

Supplementary Material

Supplement to: “AATF and SMARCA2 are associated with thyroid volume in Hashimoto’s thyroiditis patients”.

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Supplementary Table 1. Associations of genetic variants located inside +/- 500 kb genomic regions around the most associated genetic variants with thyroid volume from the present study.**Genomic region around rs7212416 (17:36475441-37475441)**

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
Genome-wide associations:							
rs78943308	<0,01	36602169	2,00E-81	missense_variant	<i>MRM1</i>	Macrophage inflammatory protein 1b levels	27989323
rs76842834	<0,01	36528017	1,00E-35	intron_variant	<i>MYO19</i>	Macrophage inflammatory protein 1b levels	27989323
rs184920307	<0,01	36522456	4,00E-30	intron_variant	<i>MYO19</i>	Macrophage inflammatory protein 1b levels	27989323
rs143653036	<0,01	36782901	1,00E-25	intergenic_variant	<i>LOC105371750 - LOC102723471</i>	Macrophage inflammatory protein 1b levels	27989323
rs11263779	<0,01	36627751	5,00E-16	intergenic_variant	<i>MRM1</i>	Macrophage inflammatory protein 1b levels	27989323
rs67796445	<0,01	36483820	4,00E-13	upstream_gene_variant	<i>ZNHIT3</i>	Red cell distribution width	27863252
rs9910727	<0,01	36903260	5,00E-12	intron_variant	<i>LOC102723471</i>	Macrophage inflammatory protein 1b levels	27989323
rs12150665	<0,01	36558947	5,00E-11	intron_variant	<i>GGNBP2</i>	Body mass index	28892062
rs3744593	<0,01	36587289	4,00E-10	missense_variant	<i>GGNBP2</i>	Intelligence (multi-trait analysis)	29326435
rs185128671	<0,01	37365406	2,00E-09	intron_variant	<i>ACACA</i>	Macrophage inflammatory protein 1b levels	27989323
rs186218230	<0,01	37027128	3,00E-09	intron_variant	<i>AATF</i>	Macrophage inflammatory protein 1b levels	27989323
Suggestive associations:							
rs12150665	<0,01	36558947	8,00E-08	intron_variant	<i>GGNBP2</i>	Body mass index	25673413
rs12150665	<0,01	36558947	2,00E-07	intron_variant	<i>GGNBP2</i>	Body mass index	25673413
rs182210624	<0,01	37159111	2,00E-07	intron_variant	<i>ACACA</i>	Macrophage inflammatory protein 1b levels	27989323
rs17138064	<0,01	36831827	5,00E-07	intergenic_variant	<i>LOC105371750 - LOC102723471</i>	Orofacial clefts	22419666
rs8081319	<0,01	37374139	8,00E-07	intron_variant	<i>HOXB9, ACACA</i>	Celiac disease	24999842
rs12950363	<0,01	36659471	2,00E-06	intergenic_variant	<i>MRM1 - LOC105371751</i>	Hippocampal sclerosis	25188341
rs2003347	<0,01	36916062	2,00E-06	intron_variant	<i>LOC102723471</i>	Post bronchodilator FEV1/FVC ratio	26634245
rs2306658	<0,01	36949012	2,00E-06	5_prime_UTR_variant	<i>AATF</i>	Obesity-related traits (body composition)	23251661
rs12185265	<0,01	36916999	3,00E-06	intron_variant	<i>LOC102723471</i>	Post bronchodilator FEV1/FVC ratio	26634245
rs55955238	<0,01	36913639	3,00E-06	intron_variant	<i>LOC102723471</i>	Post bronchodilator FEV1/FVC ratio	26634245
rs4796285	<0,01	36824731	7,00E-06	intergenic_variant	<i>LOC105371750 - LOC102723471</i>	Obstructive sleep apnea trait (apnea hypopnea index)	26977737
rs2306658	<0,01	36949012	9,00E-06	5_prime_UTR_variant	<i>AATF</i>	Obesity-related traits (hip circumference)	23251661

Genomic region around rs10738556 (9:1507878-2507878)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
Genome-wide associations:							
rs11998763	<0,01	1787687	5,00E-14	intergenic_variant	<i>LOC105375951</i>	Educational attainment (years of education)	27225129
rs3847225	<0,01	1790685	4,00E-10	intergenic_variant	<i>LOC105375951</i>	Educational attainment	27046643
rs872256	<0,01	2496480	9,00E-09	intron_variant	<i>SMARCA2, VLDLR</i>	Systolic blood pressure	26969751
Suggestive associations:							
rs377310910	<0,01	1940937	2,00E-07	regulatory_region_variant	<i>LOC105375951</i>	Parental extreme longevity (95 years and older)	27015805
rs1478110	<0,01	1721478	4,00E-07	intergenic_variant	<i>LOC105375951</i>	Educational attainment	25201988
rs866991	<0,01	2403909	4,00E-07	regulatory_region_variant	<i>LOC101930053</i>	Low white blood cell count (conditioned on rs2814778)	29596498
rs4741700	<0,01	2404563	4,00E-07	intergenic_variant	<i>LOC101930053</i>	Low white blood cell count (conditioned on rs2814778)	29596498
rs36030485	<0,01	2411646	9,00E-07	regulatory_region_variant	<i>LOC105375956</i>	Bipolar disorder or attention deficit hyperactivity disorder	27890468
rs16938145	<0,01	2256092	1,00E-06	intergenic_variant	<i>SMARCA2</i>	Amyotrophic lateral sclerosis (sporadic)	24529757
						Adverse response to chemotherapy in breast cancer (alopecia)	
rs6475600	<0,01	2203938	2,00E-06	intergenic_variant	<i>SMARCA2</i>	(cyclophosphamide+doxorubicin+/-5FU)	24025145

rs10966132	<0,01	2400701	2,00E-06	intergenic_variant	<i>LOC101930053</i>	Low white blood cell count (conditioned on rs2814778)	29596498
rs10962181	<0,01	1595160	3,00E-06	intergenic_variant	<i>SMARCA2</i>	Superior frontal gyrus grey matter volume	25335168
rs1123970	<0,01	2328213	4,00E-06	intergenic_variant	<i>LOC105375955 - LOC101930053</i>	Warfarin maintenance dose	26265036
rs12686800	<0,01	2489728	4,00E-06	intron_variant	<i>FLJ35024, LOC101930053</i>	Venous thromboembolism adjusted for sickle cell variant rs77121243-T	28203683
rs10811256	0,1	1995749	5,00E-06	intron_variant	<i>SMARCA2</i>	Asthma (childhood onset)	27611488
rs4741652	<0,01	2194227	7,00E-06	downstream_gene_variant	<i>SMARCA2</i>	Autism spectrum disorder, attention deficit-hyperactivity disorder, bipolar disorder, major depressive disorder, and schizophrenia (combined)	23453885

Genomic region around rs201666766 (5:13329978-14329978)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
Genome-wide associations:							
rs7720298	<0,01	13858219	3,00E-08	intron_variant	<i>DNAH5</i>	Response to radiotherapy in prostate cancer (toxicity, decreased urine stream)	27515689
Suggestive associations:							
rs10036995	<0,01	13693461	5,00E-07	intron_variant	<i>DNAH5</i>	Bacterial meningitis	28928442
rs163818	<0,01	14071948	6,00E-07	intergenic_variant	<i>DNAH5 - TRIO</i>	Adverse response to chemotherapy in breast cancer (alopecia) (paclitaxel)	24025145
rs924633	<0,01	13859170	9,00E-07	intron_variant	<i>DNAH5</i>	Emphysema imaging phenotypes	26030696
rs795544	0,02	13798450	1,00E-06	intron_variant	<i>DNAH5</i>	Corneal astigmatism	23322567
rs6881967	<0,01	13741054	1,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1 in COPD	26634245
rs9765543	0,03	13748060	2,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs6554809	<0,01	13740867	3,00E-06	intron_variant	<i>DNAH5</i>	IgE grass sensitization	22036096
rs2134257	0,03	13756020	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs2134259	0,03	13755842	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs1604476	0,03	13743975	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs9687653	0,03	13746951	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs34476088	0,03	13747718	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs1502045	<0,01	13745610	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs6889428	0,03	13750866	3,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs6881967	<0,01	13741054	4,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs6897741	0,03	13749128	4,00E-06	intron_variant	<i>DNAH5</i>	Post bronchodilator FEV1/FVC ratio in chronic obstructive pulmonary disease	26634245
rs2896103	<0,01	13764310	5,00E-06	intron_variant	<i>DNAH5</i>	Subclinical atherosclerosis traits (ankle brachial index)	17903303
rs7715811	<0,01	13769865	6,00E-06	intron_variant	<i>DNAH5</i>	Subclinical atherosclerosis traits (ankle brachial index)	17903303
rs1502050	<0,01	13779634	9,00E-06	intron_variant	<i>DNAH5</i>	Subclinical atherosclerosis traits (ankle brachial index)	17903303

Genomic region around rs170884 (1:184442995-185442995)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
Genome-wide associations:							
rs10732976	<0,01	185439929	2,00E-16	downstream_gene_variant	<i>CTA-277P6.1</i>	Monocyte percentage of white cells	27863252
rs10489481	<0,01	185422035	2,00E-15	intergenic_variant	<i>LOC107985455 - RNU7-183P</i>	Monocyte count	27863252
rs10911628	<0,01	184680369	2,00E-13	intergenic_variant	<i>EDEM3</i>	Systemic lupus erythematosus	24871463
rs10732976	<0,01	185439929	5,00E-10	downstream_gene_variant	<i>CTA-277P6.1</i>	Granulocyte percentage of myeloid white cells	27863252
Suggestive associations:							
rs72392086	<0,01	185064685	2,00E-07	intron_variant	<i>RNF2</i>	Clopidogrel active metabolite levels	28207573
rs34199165	<0,01	184861124	4,00E-07	intron_variant	<i>FAM129A</i>	Cough in response to angiotensin-converting enzyme inhibitor drugs	28084903
rs12136737	0,01	184482448	1,00E-06	intron_variant	<i>C1orf21</i>	Colonoscopy-negative controls vs population controls	29228715
rs72739697	0,03	185072240	2,00E-06	intron_variant	<i>RNF2</i>	Itch intensity from mosquito bite adjusted by bite size	28199695
rs3753573	<0,01	185044870	2,00E-06	upstream_gene_variant	<i>RNF2</i>	Obesity-related traits	23251661

rs682331	0,07	184792231	4,00E-06	3_prime_UTR_variant	<i>FAM129A</i>	Obesity-related traits	23251661
rs185610185	<0,01	184914373	5,00E-06	intron_variant	<i>FAM129A</i>	Number of common colds	28928442
rs3736757	0,02	184708330	6,00E-06	synonymous_variant	<i>EDEM3</i>	Obesity-related traits	23251661
rs144658860	<0,01	185197819	8,00E-06	intron_variant	<i>SWT1</i>	Number of common colds	28928442
rs188560777	<0,01	185330214	8,00E-06	intron_variant	<i>GS1-279B7.1, LOC102724897</i>	Number of common colds	28928442
rs201130852	<0,01	184795373	9,00E-06	synonymous_variant	<i>FAM129A</i>	Epstein-Barr virus copy number in lymphoblastoid cell lines	28654678

Genomic region around rs4747268 (10:15769537-16769537)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
Genome-wide associations:							
rs12265790	<0,01	15831289	2,00E-08	intron_variant	<i>ITGA8</i>	Cerebrospinal fluid t-tau:AB1-42 ratio	28641921
rs7896076	<0,01	15830828	2,00E-08	intron_variant	<i>ITGA8</i>	Cerebrospinal fluid t-tau:AB1-42 ratio	28641921
Suggestive associations:							
rs10508503	0,02	16257952	2,00E-07	intergenic_variant	<i>PTER</i>	Obesity	19151714
rs7916663	<0,01	16706611	4,00E-07	intron_variant	<i>RSU1</i>	Obesity-related traits	23251661
rs7916663	<0,01	16706611	2,00E-06	intron_variant	<i>RSU1</i>	Obesity-related traits	23251661
rs7068341	<0,01	16592300	2,00E-06	3_prime_UTR_variant	<i>RSU1</i>	Migraine	23793025
rs61842316	<0,01	16711721	3,00E-06	intron_variant	<i>RSU1</i>	Major depressive disorder	29317602
rs2069036	<0,01	16074748	3,00E-06	upstream_gene_variant	<i>FAM188A, PTER</i>	Urate levels (BMI interaction)	25811787
rs138166088	0,02	16388195	4,00E-06	intergenic_variant	<i>LOC102724039 - PTER</i>	Facial morphology (factor 14, intercanthal width)	28441456
rs2275731	<0,01	16484841	4,00E-06	intron_variant	<i>PTER</i>	Bone fracture in osteoporosis	28580392
rs200867798	<0,01	15876355	4,00E-06	intergenic_variant	<i>FAM188A - FTLP19</i>	Hepatitis B	28928442
rs7916663	<0,01	16706611	5,00E-06	intron_variant	<i>RSU1</i>	Obesity-related traits	23251661
rs11254160	<0,01	16702524	6,00E-06	intron_variant	<i>RSU1</i>	Obesity-related traits	23251661
rs2069036	<0,01	16074748	8,00E-06	upstream_gene_variant	<i>C10orf97</i>	Plasma omega-6 polyunsaturated fatty acid levels (gamma-linolenic acid)	24823311
rs11254160	<0,01	16702524	8,00E-06	intron_variant	<i>RSU1</i>	Obesity-related traits	23251661
rs10904785	<0,01	16671774	8,00E-06	intron_variant	<i>RSU1</i>	Coronary artery calcified atherosclerotic plaque (130 HU threshold) in type 2 diabetes	29221444
rs11253668	<0,01	15883967	9,00E-06	intergenic_variant	<i>FAM188A - FTLP19</i>	Eotaxin levels	27989323

Genomic region around rs193145729 (11:22825719-23825719)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
No genome-wide associations in this region.							
Suggestive associations:							
rs11027001;							
rs11828289;							
rs17234274;							
rs7115663;				intergenic_variant; intron_variant;			
rs4472938;				intron_variant; intergenic_variant;			
rs10160246;		23133679;23174695;		intergenic_variant;			
rs10833965;		23192820;23139953;		intergenic_variant; intron_variant;			
rs16910800;		23149298;23153770;		intron_variant;			
rs11602836;		23193334;23181239;		regulatory_region_variant;			
rs971535	<0,01	23211338;23123974	6,00E-07	regulatory_region_variant	<i>RP11-266A24.1</i>	Cancer	29299148
rs11027293	<0,01	23530907	7,00E-07	intergenic_variant	<i>SVIP</i>	Allergic rhinitis	25085501
rs10833905	<0,01	23023046	7,00E-07	intergenic_variant	<i>GAS2 - LOC105376591</i>	Sudden cardiac arrest	21658281
rs12364177	<0,01	22877431	1,00E-06	intron_variant	<i>GAS2</i>	Trans fatty acid levels	25646338

rs143569928	<0,01	23783102	2,00E-06	intron_variant	<i>LOC105376593 - LOC100288844</i>	Facial morphology (factor 6, height of vermillion lower lip)	28441456
rs187478995	<0,01	23413389	2,00E-06	intergenic_variant	<i>WIZP1 - MIR8054</i>	Post bronchodilator FEV1	26634245
rs147831109	<0,01	23360815	4,00E-06	intergenic_variant	<i>LOC105376592 - LOC100131557</i>	Post bronchodilator FEV1	26634245
rs35833321	<0,01	23112480	4,00E-06	intergenic_variant	<i>GAS2 - LOC105376591</i>	Interferon gamma levels	27989323
rs117285774	<0,01	23670881	6,00E-06	intergenic_variant	<i>RPS2P38 - LOC105376593</i>	3-hydroxypropylmercapturic acid levels in smokers	26053186
rs11027293	<0,01	23530907	7,00E-06	intergenic_variant	<i>SVIP</i>	Allergic rhinitis	25085501

Genomic region around rs11247367 (15:98193047-99193047)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
Genome-wide associations:							
rs2871865	<0,01	98651667	6,00E-23	intron_variant	<i>IGF1R</i>	Height	25429064
rs2871865	<0,01	98651667	3,00E-21	intron_variant	<i>IGF1R</i>	Height	20881960
rs6598541	<0,01	98727906	5,00E-15	intron_variant	<i>IGF1R</i>	Urate levels	23263486
rs4965426	<0,01	98704812	2,00E-12	intron_variant	<i>IGF1R</i>	Platelet count	27863252
rs4965426	<0,01	98704812	1,00E-11	intron_variant	<i>IGF1R</i>	Plateletcrit	27863252
rs7402982	0,05	98650040	1,00E-09	intron_variant	<i>IGF1R</i>	Birth weight	27680694
rs4966038	<0,01	98903403	2,00E-09	intron_variant	<i>IGF1R</i>	Endometriosis	27506219
rs6598351	<0,01	98264882	2,00E-08	intron_variant	<i>FAM169B</i>	Optic cup area	28073927
rs2018860	<0,01	98715481	3,00E-08	intron_variant	<i>IGF1R</i>	Fasting plasma glucose	25187374
Suggestive associations:							
rs8035887	<0,01	98618223	4,00E-07	intergenic_variant	<i>FAM169B - IRAIN</i>	3-hydroxy-1-methylpropylmercapturic acid levels in smokers	26053186
rs12719740	<0,01	98529676	7,00E-07	intron_variant	<i>FAM169B, IGF1R</i>	Arthritis (juvenile idiopathic)	22354554
rs1442808	<0,01	98221618	1,00E-06	intron_variant	<i>LOC728459, FAM169B</i>	Diisocyanate-induced asthma	25918132
rs970843	<0,01	98332800	5,00E-06	intergenic_variant	<i>FLJ39743</i>	Obesity (extreme)	21935397
rs8032194	<0,01	99074939	7,00E-06	intron_variant	<i>SYNM</i>	Carotid plaque burden	28282560
rs1670273	<0,01	99073491	8,00E-06	intron_variant	<i>DMN, SYNM</i>	Low high density lipoprotein cholesterol levels	26879886

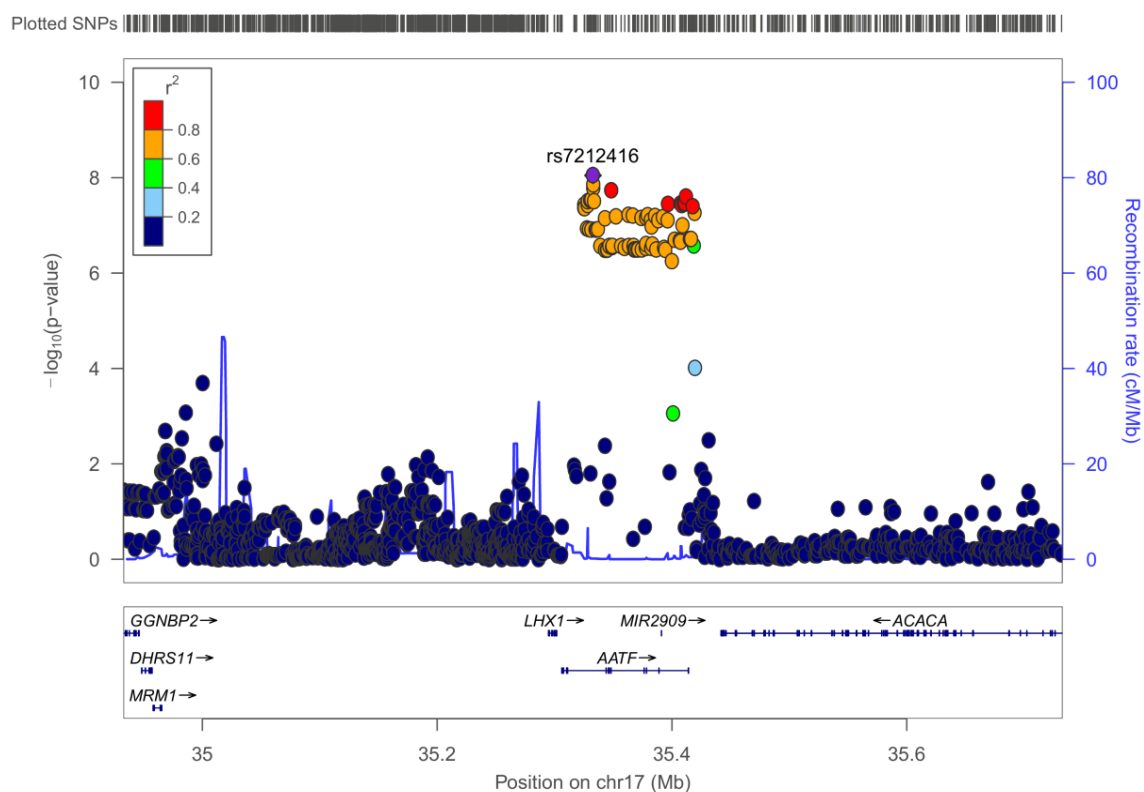
Genomic region around rs10767013 (11:22650139-23650139)

Associated SNP	R ²	Position	P	Functional effect	Gene/Nearest gene	Associated trait	PMID
No genome-wide associations in this region.							
Suggestive associations:							
rs11027001;							
rs11828289;							
rs17234274;							
rs7115663;				intergenic_variant; intron_variant;			
rs4472938;				intron_variant; intergenic_variant;			
rs10160246;		23133679;23174695;		intergenic_variant;			
rs10833965;		23192820;23139953;		intergenic_variant; intron_variant;			
rs16910800;		23149298;23153770;		intron_variant;			
rs11602836;		23193334;23181239;		regulatory_region_variant;			
rs971535	<0.01	23211338;23123974	6,00E-07	regulatory_region_variant	<i>RP11-266A24.1</i>	Cancer	29299148
rs11027293	<0,01	23530907	7,00E-07	intergenic_variant	<i>SVIP</i>	Allergic rhinitis	25085501
rs10833905	<0.01	23023046	7,00E-07	intergenic_variant	<i>GAS2 - LOC105376591</i>	Sudden cardiac arrest	21658281
rs12364177	<0,01	22877431	1,00E-06	intron_variant	<i>GAS2</i>	Trans fatty acid levels	25646338
rs7111546	<0.01	22808211	2,00E-06	intron_variant	<i>GAS2</i>	Dialysis-related mortality	21546767

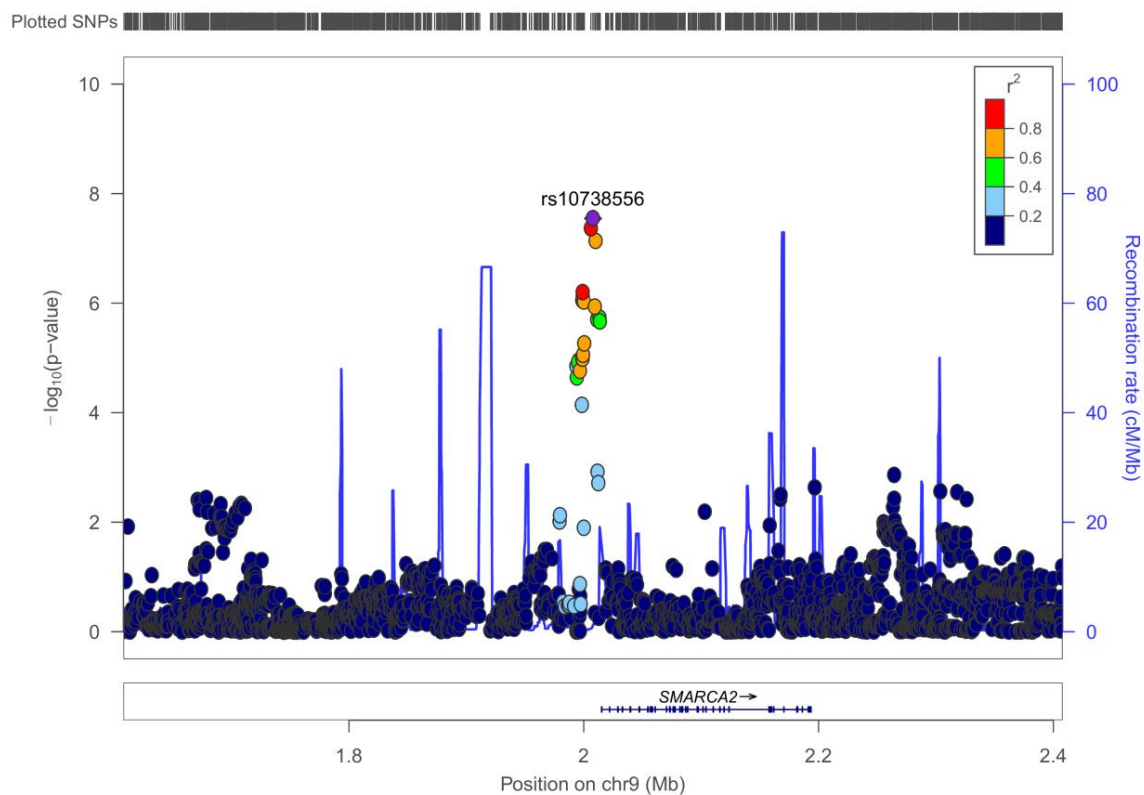
rs187478995	<0,01	23413389	2,00E-06	intergenic_variant	<i>WIZP1 - MIR8054</i>	Post bronchodilator FEV1	26634245
rs147831109	<0.01	23360815	4,00E-06	intergenic_variant	<i>LOC105376592 - LOC100131557</i>	Post bronchodilator FEV1	26634245
rs35833321	<0,01	23112480	4,00E-06	intergenic_variant	<i>GAS2 - LOC105376591</i>	Interferon gamma levels	27989323
rs712022	<0.01	22821609	6,00E-06	3_prime_UTR_variant	<i>SVIP</i>	Dialysis-related mortality	21546767
rs11027293	<0,01	23530907	7,00E-06	intergenic_variant	<i>SVIP</i>	Allergic rhinitis	25085501

Positions are based on the GRCh 38 build.

A

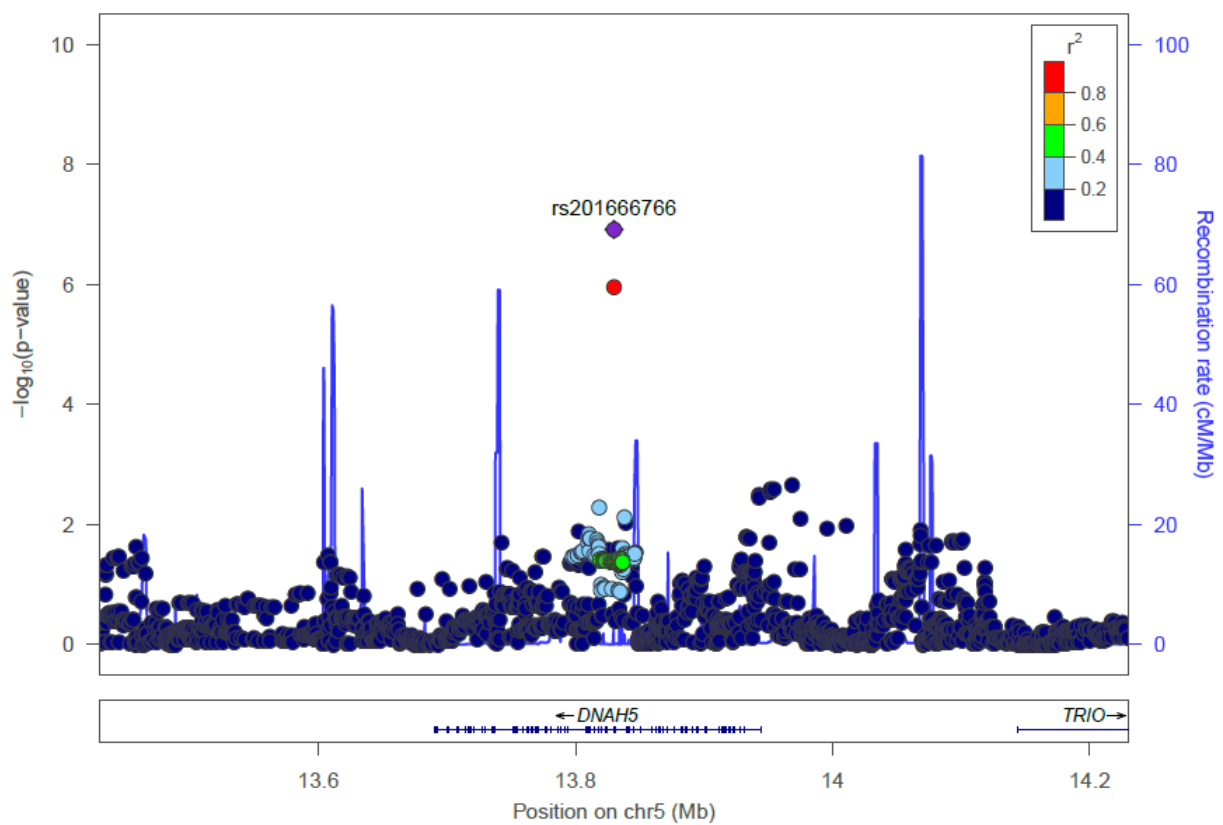


B

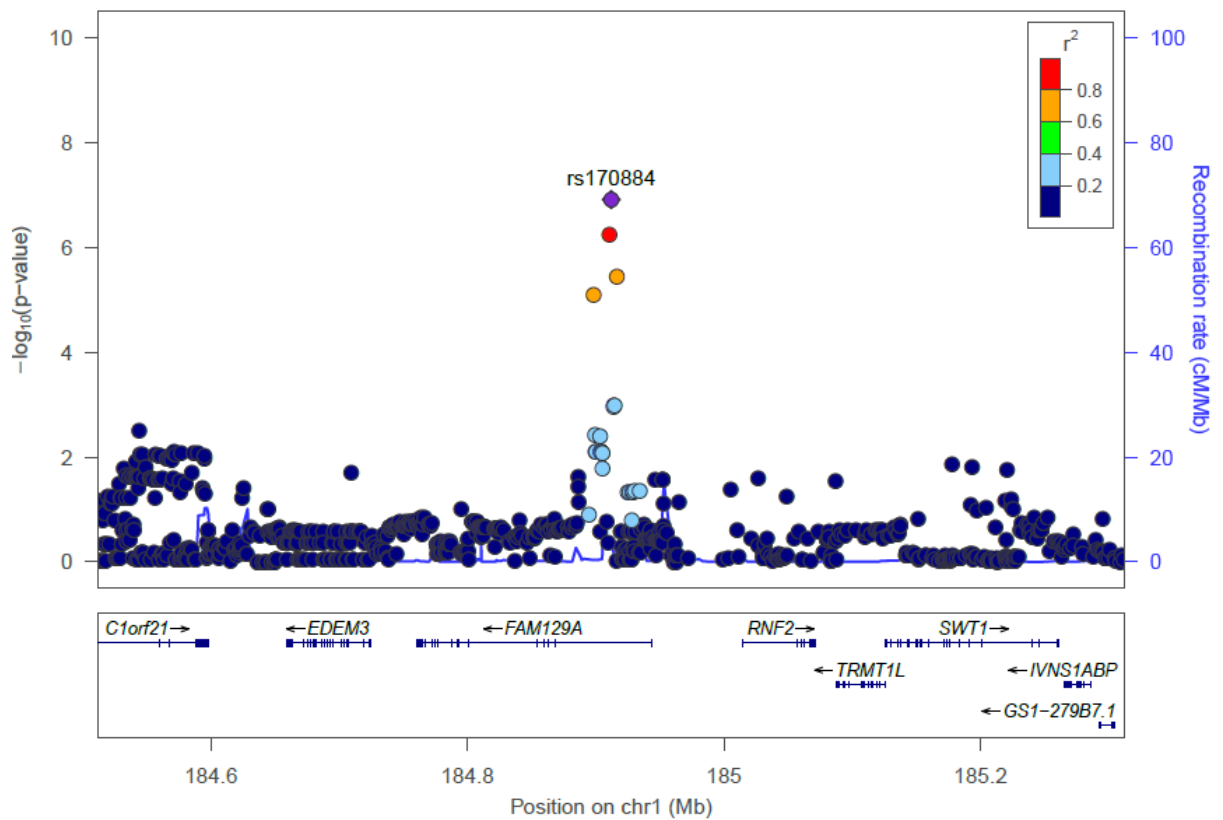


Supplementary Figure 1. Regional association plots for two genome-wide significant hits: rs7212416 (A) and rs10738556 (B).

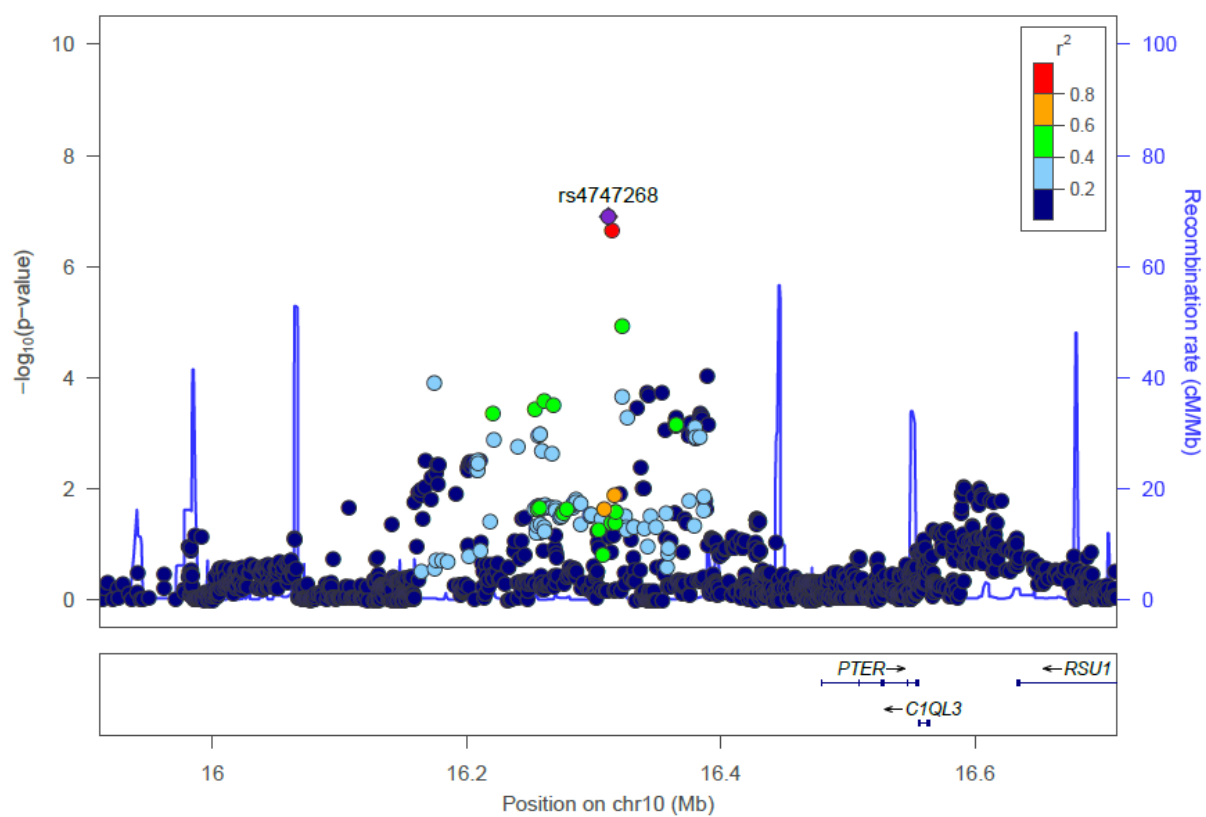
A



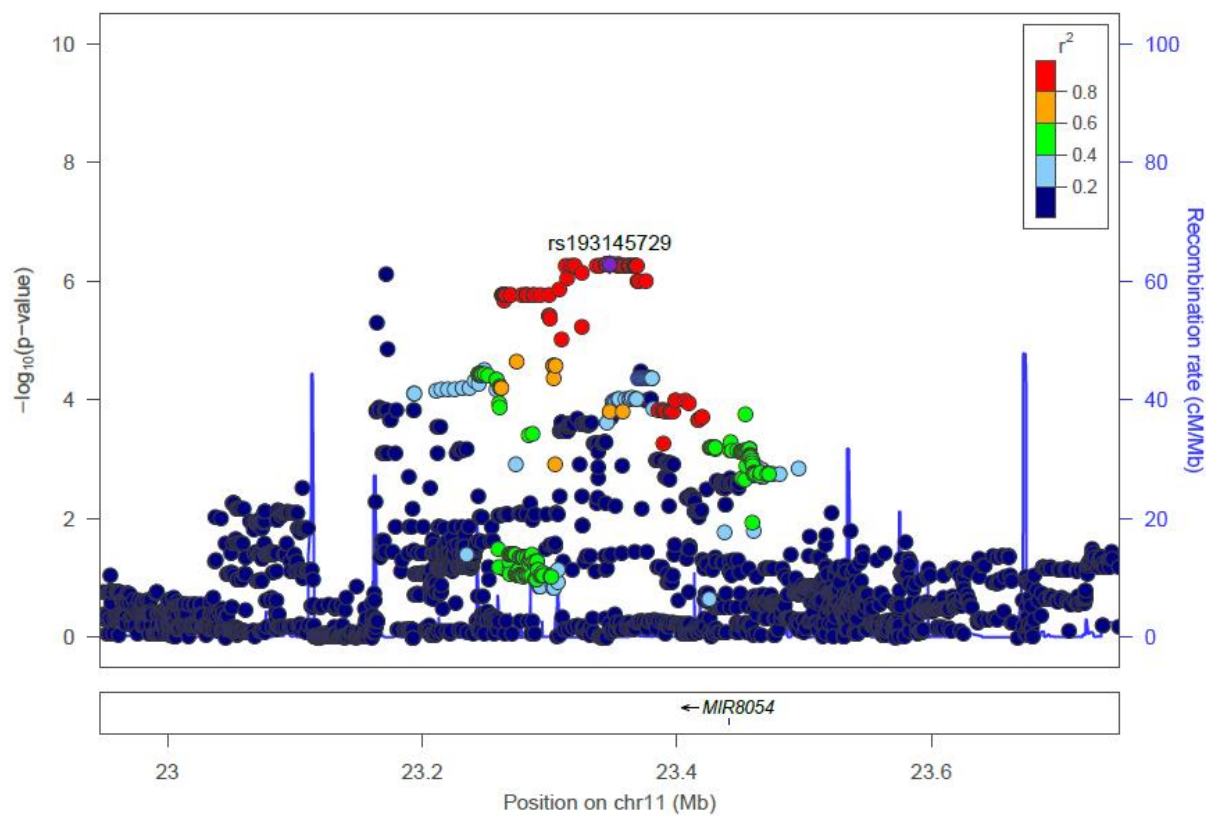
B



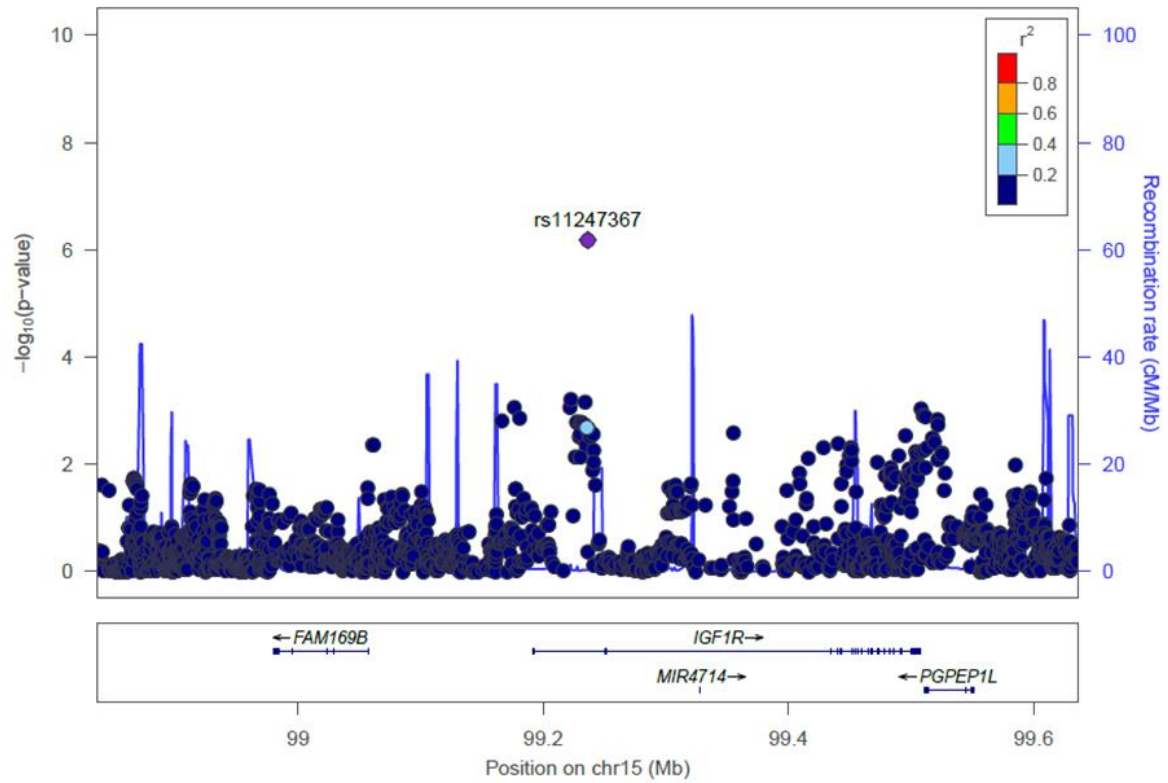
C



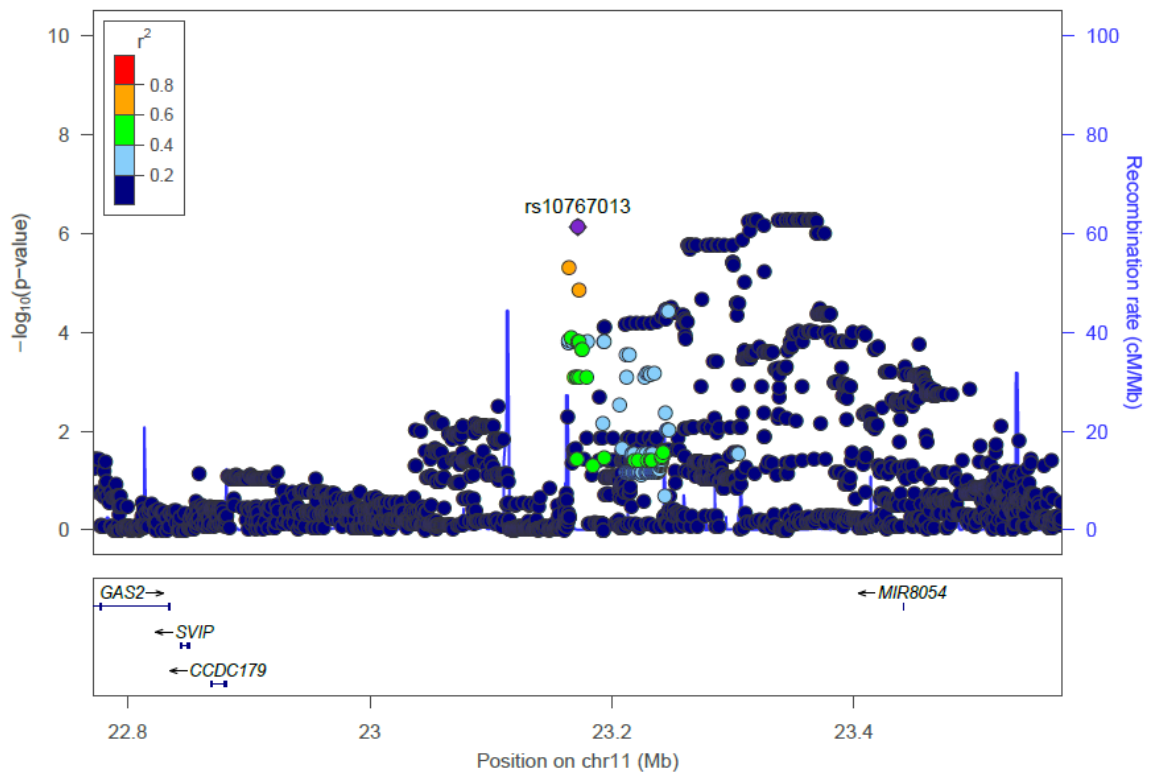
D



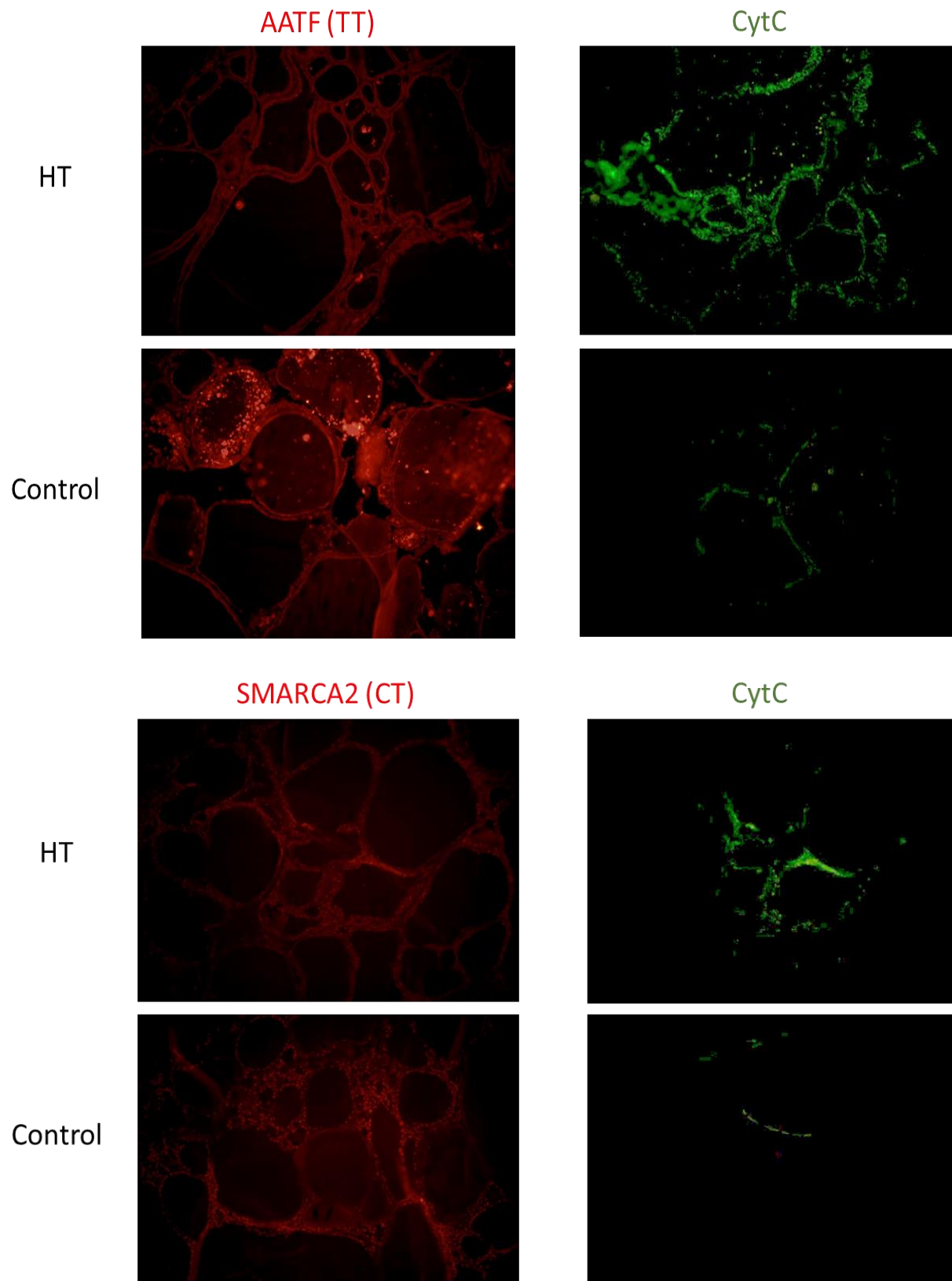
E



F



Supplementary Figure 2. Regional association plots for suggestively associated genetic variants: rs201666766 (A), rs170884 (B), rs4747268 (C), rs193145729 (D), rs11247367 (E) and rs10767013 (F).



Supplementary Figure 3. Representative photo-micrographs of AATF and CytC expression in thyroid tissues of HT (n=3) and control (n=7) participants with rs7212416 TT genotype, and SMARCA2 and CytC expression in thyroid tissues of HT (n=5) and control (n=7) participants with rs10738556 CT genotype.