup>-13</sup>	CHRNB4
rs12594247	76,733,688	T	C	0.095	7.84X10 <sup>-05</sup>	7.1X10 <sup>-12</sup>	
rs4887074	76,739,165	G	C	0.032	9.51X10 <sup>-05</sup>	9.47X10 <sup>-09</sup>	
rs8023822	76,732,095	G	C	0.052	0.000127	5.06X10 <sup>-09</sup>	

rs578776	76,675,455	G	A	0.212	0.000135	2.68X10 <sup>-19</sup>	CHRNA3
rs16970006	76,757,314	T	C	0.041	0.00016	6.55X10 <sup>-08</sup>	
rs12148319	76,743,247	G	A	0.075	0.000249	4.5X10 <sup>-09</sup>	
rs518425	76,670,868	G	A	0.227	0.000272	2.11X10 <sup>-18</sup>	CHRNA5
rs12594550	76,746,092	G	C	0.083	0.000322	1.1X10 <sup>-08</sup>	
rs11634628	76,792,634	G	A	0.032	0.000638	4.03X10 <sup>-07</sup>	
rs11072794	76,793,637	T	C	0.034	0.000683	4.14X10 <sup>-07</sup>	
rs12899940	76,788,754	T	C	0.034	0.000712	4.31X10 <sup>-07</sup>	
rs4362358	76,583,159	T	C	0.23	0.000727	4.11X10 <sup>-17</sup>	
rs4887078	76,798,128	T	C	0.034	0.0008	7.69X10 <sup>-07</sup>	
rs11072793	76,793,497	G	A	0.034	0.000801	8.17X10 <sup>-07</sup>	
rs1062980	76,579,582	T	C	0.224	0.000819	5.98X10 <sup>-16</sup>	IREB2
rs12904234	76,566,439	T	C	0.221	0.000851	6.09X10 <sup>-16</sup>	IREB2
rs7173512	76,636,969	T	C	0.333	0.000858	2.41X10 <sup>-05</sup>	
rs1964678	76,541,055	G	A	0.23	0.000891	5.03X10 <sup>-16</sup>	IREB2
rs8042238	76,561,326	T	C	0.223	0.000903	4.17X10 <sup>-16</sup>	IREB2
rs4299116	76,553,249	T	A	0.219	0.000904	4.31X10 <sup>-16</sup>	IREB2
rs3743075	76,696,507	T	C	0.309	0.000907	0.000084	CHRNA3
rs8043227	76,555,926	G	C	0.23	0.000909	4.27X10 <sup>-16</sup>	IREB2
rs8042260	76,561,429	G	A	0.206	0.000909	4.19X10 <sup>-16</sup>	IREB2
rs12910910	76,554,905	T	C	0.224	0.000913	4.28X10 <sup>-16</sup>	IREB2
rs12903295	76,566,027	G	A	0.229	0.000921	4.38X10 <sup>-16</sup>	IREB2
rs965604	76,576,278	G	A	0.23	0.000939	4.51X10 <sup>-16</sup>	IREB2
rs13180	76,576,543	T	C	0.23	0.001027	1.56X10 <sup>-15</sup>	IREB2
rs11633519	76,786,607	G	A	0.037	0.001053	9.16X10 <sup>-07</sup>	
rs8032552	76,758,191	T	C	0.039	0.001294	4.1X10 <sup>-07</sup>	
rs8043123	76,760,448	T	C	0.045	0.001336	4.96X10 <sup>-07</sup>	
rs11072787	76,760,032	T	C	0.034	0.001471	2.64X10 <sup>-07</sup>	
rs12914385	76,685,778	T	C	0.774	0.001913	4.23X10 <sup>-35</sup>	CHRNA3
rs11629637	76,806,079	T	C	0.413	0.002506	1.35X10 <sup>-20</sup>	
rs11638490	76,795,005	T	C	0.371	0.002642	6.65X10 <sup>-21</sup>	
rs12910627	76,781,988	G	C	0.399	0.003733	3.67X10 <sup>-21</sup>	
rs899997	76,806,633	T	G	0.034	0.003851	2.72X10 <sup>-06</sup>	
rs11072791	76,784,131	C	A	0.399	0.003977	5.04X10 <sup>-21</sup>	
rs11634351	76,731,773	G	A	0.502	0.004128	7.64X10 <sup>-25</sup>	
rs1383634	76,816,451	T	C	0.034	0.004272	3.18X10 <sup>-06</sup>	
rs2219939	76,816,778	G	A	0.039	0.00442	3.42X10 <sup>-06</sup>	
rs922692	76,771,269	C	A	0.399	0.00442	5.69X10 <sup>-21</sup>	
rs4887091	76,830,635	T	C	0.018	0.004511	4.95X10 <sup>-06</sup>	
rs11638372	76,770,614	T	C	0.399	0.004535	6.77X10 <sup>-21</sup>	
rs11072785	76,755,284	T	C	0.478	0.004789	7.69X10 <sup>-22</sup>	
rs1021071	76,755,234	G	C	0.47	0.004805	7.06X10 <sup>-22</sup>	
rs4887077	76,765,419	T	C	0.399	0.004815	7.64X10 <sup>-21</sup>	
rs7182567	76,832,109	G	A	0.021	0.004886	5.44X10 <sup>-06</sup>	
rs11638830	76,735,374	G	C	0.491	0.004942	3.46X10 <sup>-23</sup>	
rs12902602	76,754,456	G	A	0.457	0.004953	6.97X10 <sup>-22</sup>	
rs4886580	76,756,440	T	G	0.444	0.005104	8.96X10 <sup>-22</sup>	
rs6495314	76,747,584	C	A	0.47	0.005173	7.69X10 <sup>-23</sup>	
rs1996371	76,743,861	T	C	0.47	0.005284	4.35X10 <sup>-23</sup>	
rs12899135	76,741,434	G	A	0.461	0.005321	1.56X10 <sup>-22</sup>	
rs11639372	76,753,710	T	C	0.483	0.006441	1.01X10 <sup>-21</sup>	

rs3813565	76,806,665	T	G	0.441	0.007192	3.26X10 <sup>-21</sup>	
rs7403393	76,922,857	G	C		0.008749	1.57X10 <sup>-08</sup>	
rs7164529	76,932,853	G	A		0.009419	4.39X10 <sup>-09</sup>	
rs12286	76,838,814	G	A	0.372	0.01246	1.06X10 <sup>-18</sup>	ADAMTS7
rs12595538	76,941,508	T	A		0.01305	7.8X10 <sup>-09</sup>	
rs4887082	76,812,122	T	C	0.399	0.01376	2.88X10 <sup>-19</sup>	
rs1809420	76,843,824	T	C		0.01609	3.23X10 <sup>-18</sup>	ADAMTS7
rs7174367	76,851,722	G	A	0.337	0.01751	7X10 <sup>-18</sup>	ADAMTS7
rs11072810	76,919,261	T	C		0.01815	1.15X10 <sup>-08</sup>	
rs11072811	76,919,385	C	A		0.01818	1.22X10 <sup>-08</sup>	
rs17243470	76,959,821	T	G		0.01975	1.28X10 <sup>-07</sup>	MORF4L1
rs17487514	76,740,840	T	C	0.227	0.02294	3.25X10 <sup>-05</sup>	
rs4539564	76,915,554	G	A		0.02634	1.91X10 <sup>-09</sup>	
rs11852830	76,912,484	T	A		0.02937	6.16X10 <sup>-08</sup>	
rs11857532	76,755,323	T	G	0.41	0.03034	6.35X10 <sup>-18</sup>	
rs8032771	76,913,114	G	A		0.03042	5.54X10 <sup>-08</sup>	
rs8040868	76,698,236	T	C	0.753	0.0307	4.03X10 <sup>-08</sup>	CHRNA3
rs8035039	76,916,878	G	A		0.03152	3.12X10 <sup>-09</sup>	
rs6495337	76,912,744	G	C		0.04394	1.55X10 <sup>-07</sup>	
rs7171916	76,855,006	G	C	0.291	0.05961	1.23X10 <sup>-14</sup>	ADAMTS7
rs7173743	76,928,839	T	C		0.08455	2.14X10 <sup>-08</sup>	
rs5029904	76,939,477	G	C		0.1404	1.65X10 <sup>-07</sup>	
rs931794	76,613,235	G	A	0.872	0.1447	1.64X10 <sup>-31</sup>	LOC123688
rs8031948	76,603,112	T	G	0.87	0.1578	3.15X10 <sup>-31</sup>	LOC123688
rs10519203	76,601,101	G	A	0.872	0.1835	4.89X10 <sup>-31</sup>	LOC123688
rs9788721	76,589,924	T	C	0.872	0.1851	4.14X10 <sup>-31</sup>	LOC123688
rs12910237	76,743,393	T	C	0.351	0.1947	1.43X10 <sup>-07</sup>	
rs922691	76,751,049	G	A	0.308	0.2096	6.04X10 <sup>-07</sup>	
rs1504550	76,553,305	G	A	0.72	0.217	4.53X10 <sup>-26</sup>	IREB2
rs17484524	76,559,731	G	A	0.701	0.2192	2.01X10 <sup>-26</sup>	IREB2
rs2009746	76,541,157	G	A	0.732	0.2211	1.52X10 <sup>-25</sup>	IREB2
rs17484235	76,548,469	G	C	0.711	0.2232	1.14X10 <sup>-25</sup>	IREB2
rs8034191	76,593,078	T	C	0.872	0.2322	1.68X10 <sup>-31</sup>	LOC123688
rs2568494	76,528,019	G	A	0.72	0.2592	3.39X10 <sup>-24</sup>	IREB2
rs2656052	76,527,987	C	A	0.711	0.261	3.76X10 <sup>-24</sup>	IREB2
rs7181486	76,528,673	T	C	0.71	0.2628	2.46X10 <sup>-24</sup>	IREB2
rs17483929	76,529,431	G	A	0.711	0.2645	2.7X10 <sup>-24</sup>	IREB2
rs17483548	76,517,368	G	A	0.711	0.2661	9.66X10 <sup>-24</sup>	
rs2656065	76,537,604	G	A	0.699	0.2681	4.88X10 <sup>-25</sup>	IREB2
rs17483721	76,520,786	T	C	0.711	0.2733	7.34X10 <sup>-24</sup>	IREB2
rs17405217	76,518,204	T	C	0.711	0.274	9.09X10 <sup>-24</sup>	IREB2
rs1021070	76,733,918	G	C	0.346	0.2846	2.16X10 <sup>-08</sup>	
rs7181405	76,735,207	G	A	0.339	0.2858	2.31X10 <sup>-08</sup>	
rs2036527	76,638,670	G	A	0.837	0.3942	1.2X10 <sup>-32</sup>	
rs12905641	76,751,417	T	C	0.314	0.4385	1.07X10 <sup>-07</sup>	
rs951266	76,665,596	G	A	0.867	0.5209	3X10 <sup>-33</sup>	CHRNA5
rs8038920	76,761,600	G	A	0.321	0.5446	6.98X10 <sup>-08</sup>	
rs1994016	76,867,289	T	C	0.134	0.5454	3.33X10 <sup>-10</sup>	ADAMTS7
rs7180002	76,661,048	T	A	0.867	0.5528	4.11X10 <sup>-33</sup>	CHRNA5
rs17486278	76,654,537	C	A	0.89	0.5929	5.91X10 <sup>-33</sup>	CHRNA5
rs3743057	76,876,062	T	C	0.204	0.5941	9.45X10 <sup>-06</sup>	ADAMTS7

rs7177699	76,876,789	T	C	0.212	0.5983	6.78X10 <sup>-11</sup>	ADAMTS7
rs3825807	76,876,166	G	A	0.212	0.6064	1.29X10 <sup>-10</sup>	ADAMTS7
rs16969968	76,669,980	G	A	0.9	0.6075	4.48X10 <sup>-33</sup>	CHRNA5
rs2277545	76,870,646	T	C	0.196	0.6162	7.55X10 <sup>-11</sup>	ADAMTS7
rs12903203	76,871,988	T	C	0.256	0.6198	1.08X10 <sup>-10</sup>	ADAMTS7
rs7178051	76,905,351	T	C		0.6273	1.07X10 <sup>-05</sup>	
rs1564499	76,871,863	T	C	0.204	0.63	4.7X10 <sup>-06</sup>	ADAMTS7
rs1317286	76,683,184	G	A	0.897	0.6598	5.26X10 <sup>-33</sup>	CHRNA3
rs2904228	76,873,154	G	A	0.194	0.6727	5.99X10 <sup>-06</sup>	ADAMTS7
rs12905740	76,869,419	T	C	0.173	0.674	3.08X10 <sup>-06</sup>	ADAMTS7
rs1994017	76,867,361	T	C	0.204	0.6782	2.86X10 <sup>-06</sup>	ADAMTS7
rs4380028	76,898,148	T	C		0.6893	8.92X10 <sup>-06</sup>	
rs6495335	76,904,188	T	G		0.7042	8.7X10 <sup>-06</sup>	
rs7176187	76,908,428	T	C		0.7066	5.13X10 <sup>-06</sup>	
rs1394371	76,511,524	T	C	0.592	0.8119	2.36X10 <sup>-18</sup>	
rs17487223	76,711,042	T	C	0.747	0.887	4.23X10 <sup>-29</sup>	CHRNA4
rs1383636	76,893,275	G	A		0.929	1.24X10 <sup>-06</sup>	
rs922693	76,886,593	G	A		0.9355	8.09X10 <sup>-07</sup>	ADAMTS7
rs8038189	76,886,081	G	C		0.9568	6.75X10 <sup>-07</sup>	ADAMTS7

# 1 rs1051730

## Gene near 50kb

CHRNA5 CHRNB4  
CHRNA3 LOC123688 PSMA4  
IREB2 PSMA4  
CHRNA5 IREB2 PSMA4  
IREB2 PSMA4  
CHRNA3 LOC123688 PSMA4  
CHRNA5 IREB2 PSMA4  
CHRNA5 IREB2 PSMA4  
CHRNA5 CHRNB4  
CHRNA5 CHRNB4  
CHRNA5 IREB2 LOC123688  
CHRNA5 CHRNB4  
CHRNA3 CHRNB4 LOC123688 PSMA4  
CHRNA5 CHRNB4  
CHRNA5 CHRNB4  
CHRNA5 CHRNB4  
CHRNA5 CHRNB4  
CHRNA5 CHRNB4  
IREB2  
CHRNA5 CHRNB4  
CHRNA3 CHRNA5 CHRNB4  
CHRNA3 CHRNA5  
IREB2  
IREB2  
IREB2  
IREB2 LOC123688 PSMA4  
LOC123688  
LOC123688  
LOC123688

CHRNA3 CHRNA5  
CHRNA5 CHRNB4  
CHRNA3 CHRNA5  
CHRNA3 CHRNA5  
CHRNA3 CHRNA5  
CHRNA3 CHRNA5  
CHRNA3 CHRNB4 LOC123688 PSMA4  
CHRNA3 CHRNB4  
CHRNA3 CHRNA5  
CHRNA3 CHRNB4  
CHRNA3 CHRNB4  
CHRNA3 CHRNB4



CHRNA5 CHRNB4 PSMA4  
CHRNB4  
CHRNA3 CHRNB4  
CHRNA3 CHRNB4 PSMA4  
CHRNA3 CHRNB4  
ADAMTS7  
ADAMTS7  
ADAMTS7  
IREB2 LOC123688 PSMA4  
ADAMTS7  
ADAMTS7  
LOC123688 PSMA4  
LOC123688  
CHRNA3 CHRNA5 LOC123688 PSMA4  
LOC123688  
LOC123688  
LOC123688  
CHRNA5 CHRNB4  
LOC123688  
LOC123688  
LOC123688  
LOC123688  
LOC123688 PSMA4  
LOC123688 PSMA4

CHRNB4  
CHRNB4  
CHRNB4  
CHRNA5 CHRNB4  
ADAMTS7  
ADAMTS7

ADAMTS7

CHRNA3 CHRNB4  
ADAMTS7  
ADAMTS7

ADAMTS7  
CHRNB4  
CHRNB4  
CHRNB4  
CHRNB4  
ADAMTS7  
CHRNA3 CHRNB4  
CHRNB4  
CHRNB4  
CHRNA3 CHRNB4  
CHRNA3 CHRNB4  
CHRNA3 CHRNB4  
CHRNB4

ADAMTS7  
ADAMTS7 MORF4L1  
ADAMTS7 MORF4L1

MORF4L1  
ADAMTS7

ADAMTS7 MORF4L1  
ADAMTS7 MORF4L1  
CTSH  
CHRNA3 CHRNB4  
ADAMTS7 MORF4L1  
ADAMTS7 MORF4L1  
CHRNB4  
ADAMTS7 MORF4L1  
CHRNA5 CHRNB4  
ADAMTS7 MORF4L1  
ADAMTS7 MORF4L1

ADAMTS7 MORF4L1  
ADAMTS7 MORF4L1  
CHRNA5 IREB2 PSMA4  
CHRNA5 IREB2 PSMA4  
CHRNA5 IREB2 PSMA4  
IREB2 PSMA4  
CHRNA3 CHRNB4  
CHRNB4  
LOC123688  
LOC123688  
LOC123688  
LOC123688  
IREB2 PSMA4

IREB2  
LOC123688

CHRNA3 CHRNB4  
CHRNA3 CHRNB4  
CHRNA3 CHRNA5 LOC123688 PSMA4  
CHRNB4  
CHRNA3 CHRNB4 LOC123688 PSMA4  
CHRNB4

CHRNA3 CHRNB4 LOC123688 PSMA4  
CHRNA3 CHRNB4 LOC123688 PSMA4

*CHRNA3 CHRNB4 PSMA4*

*ADAMTS7 MORF4L1*

*CHRNA5 CHRNB4*

*ADAMTS7*

*ADAMTS7 MORF4L1*

*ADAMTS7 MORF4L1*

*IREB2*

*CHRNA3 CHRNA5*

*ADAMTS7*