AJRCMB Articles in Press. Published on 07-February-2017 as 10.1165/rcmb.2016-0331OC

Title: Genetic Association and Risk Scores in a COPD Meta-Analysis of 16,707 Subjects

Brief Title: Genetic Association and Risk Scores in COPD

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All of the authors listed have contributed sufficiently to the project to be included as authors by the ICMJE guidelines, including involvement in the conception and design, analysis and interpretation, and drafting the manuscript for important intellectual content. All authors have agreed to be accountable for the work, and all those who are qualified to be authors are listed in the author byline.

Supplement:
This manuscript is accompanied by a Methods and Data Supplement

Funding: This project was supported by NIH grants including T32 HL007427, R01 HL089856 (EKS), R01 HL089897 (JDC), R01 HL113264 (MHC and EKS), P01 HL105339 (EKS), and P01 HL114501 (AMKC). The COPDGene project (NCT00608764) is also supported by the COPD Foundation through contributions made to an Industry Advisory Board comprised of AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pfizer, Siemens and Sunovion. The National Emphysema Treatment Trial was supported by the National Heart, Lung, and Blood Institute, the Centers for Medicare and Medicaid Services and the Agency for Healthcare Research and Quality. The Normative Aging Study is supported by the Cooperative Studies Program/ERIC of the US Department of Veterans Affairs and is a component of the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC). The Norway GenKOLS study (Genetics of Chronic Obstructive Lung Disease, GSK code RES11080), the ECLIPSE study (clinicaltrials.gov identifierNCT00292552; GSK code SCO104960) and the ICGN study are funded by GlaxoSmithKline.

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ABSTRACT:

The heritability of chronic obstructive pulmonary disease (COPD) cannot be fully explained by recognized genetic risk factors identified as achieving genome-wide significance. In addition, the combined contribution of genetic variation to COPD risk has not been fully explored. We sought to determine 1) whether studies of variants from previous studies of COPD or lung function in a larger sample could identify additional associated variants, particularly for severe COPD, and 2) the impact of genetic risk scores on COPD. We genotyped 3,346 single nucleotide polymorphisms (SNP) in 2,588 cases (1,803 severe COPD) and 1,782 controls from four cohorts, and performed association testing with COPD, combining these results with existing genotyping data from 6,633 cases (3,497 severe COPD) and 5,704 controls. Additionally, we developed genetic risk scores from SNPs associated with lung function and COPD and tested their discriminatory power for COPD-related measures. We identified significant associations between SNPs near *PPIC* ($p=1.28x10^{-8}$) and *PPP4R4/SERPINA1* ($p=1.01x10^{-8}$) and severe COPD; the latter association may be driven by recognized variants in *SERPINA1*. Genetic risk scores based on SNPs previously associated with COPD and lung function had a modest ability to discriminate COPD (AUC ~0.6), and accounted for a mean 0.9-1.9% lower FEV1 percent-predicted for each additional risk allele. In a large genetic association analysis, we identified associations with severe COPD near *PPIC* and *SERPINA1*. A risk score based on combining genetic variants had modest but significant effects on risk of COPD and lung function.

Key Words: chronic obstructive pulmonary disease, genetic epidemiology, genetic risk factors, alpha-1 antitrypsin, genetic risk score

Introduction

Chronic obstructive pulmonary disease (COPD), a progressive lung disease characterized by irreversible airflow obstruction, is a leading cause of morbidity and mortality worldwide(1, 2). While cigarette smoking is the major determinant of COPD susceptibility in the industrialized world (3-5), pulmonary response to cigarette smoking is highly variable(6). Genetic factors contribute to variability in response to smoking, and multiple studies have identified genetic variants associated with increased COPD susceptibility(7-12). Nonetheless, the majority of estimated heritability for risk to COPD remains unexplained(13). In addition, the effect of several recognized risk alleles on lung function or risk of COPD , particularly in cohorts of severely affected subjects, has not been well studied. Meta-analysis of genetic associations across multiple cohorts has the advantage of improving power to detect additional susceptibility risk variants by combining information across studies, which may add to our understanding of disease mechanisms(14) as well as providing potential new targets for COPD therapy development(15, 16).

This study had two primary goals: First, we wished to investigate a panel of variants in a larger meta-analysis of cross-sectional data to increase our power to detect associations(17) with moderate-to-severe and severe COPD. The marker panel was composed of two groups of SNPs. The first group included top associations from previous GWAS studies including SNPs that did not reach genome-wide significance(18), and the second group included genetic variants hypothesized to affect COPD (19) including SNPs previously associated with lung function(20-22). We hypothesized some of these loci would reach pre-defined levels of statistical significance with our additional sample size in this meta-analysis.

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Since genetic variation is fixed at birth, genetic risk scores in cross-sectional data may offer a way to consolidate genetic information(23) into a clinically meaningful tool that could help clinicians to predict disease susceptibility, progression, and outcomes(24, 25). Our second goal was to determine the relevance of genetic risk scores to COPD by modeling the effect of COPD- and lung function-associated risk alleles on clinical status, severe COPD-affection status, and forced expiratory volume in one second (FEV_1) percent predicted. We hypothesized a combined risk score composed of SNPs shown to influence risk to COPD and lung function would explain the genetic contribution to COPD-related outcomes in a clinically useful manner.

Materials and Methods

We performed genetic meta-analysis using eight cohorts, including a total of 16,707 subjects (Table 1). We genotyped 3,346 SNPs (see Supplement) in 5358 subjects from four cohorts: the Transcontinental COPD Genetics Study (TCGS)-Korea and TCGS-Poland(26), The International COPD Genetics Network (ICGN)(27, 28), and the Boston Early-Onset COPD Study (EOCOPD)(29). To maximize power for meta-analysis, we combined these results with existing data from five additional cohorts with: COPDGene non-Hispanic Whites (NHW) and African-Americans (AA), (30), Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-Points (ECLIPSE)(31), National Emphysema Treatment Trial (NETT)(32)/Normative Aging Study (NAS)(33), and Genetics of COPD in Norway (GenKOLS)(34). Detailed description of these cohorts have been previously published(35).

All subjects were current or former cigarette smokers with and without COPD, except for EOCOPD which included a small number of non-smokers. We defined "moderate to severe" COPD as GOLD(2) spirometric Grade 2-4 COPD (post-bronchodilator $FEV_1/FVC < 0.7$, $FEV_1 < 80\%$ predicted), while "severe" COPD was defined as Grade 3-4 COPD ($FEV_1/FVC < 0.7$, $FEV_1 < 50\%$ predicted). Controls had normal spirometry ($FEV_1/FVC \geq 0.7$, $FEV_1 \geq 80\%$). Previously diagnosed alpha-1 antitrypsin deficiency was an exclusion criterion for all cohorts.

Genetic Analysis

We used PLINK v1.9(36) and GWAF(37) for case-control and family-based data, respectively, to perform multiple logistic regression within each dataset and then performed fixed-effect meta-analysis using METAL(38). Given that many of our SNPs were chosen from top findings from prior GWAS (see Supplemental Table 1 for full list of SNPs and provenance), we required an overall P-value of $< 5x10^{-8}$ for statistical significance. We also considered a more liberal suggestive threshold based on a Bonferroni correction for the number of tested SNPs ($p<1.49x10^{-5}$).

Genetic Risk Scores

We used PLINK v1.9 to create genetic scores based on significant associations from prior genome-wide association studies of COPD and lung function (Table 4 and Supplemental Table 5) (20, 21, 39). We oriented risk alleles to be consistent with prior reports, and gave each allele equal weight. We applied these scoring systems to the ICGN cohort, the largest individual cohort not used in the discovery of any of the risk score variants. Risk scores were also applied to the COPDGene and TCGS Poland cohorts using analogous methods.

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The resultant risk scores were used as predictors in a linear mixed model of FEV_1 percent predicted, as well as logistic regression models of both moderate-to-severe and severe COPD incorporating generalized estimating equations. Models were controlled for age, pack-years of smoking, principal components of genetic ancestry, and for familial correlation. In addition, we used the pROC(40) and GenAbel(41) packages in R to compare the accuracy of two models (i.e. model with genetic risk factors and clinical predictors versus the clinical predictors alone) through receiver operator characteristic (ROC) curves and net reclassification index (NRI). Subjects were divided into three tiers of COPD risk (low 0-33.3%, intermediate 33.4-66.7%, and high 66.8-100%) for NRI analysis to assess the discriminatory benefit of adding genetic information to the clinical risk model of age and pack-years of smoking alone.

Additional details regarding the SNPs and cohorts used in this study; genotype-, marker-, and subject-level quality control; and risk score modeling and NRI analysis are available in the Methods and Data Supplement.

Results

The baseline characteristics of all cohorts are shown in Table 1. Notably, the TCGS-Korea, TCGS-Poland, and NETT/NAS studies were designed to contain only severe COPD cases, which is reflected in the low average FEV_1 percent predicted seen among cases for these studies.

Genetic Association Analysis

The moderate-to-severe analysis included 9,221 cases and 7,486 controls, and confirmed signals in the previously described *TGFB2*, *FAM13A*, *HHIP*, *CHRNA3/CHRNA5/IREB2,* and *RIN3* regions; in

addition, a SNP in 16p11.2, recently described in an exome chip analysis of these same cohorts(42), was associated with moderate-to-severe COPD (rs40834, $p=1.90x10^{-8}$, estimated OR=1.17, Supplemental Table 2). The analysis of severe COPD (Table 2) included 5,300 cases and 7,486 controls. We confirmed significance of SNPs in the *TGFB2*, *FAM13A*, *HHIP*, *MMP3/MMP12*, and *CHRNA3/CHRNA5/IREB2* regions. We also identified two SNPs at loci not previously described as genome-wide significant: 5q23.2 between the *PRDM6* and *PPIC* genes (rs6860095, $p=1.01x10^{-8}$, estimated OR=1.24), and an intronic SNP within the *PPP4R4* gene (rs112458284, $p=1.28x10^{-8}$, estimated OR=1.69) in 14q32.13.

We examined these loci using the GTEx eQTL database(43) and Haploreg v4.1(44). SNP rs6860095 affected gene expression levels of *PPIC*, *snoU13*, *SNX2* and *RN7SL689P* in multiple tissues, although not in lung tissue. No significant eQTLs were found for SNP rs112458284; however, it lies approximately 200kb away from *SERPINA1,* which encodes the protein responsible for alpha-1 antitrypsin deficiency(45, 46).

We investigated whether rs112458284 could be tagging alleles of *SERPINA1* known to contribute to risk of COPD (e.g. the Z-allele rs28929474 or S-allele rs17580). rs112458284 showed LD with the Z-allele in directly genotyped (i.e. not imputed) samples from COPDGene NHW subjects (r^2= 0.41, D'= 0.78) and, to a lesser extent, the S-Allele ($r^2= 8.63x10^{-5}$, D'= 0.25). Consistent with this hypothesis, the Z-allele was associated with COPD at near-genome-wide significance in our primary analysis using imputed data in COPDGene ($p=1.53x10^{-7}$, OR=1.78, CI=1.44-2.21); this signal improved using genotyping data ($p=2.05x10^{-8}$, OR=1.84, CI=1.49-2.27), although rs112458284 was still the strongest association signal in the region. To further investigate

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whether there was any association signal at the rs112458284 that was independent from the Z-allele, we also conditioned on the Z-allele in a meta-analysis model, and found that the association signal for rs112458284 was attenuated (p=0.0087).

Known alpha-1 antitrypsin deficiency was an exclusion criterion in our study; however, our genotyping (and imputed data) identified three previously unrecognized Z-allele homozygotes in the Poland cohort(35) and six additional Z-allele homozygotes in the ECLIPSE cohort(47). After removing these subjects, the rs112458284 association was only mildly attenuated ($p=7.22x10^{-8}$), as was the association with the Z-allele ($p=9.29x10^{-8}$, OR=1.80, CI=1.45-2.23). Thus, heterozygous carriers of the Z-allele appear to be driving a large proportion of the association, consistent with prior studies showing an increased risk of COPD for MZ heterozygotes(48). In addition, these results suggest if we had not specifically excluded subjects with known alpha-1 antitrypsin deficiency in our other populations, the association with SNP rs112458284 would likely be even more extreme(49). Allele frequencies for the Z-allele in each cohort are provided in the Supplemental Table 3. The poor imputation quality of the S-allele in our cohorts prevented us from further assessing its impact on the rs112458284 association.

We next examined our other SNPs, at a more liberal P-value threshold. Using a Bonferroni significance threshold for 3,346 SNPs ($p<1.49x10^{-5}$), we identified suggestive associations at three loci. All of these (*THSD4*, *AGER/PPT2,* and *ADAM19*) were in regions previously associated in genome-wide association studies of lung function. We then examined linkage disequilibrium within each candidate locus to further explore whether these associations represented the same variants as previous associations. We defined "lead SNP" as the association yielding the lowest p-

value in a given region, and the "candidate SNP" as the previously described variant. In 14 of these lead SNPs, LD with the candidate SNP measured by D' was >0.8, while eight also had an r^2 >0.3 (Table 3). Notably, SNPs associated with lower lung function showed a directionally consistent increased risk for COPD in 23 of 25 previously reported SNPs directly genotyped in our meta-analysis (binomial for enrichment, $p=9.7x10^{-6}$). These 23 lung function risk alleles included 12 showing a nominally statistically significant ($p<0.05$) effect on COPD risk (see Table 3); only lung function risk-alleles in the *ZKSCAN3* and *NCR3-AIF1* genes showed a directionally discordant effect on COPD susceptibility (lower risk of COPD), though these discordant association results were not statistically significant. Additional results for other variants are reported in Supplemental Table 4.

Genetic Risk Scores

We next examined the ability of genetic risk scores to explain both FEV_1 percent predicted and COPD affection status. Based on our results above, we constructed risk scores using genome-wide significant SNPs associated with COPD (COPD7 score) and also including genome-wide significant SNPs associated with lung function in population-based studies (LUNG 30); Table 4 describes the loci involved in each score. We evaluated the risk scores using the ICGN cohort, the largest available cohort not used in the discovery of these risk loci. Results from the unadjusted model are shown in Figure 1. In a linear mixed model adjusting for age, pack-years of smoking, principal components of ancestry, and a within-family component, we found the COPD7 risk score (ranging from 0 to 14 possible alleles) was associated with a 1.86% reduction in FEV_1 percent predicted for each additional risk allele carried (Table 5a). Using generalized estimating equations for models of moderate-to-severe and severe COPD (Table 5b), each additional risk allele in the COPD7 risk

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score was associated with an odds ratio (OR) of 1.18 for moderate-to-severe COPD and 1.19 for severe COPD ($p=4.1x10^{-8}$ and $p=4.4\ x10^{-8}$, respectively). We found nearly identical results for a standard logistic regression (OR=1.17 and OR=1.19, respectively) without family adjustment, and therefore used these simpler models to generate receiver operator characteristic (ROC) curves for affection status using genetic variants alone, age and pack-years, and the combination of age, pack-years, and genetic information. The area under the curve (AUC) for the genetic model was 0.58 for moderate-to-severe COPD and 0.59 for severe COPD. Additionally, adding genetic risk scores (COPD7) only modestly increased the AUC (Figure 2) over the AUC of the clinical model. Three-tiered categorical analysis of reclassification(50) after addition of the COPD7 risk score and adjustment for genetic components of ancestry into the clinical model (containing only age and pack-years of smoking) resulted in a NRI of 0.053 ($p=2.32x10^{-3}$) for the combined model risk stratification of moderate-to-severe COPD, and an NRI of 0.047 for risk stratification of severe COPD (p=0.01). For the expanded LUNG30 score, we found a lower per-allele effect, but larger overall effect because more factors went into the score (Tables 5a and 5b). We also tested risk scores in the TCGS Poland and COPDGene cohorts and found comparable results (see Methods and Data Supplement).

Discussion

Genetic association studies in COPD have identified well-replicated genome-wide associations with COPD, but the majority of genetic susceptibility remains unexplained. In a large-scale genetic association meta-analysis of 9 cohorts, analyzing both moderate to severe and severe COPD, we identified two new associations at genome-wide significance with severe COPD, including one in strong LD with *SERPINA1*, and associations at a more liberal significance threshold in regions

previously associated with population-based lung function. We found consistent directions of effect on risk to COPD in 23 previously identified markers associated with lung function, consistent with recent reports(7). We also constructed genetic risk scores that showed compelling relationships for quantitative measures of lung function and modest discrimination for COPD affection status. Our results further inform the discussion of how genetic variants could influence COPD susceptibility.

The discovery that variants in LD with *SERPINA1* are associated with severe COPD demonstrates how genetic association studies can confirm known disease mechanisms. This rs112458284 variant is also in strong LD with rs45505795 near *SERPINA10* (r^2= 0.96 and D'= 1.0 in 1000 Genomes EUR Phase I v3 data), which we recently described in a GWAS of quantitative measures of emphysema(47). The 5q23.2 region containing SNP rs6860095 is strongly associated with severe COPD risk. Both *PPIC* and *PRDM6* lie in this region. Peptidylprolyl Isomerase C (PPIC, also known as Cyclophilin C) has functions related to mitochondrial metabolism, inflammation, and immune response through its interactions with cyclosporine A. While the related protein Cyclophilin A has been associated with both COPD(51) and lung cancer(52), to our knowledge no prior study has shown significant association between *PPIC* and risk of COPD. The PRDI-BF1 and RIZ homology Domain Containing 6 (*PRDM6*) protein is involved in chromatin remodeling and transcriptional control of smooth muscle gene expression(53). Expression of *PRDM6* has been implicated in the pseudoglandular and canalicular stages of lung morphogenesis in murine models, and expression has been documented in smooth muscle of the developing murine trachea, bronchi, and pulmonary trunk(53). Additional studies are needed to confirm association between markers in 5q23.2 and severe COPD.

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We examined genomic loci previously associated with FEV1, FEV1/FVC, and additional variants previously hypothesized to be associated with COPD(19). SNPs that met criteria for suggestive association were found in regions previously associated with lung function, including the *AGER/PPT2* and the *THSD4* regions. Additionally, the majority of variants associated with quantitative measures of lung function showed consistent directions of effect for both COPD and low lung function.

Genetic risk scores using selected risk variants from COPD-based cohorts could provide a clinically relevant context to individual level genetic data, and could have applications in assessing risk to COPD and its severity (25). We investigated the ability of genetic risk scores to explain COPD risk and FEV_1 percent predicted. Genetic data alone only achieved an AUC of ~0.6 in our modeling of moderate-to-severe COPD risk. This finding is comparable to the AUC of genetic risk scores in other complex diseases, such as coronary artery disease(54) and Type II diabetes(55). This low AUC of our risk score may be due to the fact that genetic data does not account for the contributions to COPD of other significant risk factors such as age and environmental exposures like pack-years of smoking. The addition of genetic data to the clinical model including age and pack-years of smoking resulted in statistically significant, but small, increases in AUCs and in statistically significant NRI values when classifying risk for severe COPD. Interpretation of the NRI is more straightforward for clinically-actionable consensus endpoints, such as primary prevention statin therapy for coronary artery disease outcomes, which are less well-defined for COPD. Despite these concerns, the clinical relevance of this model is most apparent in the risk score coefficient itself. The LUNG30 model implies that a subject with 35 risk alleles would show a 3-fold

increase in risk of COPD compared with a subject with a score of 25, all other variables being equal.

Similarly, in our modeling of FEV_1 percent predicted, we found a small, but detectable effect of each individual risk allele, though the cumulative effect of this score may be clinically relevant. For example, within the ICGN dataset we had subjects with as few as 16 and as many as 45 alleles in their LUNG30 score. Based on our model, this difference in alleles would account for an approximately 30% difference in FEV1 percent predicted, holding all other variables equal. Such a 30% FEV1 percent predicted difference implies that two people (with similar age and pack-years of smoking) may fall into different GOLD severity classes due to the effect of these risk alleles alone. While the COPD-based ascertainment of the ICGN pedigrees may have led to enrichment of these risk-alleles in this cohort, the significance of the risk scores was robust when tested in two additional case-control cohorts.

Despite having analyzed over 16,000 subjects, our study and the experience in other GWAS suggests power is still a major limitation in detecting additional COPD associations. The definition of COPD phenotypes and its severity by spirometric criteria alone(2) was consistent in our meta-analysis; however, this does not address other aspects of heterogeneity in COPD that may be under genetic control (such as emphysema or exacerbations). The study was cross-sectional in design with lung function assessment at only one point of time, so we cannot assess the impact of lung function trajectories(56) in our models. This study was not a comprehensive survey of genome-wide data, and its ability to detect new associations was limited to previously identified loci and their surrounding regions. Four of the datasets in our meta-analysis were previously

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investigated for genetic associations for COPD status(18), so our results are enriched for previously discovered associations. Additionally, genotyping was performed before the results of recent COPD and lung function GWAS studies in the UK BiLeve group(7) and Soler Artigas et al(57, 58) were published, and the additional risk loci for COPD and lung function found in these studies were not included in our analysis. We chose to use a simple model for our genetic (and clinical) risk scores. More sophisticated models using these SNPs, based on genome-wide results, and incorporating additional clinical factors, may result in improved prediction. In pathway analysis in Gene Ontology, Kyoto Encyclopedia of Genes and Genomes, and the Reactome (see Supplemental Methods and Results) the closest gene(s) to the LUNG30 risk score variants showed enrichment in gene sets related to structural components of lung development, control of lung development, inflammatory response, and response to steroid hormone, among others. These enriched terms and pathways may help to provide insight into the pathophysiologic mechanisms of COPD pathogenesis that are represented by the LUNG30 association signal. However, our risk scores focused on SNPs previously associated with lung function and COPD; most of the causal genes at these loci are not known, and these signals capture only a minority of relevant genetic mechanisms contributing to COPD pathogenesis. The performance of our genetic risk scores in other racial groups and in never-smokers has not been tested, although this is an area of interest for follow-up investigations. While associations with SNPs rs112458284 and rs6860095 did achieve genome-wide levels of significance in our severe COPD analysis, these results still need to be replicated in independent populations.

In summary, we performed a meta-analysis of markers in selected genes and discovered two new SNPs associated with severe COPD that reached significance levels equivalent to accepted

thresholds of genome-wide significance, one of which tags recognized risk alleles in *SERPINA1* . Our study is one of the largest genetic association studies of severe COPD, the first to identify *SERPINA1* at genome-wide significance for COPD. Our study supports the idea that loci associated with lung function play some role in susceptibility to COPD. We also showed the clinical applicability of simple genetic risk scores for explaining COPD spirometric severity in an independent cohort. This study adds to the growing body of genetic knowledge about COPD, including efforts at subtyping, prediction, and mechanistic investigation, which may ultimately inform patient counseling, clinical decision-making, and lead to new therapies for this disease.

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Acknowledgements

We would like to acknowledge and thank Augustine M K Choi, MD for his support of this project. In addition, we would like to thank the following members of the individual study cohorts, without whom this work would not have been possible.

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Health Partners Research Foundation, Minneapolis, MN: Charlene McEvoy, MD, MPH, Joseph Tashjian, MD

Johns Hopkins University, Baltimore, MD: Robert Wise, MD, Nadia Hansel, MD, MPH, Robert Brown, MD, Karen Horton, MD, Nirupama Putcha, MD, MHS,

Los Angeles Biomedical Research Institute at Harbor UCLA Medical Center, Torrance, CA: Richard Casaburi, PhD, MD, Alessandra Adami, PhD, Janos Porszasz, MD, PhD, Hans Fischer, MD, PhD, Matthew Budoff, MD, Harry Rossiter, PhD

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AJRCMB Articles in Press. Published on 07-February-2017 as 10.1165/rcmb.2016-0331OC

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The Norway **GenKOLS** study (Genetics of Chronic Obstructive Lung Disease, GSK code RES11080) and the ECLIPSE study (NCT00292552; GSK code SCO104960) were funded by GlaxoSmithKline.

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AJRCMB Articles in Press. Published on 07-February-2017 as 10.1165/rcmb.2016-0331OC

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DAL is supported by the Medical Research Council (UK) and UCLH NIHR Biomedical Research Centre.

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NETT was supported by NHLBI grants N01HR76101, N01HR76102, N01HR76103, N01HR76104, N01HR76105, N01HR76106, N01HR76107, N01HR76108, N01HR76109, N01HR76110, N01HR76111, N01HR76112, N01HR76113, N01HR76114, N01HR76115, N01HR76116,

N01HR76118, and N01HR76119; the Centers for Medicare and Medicaid Services; and the Agency for Healthcare Research and Quality. The Normative Aging Study (**NAS**) is supported by the Cooperative Studies Program/ERIC of the US Department of Veterans Affairs, and is a component of the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC).

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Tables

		COPDGene NHW	**COPDGene AA**	**ICGN** (1103 Pedigrees)	**ECLIPSE**	**GenKOLS**	**NETT/NAS**	**EOCOPD** (201 pedigrees)	**TCGS Poland**	**TCGS Korea**
Control	N	2534	1749	696	178	808	435	560	307	219
	Sex (% male)	49.3	58.1	48.3	57.9	50.1	100	41.6	67.4	96.8
	Age	59.5 (± 8.7)	52.8 (± 6.0)	54.4 (± 8.9)	57.5 (± 9.4)	55.6 (± 9.7)	69.8 (± 7.5)	40.8 (± 17.5)	58.8 (± 7.3)	52.9 (± 8.41)
	Pack-years	37.8 (± 20.3)	36.4 (± 20.1)	29.4 (± 19.8)	32.1 (± 24.8)	19.7 (± 13.6)	40.7 (± 27.9)	10.8 (± 18.4)	34 (± 15.2)	27.3 (± 14.9)
	FEV_1, % predicted	96.8 (±11)	98.4 (± 12.2)	99.1 (± 14.4)	107.8 (± 13.6)	94.9 (± 9.2)	100.0 (± 13.2)	95.7 (± 11.5)	103 (± 12.7)	94.4 (± 9.4)
Moderate to Severe COPD (GOLD II-IV)	N	2812	821	1769	1764	863	373	366	304	149
	Sex (% male)	55.7	55.2	58.6	67.0	60.1	63.8	39.9	70.1	99.3
	Age	64.7 (± 8.2)	59.0 (± 8.2)	59.2 (± 6.9)	63.6 (± 7.1)	65.5 (± 10.0)	67.5 (± 5.8)	53.2 (± 12)	62.6 (± 7.41)	68.9 (± 6.21)
	Pack-years	56.3 (± 28.0)	42.4 (± 23.0)	51.3 (± 28.2)	50.3 (± 27.4)	32.0 (± 18.5)	66.4 (± 30.7)	41.1 (± 24.4)	44.5 (± 22.4)	44.9 (± 24.5)
	FEV_1, % predicted	49.6 (± 18.0)	52.2 (± 17.8)	40.5 (± 16.7)	47.6 (± 15.6)	50.6 (± 17.4)	28.1 (± 7.4)	35.1 (± 20)	29.1 (± 9.22)	33.8 (± 8.28)
Severe COPD (GOLD III-IV)	N	1390	352	1099	999	383	373	251	304	149
	Sex (% male)	57.8	58	60.9	69.9	61.5	63.8	33.1	70.1	99.3
	Age	65.2 (± 7.8)	60.6 (± 8.1)	59.2 (± 6.27)	63.5 (± 7.0)	66.7 (± 9.7)	67.5 (± 5.8)	51.3 (± 10.1)	62.6 (± 7.41)	68.9 (± 6.21)
	Pack-years	58.7 (± 28.4)	43.9 (± 23.4)	53.6 (± 28.8)	50.7 (± 26.3)	33.0 (± 19.9)	66.4 (± 30.7)	41.7 (± 22.6)	44.5 (± 22.4)	44.9 (± 24.5)
	FEV_1, % predicted	34.0 (± 9.9)	34.8 (± 10.4)	30 (± 9.96)	36.5 (± 8.6)	34.4 (± 10.3)	28.1 (± 7.4)	23.3 (± 9.44)	29.1 (± 9.22)	33.8 (± 8.28)

Table 1. Baseline Characteristics of Meta-Analysis Cohorts

ICGN = International COPD Genetics Network; ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points, GenKOLS = Genetics of Chronic Obstructive Lung Disease, Norway, NETT = National Emphysema Treatment Trial, NAS = Normative Aging Study, EOCOPD = Boston Early-Onset COPD Study, TCGS = Transcontinental COPD Genetics Study. Number of subjects is presented as N, gender is presented as percent male. Mean values for age, pack-years, and FEV_1 (% predicted) are shown as mean followed by standard deviation. Age is displayed in years. Moderate to Severe COPD represents GOLD II-IV COPD cases, while Severe COPD represents GOLD III-IV COPD cases. Number of pedigrees is presented adjacent to the study name for the pedigree-bases studies ICGN and EOCOPD.

rs ID	Chromosome	Base Position	Effect Allele	p-value	Odds Ratio	Lower 95% CI	Upper 95% CI	Effect Allele Frequency	Nearest Gene(s)
rs1890995	1	218604678	A	3.79×10^{-11}	1.27	1.37	1.19	0.73	*TGFB2*
rs4416442	4	89866713	T	5.38×10^{-17}	1.32	1.39	1.23	0.43	*FAM13A*
rs13141641	4	145506456	T	1.69×10^{-21}	1.38	1.29	1.48	0.61	*HHIP*
rs6860095	5	122405957	A	1.01×10^{-8}	1.24	1.15	1.33	0.74	*PRDM6/PPIC*
rs679620	11	102713620	T	1.87×10^{-8}	1.19	1.12	1.27	0.54	*MMP3/MMP12*
rs112458284	14	94672731	T	1.28×10^{-8}	1.69	2.04	1.41	0.04	*PPP4R4*
rs17486278	15	78867482	A	1.70×10^{-27}	1.43	1.54	1.35	0.37	*CHRNA5*

Table 2. Genome-wide significant Severe COPD Associations

Significant associations for GOLD spirometric stage III-IV COPD, organized by chromosome. In each case, the lead SNP for the locus is presented. Effect alleles represent the allele that is associated with the stated odds ratio for COPD-risk. Base Position was calculated using hg19 coordinates.

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Previously Reported Variant					Lead Variant in Meta-Analysis Window		Linkage Disequilibrium Between Previously Reported and Lead Variants	
Chromosome	rsID	Base Position	Nearest Gene	Meta-analysis p-value	rsID	Meta-analysis p-value	r^2	D'
1	rs2284746	17306675	*MFAP2*	0.12	rs3170740	0.10	0.91	0.98
1	rs993925	218860068	*TGFB2-LYPLAL1*	0.56	rs72738847	$4.56x10^{-6}$	0.00	0.34
2	rs2571445 (rs918949)	218683153	*TNS1*	0.07	rs3791953	$1.75x10^{-2}$	0.00	0.12
2	rs7594321	230224031	*DNER*	0.09	rs12995479	0.02	0.00	0.02
2	**rs12477314**	**239877148**	***HDAC4-FLJ43879***	**$2.37x10^{-3}$**	rs35877146	$1.26x10^{-3}$	0.72	0.90
3	**rs1529672**	**25520582**	***RARB***	**$3.08x10^{-4}$**	rs1529672	$3.08x10^{-4}$	N/A	N/A
3	rs1344555	169300219	*MECOM / EVI1*	0.68	rs933607	$2.29x10^{-4}$	0.03	0.24
4	**rs7671167**	**89883979**	***FAM13A***	**$2.45x10^{-15}$**	rs4416442	$1.84x10^{-17}$	0.65	0.99
4	**rs10516526**	**106688904**	***GSTCD/INTS12/ NPNT***	**$7.39x10^{-4}$**	rs11735213	$5.12x10^{-5}$	0.67	0.91
4	**rs1032296**	**145434688**	***HHIP***	**$4.13x10^{-10}$**	rs13141641	$1.26x10^{-18}$	0.41	0.89
5	**rs153916**	**95036700**	***SPATA9-RHOBTB3***	**$2.90x10^{-3}$**	rs153916	$2.90x10^{-3}$	N/A	N/A
5	**rs11168048**	**147842353**	***HTR4***	**0.01**	rs17720155	$4.41x10^{-4}$	0.33	0.78
5	**rs11134779 (rs1422795)**	**156936766**	***ADAM19***	**$7.98x10^{-3}$**	rs62390771	$4.16x10^{-7}$	0.02	0.38
6	rs6903823$^{\Phi}$	28322296	*ZKSCAN3*	0.75	rs3800326	0.10	0.09	1.00
6	rs2857595$^{\Phi}$	31568469	*NCR3-AIF1*	0.71	rs2844479	0.03	0.03	0.51
6	**rs2070600**	**32151443**	***AGER/ PPT2***	**$7.05x10^{-6}$**	rs2070600	$7.05x10^{-6}$	N/A	N/A
6	rs7765379	32680928	*HLA-DQB1*	0.12	rs9275141	$5.67x10^{-3}$	0.14	1.00
6	**rs2798641**	**109268050**	***ARMC2***	**$1.15x10^{-4}$**	rs2848598	$2.06x10^{-5}$	0.31	0.89
6	**rs3817928**	**142750516**	***GPR126***	**$5.71x10^{-3}$**	rs9399401	$1.91x10^{-4}$	0.63	0.96
9	rs16909898	98231008	*PTCH1*	0.12	rs357523	$7.77x10^{-3}$	0.47	0.73
10	rs7068966	12277992	*CDC123*	0.05	rs10906083	0.03	0.01	0.13
10	rs11001819	78315224	*C10orf11*	0.39	rs7904646	$2.08x10^{-3}$	0.00	0.33
12	**rs11172113**	**57527283**	***LRP1***	**$2.28x10^{-4}$**	rs2122692	$9.12x10^{-5}$	0.44	0.80
12	**rs1036429 (rs7307510)**	**96271427**	***CCDC38***	**$6.35\ x10^{-3}$**	rs7306887	$7.35x10^{-4}$	0.13	0.87
15	**rs12899618**	**71645120**	***THSD4***	**0.01**	rs10459646	$4.37x10^{-7}$	0.09	1.00
16	rs12447804	58075282	*MMP15*	0.16	rs2550370	$9.55x10^{-3}$	0.03	0.63
16	**rs2865531 (rs4888380)**	**75390315**	***CFDP1***	**$3.09\ x10^{-3}$**	rs37586	$4.88x10^{-4}$	0.13	1.00
17	rs11654749	69125606	*KCNJ2*	0.39	rs35883109	0.01	0.00	0.08
21	rs9978142	35652239	*KCNE2-LINC00310 /C21orf82*	0.98	rs73205216	$8.96x10^{-5}$	0.02	1.00

Table 3. Lung Function Variants

For each previously reported variant and lead variant, the p-value refers to the association with moderate-to-severe COPD in our analysis. Risk alleles showing a discordant association direction of effect for COPD risk and decreased lung function risk are marked with **Φ**. Nominally significant associations ($p < 0.05$) among previously reported variants are shown in bold. Linkage disequilibrium values (r^2) between the previously reported variant and the lead variant in meta-analysis window were obtained using data from 1000 Genomes Project Phase 1 v3. Proxies for variants not available in our dataset are in parentheses, and p-values displayed are for the proxy variant. D' represents the normalized coefficient of linkage disequilibrium, and r^2 represents the between-locus correlation coefficient.

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CHRNA3 rs12914385	***HHIP*** rs13141641	***DNER*** rs7594321	***RARB*** rs1529672	***ZKSCAN3*** rs6903823	***GPR126*** rs3817928
RAB4B/ EGLN2/ MIA/CYP2A6 rs7937	***FAM13A*** rs4416442	***HDAC4-FLJ43879*** rs12477314	***GSTCD/INTS12 / NPNT*** rs10516526	***SPATA9-RHOBTB3*** rs153916	***TGFB2-LYPLAL1*** rs993925
RIN3 rs754388	***PTCH1*** rs16909898	***MFAP2*** rs2284746	***NCR3-AIF1*** rs2857595	***MMP15*** rs12447804	***CDC123*** rs7068966
TGFB2 rs4846480	***C10orf11*** rs11001819	***ARMC2*** rs2798641	***MECOM/EVI1*** rs1344555	***HLA-DQB1*** rs7765379	***KCNE2-LINC00310/ C21orf82*** rs9978142
MMP12 rs626750	***HTR4*** rs11168048	***LRP1*** rs11172113	***AGER/PPT2*** rs2070600	***KCNJ2/ CASC17*** rs11654749	***THSD4*** rs12899618

Table 4. Genetic Risk Score Loci

Genetic risk scores were composed using previous COPD and lung function associated loci, here labeled by the closest gene (SNP identifier shown below gene). The LUNG30 score included all of the loci listed in the above table, the COPD7 Score included only those in the gray boxes. Loci names are based on previously reported SNP-associations annotated to the nearest gene or region.

	FEV_1 % per Risk Allele (unadjusted)	p-value	FEV_1 % per Risk Allele (adjusted)	p-value
COPD7	-2.02 (-1.34, -2.70)	$6.74x10^{-9}$	-1.86 (-1.24, -2.50)	$7.90x10^{-9}$
LUNG30	-1.18 (-0.83,-1.53)	$4.70x10^{-11}$	-1.10 (-0.78, -1.43)	$3.78x10^{-11}$

Table 5a: Genetic Risk Scores: Lung Function in ICGN

For each risk score (COPD7 and LUNG30), the linear mixed model coefficient is presented with 95% confidence interval in parentheses and p-value. Final model included adjustment for age, pack years, familial correlation, and principal components for genetic ancestry, while the unadjusted model was not adjusted for age and pack years. FEV_1 % represents the unit change in FEV_1 percent predicted . COPD7: 7 COPD risk SNPs (14 risk alleles); LUNG30: 30 COPD and lung function SNPs (60 risk alleles)

		Moderate COPD	p-value	Severe COPD	p-value
COPD7	OR per Risk Allele	1.18 (1.11, 1.25)	$4.10x10^{-8}$	1.19 (1.12, 1.27)	$4.43x10^{-8}$
	AUC	0.58 (0.56, 0.61)		0.59 (0.56, 0.61)	
	Total NRI	0.053 (0.019-0.086)	$2.32x10^{-3}$	0.047 (0.01, 0.084)	$1.32x10^{-2}$
	Event NRI	0.23%		0.83%	
	Nonevent NRI	5.03%		3.88%	
LUNG30	OR per Risk Allele	1.12 (1.09, 1.15)	$1.25x10^{-13}$	1.12 (1.09, 1.15)	$1.25x10^{-13}$
	AUC	0.60 (0.57, 0.62)		0.60 (0.57, 0.63)	
	NRI	0.090 (0.053, 0.126)	$1.72x10^{-6}$	0.047 (0.007, 0.087)	$2.22x10^{-2}$
	Event NRI	2.35%		0.65%	
	Nonevent NRI	6.61%		4.67%	

Table 5b. Genetic Risk Scores: Affection Status in ICGN

For each risk score (COPD7 and LUNG30), OR represents the odds ratio of each additional risk allele on the outcome of either Moderate COPD (GOLD II-IV) or Severe COPD (GOLD III-IV). AUC represents Area Under the Curve of a model including only the genetic data of risk score alleles adjusted for principal components of genetic ancestry. NRI represents the three-tiered net reclassification index value of the model combining genetic risk score, age, pack-years of smoking, and principal components of genetic ancestry compared to the model containing age and pack-years alone. Event NRI represents the percentage of subjects with the outcome of COPD adding correctly reclassified to a higher risk group after adding genetic data. Nonevent NRI represents the percentage of subjects without the outcome of COPD correctly reclassified to a lower risk group after genetic data. Data is presented with 95% confidence intervals in parentheses. COPD7: 14 COPD risk allelesLUNG30: 60 COPD and lung function risk alleles

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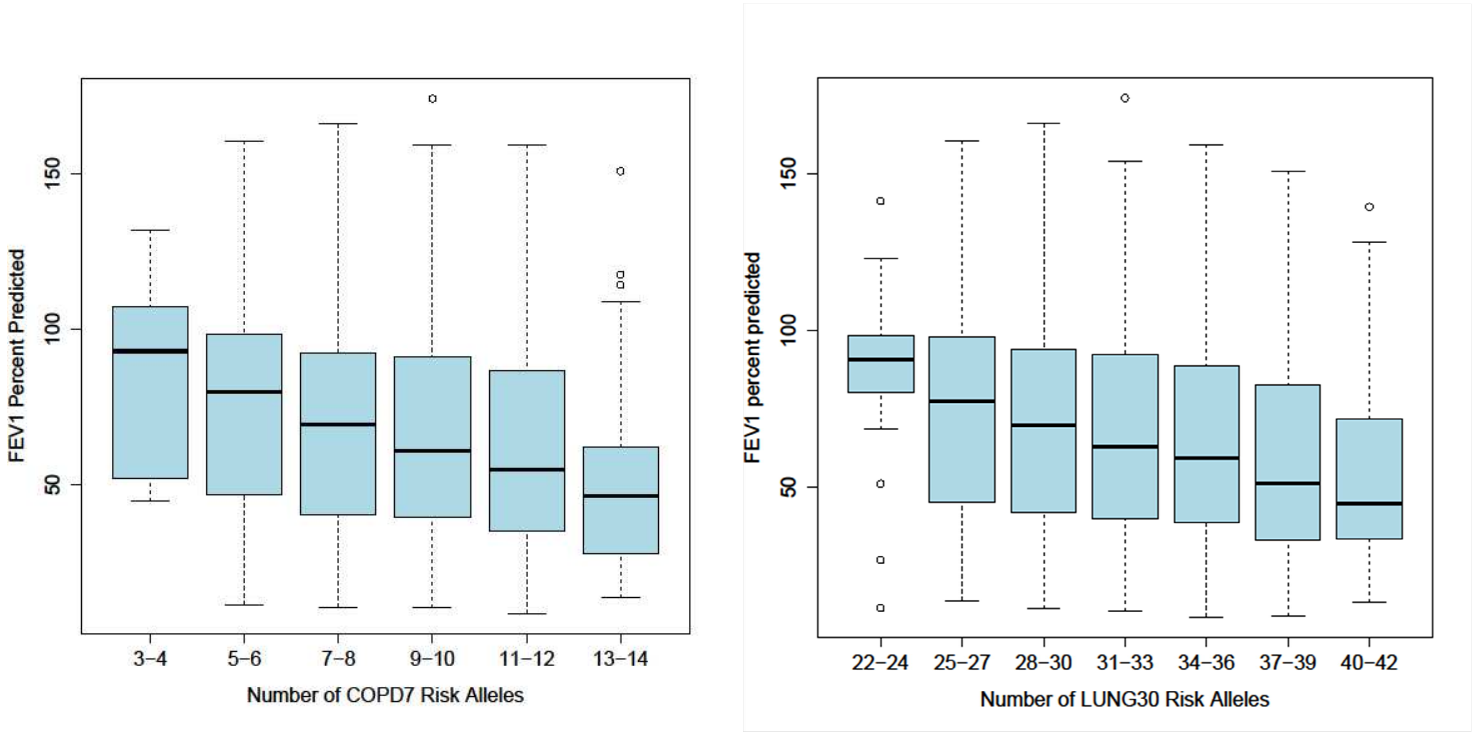
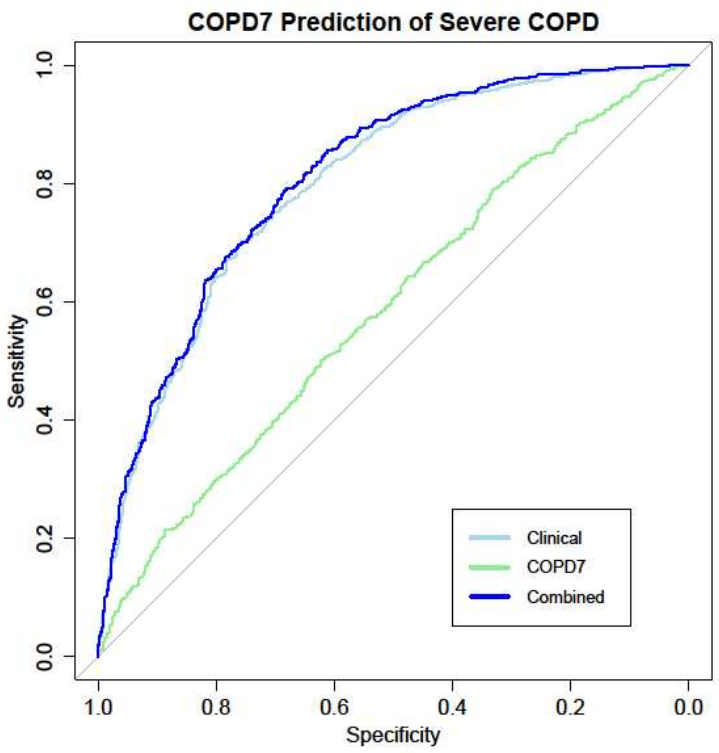
Figures:

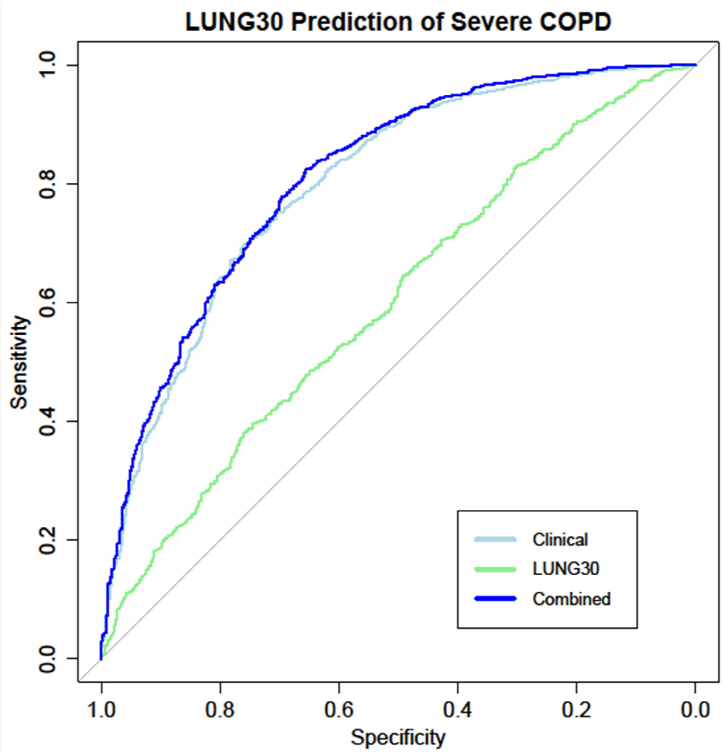
Figure 1. Unadjusted FEV1 by number of COPD7 and LUNG 30 Risk Alleles



Boxplots showing FEV_1 percent predicted stratified by number of risk alleles in the ICGN pedigree-based cohort. The figure on the left shows the COPD7 risk score, while the figure on the right shows the LUNG30 risk score.

Figure2: Severe COPD Diagnosis using COPD7 and LUNG30





Receiver operator characteristic curves showing diagnostic accuracy of models based on clinical variables (age and pack-years of smoking alone, shown light blue), COPD7 or LUNG30 risk allele data alone (light green), and the combination of clinical and FX25 data (blue) for predicting GOLD spirometric stage III-IV COPD affection status in the ICGN cohort. The differences between the clinical and combined curves were statistically significant in both the COPD7 (difference 0.010, p-value 4.4×10^{-3}) and the LUNG30 scores (difference 0.012, p-value 4.7×10^{-3}).

AJRCMB Articles in Press. Published on 07-February-2017 as 10.1165/rcmb.2016-0331OC

Genetic Association and Risk Scores in a COPD Meta-Analysis of 16,707 Subjects

Methods and Data Supplement

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Supplemental Methods

Study Populations

The Boston Early Onset COPD (EOCOPD) study (ClinicalTrials.gov study NCT01177618) is a pedigree-based genetic study of severe, early-onset COPD that enrolled probands as well as first-degree and more extended relatives. Enrolled probands were less than 53 years of age, with FEV_1 <40% predicted. The International COPD Genetics Network (ICGN) study is a multicenter pedigree-based trial of COPD probands, parents, and siblings. Probands were between the ages of 45-65 years and had a clinical diagnosis of COPD, spirometry with post-bronchodilator values of FEV_1 <60% predicted and FEV_1/FVC ratio of <90% predicted. In both of the preceding

studies, investigation was limited to the non-Hispanic and Hispanic White subjects due to underrepresentation of other racial groups (<5% non-white). The Transcontinental COPD Genetics Study was a case-control study of severe COPD, with cohorts drawn from Poland (TCGS-Poland) and Korea (TCGS-Korea). Both of these cohorts included current or ex-smoking subjects between the ages of 40 and 80 years with >10 pack-years of smoking history. Cases were defined by the presence of severe or very severe COPD (FEV_1 <50% predicted), while controls had normal spirometry. The TCGS Poland cohort consisted of non-Hispanic White subjects, while the TCGS Korea cohort consisted of subjects with Korean ancestry.

COPDGene (ClinicalTrials.gov NCT00608764) is a multicenter case-control study of current and former smokers with and without COPD, designed to investigate epidemiologic and genetic risk factors for COPD(1). COPDGene included subjects between the ages of 45-80, self-described as non-Hispanic White or African-American. ECLIPSE (ClinicalTrials.gov NCT00292552) and GenKOLS (GSK code RES11080) were case-control studies of ever-smokers with and without COPD. The NETT/NAS cohort is composed of cases from NETT (ClinicalTrials.gov NCT00000606) and controls from NAS. Subjects in all cohorts completed lifestyle and symptom questionnaires, spirometry, and genotyping. Further details of study design, genotyping, imputation, and quality control have been previously described(1-7).

All subjects in the COPDGene, ECLIPSE, GenKOLS, NETT/NAS, TCGS, and ICGN study were current or former cigarette smokers; EOCOPD included a small number of non-smokers, both with and without COPD.
We classified subjects in each dataset using a consistent definition of case and control status. We defined "moderate to severe" COPD as GOLD(8) spirometric Grade 2-4 COPD (post-bronchodilator FEV_1/FVC <0.7, FEV_1 <80% predicted), while "severe" COPD was defined as Grade 3-4 COPD (FEV_1/FVC <0.7, FEV_1 <50% predicted). Controls had normal spirometry ($FEV_1/FVC \geq 0.7$, $FEV_1 \geq 80\%$).

Genotyping

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A total of 4900 non-Hispanic White subjects (ICGN= 3043, EOCOPD = 1198, TCGS-Poland = 659) and 458 Korean subjects from TCGS-Korea were genotyped using the HumanExome v1.2 (Illumina, San Diego, CA) platform with the addition of a set of 3,346 custom markers. This custom content included top results from a previously published COPD GWAS(9), using results with $P < 10^{-4}$ using PLINK '—clump' on the COPDGene non-Hispanic whites (NHW) to perform linkage disequilibrium pruning ($r^2 < 0.8$), preferentially retaining both an imputed and genotyped top SNP at each locus. An additional set of candidate SNPs came from a previous analysis of COPD by Castaldi et al (10), which included both genome-wide significant associations identified from population-based GWAS of spirometric lung function (11-14) and biological candidate gene regions; for the former, we included the lead SNP and SNPs within a 200kb region around that SNP pruned for variants with $P < 0.01$ and $r^2 < 0.8$. A complete table of the SNPs considered for our analysis (and their provenance) is provided in Supplemental Table 1.

Genotyping and imputation of the COPDGene, ECLIPSE, NETT/NAS, and Norway (GenKOLS) studies have been previously described(9) including information regarding quality control. In all cohorts, genotyping was performed using Illumina arrays, and imputation was performed using MaCH(15) and minimac. 1000 Genomes Phase I v3 EUR(16) served as a reference panel for the European ancestry cohorts, and cosmopolitan reference panels were used for the African-Americans (AA).

Genotyping Quality Control

Genotyping quality control at a subject level was identical to that used for the exome array analysis(17). Briefly, systematic evaluation of kinship errors was performed using KING relationship inference software. Further subject-level controls were performed using PLINK v1.07(18) and v1.9(19), including assessment of X-chromosome heterozygosity (gender check), excess homozygosity (consanguinity check), assessment of overall subject genotyping success rate, and assessment of Mendelian transmission errors (EOCOPD study only). For the pedigree-based studies, we manually reviewed errors in reported relationships using the

kinship2 package in R to draw all pedigrees that contained errors. All kinship errors except those detailed below were dropped from the analysis. Subjects with suspected non-paternity in the ICGN study were kept in the study as half-siblings. Subjects with suspected non-paternity in the EOCOPD study were kept in the analysis if there was evidence of non-paternity when examining all first-degree relationships. Relationship errors in the EOCOPD study that involved third-degree or more distant relatives of the probands were reviewed, and retained if relationships between these subjects and first- and second-degree relatives conformed to the predicted relationship values.

Subject Quality Control

We identified population outliers in the COPDGene, ECLIPSE, NETT/NAS, and GenKOLS cohorts using principal component analysis in smartpca. Population outliers were identified in the EOCOPD, ICGN, TCGS-Poland, and TCGS-Korea studies using TRACE software using the HapMap as a reference group. Marker quality control included discordances between subject replicates, markers out of Hardy-Weinberg equilibrium (p-value $<1x10^{-8}$) in controls, and call rate <95%.

Marker Quality Control

Markers were removed for discordances between subject replicates, markers out of Hardy-Weinberg equilibrium (p-value $<1x10^{-8}$) in the controls of any cohort, and call rate <95% in any cohort.

Genetic Analysis: Association Analysis

PLINK v1.9(19) and GWAF(20) were used to perform multiple logistic regression within each dataset case-control and pedigree dataset, respectively, adjusting for age, pack-years of smoking, and principal components of genetic ancestry as previously described. Family-based data were also adjusted for within-family variability using generalized estimating equations with an exchangeable correlation structure. We performed fixed-

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effects meta-analysis across all studies using METAL(21).Family-based cohorts were analyzed together, with a covariate to indicate study.

For our signal near *SERPINA1*, we repeated the analysis after excluding ZZ-homozygotes for alpha-1 antitrypsin deficiency identified through our genotyping (three in the Poland cohort and six in the ECLIPSE cohort) to verify that the chromosome 14 association was robust to the removal of these subjects. We also performed a meta-analysis of rs112458284 conditioning on the *SERPINA1* Z-allele.

For variants previously associated with FEV1 or FEV1/FVC that were not successfully genotyped, we identified proxies (within 250kb and r^2>0·8) using 1000 Genomes data. For lead SNPs previously reported to be associated with lung function, we additionally examined whether the direction of effect for COPD was consistent with the previously reported SNP's effect on spirometric phenotypes.

Genetic Analysis: Genetic Risk Scores

We used PLINK (v1.9) to create genetic scores based on prior genome-wide association studies of COPD and lung function. We oriented risk alleles to be consistent with prior reports, and gave each allele equal weight. We applied the scoring systems to the ICGN cohort, the largest individual cohort not used in the discovery of any of the risk score variants. The resulting combined risk scores were used as predictors in a linear mixed model of FEV_1 percent predicted, as well as logistic regression models of both moderate-to-severe and severe COPD incorporating generalized estimating equations. Models were controlled for age, pack-years of smoking, principal component of genetic ancestry, and for familial correlation. In addition, we used the pROC(22) and GenAbel(23) packages in R to compare the accuracy of two models (i.e. model with genetic risk factors and clinical predictors versus the clinical predictors alone) through receiver operator characteristic (ROC) curves and net reclassification index (NRI) at explaining risk to moderate-to-severe and severe COPD separately. In addition to examining ROC curves, we also used the net reclassification index (24) (NRI) to

characterize the efficacy of these risk scores. The NRI evaluates risk in the decision-making context, and offers an alternative interpretation of classification results. We used the NRI to evaluate the added discriminatory benefit of adding genetic information from genetic risk score SNPs to a clinical model by dividing subjects into three tiers of COPD risk (low 0-33.3%, intermediate 33.4-66.8%, and high 66.7-100%) under a clinical risk model based on age and pack-years of smoking alone. NRI was calculated using the PredictAbel package(25), and data are presented as total NRI as well as event NRI and non-event NRI components.

Coefficient p-values for linear mixed models were calculated using effective degrees of freedom based on the Satterthwaite approximation(26). The calculated genetic risk scores were used as predictors in linear mixed models of FEV_1 percent predicted adjusted for age, pack-years of smoking, principal components of genetic ancestry, and family membership (as a random effect). The scores were also used as predictors in logistic regression models incorporating generalized estimating equations for both moderate-to-severe and severe COPD, controlling for age, pack-years of smoking, principal component of genetic ancestry, and adjustment for familial correlation.

The net reclassification index (NRI) was used to evaluate the added benefit of the addition of genetic information on the risk score SNPs to the clinical model of age and pack-years of smoking using the method of Pencina, et al(24). Subjects were stratified into low (0-33% risk), medium (33-66% risk), and high (66-100% risk) risk groups for the outcome of COPD or severe COPD using only age and pack-years of smoking data; after addition of the risk score SNPs to the model, each subject was reclassified into low, medium, or high risk groups. The event NRI was defined as the number of subjects with COPD who were appropriately reclassified to a higher risk group minus the number of subjects with COPD who were inappropriately reclassified to a lower risk group, divided by the total number of subjects with COPD. The nonevent NRI was defined as the number of subjects without COPD who were appropriately reclassified to a lower risk group minus the number

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of subjects without COPD who were inappropriately reclassified to a higher risk group, divided by the total number of subjects without COPD. The sum of these two component NRI values yielded the total NRI.

We performed pathway analysis of the LUNG30 score risk loci with ConsensusPathDB(27) and SNPsea(28). We selected the closest gene(s) by distance to each variant of the LUNG30 score (listed in Table 4 of the manuscript), and these gene names were used as input for ConsensusPathDB hypergeometric testing in the Gene Ontology (GO) Biological Process(29) ontology (Level 1-5), Kyoto Encyclopedia of Genes and Genomes(30) (KEGG), and the Reactome(31). We required a threshold for enrichment of three genes matching a given gene set, and filtered our results for a false discovery rate (FDR) adjusted q-value of 0.01. Using SNPsea software with default settings, we created a tissue-specific score for each gene in linkage-disequilibrium with a LUNG30 score SNP. This aggregate score for each tissue was then compared against the scores of random SNP sets of similar size to create a null distribution, and an association statistic for tissue-specific enrichment of gene expression was calculated for each tissue.

Supplemental Results:

Genetic Analysis

Genome-wide significant results of the moderate-to-severe COPD candidate SNP association meta-analysis are presented below in Supplemental table 2, while the genome-wide significant results of the severe COPD association were presented in the main manuscript. Supplemental Table 3 shows effect allele frequencies stratified by case and control status for each cohort included in the meta-analysis. Supplemental Table 4 describes association results and LD characteristics of additional candidate regions identified in the work of Castaldi et al(10).

Genetic Risk Scores

The loci included in the COPD7 and LUNG30 risk scores are described in detail in Supplemental Table 5.

The LUNG30 risk score had a smaller per-allele effect but was significantly associated with FEV_1 percent predicted, moderate-to-severe and severe COPD prediction, and reclassification when added to a model composed of clinical data only. The LUNG30 score (with a range of 0-60 possible alleles) also showed a statistically and clinically significant association with lung function in the ICGN cohort, with a 1.10% lower FEV_1 percent predicted per risk allele (p-value $3.8x10^{-11}$). For moderate-to-severe affection status, the NRI showed modest benefit (NRI = 0.090, p-value $1.72x10^{-6}$).

Application of the COPD7, and LUNG30 risk scores on the COPDGene and TCGS Poland datasets are provided in Supplemental Table 6 and 7.

Hypergeometric testing of the genes in the LUNG30 score against KEGG and Reactome gene sets yielded enrichment for terms related to the hedgehog signaling pathway, while testing against the Reactome database also yielded additional enrichments for processes that are potentially involved in COPD pathogenesis such as structural components of lung development like elastic fiber formation, collagen degradation, and extracellular matrix organization. The LUNG30 genes also showed enrichment in Gene Ontology gene sets that could be related to COPD. Multiple sets were related to components of lung development such as the GO terms tube development, morphogenesis of an epithelium, epithelial cell proliferation, extracelular structure organization, smooth muscle proliferation, and branching morphogenesis of an epithelial tube. Others were related to response to stimuli that were potentially relevant for COPD including response to steroid hormone, response to organic substance, inflammatory response, and regulation of reactive oxygen species metabolic process. We then used the SNPsea algorithm to identify tissue types that were likely to be affected by the risk loci in our LUNG30 score. Using a p-value threshold of 0.1, we saw enrichment of the LUNG30 SNPs in fetal lung, trachea, and smooth muscle tissue, among others. Results of KEGG, Reactome, and GO enrichment analysis are presented in Supplemental Table 8, and SNPsea results are presented in Supplemental Table 9.

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SUPPLEMENTAL TABLE 1

CHR	BP	SNP	Source
1	7133059	rs147005162	GWAS Follow-Up
1	9708688	rs6540985	GWAS Follow-Up
1	9709735	rs4529711	GWAS Follow-Up
1	9718087	rs6540991	GWAS Follow-Up
1	17292223	rs78888579	GWAS Follow-Up
1	17306675	rs2284746	Candidate
1	17312743	rs3170740	GWAS Follow-Up
1	17331676	rs3738814	GWAS Follow-Up
1	17354297	rs33927012	GWAS Follow-Up
1	17395480	rs2076599	GWAS Follow-Up
1	18859887	rs35192516	GWAS Follow-Up
1	18860592	rs12120885	GWAS Follow-Up
1	18864374	rs68124995	GWAS Follow-Up
1	27532529	rs12747236	GWAS Follow-Up
1	27537101	rs6687674	GWAS Follow-Up
1	33871246	rs12131910	GWAS Follow-Up
1	54940234	rs115159278	GWAS Follow-Up
1	57913227	rs12033655	GWAS Follow-Up
1	62204308	rs12738921	GWAS Follow-Up
1	68100394	rs629112	GWAS Follow-Up
1	72455832	rs6677919	GWAS Follow-Up
1	72458685	rs6661979	GWAS Follow-Up
1	74470568	rs10890102	GWAS Follow-Up
1	74522532	rs1072936	GWAS Follow-Up
1	74699912	rs518769	GWAS Follow-Up
1	78723269	rs1417100	GWAS Follow-Up
1	78724748	rs34125922	GWAS Follow-Up
1	78732801	rs4650408	GWAS Follow-Up
1	78756602	rs12144203	GWAS Follow-Up
1	78772046	rs11162456	GWAS Follow-Up
1	90328483	rs12045824	GWAS Follow-Up
1	90338129	rs17130908	GWAS Follow-Up
1	92031009	rs11164953	Candidate
1	92031175	rs925190	Candidate
1	92032613	rs7549735	Candidate
1	96749714	rs161989	GWAS Follow-Up
1	96818456	rs325953	GWAS Follow-Up
1	108572106	rs4915093	Candidate
1	108578125	rs12119029	Candidate
1	108580998	rs9787114	Candidate
1	108584103	rs12409794	Candidate

1	108587458	rs4423038	Candidate
1	108600490	rs78362906	Candidate
1	108607992	rs12126230	Candidate
1	108616858	rs10494088	Candidate
1	108637557	rs12132365	Candidate
1	108661569	rs12116716	Candidate
1	108669146	rs56006067	Candidate
1	108681944	rs12076095	Candidate
1	109999838	rs1933182	GWAS Follow-Up
1	110019439	rs62623713	GWAS Follow-Up
1	110031188	rs12049330	GWAS Follow-Up
1	110078434	rs501163	GWAS Follow-Up
1	110082886	rs7550711	GWAS Follow-Up
1	110119732	rs6537837	GWAS Follow-Up
1	110151395	rs3738766	GWAS Follow-Up
1	110163879	rs28362581	GWAS Follow-Up
1	110186563	rs12745189	Candidate
1	110279701	rs7483	GWAS Follow-Up
1	110299691	rs11102001	GWAS Follow-Up
1	110300441	rs3818562	GWAS Follow-Up
1	110301260	rs6693815	GWAS Follow-Up
1	110346355	rs7520172	GWAS Follow-Up
1	110352477	rs10494112	GWAS Follow-Up
1	110366083	rs484959	GWAS Follow-Up
1	111306729	rs12118017	Candidate
1	111318158	rs12084202	Candidate
1	111320253	rs12127060	Candidate
1	111832469	rs61803519	Candidate
1	113240577	rs72701116	GWAS Follow-Up
1	151456548	rs11204827	GWAS Follow-Up
1	151457638	rs11590129	GWAS Follow-Up
1	151458193	rs11204828	GWAS Follow-Up
1	151699416	rs12402668	GWAS Follow-Up
1	151700214	rs2275920	GWAS Follow-Up
1	151703474	rs57696433	GWAS Follow-Up
1	164733504	rs2789443	GWAS Follow-Up
1	164735436	rs1780360	GWAS Follow-Up
1	165958942	rs75331080	GWAS Follow-Up
1	167454312	rs858558	GWAS Follow-Up
1	167454346	rs858557	GWAS Follow-Up
1	167454562	rs858555	GWAS Follow-Up
1	167454914	rs858554	GWAS Follow-Up
1	167455145	rs858553	GWAS Follow-Up
1	168251144	rs12083107	Candidate
1	168251333	rs3767480	Candidate

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1	168251535	rs3767481	Candidate
1	172450689	rs4916263	GWAS Follow-Up
1	172451442	rs9425628	GWAS Follow-Up
1	172451886	rs2032530	GWAS Follow-Up
1	175276630	rs74566648	GWAS Follow-Up
1	177411322	rs80065677	Candidate
1	179130359	rs6672395	GWAS Follow-Up
1	179290889	rs12031660	GWAS Follow-Up
1	179302003	rs7531307	GWAS Follow-Up
1	179306200	rs12039261	GWAS Follow-Up
1	191153510	rs12756536	Candidate
1	191156476	rs10920911	Candidate
1	191167624	rs7554791	Candidate
1	191320291	rs7550126	Candidate
1	193938733	rs34990096	GWAS Follow-Up
1	193938975	rs35168515	GWAS Follow-Up
1	193942375	rs1323086	GWAS Follow-Up
1	193942506	rs17548640	GWAS Follow-Up
1	193970745	rs12725939	GWAS Follow-Up
1	196686652	rs3753395	Candidate
1	196687329	rs10465586	Candidate
1	196701284	rs7540032	Candidate
1	196702810	rs1329428	Candidate
1	196704559	rs1329427	Candidate
1	196880005	rs1409153	Candidate
1	196937536	rs6428379	Candidate
1	206834908	rs77013051	Candidate
1	206836651	rs12042566	Candidate
1	206879122	rs4072677	GWAS Follow-Up
1	206939904	rs3024505	GWAS Follow-Up
1	206943968	rs3024493	GWAS Follow-Up
1	206944233	rs1554286	Candidate
1	206944645	rs1518111	GWAS Follow-Up
1	206946634	rs1800871	GWAS Follow-Up
1	206970470	rs4845140	Candidate
1	207015957	rs2243191	GWAS Follow-Up
1	207074905	rs1150258	GWAS Follow-Up
1	207106478	rs291102	GWAS Follow-Up
1	207109116	rs2275531	GWAS Follow-Up
1	207110936	rs291096	GWAS Follow-Up
1	207134104	rs61729352	GWAS Follow-Up
1	218274763	rs7536760	GWAS Follow-Up
1	218274933	rs7550557	GWAS Follow-Up
1	218563693	rs12129220	Candidate
1	218571757	rs61823428	GWAS Follow-Up

1	218575202	rs1317681	Candidate
1	218575887	rs10746379	GWAS Follow-Up
1	218579985	rs1891467	GWAS Follow-Up
1	218582778	rs17047804	GWAS Follow-Up
1	218586132	rs2796822	Candidate
1	218587636	rs2000220	Candidate
1	218588279	rs10863398	GWAS Follow-Up
1	218593037	rs12048582	GWAS Follow-Up
1	218597632	rs72738830	GWAS Follow-Up
1	218597859	rs1342586	Candidate
1	218598328	rs4846478	GWAS Follow-Up
1	218598410	rs4846479	Candidate
1	218598469	rs4846480	GWAS Follow-Up
1	218598484	rs4846481	Candidate
1	218604678	rs1890995	GWAS Follow-Up
1	218605609	rs10482795	Candidate
1	218605635	rs10482796	GWAS Follow-Up
1	218622319	rs1473527	GWAS Follow-Up
1	218622639	rs12023953	Candidate
1	218623888	rs72738834	GWAS Follow-Up
1	218624533	rs10429950	Candidate
1	218626620	rs7515360	GWAS Follow-Up
1	218634362	rs6604615	GWAS Follow-Up
1	218634787	rs1108548	GWAS Follow-Up
1	218639589	rs7547759	GWAS Follow-Up
1	218640261	rs2001552	Candidate
1	218643940	rs725033	Candidate
1	218645873	rs7526672	Candidate
1	218656286	rs35450021	GWAS Follow-Up
1	218656387	rs1845463	Candidate
1	218657788	rs7534133	Candidate
1	218666429	rs6656288	Candidate
1	218670357	rs622912	Candidate
1	218672807	rs72738842	Candidate
1	218673257	rs11118112	GWAS Follow-Up
1	218674236	rs72738843	Candidate
1	218674597	rs72738844	GWAS Follow-Up
1	218676444	rs72738847	GWAS Follow-Up
1	218681971	rs796395	Candidate
1	218683684	rs72738855	Candidate
1	218689155	rs3009947	Candidate
1	218690577	rs6665024	GWAS Follow-Up
1	218698728	rs72738863	Candidate
1	218701451	rs60831762	Candidate
1	218730751	rs12022686	Candidate

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1	218738103	rs6666438	Candidate
1	218739482	rs682483	Candidate
1	218744152	rs17048147	Candidate
1	218746863	rs62817	Candidate
1	218756684	rs259471	Candidate
1	218760982	rs259476	Candidate
1	218775194	rs2929333	Candidate
1	218798710	rs2993030	Candidate
1	218827855	rs1481345	Candidate
1	218832257	rs6690218	Candidate
1	218833890	rs17048367	Candidate
1	218835037	rs11488570	Candidate
1	218838553	rs17505020	Candidate
1	218860068	rs993925	Candidate
1	218907657	rs17512596	Candidate
1	218910704	rs57548624	Candidate
1	218931976	rs7542694	Candidate
1	218938564	rs9431104	Candidate
1	218938961	rs6541199	Candidate
1	218940576	rs17048556	Candidate
1	218950403	rs2889809	GWAS Follow-Up
1	218972552	rs12081079	Candidate
1	218979635	rs116167583	Candidate
1	218988754	rs17514738	Candidate
1	219001663	rs6541234	Candidate
1	219004755	rs2647119	Candidate
1	219006382	rs2244622	Candidate
1	219009835	rs2647116	GWAS Follow-Up
1	219024035	rs17574573	Candidate
1	219039895	rs80261364	Candidate
1	219043164	rs79112139	Candidate
1	219053082	rs17575281	GWAS Follow-Up
1	221197094	rs61819230	GWAS Follow-Up
1	221624945	rs74743345	GWAS Follow-Up
1	221631207	rs17010062	GWAS Follow-Up
1	221657985	rs77012522	GWAS Follow-Up
1	221662052	rs76184324	GWAS Follow-Up
1	222078600	rs4457591	Candidate
1	222083595	rs11118892	Candidate
1	225965803	rs3738037	Candidate
1	226019633	rs1051740	GWAS Follow-Up
1	226020988	rs2740168	GWAS Follow-Up
1	226040404	rs1009668	GWAS Follow-Up
1	226054333	rs45492299	GWAS Follow-Up
1	233782353	rs6660631	GWAS Follow-Up

1	233782896	rs11576834	GWAS Follow-Up
1	233805172	rs7552738	GWAS Follow-Up
1	239079309	rs6676535	Candidate
1	239090514	rs9970786	Candidate
1	241400970	rs10926435	Candidate
1	241405041	rs10926436	Candidate
1	241421911	rs10926443	Candidate
1	247278125	rs60176339	GWAS Follow-Up
1	247348586	rs3820508	GWAS Follow-Up
1	247348738	rs3738444	GWAS Follow-Up
1	247348774	rs2068050	GWAS Follow-Up
1	247352621	rs10754538	GWAS Follow-Up
2	26940294	rs12468863	GWAS Follow-Up
2	26941482	rs56083993	GWAS Follow-Up
2	26942256	rs2384463	GWAS Follow-Up
2	26948209	rs7595648	GWAS Follow-Up
2	26948279	rs7586627	GWAS Follow-Up
2	26953354	rs1731260	GWAS Follow-Up
2	28778679	rs12618917	GWAS Follow-Up
2	28782922	rs6725700	GWAS Follow-Up
2	28785621	rs6738552	GWAS Follow-Up
2	32891483	rs1807918	GWAS Follow-Up
2	33809294	rs11066	Candidate
2	33815384	rs6708570	Candidate
2	42388003	rs56398784	GWAS Follow-Up
2	42446076	rs6743809	GWAS Follow-Up
2	42458640	rs10182302	GWAS Follow-Up
2	44049795	rs55680582	GWAS Follow-Up
2	45549305	rs12473388	GWAS Follow-Up
2	61183525	rs7560570	GWAS Follow-Up
2	61347626	rs1177292	GWAS Follow-Up
2	61349446	rs1177284	GWAS Follow-Up
2	61352163	rs1177287	GWAS Follow-Up
2	61394851	rs2600671	GWAS Follow-Up
2	61413723	rs1809028	GWAS Follow-Up
2	61478497	rs4672428	GWAS Follow-Up
2	61751642	rs3771262	GWAS Follow-Up
2	61763207	rs9309337	GWAS Follow-Up
2	61837947	rs4494731	GWAS Follow-Up
2	61879276	rs6545894	GWAS Follow-Up
2	69369989	rs115308740	GWAS Follow-Up
2	79140196	rs73939929	GWAS Follow-Up
2	79142387	rs17015845	GWAS Follow-Up
2	85696551	rs12616455	Candidate
2	85699750	rs7577642	GWAS Follow-Up

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2	85769711	rs1078004	GWAS Follow-Up
2	85780536	rs699664	GWAS Follow-Up
2	85794114	rs10187218	Candidate
2	85798858	rs2121397	Candidate
2	85809989	rs1561198	GWAS Follow-Up
2	85824039	rs1127974	GWAS Follow-Up
2	85824251	rs6643	GWAS Follow-Up
2	85866118	rs17736515	Candidate
2	85893741	rs1130866	GWAS Follow-Up
2	85895338	rs2077079	GWAS Follow-Up
2	85924729	rs11127	GWAS Follow-Up
2	86010098	rs2001593	Candidate
2	86010243	rs869778	Candidate
2	86013029	rs13386681	Candidate
2	86025331	rs6706567	GWAS Follow-Up
2	86036870	rs13347170	Candidate
2	86054300	rs56035936	Candidate
2	86054301	rs56363459	Candidate
2	86063044	rs13420465	Candidate
2	86063465	rs11900847	Candidate
2	104586416	rs78999012	Candidate
2	108659330	rs2889821	GWAS Follow-Up
2	108659446	rs35227180	GWAS Follow-Up
2	108664582	rs35586373	GWAS Follow-Up
2	108812855	rs12329189	Candidate
2	108816885	rs6761157	Candidate
2	113389232	rs908545	GWAS Follow-Up
2	113405483	rs77746742	Candidate
2	113468896	rs58533146	GWAS Follow-Up
2	113496554	rs116342308	GWAS Follow-Up
2	113498566	rs3811040	GWAS Follow-Up
2	113513825	rs6731822	GWAS Follow-Up
2	113514763	rs17042344	GWAS Follow-Up
2	113520129	rs36093393	GWAS Follow-Up
2	113529183	rs6542095	GWAS Follow-Up
2	113537223	rs17561	GWAS Follow-Up
2	113579866	rs3917386	Candidate
2	113594387	rs1143627	GWAS Follow-Up
2	113671410	rs3811047	GWAS Follow-Up
2	113674721	rs2723183	GWAS Follow-Up
2	113675269	rs2723187	GWAS Follow-Up
2	113676219	rs2708947	GWAS Follow-Up
2	113676381	rs2723192	GWAS Follow-Up
2	113763575	rs895497	GWAS Follow-Up
2	113765587	rs34817588	GWAS Follow-Up

2	113773561	rs1867831	Candidate
2	113775573	rs4849140	Candidate
2	113775749	rs7595507	Candidate
2	113778642	rs6745709	Candidate
2	113778986	rs6749299	Candidate
2	113779206	rs13033574	Candidate
2	113789316	rs2305150	GWAS Follow-Up
2	113790258	rs11123155	GWAS Follow-Up
2	113791482	rs2862772	GWAS Follow-Up
2	113792419	rs11891020	GWAS Follow-Up
2	182390953	rs3770107	GWAS Follow-Up
2	182396032	rs6433921	GWAS Follow-Up
2	182424718	rs12693280	GWAS Follow-Up
2	182429735	rs10490687	GWAS Follow-Up
2	182443391	rs11687348	GWAS Follow-Up
2	182451737	rs10490684	GWAS Follow-Up
2	182491014	rs6719421	GWAS Follow-Up
2	182495701	rs1372119	GWAS Follow-Up
2	182501005	rs62189989	GWAS Follow-Up
2	187901064	rs6748392	GWAS Follow-Up
2	187926271	rs10931269	GWAS Follow-Up
2	187976717	rs9646745	GWAS Follow-Up
2	189883851	rs58099040	GWAS Follow-Up
2	189915813	rs61664338	GWAS Follow-Up
2	189962098	rs73051214	GWAS Follow-Up
2	189967528	rs73051217	GWAS Follow-Up
2	194194121	rs77734878	GWAS Follow-Up
2	202721424	rs2882324	GWAS Follow-Up
2	204740171	rs10197010	GWAS Follow-Up
2	204744097	rs231730	GWAS Follow-Up
2	204744530	rs231731	GWAS Follow-Up
2	204745132	rs11571299	GWAS Follow-Up
2	218669225	rs61741262	GWAS Follow-Up
2	218674697	rs918949	GWAS Follow-Up
2	218683139	rs34291329	GWAS Follow-Up
2	218712290	rs61746994	GWAS Follow-Up
2	218713282	rs3796033	GWAS Follow-Up
2	218713469	rs3815849	GWAS Follow-Up
2	218725480	rs3791953	Candidate
2	218732851	rs17790748	Candidate
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2	218734362	rs3791949	Candidate
2	218734953	rs10204348	Candidate
2	218739732	rs1424917	Candidate
2	218795794	rs7585036	Candidate

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2	218864319	rs6712327	GWAS Follow-Up
2	224824617	rs11546405	GWAS Follow-Up
2	224837600	rs12694624	GWAS Follow-Up
2	224866427	rs34078713	GWAS Follow-Up
2	224931733	rs282249	GWAS Follow-Up
2	224947170	rs16865545	Candidate
2	225047744	rs2629046	GWAS Follow-Up
2	229502503	rs10498230	Candidate
2	229510929	rs1435867	GWAS Follow-Up
2	229533885	rs1881204	GWAS Follow-Up
2	229552897	rs62201158	Candidate
2	229561895	rs62202378	GWAS Follow-Up
2	229581891	rs4973113	Candidate
2	229590717	rs4973115	Candidate
2	229591965	rs62202385	Candidate
2	229723426	rs10206541	Candidate
2	229729917	rs800736	Candidate
2	229736292	rs55898636	Candidate
2	229755868	rs60975031	Candidate
2	229841213	rs74000792	Candidate
2	229853850	rs2193390	Candidate
2	229892748	rs7580152	Candidate
2	229899441	rs34025994	Candidate
2	229906421	rs12463741	Candidate
2	229921340	rs111827343	Candidate
2	229977915	rs2536217	GWAS Follow-Up
2	230022826	rs11903631	Candidate
2	230023296	rs4973164	Candidate
2	230025158	rs12995479	Candidate
2	230029966	rs9973934	Candidate
2	230030405	rs4973171	Candidate
2	230030822	rs72617162	Candidate
2	230032055	rs2396618	Candidate
2	230033560	rs1419958	Candidate
2	230209923	rs2894676	Candidate
2	230211114	rs6756789	Candidate
2	230224031	rs7594321	Candidate
2	233319911	rs1213008	GWAS Follow-Up
2	233349588	rs1529874	GWAS Follow-Up
2	239877148	rs12477314	Candidate
2	239887220	rs35877146	Candidate
2	239893783	rs35945722	Candidate
2	239896861	rs10199914	GWAS Follow-Up
3	2638138	rs9866546	GWAS Follow-Up
3	3732283	rs2044094	GWAS Follow-Up

3	3733372	rs2165631	GWAS Follow-Up
3	3733390	rs2165630	GWAS Follow-Up
3	4400735	rs2819563	GWAS Follow-Up
3	4843506	rs80129583	GWAS Follow-Up
3	12504295	rs1699346	Candidate
3	12507564	rs1699348	Candidate
3	12622623	rs9849171	Candidate
3	12626516	rs3729931	Candidate
3	18111142	rs12488761	GWAS Follow-Up
3	18133070	rs62240234	GWAS Follow-Up
3	20112187	rs114491517	GWAS Follow-Up
3	20275194	rs17191318	GWAS Follow-Up
3	22020956	rs34866662	GWAS Follow-Up
3	22021125	rs10510522	GWAS Follow-Up
3	25320733	rs1825370	Candidate
3	25325452	rs322659	Candidate
3	25341251	rs12108115	Candidate
3	25341255	rs185990320	Candidate
3	25423265	rs9876345	GWAS Follow-Up
3	25520582	rs1529672	GWAS Follow-Up
3	25528376	rs1286662	GWAS Follow-Up
3	25529280	rs1286664	Candidate
3	25534688	rs35536382	Candidate
3	25560231	rs1435703	GWAS Follow-Up
3	25639828	rs61739570	GWAS Follow-Up
3	31427154	rs12490017	GWAS Follow-Up
3	31428425	rs17027566	GWAS Follow-Up
3	31430001	rs55985928	GWAS Follow-Up
3	31430754	rs9877237	GWAS Follow-Up
3	31431024	rs9877602	GWAS Follow-Up
3	31431722	rs12497875	GWAS Follow-Up
3	31432835	rs17027580	GWAS Follow-Up
3	31433240	rs10510650	GWAS Follow-Up
3	31433893	rs9845596	GWAS Follow-Up
3	31435901	rs9855940	GWAS Follow-Up
3	63146329	rs72874557	GWAS Follow-Up
3	69430452	rs62251411	GWAS Follow-Up
3	69434402	rs34685652	GWAS Follow-Up
3	69437171	rs981054	GWAS Follow-Up
3	69438053	rs11717499	GWAS Follow-Up
3	69440851	rs7648449	GWAS Follow-Up
3	69443677	rs62251413	GWAS Follow-Up
3	69460531	rs6549217	GWAS Follow-Up
3	69471552	rs73109466	GWAS Follow-Up
3	69498897	rs56840526	GWAS Follow-Up

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3	69503920	rs62252290	GWAS Follow-Up
3	72413687	rs4677155	GWAS Follow-Up
3	72420023	rs35172111	GWAS Follow-Up
3	73670346	rs6801447	GWAS Follow-Up
3	73687663	rs4677321	GWAS Follow-Up
3	75238423	rs79210092	GWAS Follow-Up
3	75239485	rs76794935	GWAS Follow-Up
3	85370873	rs9831374	Candidate
3	85391672	rs9811546	Candidate
3	85403892	rs28732378	Candidate
3	85404030	rs62253107	Candidate
3	85405501	rs9822731	Candidate
3	85409313	rs9824178	Candidate
3	85409353	rs9861451	Candidate
3	85414291	rs7627971	Candidate
3	85415875	rs73134727	Candidate
3	85429172	rs13085170	Candidate
3	85574891	rs73130304	Candidate
3	85608137	rs1375547	Candidate
3	100822032	rs35904383	GWAS Follow-Up
3	100843733	rs62280585	GWAS Follow-Up
3	109037249	rs2699984	GWAS Follow-Up
3	109037738	rs2625619	GWAS Follow-Up
3	109047928	rs1163439	GWAS Follow-Up
3	109052935	rs1351737	GWAS Follow-Up
3	109057397	rs1163448	GWAS Follow-Up
3	112303559	rs79058794	GWAS Follow-Up
3	122010679	rs35467281	GWAS Follow-Up
3	122018967	rs13058991	GWAS Follow-Up
3	122031859	rs4247197	GWAS Follow-Up
3	127715196	rs17282209	Candidate
3	127794248	rs11709060	Candidate
3	127854527	rs35347185	Candidate
3	127857933	rs11709725	Candidate
3	127893564	rs11715394	Candidate
3	127898783	rs2811477	Candidate
3	127931340	rs2999090	GWAS Follow-Up
3	127935159	rs2999089	GWAS Follow-Up
3	127956188	rs2999082	Candidate
3	127956272	rs2999081	Candidate
3	127961305	rs2955084	Candidate
3	127977978	rs2999068	Candidate
3	127991527	rs2811415	Candidate
3	127991938	rs2811416	GWAS Follow-Up
3	128004531	rs4593050	Candidate

3	128012277	rs2811520	Candidate
3	128039895	rs11708733	Candidate
3	128044372	rs6772407	GWAS Follow-Up
3	128067275	rs11709611	GWAS Follow-Up
3	128072502	rs11711096	GWAS Follow-Up
3	128097496	rs2293947	GWAS Follow-Up
3	128103714	rs78360844	Candidate
3	128106536	rs2977561	GWAS Follow-Up
3	133575865	rs7644124	GWAS Follow-Up
3	133577269	rs1534167	GWAS Follow-Up
3	133578594	rs1467334	GWAS Follow-Up
3	134098876	rs2052830	Candidate
3	134099218	rs2052832	Candidate
3	135313695	rs75027740	Candidate
3	156492758	rs9818780	GWAS Follow-Up
3	156493213	rs9878566	GWAS Follow-Up
3	156512817	rs9859058	GWAS Follow-Up
3	156524220	rs9818684	GWAS Follow-Up
3	156532666	rs10936038	GWAS Follow-Up
3	156533403	rs4680305	GWAS Follow-Up
3	156601655	rs2321291	GWAS Follow-Up
3	156619137	rs4680313	GWAS Follow-Up
3	156626091	rs12638253	GWAS Follow-Up
3	156645757	rs7637701	GWAS Follow-Up
3	156655494	rs6784421	GWAS Follow-Up
3	156696506	rs10936043	GWAS Follow-Up
3	156704742	rs9829685	GWAS Follow-Up
3	156707330	rs1032044	GWAS Follow-Up
3	156733521	rs7637445	GWAS Follow-Up
3	156734799	rs1600978	GWAS Follow-Up
3	157232900	rs75703125	GWAS Follow-Up
3	165070685	rs822719	GWAS Follow-Up
3	165080780	rs7648573	GWAS Follow-Up
3	169100899	rs448378	GWAS Follow-Up
3	169300219	rs1344555	Candidate
3	169316165	rs933607	Candidate
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3	169364599	rs34781085	Candidate
3	169371036	rs11928083	Candidate
3	169413590	rs6782665	Candidate
3	169414042	rs10460793	Candidate
3	169416247	rs59908764	Candidate
3	169416569	rs16854319	Candidate
3	169442363	rs9880534	Candidate
3	169481271	rs12696304	GWAS Follow-Up

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3	169485588	rs34273285	GWAS Follow-Up
3	169485639	rs2068178	GWAS Follow-Up
3	169492101	rs10936599	GWAS Follow-Up
3	183936680	rs2668193	GWAS Follow-Up
3	185931624	rs57816510	Candidate
3	186497254	rs62294445	GWAS Follow-Up
3	186505900	rs1354091	GWAS Follow-Up
3	186515844	rs3917117	GWAS Follow-Up
3	186518652	rs3917110	GWAS Follow-Up
3	187436079	rs59761878	GWAS Follow-Up
3	187438897	rs55934024	GWAS Follow-Up
4	3303976	rs994426	GWAS Follow-Up
4	3312883	rs35720136	GWAS Follow-Up
4	3313808	rs61211078	GWAS Follow-Up
4	8234562	rs115561809	Candidate
4	8276491	rs79614502	Candidate
4	17062043	rs28479818	GWAS Follow-Up
4	17062269	rs10022937	GWAS Follow-Up
4	17062676	rs949587	GWAS Follow-Up
4	17069489	rs7657395	GWAS Follow-Up
4	17070309	rs28524821	GWAS Follow-Up
4	17073543	rs1533361	GWAS Follow-Up
4	17075697	rs10939704	GWAS Follow-Up
4	17094967	rs73135080	GWAS Follow-Up
4	17106331	rs2056393	GWAS Follow-Up
4	17106462	rs2056392	GWAS Follow-Up
4	17107945	rs955609	GWAS Follow-Up
4	17113151	rs10008516	GWAS Follow-Up
4	17113440	rs10018968	GWAS Follow-Up
4	17168001	rs16894543	GWAS Follow-Up
4	17171130	rs10019583	GWAS Follow-Up
4	17172914	rs1108802	GWAS Follow-Up
4	17173148	rs6838488	GWAS Follow-Up
4	17173670	rs74837368	GWAS Follow-Up
4	17174275	rs78326497	GWAS Follow-Up
4	17176095	rs76785184	GWAS Follow-Up
4	17176796	rs4698543	GWAS Follow-Up
4	17178058	rs1522075	Candidate
4	17187440	rs574427	GWAS Follow-Up
4	17203295	rs10805352	GWAS Follow-Up
4	17209596	rs12640889	GWAS Follow-Up
4	17224847	rs57016776	GWAS Follow-Up
4	17239066	rs4698557	GWAS Follow-Up
4	17239151	rs4698174	GWAS Follow-Up
4	23565305	rs58874680	GWAS Follow-Up

4	23565839	rs73105087	GWAS Follow-Up
4	24790680	rs17622933	Candidate
4	24796568	rs8192287	GWAS Follow-Up
4	24796678	rs8192288	GWAS Follow-Up
4	24796803	rs699473	GWAS Follow-Up
4	24810094	rs74764772	GWAS Follow-Up
4	24896658	rs12511068	GWAS Follow-Up
4	24981689	rs764497	GWAS Follow-Up
4	29929502	rs1503966	GWAS Follow-Up
4	29940277	rs28368922	GWAS Follow-Up
4	34973964	rs874936	GWAS Follow-Up
4	34974596	rs58966196	GWAS Follow-Up
4	34987181	rs4290912	GWAS Follow-Up
4	34991642	rs55892081	GWAS Follow-Up
4	42281021	rs116415202	GWAS Follow-Up
4	72608383	rs2282679	GWAS Follow-Up
4	72618323	rs4588	GWAS Follow-Up
4	72618334	rs7041	GWAS Follow-Up
4	72699705	rs9291163	Candidate
4	72706235	rs1476272	GWAS Follow-Up
4	72774077	rs1915189	Candidate
4	72774622	rs72607837	Candidate
4	72835953	rs1520503	GWAS Follow-Up
4	82647939	rs6829367	Candidate
4	84175235	rs4346637	GWAS Follow-Up
4	84178980	rs57516559	GWAS Follow-Up
4	84182361	rs61587542	GWAS Follow-Up
4	89456219	rs7435410	GWAS Follow-Up
4	89456677	rs11735201	GWAS Follow-Up
4	89458051	rs11736472	GWAS Follow-Up
4	89469328	rs10007151	GWAS Follow-Up
4	89470295	rs78011872	GWAS Follow-Up
4	89477002	rs11929822	GWAS Follow-Up
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4	89485105	rs72663434	GWAS Follow-Up
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4	89497079	rs6532072	GWAS Follow-Up
4	89514572	rs6857847	GWAS Follow-Up
4	89524695	rs17737045	GWAS Follow-Up
4	89527323	rs17799056	GWAS Follow-Up
4	89540209	rs10028621	GWAS Follow-Up
4	89540939	rs28413084	GWAS Follow-Up

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4	89541016	rs17014307	GWAS Follow-Up
4	89542281	rs2869663	GWAS Follow-Up
4	89579183	rs2915427	Candidate
4	89581654	rs78232283	Candidate
4	89584697	rs75177363	Candidate
4	89586243	rs3852086	Candidate
4	89588067	rs10516817	Candidate
4	89599570	rs3017919	Candidate
4	89599839	rs3017918	GWAS Follow-Up
4	89603085	rs2972038	GWAS Follow-Up
4	89606980	rs80288725	Candidate
4	89612583	rs2904250	Candidate
4	89613579	rs3756051	Candidate
4	89617387	rs8605	Candidate
4	89617931	rs28435799	Candidate
4	89618837	rs710834	Candidate
4	89619276	rs2972011	Candidate
4	89621072	rs2604209	GWAS Follow-Up
4	89624219	rs76432068	Candidate
4	89644197	rs2924941	Candidate
4	89647070	rs2860500	Candidate
4	89665193	rs3775391	GWAS Follow-Up
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4	89667854	rs6855961	Candidate
4	89668210	rs2278877	GWAS Follow-Up
4	89670155	rs3756050	Candidate
4	89672738	rs10428273	GWAS Follow-Up
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4	89708850	rs11725153	Candidate
4	89710789	rs6825776	Candidate
4	89717298	rs77140172	GWAS Follow-Up
4	89718313	rs112542013	Candidate
4	89718378	rs75621874	GWAS Follow-Up
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4	89725505	rs75581102	Candidate
4	89727979	rs10516821	Candidate
4	89734828	rs1817279	GWAS Follow-Up
4	89736565	rs17014616	GWAS Follow-Up
4	89737376	rs17014620	Candidate
4	89739479	rs13131633	GWAS Follow-Up
4	89739808	rs3775380	Candidate

4	89740128	rs13133548	GWAS Follow-Up
4	89741269	rs3822072	Candidate
4	89742764	rs2869950	GWAS Follow-Up
4	89743780	rs2869951	Candidate
4	89743821	rs3775373	Candidate
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4	89744825	rs3806788	GWAS Follow-Up
4	89746220	rs35019968	Candidate
4	89746849	rs73842249	Candidate
4	89747394	rs71609539	GWAS Follow-Up
4	89750361	rs10021465	GWAS Follow-Up
4	89750668	rs13149209	GWAS Follow-Up
4	89752276	rs57400569	GWAS Follow-Up
4	89753225	rs4425336	GWAS Follow-Up
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4	89760151	rs74610824	Candidate
4	89765661	rs7682431	GWAS Follow-Up
4	89765872	rs9991039	Candidate
4	89772301	rs7680970	GWAS Follow-Up
4	89772321	rs115194267	GWAS Follow-Up
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4	89779909	rs2085600	Candidate
4	89781164	rs11729108	Candidate
4	89781166	rs11724744	Candidate
4	89781277	rs10022272	Candidate
4	89789067	rs922026	Candidate
4	89789478	rs1979290	Candidate
4	89789799	rs17815876	Candidate
4	89791075	rs17815912	Candidate
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4	89797667	rs4693973	Candidate
4	89803695	rs78366141	GWAS Follow-Up
4	89810395	rs4693974	Candidate
4	89811195	rs2609255	GWAS Follow-Up
4	89813284	rs6815970	GWAS Follow-Up
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4	89827071	rs6813090	GWAS Follow-Up
4	89828544	rs79524934	Candidate
4	89832532	rs10019681	GWAS Follow-Up
4	89835762	rs56221166	Candidate
4	89836819	rs2609260	GWAS Follow-Up
4	89839840	rs4693976	Candidate
4	89847655	rs6835019	GWAS Follow-Up

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4	89850005	rs2704587	Candidate
4	89850263	rs2609282	GWAS Follow-Up
4	89850542	rs2125409	Candidate
4	89853598	rs1458562	Candidate
4	89854079	rs4693977	Candidate
4	89854167	rs4693978	Candidate
4	89860819	rs7660385	Candidate
4	89860843	rs2464522	Candidate
4	89860847	rs2464523	Candidate
4	89861309	rs2904256	Candidate
4	89862169	rs987314	Candidate
4	89864998	rs59489826	Candidate
4	89866713	rs4416442	Candidate
4	89869078	rs2869966	Candidate
4	89869332	rs2869967	Candidate
4	89873092	rs6837671	Candidate
4	89875694	rs56162738	Candidate
4	89879488	rs34749134	Candidate
4	89879663	rs2464526	Candidate
4	89883818	rs7671261	GWAS Follow-Up
4	89883979	rs7671167	GWAS Follow-Up
4	89885086	rs2013701	GWAS Follow-Up
4	89885714	rs2904259	GWAS Follow-Up
4	89886297	rs1903003	GWAS Follow-Up
4	89886358	rs1903004	Candidate
4	89891597	rs1458560	Candidate
4	89895944	rs2085601	Candidate
4	89896036	rs6838424	GWAS Follow-Up
4	89898476	rs11737182	Candidate
4	89898681	rs11737260	Candidate
4	89900452	rs10470936	GWAS Follow-Up
4	89906598	rs78681184	GWAS Follow-Up
4	89907604	rs7691363	GWAS Follow-Up
4	89908727	rs11737016	GWAS Follow-Up
4	89917563	rs4693981	GWAS Follow-Up
4	89918312	rs7659904	GWAS Follow-Up
4	89921288	rs12508371	GWAS Follow-Up
4	89925320	rs2178586	GWAS Follow-Up
4	89925969	rs6852373	GWAS Follow-Up
4	89926193	rs6852928	Candidate
4	89927612	rs13129885	Candidate
4	89928203	rs10015415	Candidate
4	89928489	rs6849143	Candidate
4	89928532	rs6823536	GWAS Follow-Up
4	89929610	rs1708667	GWAS Follow-Up

4	89930392	rs1398942	GWAS Follow-Up
4	89930434	rs1795738	GWAS Follow-Up
4	89931070	rs12505696	Candidate
4	89933630	rs1795734	Candidate
4	89934550	rs1849597	GWAS Follow-Up
4	89935386	rs12509305	Candidate
4	89937184	rs1398940	Candidate
4	89938362	rs12508524	Candidate
4	89947352	rs1708669	GWAS Follow-Up
4	89948639	rs2464514	GWAS Follow-Up
4	89948897	rs34624010	GWAS Follow-Up
4	89951561	rs1708668	Candidate
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4	89960285	rs2704571	GWAS Follow-Up
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4	89973910	rs2670623	GWAS Follow-Up
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4	90003669	rs35652620	GWAS Follow-Up
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4	90019365	rs6843986	GWAS Follow-Up
4	90020087	rs6846010	GWAS Follow-Up
4	90024204	rs62306363	Candidate
4	90024321	rs4325981	GWAS Follow-Up
4	90024793	rs62306364	GWAS Follow-Up
4	90024960	rs10009665	Candidate
4	90025750	rs13113298	GWAS Follow-Up
4	90028412	rs7440590	Candidate
4	90028653	rs4285052	GWAS Follow-Up
4	90031328	rs62306390	GWAS Follow-Up
4	90034686	rs17015027	Candidate
4	90035549	rs2280099	GWAS Follow-Up
4	90045646	rs35624987	Candidate
4	90049404	rs6844490	Candidate
4	90052321	rs58377799	Candidate
4	90053943	rs5029557	Candidate
4	90055959	rs7692291	GWAS Follow-Up
4	90056378	rs12647781	Candidate
4	90057814	rs1398944	Candidate
4	90057983	rs7658455	Candidate
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4	90059434	rs6828137	Candidate
4	90062409	rs7690336	GWAS Follow-Up
4	90062555	rs75140020	Candidate
4	90073214	rs756345	GWAS Follow-Up

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4	90075384	rs7684332	GWAS Follow-Up
4	90076233	rs62306424	GWAS Follow-Up
4	90077090	rs4491985	Candidate
4	90077367	rs7672716	GWAS Follow-Up
4	90077431	rs7672894	GWAS Follow-Up
4	90077986	rs79013678	GWAS Follow-Up
4	90113524	rs78122929	GWAS Follow-Up
4	90117271	rs79757761	GWAS Follow-Up
4	90124852	rs80007183	GWAS Follow-Up
4	104156174	rs6855414	GWAS Follow-Up
4	106395144	rs35571699	GWAS Follow-Up
4	106448900	rs4082504	GWAS Follow-Up
4	106457330	rs7669317	GWAS Follow-Up
4	106510470	rs2276970	GWAS Follow-Up
4	106511488	rs17324954	Candidate
4	106520742	rs17035917	Candidate
4	106523319	rs73837046	Candidate
4	106523932	rs1374531	Candidate
4	106526544	rs17035939	Candidate
4	106527508	rs11735213	Candidate
4	106531846	rs17035960	Candidate
4	106556518	rs17036027	Candidate
4	106592617	rs12512339	Candidate
4	106593574	rs17036090	Candidate
4	106593850	rs4235415	Candidate
4	106624529	rs17036129	GWAS Follow-Up
4	106625263	rs10516523	GWAS Follow-Up
4	106631870	rs11727735	Candidate
4	106684022	rs62317671	Candidate
4	106688904	rs10516526	Candidate
4	106698892	rs2553449	Candidate
4	106718253	rs72673821	Candidate
4	106729933	rs11097901	Candidate
4	106741163	rs11723639	Candidate
4	106746012	rs11731417	Candidate
4	106755996	rs11728716	Candidate
4	106766430	rs11722225	Candidate
4	106767741	rs17036337	Candidate
4	106768598	rs72673865	Candidate
4	106792380	rs2553440	Candidate
4	106808107	rs17331332	Candidate
4	106808181	rs72673888	Candidate
4	106812732	rs11933466	Candidate
4	106814302	rs72673891	Candidate
4	106843958	rs7664805	Candidate

4	106861730	rs4340795	GWAS Follow-Up
4	106922960	rs11730681	GWAS Follow-Up
4	107232695	rs114723682	GWAS Follow-Up
4	108009235	rs72666083	GWAS Follow-Up
4	109757451	rs10015699	GWAS Follow-Up
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4	119412100	rs17642633	Candidate
4	119454437	rs56203850	Candidate
4	119454442	rs34983100	Candidate
4	119462685	rs2200517	Candidate
4	119605009	rs298982	Candidate
4	119641941	rs298992	Candidate
4	119646000	rs298991	Candidate
4	119648689	rs6820588	Candidate
4	119657920	rs17323606	Candidate
4	119686551	rs2288306	Candidate
4	119886214	rs78300132	GWAS Follow-Up
4	132496237	rs9997012	GWAS Follow-Up
4	132501395	rs36124350	GWAS Follow-Up
4	132507123	rs28679731	GWAS Follow-Up
4	132509731	rs28714103	GWAS Follow-Up
4	145227600	rs13118083	Candidate
4	145229710	rs13106167	GWAS Follow-Up
4	145234515	rs6828489	GWAS Follow-Up
4	145240011	rs4256191	Candidate
4	145240152	rs4321584	GWAS Follow-Up
4	145242662	rs6537275	GWAS Follow-Up
4	145249275	rs12512788	Candidate
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4	145254685	rs7377575	Candidate
4	145257681	rs2202507	Candidate
4	145258754	rs9995482	Candidate
4	145259126	rs13118748	GWAS Follow-Up
4	145260495	rs7661046	GWAS Follow-Up
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4	145263756	rs6822064	Candidate
4	145264014	rs6840871	Candidate
4	145270867	rs987246	GWAS Follow-Up
4	145272119	rs34991888	Candidate
4	145272692	rs17766168	Candidate
4	145273928	rs4835177	GWAS Follow-Up
4	145275039	rs6537279	Candidate
4	145278837	rs17766287	Candidate
4	145302155	rs1394998	Candidate
4	145310689	rs72731541	Candidate

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4	145321006	rs7654571	Candidate
4	145333609	rs17019336	Candidate
4	145363247	rs1602238	Candidate
4	145363781	rs11735249	Candidate
4	145371436	rs13142439	GWAS Follow-Up
4	145372248	rs12510916	GWAS Follow-Up
4	145375299	rs71614507	Candidate
4	145375405	rs17019368	GWAS Follow-Up
4	145381766	rs17019370	GWAS Follow-Up
4	145388834	rs2130499	GWAS Follow-Up
4	145388954	rs62343635	GWAS Follow-Up
4	145417318	rs17019390	Candidate
4	145418294	rs11736238	Candidate
4	145418803	rs72731582	GWAS Follow-Up
4	145425040	rs12639777	Candidate
4	145425849	rs35937742	Candidate
4	145425936	rs34265962	Candidate
4	145428569	rs12500946	Candidate
4	145429056	rs11935246	Candidate
4	145431497	rs1512282	GWAS Follow-Up
4	145432894	rs7654793	Candidate
4	145434584	rs1032295	Candidate
4	145434688	rs1032296	Candidate
4	145434744	rs1032297	Candidate
4	145434901	rs1512281	Candidate
4	145436324	rs12504628	Candidate
4	145436894	rs7697189	GWAS Follow-Up
4	145437014	rs7681384	GWAS Follow-Up
4	145437081	rs7698984	Candidate
4	145437319	rs7677035	GWAS Follow-Up
4	145444039	rs13107186	Candidate
4	145450959	rs1512285	Candidate
4	145452783	rs6845536	GWAS Follow-Up
4	145460230	rs13147758	GWAS Follow-Up
4	145469373	rs62346060	Candidate
4	145469968	rs6537292	GWAS Follow-Up
4	145474297	rs1489760	GWAS Follow-Up
4	145478777	rs4834988	GWAS Follow-Up
4	145479167	rs28758624	Candidate
4	145480780	rs1828591	GWAS Follow-Up
4	145482243	rs28626624	GWAS Follow-Up
4	145484638	rs12510044	GWAS Follow-Up
4	145485738	rs1980057	Candidate
4	145485915	rs7655625	Candidate
4	145486389	rs13118928	GWAS Follow-Up

4	145489098	rs13140176	GWAS Follow-Up
4	145499389	rs34544231	GWAS Follow-Up
4	145499473	rs78652667	GWAS Follow-Up
4	145500596	rs13136959	GWAS Follow-Up
4	145502121	rs71614512	GWAS Follow-Up
4	145506456	rs13141641	GWAS Follow-Up
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4	145506871	rs6537298	Candidate
4	145511040	rs11724319	Candidate
4	145511875	rs7670758	Candidate
4	145515769	rs1542726	GWAS Follow-Up
4	145516378	rs1489765	GWAS Follow-Up
4	145517578	rs2353397	Candidate
4	145520608	rs4835180	Candidate
4	145521189	rs10023833	Candidate
4	145521867	rs2035901	Candidate
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4	145974688	rs11734845	Candidate
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4	146056320	rs1804528	GWAS Follow-Up
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4	147351628	rs10017463	GWAS Follow-Up
4	147354570	rs11726588	GWAS Follow-Up
4	147355224	rs10030464	GWAS Follow-Up
4	147389169	rs10012310	GWAS Follow-Up
4	147393001	rs6537424	GWAS Follow-Up
4	147394565	rs3914627	GWAS Follow-Up
4	147425114	rs7439061	GWAS Follow-Up
4	147442492	rs12500663	GWAS Follow-Up
4	147446692	rs2357087	GWAS Follow-Up
4	147466990	rs2102252	GWAS Follow-Up
4	147467353	rs6840503	GWAS Follow-Up
4	147469133	rs1504355	GWAS Follow-Up
4	169644989	rs17542430	GWAS Follow-Up
4	169670530	rs6817535	GWAS Follow-Up

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4	180192751	rs28502482	Candidate
4	180193431	rs6848106	Candidate
4	180193914	rs6828433	Candidate
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5	7438910	rs6878468	Candidate
5	7442910	rs6881726	Candidate
5	7520881	rs13166360	GWAS Follow-Up
5	7527521	rs2055388	GWAS Follow-Up
5	7564015	rs11134242	Candidate
5	7757647	rs52827085	GWAS Follow-Up
5	7900833	rs8659	GWAS Follow-Up
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5	13750975	rs6889428	Candidate
5	13753984	rs3734108	Candidate
5	13755951	rs2134259	Candidate
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5	13761321	rs61016840	Candidate
5	35141661	rs75433606	GWAS Follow-Up
5	35145815	rs79642114	GWAS Follow-Up
5	35149100	rs78493119	GWAS Follow-Up
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5	38910764	rs72732729	GWAS Follow-Up
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5	38923732	rs357292	GWAS Follow-Up
5	38935244	rs1051942	Candidate
5	38964026	rs28684455	Candidate
5	39004105	rs62359819	GWAS Follow-Up
5	39009131	rs10060696	GWAS Follow-Up
5	39018114	rs62359835	GWAS Follow-Up
5	39019612	rs61343691	GWAS Follow-Up
5	39051341	rs10037713	Candidate
5	39062977	rs9292730	GWAS Follow-Up
5	39063119	rs9292731	GWAS Follow-Up
5	40704090	rs6872282	GWAS Follow-Up

5	43477344	rs74826072	GWAS Follow-Up
5	49860118	rs12657678	GWAS Follow-Up
5	49870703	rs4605740	GWAS Follow-Up
5	49872016	rs7721806	GWAS Follow-Up
5	49872572	rs7704183	GWAS Follow-Up
5	49917122	rs11951835	GWAS Follow-Up
5	50068245	rs154140	GWAS Follow-Up
5	50089919	rs27466	GWAS Follow-Up
5	50095914	rs32376	GWAS Follow-Up
5	50140456	rs27389	GWAS Follow-Up
5	50584237	rs4141541	GWAS Follow-Up
5	50595433	rs1501985	GWAS Follow-Up
5	50600177	rs10066412	GWAS Follow-Up
5	53502468	rs13358454	GWAS Follow-Up
5	53502836	rs445953	GWAS Follow-Up
5	54398049	rs2069187	GWAS Follow-Up
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5	58267976	rs829259	GWAS Follow-Up
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5	59065790	rs1504982	GWAS Follow-Up
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5	62703874	rs10058963	GWAS Follow-Up
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5	62717532	rs10073868	GWAS Follow-Up
5	62720889	rs56356819	GWAS Follow-Up
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5	78944371	rs72768817	Candidate
5	78946215	rs55687040	Candidate
5	78963323	rs12657392	Candidate
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5	89830456	rs679568	GWAS Follow-Up
5	89844438	rs27201	GWAS Follow-Up
5	89853069	rs42467	GWAS Follow-Up
5	89854448	rs154568	GWAS Follow-Up
5	94246553	rs469843	GWAS Follow-Up

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5	94252861	rs159349	GWAS Follow-Up
5	94861118	rs17084873	GWAS Follow-Up
5	94939193	rs17084927	GWAS Follow-Up
5	94994467	rs34297786	GWAS Follow-Up
5	95036700	rs153916	Candidate
5	95091201	rs34899	GWAS Follow-Up
5	95115959	rs41276257	GWAS Follow-Up
5	95234350	rs3777204	GWAS Follow-Up
5	95236459	rs3815768	GWAS Follow-Up
5	95236474	rs113894818	GWAS Follow-Up
5	108107311	rs114508915	GWAS Follow-Up
5	108581219	rs61701247	GWAS Follow-Up
5	108581474	rs17161655	GWAS Follow-Up
5	111083884	rs3797734	GWAS Follow-Up
5	111084118	rs17133711	GWAS Follow-Up
5	111479750	rs62372418	GWAS Follow-Up
5	111501334	rs1020951	GWAS Follow-Up
5	111501729	rs6594566	GWAS Follow-Up
5	111503142	rs6594567	GWAS Follow-Up
5	111503308	rs2114991	GWAS Follow-Up
5	111503618	rs10070995	GWAS Follow-Up
5	111590409	rs34819608	GWAS Follow-Up
5	111595745	rs28620667	GWAS Follow-Up
5	111602713	rs13358904	GWAS Follow-Up
5	111603683	rs10478074	GWAS Follow-Up
5	111669737	rs10037235	GWAS Follow-Up
5	111675130	rs13190229	GWAS Follow-Up
5	120141352	rs9327168	Candidate
5	120144768	rs7715474	Candidate
5	120755648	rs11951505	Candidate
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5	120889325	rs1896740	GWAS Follow-Up
5	120897889	rs2217319	GWAS Follow-Up
5	120899371	rs7723363	GWAS Follow-Up
5	122087617	rs79177619	GWAS Follow-Up
5	122116803	rs56364502	GWAS Follow-Up
5	122131511	rs17149627	GWAS Follow-Up
5	122225480	rs246283	GWAS Follow-Up
5	122259553	rs451897	GWAS Follow-Up
5	122321622	rs882143	GWAS Follow-Up
5	122328421	rs1551937	GWAS Follow-Up
5	122354298	rs3813313	GWAS Follow-Up
5	122405090	rs7700388	GWAS Follow-Up
5	122405957	rs6860095	GWAS Follow-Up
5	122411771	rs4836423	GWAS Follow-Up

5	122412709	rs6595430	GWAS Follow-Up
5	122413016	rs7704775	GWAS Follow-Up
5	122418041	rs4469193	GWAS Follow-Up
5	124504333	rs10463784	GWAS Follow-Up
5	126569039	rs10065046	Candidate
5	126610750	rs60477974	Candidate
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5	131801726	rs2522056	GWAS Follow-Up
5	131839618	rs4705952	GWAS Follow-Up
5	131862977	rs4143832	GWAS Follow-Up
5	131867702	rs2706399	GWAS Follow-Up
5	131870689	rs11242120	GWAS Follow-Up
5	131901225	rs2244012	GWAS Follow-Up
5	131973177	rs2040704	GWAS Follow-Up
5	131995843	rs1295686	GWAS Follow-Up
5	131995964	rs20541	Candidate
5	132030284	rs17690923	Candidate
5	132074695	rs57586624	GWAS Follow-Up
5	132132647	rs803137	GWAS Follow-Up
5	132759324	rs29545	Candidate
5	146714174	rs75404872	GWAS Follow-Up
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5	147779935	rs17720155	Candidate
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5	147847273	rs4597955	Candidate
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5	147924255	rs17706683	Candidate
5	147936863	rs10477385	Candidate
5	147949611	rs56101651	Candidate
5	147964658	rs10040819	Candidate
5	147987866	rs79721457	Candidate

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5	148191398	rs2116714	GWAS Follow-Up
5	148206440	rs1042713	GWAS Follow-Up
5	148206473	rs1042714	GWAS Follow-Up
5	148215902	rs17108817	Candidate
5	148310587	rs10054497	Candidate
5	148388420	rs55853803	GWAS Follow-Up
5	148407893	rs6875902	GWAS Follow-Up
5	155450424	rs2116737	GWAS Follow-Up
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5	156682890	rs25777	Candidate
5	156684911	rs246750	Candidate
5	156687631	rs511133	Candidate
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5	156916611	rs10058865	Candidate
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5	156918147	rs35413759	Candidate
5	156918850	rs2287749	GWAS Follow-Up
5	156920756	rs1990950	Candidate
5	156926442	rs13361953	Candidate
5	156926777	rs12522418	Candidate
5	156928008	rs56168343	Candidate
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5	156977853	rs12189024	Candidate
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5	156989957	rs7724199	Candidate
5	156991508	rs11134819	Candidate

5	156999098	rs11738723	GWAS Follow-Up
5	157001302	rs11134822	Candidate
5	157020761	rs6873008	Candidate
5	157029138	rs62390768	Candidate
5	157030395	rs10035961	Candidate
5	157031112	rs11134828	Candidate
5	157032982	rs78827776	GWAS Follow-Up
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6	23381935	rs9393408	GWAS Follow-Up
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6	28130359	rs1150669	GWAS Follow-Up

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6	28134368	rs1150674	GWAS Follow-Up
6	28142276	rs1150678	GWAS Follow-Up
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6	31446796	rs2248462	GWAS Follow-Up
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6	31564821	rs2844480	GWAS Follow-Up
6	31567422	rs2857596	GWAS Follow-Up
6	31568469	rs2857595	Candidate

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6	31572956	rs2844479	Candidate
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6	31916951	rs541862	GWAS Follow-Up

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6	32134510	rs3096697	GWAS Follow-Up

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6	32145205	rs3134947	GWAS Follow-Up
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6	32147696	rs3130349	GWAS Follow-Up
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6	32179896	rs2071286	GWAS Follow-Up
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6	32187023	rs394657	GWAS Follow-Up
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6	32790089	rs16870908	GWAS Follow-Up
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6	32792973	rs1894411	GWAS Follow-Up
6	32794676	rs2857101	GWAS Follow-Up
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6	109078539	rs523632	Candidate
6	109082625	rs507189	Candidate

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6	109087078	rs574217	Candidate
6	109088972	rs58362680	Candidate
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6	116568773	rs1052443	Candidate
6	116571695	rs3749893	Candidate
6	116575083	rs2232470	GWAS Follow-Up
6	116575116	rs17524614	GWAS Follow-Up
6	116600453	rs3749894	GWAS Follow-Up
6	116600616	rs61746508	GWAS Follow-Up
6	116720487	rs10485183	GWAS Follow-Up
6	116720514	rs35548455	GWAS Follow-Up
6	116721656	rs2227125	GWAS Follow-Up
6	123702499	rs3813328	Candidate
6	123703983	rs2043148	Candidate
6	123715748	rs9385299	Candidate
6	123715968	rs9401668	Candidate
6	123731285	rs9388238	Candidate
6	142548099	rs225717	GWAS Follow-Up
6	142565531	rs1931983	GWAS Follow-Up
6	142655490	rs2039987	Candidate
6	142663177	rs1342060	Candidate
6	142668901	rs9399401	Candidate

6	142679572	rs6570507	GWAS Follow-Up
6	142688969	rs17280293	Candidate
6	142691549	rs11155242	Candidate
6	142703877	rs4896582	GWAS Follow-Up
6	142707133	rs6937121	Candidate
6	142725182	rs73780221	Candidate
6	142750516	rs3817928	Candidate
6	142764073	rs9403386	Candidate
6	142767633	rs3748069	GWAS Follow-Up
6	142777064	rs7776375	Candidate
6	142797289	rs7763064	GWAS Follow-Up
6	145275656	rs73613930	GWAS Follow-Up
6	145276870	rs9484931	GWAS Follow-Up
6	145281094	rs9322011	GWAS Follow-Up
6	145282579	rs73613983	GWAS Follow-Up
6	145283387	rs9497155	GWAS Follow-Up
6	145311901	rs1416295	GWAS Follow-Up
6	151427385	rs6934983	GWAS Follow-Up
6	151641001	rs12205375	GWAS Follow-Up
6	161937977	rs78008396	GWAS Follow-Up
6	162056646	rs79403850	GWAS Follow-Up
6	163543699	rs536980	GWAS Follow-Up
6	163546352	rs547539	GWAS Follow-Up
6	163551992	rs498657	GWAS Follow-Up
6	163571901	rs6455866	GWAS Follow-Up
6	163572250	rs6921357	GWAS Follow-Up
6	163578666	rs10945875	GWAS Follow-Up
6	163580885	rs12190368	GWAS Follow-Up
6	163581656	rs12190791	GWAS Follow-Up
6	163583121	rs12197200	GWAS Follow-Up
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6	169416679	rs12194918	GWAS Follow-Up
6	169418823	rs1322638	GWAS Follow-Up
6	169421120	rs11752531	GWAS Follow-Up
6	169421443	rs11755456	GWAS Follow-Up
6	169425778	rs12203323	GWAS Follow-Up
6	169429003	rs910690	GWAS Follow-Up
6	169440902	rs7741593	GWAS Follow-Up
6	169442689	rs959687	GWAS Follow-Up
7	4246412	rs7812170	GWAS Follow-Up
7	14540895	rs62443479	GWAS Follow-Up
7	14586855	rs62443522	GWAS Follow-Up
7	39409900	rs12672997	GWAS Follow-Up
7	39419781	rs6462913	GWAS Follow-Up
7	43413384	rs10282127	GWAS Follow-Up

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7	43413421	rs10281930	GWAS Follow-Up
7	43414004	rs9639873	GWAS Follow-Up
7	46435992	rs62452690	GWAS Follow-Up
7	46437330	rs6980173	GWAS Follow-Up
7	50419792	rs28733769	Candidate
7	78127027	rs4421288	GWAS Follow-Up
7	78138542	rs4730345	GWAS Follow-Up
7	78151125	rs724914	GWAS Follow-Up
7	78158840	rs10447824	GWAS Follow-Up
7	78234493	rs416102	GWAS Follow-Up
7	79804665	rs13227898	Candidate
7	79812826	rs67077197	Candidate
7	81359051	rs5745687	GWAS Follow-Up
7	96795041	rs10229181	GWAS Follow-Up
7	99872675	rs73161741	GWAS Follow-Up
7	99956290	rs2906644	GWAS Follow-Up
7	99971313	rs2405442	GWAS Follow-Up
7	100012334	rs34919929	GWAS Follow-Up
7	100013457	rs5015756	Candidate
7	100042413	rs55773945	GWAS Follow-Up
7	100079857	rs6971558	GWAS Follow-Up
7	100091795	rs12539172	GWAS Follow-Up
7	100092311	rs11971846	GWAS Follow-Up
7	104084209	rs62485096	Candidate
7	125521995	rs721118	Candidate
7	129617727	rs10808241	GWAS Follow-Up
7	136630812	rs10225215	GWAS Follow-Up
7	136642634	rs2350782	GWAS Follow-Up
7	139172868	rs67345907	GWAS Follow-Up
7	139172887	rs9642124	GWAS Follow-Up
7	140217670	rs3748088	GWAS Follow-Up
7	154460660	rs118189482	Candidate
7	156250444	rs7778219	GWAS Follow-Up
7	156259409	rs1881008	GWAS Follow-Up
7	156259583	rs1534008	GWAS Follow-Up
7	157788880	rs10258167	GWAS Follow-Up
7	157788972	rs10258292	GWAS Follow-Up
7	157791029	rs11984274	GWAS Follow-Up
7	157791818	rs12665894	GWAS Follow-Up
8	3600189	rs9650510	Candidate
8	3604955	rs10503216	Candidate
8	4483141	rs2616984	GWAS Follow-Up
8	4489315	rs62486712	GWAS Follow-Up
8	8630269	rs506960	GWAS Follow-Up
8	8632957	rs565203	GWAS Follow-Up

8	8633928	rs535094	GWAS Follow-Up
8	8635888	rs617813	Candidate
8	9740358	rs10104353	GWAS Follow-Up
8	9740636	rs6601389	GWAS Follow-Up
8	9740657	rs6601390	GWAS Follow-Up
8	9741171	rs6990268	GWAS Follow-Up
8	9741478	rs10098618	GWAS Follow-Up
8	9742525	rs12056944	GWAS Follow-Up
8	9742841	rs7828229	GWAS Follow-Up
8	9744650	rs6989793	GWAS Follow-Up
8	9973371	rs963593	GWAS Follow-Up
8	9976540	rs7843924	GWAS Follow-Up
8	9977918	rs6983332	GWAS Follow-Up
8	9978471	rs6986885	GWAS Follow-Up
8	9978940	rs12678800	GWAS Follow-Up
8	9979992	rs2062331	GWAS Follow-Up
8	9981149	rs2062333	GWAS Follow-Up
8	9981854	rs17689674	GWAS Follow-Up
8	9983369	rs17151147	GWAS Follow-Up
8	9995853	rs17151188	GWAS Follow-Up
8	9997980	rs62488714	GWAS Follow-Up
8	10005883	rs58764043	GWAS Follow-Up
8	10006664	rs4840464	GWAS Follow-Up
8	10009952	rs11993089	GWAS Follow-Up
8	10012232	rs62488738	GWAS Follow-Up
8	10077806	rs10110380	GWAS Follow-Up
8	10082746	rs11249978	GWAS Follow-Up
8	10083040	rs10089666	GWAS Follow-Up
8	10083515	rs4265190	GWAS Follow-Up
8	10084886	rs13256234	GWAS Follow-Up
8	10099624	rs12550483	GWAS Follow-Up
8	10115960	rs4258008	GWAS Follow-Up
8	10117279	rs35226696	GWAS Follow-Up
8	10117759	rs11782000	GWAS Follow-Up
8	10445702	rs12543042	GWAS Follow-Up
8	10448142	rs12681639	GWAS Follow-Up
8	10458377	rs12680137	Candidate
8	10573698	rs75731123	GWAS Follow-Up
8	11562513	rs62489319	GWAS Follow-Up
8	11567140	rs4489290	GWAS Follow-Up
8	11567376	rs7817412	GWAS Follow-Up
8	11611353	rs17153747	GWAS Follow-Up
8	11611366	rs17153752	GWAS Follow-Up
8	14660581	rs35770515	GWAS Follow-Up
8	14668859	rs7002469	GWAS Follow-Up

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8	18163452	rs73584323	GWAS Follow-Up
8	18164315	rs73666603	GWAS Follow-Up
8	27146595	rs148666973	GWAS Follow-Up
8	32303612	rs6468104	Candidate
8	32306984	rs6996957	Candidate
8	32365695	rs68189791	Candidate
8	32403573	rs7823498	Candidate
8	32410110	rs4236709	Candidate
8	32412359	rs2439312	Candidate
8	41653471	rs79432940	GWAS Follow-Up
8	41663090	rs77788808	GWAS Follow-Up
8	54453130	rs9693226	Candidate
8	54529344	rs28414831	Candidate
8	74335766	rs144404773	GWAS Follow-Up
8	76202315	rs11998486	GWAS Follow-Up
8	76216868	rs57747815	GWAS Follow-Up
8	83534705	rs16910688	Candidate
8	83538521	rs72677531	Candidate
8	96226228	rs2514560	Candidate
8	96230017	rs74956051	Candidate
8	100803907	rs62534610	GWAS Follow-Up
8	103208028	rs1265143	GWAS Follow-Up
8	103215928	rs1265154	GWAS Follow-Up
8	103265132	rs2853235	GWAS Follow-Up
8	103282518	rs2978431	GWAS Follow-Up
8	103313114	rs76081441	GWAS Follow-Up
8	108868731	rs13274153	GWAS Follow-Up
8	108894697	rs34503613	GWAS Follow-Up
8	108899439	rs72680424	GWAS Follow-Up
8	108950190	rs72680448	GWAS Follow-Up
8	121377702	rs6990426	GWAS Follow-Up
8	121465262	rs6989609	GWAS Follow-Up
8	121475611	rs77269571	GWAS Follow-Up
8	121479247	rs75201989	GWAS Follow-Up
8	124078472	rs80042305	GWAS Follow-Up
8	124264927	rs1044714	GWAS Follow-Up
8	124300658	rs11782961	GWAS Follow-Up
8	124379755	rs13248086	GWAS Follow-Up
8	125961813	rs9297704	GWAS Follow-Up
8	125962981	rs75785682	GWAS Follow-Up
8	125963969	rs78809767	GWAS Follow-Up
8	132883079	rs7006137	GWAS Follow-Up
8	140949469	rs2614717	GWAS Follow-Up
8	140954213	rs2665945	GWAS Follow-Up
8	144973617	rs72693382	GWAS Follow-Up

8	144974142	rs10100277	GWAS Follow-Up
8	144974963	rs7831595	Candidate
8	144976572	rs4077669	Candidate
8	144977279	rs4073900	Candidate
8	144981498	rs7461753	Candidate
8	144986793	rs3923387	Candidate
8	144993324	rs6984820	Candidate
8	144996029	rs7833924	Candidate
8	145001031	rs55895668	Candidate
8	145006790	rs10866916	Candidate
8	145011204	rs6993938	Candidate
8	145020477	rs12543539	Candidate
8	145031265	rs11777239	Candidate
8	145034852	rs11780978	Candidate
8	145035342	rs7357417	Candidate
8	145039400	rs72695409	Candidate
9	286491	rs3209441	Candidate
9	306277	rs35381637	Candidate
9	306734	rs62533402	Candidate
9	660970	rs10815439	GWAS Follow-Up
9	668887	rs7035770	GWAS Follow-Up
9	669125	rs9408665	GWAS Follow-Up
9	669259	rs10815451	GWAS Follow-Up
9	671053	rs4584192	GWAS Follow-Up
9	674428	rs4742217	GWAS Follow-Up
9	675377	rs4742219	GWAS Follow-Up
9	675419	rs4742220	GWAS Follow-Up
9	682330	rs9299037	GWAS Follow-Up
9	682646	rs9407359	GWAS Follow-Up
9	684096	rs1323262	GWAS Follow-Up
9	685819	rs9408677	GWAS Follow-Up
9	2808536	rs12353495	GWAS Follow-Up
9	2811731	rs12340161	GWAS Follow-Up
9	2815440	rs73394639	GWAS Follow-Up
9	2815601	rs12340564	GWAS Follow-Up
9	2839934	rs3824352	GWAS Follow-Up
9	2842672	rs12345518	GWAS Follow-Up
9	2843201	rs12343488	GWAS Follow-Up
9	3833771	rs116892582	GWAS Follow-Up
9	3968385	rs117377928	GWAS Follow-Up
9	4149475	rs982820	GWAS Follow-Up
9	4150202	rs10125159	GWAS Follow-Up
9	4150733	rs1998271	GWAS Follow-Up
9	4151202	rs12353487	GWAS Follow-Up
9	4151884	rs12344449	GWAS Follow-Up

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9	4152555	rs927322	GWAS Follow-Up
9	4153183	rs62524070	GWAS Follow-Up
9	4154267	rs12553203	GWAS Follow-Up
9	6266440	rs2026991	GWAS Follow-Up
9	6268204	rs2039386	GWAS Follow-Up
9	6268893	rs2000199	GWAS Follow-Up
9	6271238	rs1041537	GWAS Follow-Up
9	7007063	rs7025832	GWAS Follow-Up
9	7019562	rs147029433	GWAS Follow-Up
9	7641251	rs10976470	Candidate
9	7646850	rs10976473	Candidate
9	7650677	rs55833066	GWAS Follow-Up
9	7654872	rs75241563	GWAS Follow-Up
9	7655095	rs79280735	Candidate
9	7657370	rs16926508	GWAS Follow-Up
9	7657636	rs17544446	GWAS Follow-Up
9	7658421	rs78645567	GWAS Follow-Up
9	7660751	rs11790748	GWAS Follow-Up
9	7661068	rs17627322	GWAS Follow-Up
9	7662198	rs10976481	GWAS Follow-Up
9	7662660	rs10976483	Candidate
9	7665194	rs10976486	GWAS Follow-Up
9	7669918	rs74822503	Candidate
9	7670008	rs78491788	GWAS Follow-Up
9	7671218	rs77014806	Candidate
9	7681732	rs78467782	GWAS Follow-Up
9	7682063	rs10976498	GWAS Follow-Up
9	7682480	rs10815656	GWAS Follow-Up
9	7682860	rs4740904	GWAS Follow-Up
9	7700884	rs72695191	GWAS Follow-Up
9	8353593	rs75885112	GWAS Follow-Up
9	9070768	rs324513	GWAS Follow-Up
9	9072442	rs634098	GWAS Follow-Up
9	9072447	rs580780	GWAS Follow-Up
9	9073311	rs324483	GWAS Follow-Up
9	9074622	rs182720	GWAS Follow-Up
9	9076554	rs324487	GWAS Follow-Up
9	9077555	rs324474	GWAS Follow-Up
9	9077607	rs324475	GWAS Follow-Up
9	9079771	rs324479	GWAS Follow-Up
9	9080896	rs324473	GWAS Follow-Up
9	9086923	rs369166	GWAS Follow-Up
9	9088309	rs3004230	GWAS Follow-Up
9	9089810	rs324465	GWAS Follow-Up
9	9090197	rs172863	GWAS Follow-Up

9	9090876	rs324466	Candidate
9	9102409	rs324542	Candidate
9	9102650	rs10759040	GWAS Follow-Up
9	14074022	rs516325	GWAS Follow-Up
9	14074266	rs1689280	GWAS Follow-Up
9	14079067	rs480700	GWAS Follow-Up
9	14080129	rs1689282	GWAS Follow-Up
9	14089242	rs574460	GWAS Follow-Up
9	14099484	rs516090	GWAS Follow-Up
9	14117221	rs580501	GWAS Follow-Up
9	16267194	rs9298753	GWAS Follow-Up
9	16287889	rs9406608	Candidate
9	16288267	rs7874755	Candidate
9	16288424	rs7875024	Candidate
9	16289428	rs6475025	Candidate
9	16291556	rs9407736	Candidate
9	19910154	rs1887392	GWAS Follow-Up
9	19913350	rs72692011	GWAS Follow-Up
9	19916322	rs72692016	GWAS Follow-Up
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9	37684753	rs7469365	GWAS Follow-Up
9	38453822	rs80045011	GWAS Follow-Up
9	72559567	rs10868299	GWAS Follow-Up
9	72562015	rs7033495	Candidate
9	72565890	rs34131182	Candidate
9	72566736	rs1389119	Candidate
9	72572045	rs10868327	GWAS Follow-Up
9	72574727	rs7863165	GWAS Follow-Up
9	72611680	rs10868358	GWAS Follow-Up
9	72614812	rs870011	GWAS Follow-Up
9	72617499	rs4490905	GWAS Follow-Up
9	72648997	rs2975926	GWAS Follow-Up
9	72650127	rs4430153	GWAS Follow-Up
9	91397958	rs73652622	GWAS Follow-Up
9	93887773	rs13284085	GWAS Follow-Up
9	96903388	rs75373744	GWAS Follow-Up
9	96905548	rs10993067	GWAS Follow-Up
9	96910808	rs2398937	GWAS Follow-Up
9	96977650	rs10739973	GWAS Follow-Up
9	96978588	rs2768637	GWAS Follow-Up
9	96978917	rs2717488	GWAS Follow-Up
9	96993598	rs2080658	GWAS Follow-Up

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9	96997137	rs9409707	GWAS Follow-Up
9	97000398	rs2675278	GWAS Follow-Up
9	97008212	rs2675275	GWAS Follow-Up
9	97008227	rs2263455	GWAS Follow-Up
9	98153197	rs357535	Candidate
9	98167811	rs357527	Candidate
9	98177173	rs357561	Candidate
9	98189165	rs357524	Candidate
9	98189335	rs357523	Candidate
9	98191723	rs58831996	Candidate
9	98209594	rs357564	GWAS Follow-Up
9	98231008	rs16909898	Candidate
9	98256309	rs10512249	Candidate
9	98259703	rs10512248	GWAS Follow-Up
9	98319969	rs17370391	GWAS Follow-Up
9	98340320	rs7025117	GWAS Follow-Up
9	98367717	rs10818991	GWAS Follow-Up
9	98410405	rs10990303	GWAS Follow-Up
9	109495224	rs10739227	Candidate
9	109506245	rs7036275	Candidate
9	109507432	rs6477542	Candidate
9	113636793	rs551517	Candidate
9	119516230	rs13297442	GWAS Follow-Up
9	119523436	rs13291355	GWAS Follow-Up
9	119525648	rs13283406	GWAS Follow-Up
9	119529014	rs13300728	GWAS Follow-Up
9	120969775	rs10818121	GWAS Follow-Up
9	120973280	rs1327799	GWAS Follow-Up
9	120974390	rs4836712	GWAS Follow-Up
9	120981143	rs1410200	GWAS Follow-Up
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9	134258779	rs542305	GWAS Follow-Up
9	135965662	rs686246	Candidate
9	135974100	rs886017	Candidate
9	135977366	rs34170541	GWAS Follow-Up
9	136029645	rs35898523	GWAS Follow-Up
9	136037742	rs2073924	GWAS Follow-Up
9	136047393	rs2039184	GWAS Follow-Up
9	136131188	rs8176749	GWAS Follow-Up
9	136131322	rs8176746	GWAS Follow-Up
9	136131347	rs8176745	GWAS Follow-Up
9	136131350	rs8176744	GWAS Follow-Up
9	136131437	rs8176742	GWAS Follow-Up
9	136131461	rs8176741	GWAS Follow-Up
9	136131472	rs8176740	GWAS Follow-Up

9	136131576	rs55727303	GWAS Follow-Up
9	136131592	rs7853989	GWAS Follow-Up
9	136131651	rs1053878	GWAS Follow-Up
9	136132873	rs8176720	GWAS Follow-Up
9	136133506	rs512770	GWAS Follow-Up
9	136135108	rs8176707	Candidate
9	136135238	rs549446	GWAS Follow-Up
9	136136770	rs688976	GWAS Follow-Up
9	136137065	rs687621	GWAS Follow-Up
9	136139265	rs657152	GWAS Follow-Up
9	136142203	rs514659	GWAS Follow-Up
9	136149229	rs505922	GWAS Follow-Up
9	136149399	rs507666	GWAS Follow-Up
9	136153875	rs651007	GWAS Follow-Up
9	136154168	rs579459	GWAS Follow-Up
9	136155000	rs635634	GWAS Follow-Up
9	136199466	rs886089	GWAS Follow-Up
9	136199503	rs886090	GWAS Follow-Up
9	136223541	rs143037947	GWAS Follow-Up
9	136227260	rs12763	GWAS Follow-Up
9	136268952	rs33919837	GWAS Follow-Up
9	136269143	rs17150554	GWAS Follow-Up
9	136277482	rs2285487	GWAS Follow-Up
9	136277854	rs2285488	Candidate
9	136279935	rs6597630	GWAS Follow-Up
9	136287582	rs34024143	GWAS Follow-Up
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9	136310908	rs685523	GWAS Follow-Up
9	136319589	rs28503257	GWAS Follow-Up
9	136322529	rs3094327	Candidate
9	136323754	rs4962153	GWAS Follow-Up
9	136326554	rs739467	Candidate
9	136333487	rs3094381	Candidate
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9	136505241	rs1108581	Candidate
10	2628101	rs10047370	GWAS Follow-Up
10	2629002	rs4565802	GWAS Follow-Up
10	2630239	rs10794928	GWAS Follow-Up
10	2631518	rs7085508	GWAS Follow-Up
10	2635863	rs11251392	GWAS Follow-Up
10	2637008	rs7084825	GWAS Follow-Up

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10	3075076	rs17135074	Candidate
10	5996751	rs41294041	GWAS Follow-Up
10	6002697	rs41294153	GWAS Follow-Up
10	12131081	rs3740015	GWAS Follow-Up
10	12143105	rs2062988	GWAS Follow-Up
10	12179270	rs10906083	Candidate
10	12215180	rs2399786	GWAS Follow-Up
10	12277992	rs7068966	Candidate
10	12314997	rs10906115	GWAS Follow-Up
10	12546743	rs2815660	GWAS Follow-Up
10	12547135	rs7920446	GWAS Follow-Up
10	12644970	rs73572263	GWAS Follow-Up
10	12646813	rs17151970	GWAS Follow-Up
10	19093747	rs4447064	GWAS Follow-Up
10	19116011	rs12572254	GWAS Follow-Up
10	19116610	rs1329241	GWAS Follow-Up
10	19118287	rs11007193	GWAS Follow-Up
10	19120169	rs7073789	GWAS Follow-Up
10	19121271	rs7095160	GWAS Follow-Up
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10	19151542	rs1329218	GWAS Follow-Up
10	19160986	rs4748537	GWAS Follow-Up
10	19169676	rs7917968	GWAS Follow-Up
10	19169862	rs7921382	GWAS Follow-Up
10	19172869	rs4747363	GWAS Follow-Up
10	19176810	rs928058	GWAS Follow-Up
10	21393804	rs478559	GWAS Follow-Up
10	21416245	rs658096	GWAS Follow-Up
10	21417606	rs12573237	GWAS Follow-Up
10	21444603	rs1751915	GWAS Follow-Up
10	21453457	rs11012552	GWAS Follow-Up
10	21454915	rs72798503	GWAS Follow-Up
10	21469847	rs11594335	GWAS Follow-Up
10	45463220	rs10793573	Candidate
10	45464035	rs3814566	Candidate
10	61645590	rs1184089	GWAS Follow-Up
10	61655297	rs1171812	GWAS Follow-Up
10	61656044	rs2456712	GWAS Follow-Up
10	61664610	rs1171828	GWAS Follow-Up
10	61665886	rs1171830	GWAS Follow-Up
10	71525084	rs2255667	GWAS Follow-Up
10	73390724	rs56235440	Candidate
10	73393901	rs12218474	Candidate
10	73406697	rs4747179	Candidate

10	73407384	rs10999928	GWAS Follow-Up
10	73407465	rs10999929	Candidate
10	73408918	rs12414776	Candidate
10	73409978	rs4746093	Candidate
10	73416480	rs1665684	GWAS Follow-Up
10	73416753	rs1665686	GWAS Follow-Up
10	73420289	rs1665620	GWAS Follow-Up
10	73437036	rs1227039	Candidate
10	78117651	rs10430475	Candidate
10	78122729	rs12766217	GWAS Follow-Up
10	78140834	rs7904646	Candidate
10	78149043	rs7909650	Candidate
10	78151195	rs1873462	Candidate
10	78155282	rs1873463	Candidate
10	78159948	rs1907339	Candidate
10	78160976	rs1907340	Candidate
10	78315224	rs11001819	Candidate
10	78444456	rs241	GWAS Follow-Up
10	82072310	rs10788562	Candidate
10	82191255	rs4934153	Candidate
10	82203663	rs4934169	Candidate
10	82218964	rs12220642	Candidate
10	82219066	rs12220655	Candidate
10	82222178	rs7100689	Candidate
10	82222698	rs1993484	Candidate
10	82250831	rs7097656	Candidate
10	82263683	rs1902660	Candidate
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10	82280137	rs1878036	Candidate
10	82284512	rs7096909	Candidate
10	82301536	rs11185951	Candidate
10	82304297	rs7084416	Candidate
10	89889086	rs192758397	GWAS Follow-Up
10	94782567	rs10786066	GWAS Follow-Up
10	94783777	rs7895716	GWAS Follow-Up
10	97057643	rs7900898	GWAS Follow-Up
10	102056508	rs2278843	GWAS Follow-Up
10	102072092	rs3844556	GWAS Follow-Up
10	119225035	rs11198003	GWAS Follow-Up
10	119225982	rs171444	GWAS Follow-Up
10	119226791	rs4752065	GWAS Follow-Up
10	119229740	rs74162318	GWAS Follow-Up
10	119234786	rs242966	GWAS Follow-Up
10	120422764	rs10736269	GWAS Follow-Up
10	120424177	rs10886280	GWAS Follow-Up

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10	120425908	rs11198553	GWAS Follow-Up
10	120426758	rs10886282	GWAS Follow-Up
10	120428781	rs17097926	GWAS Follow-Up
10	122693564	rs1659592	Candidate
10	122697162	rs35361560	Candidate
10	129649177	rs10830186	GWAS Follow-Up
10	129649561	rs11018347	GWAS Follow-Up
10	129649832	rs74570725	GWAS Follow-Up
10	129652382	rs4751539	GWAS Follow-Up
10	129652386	rs4751540	GWAS Follow-Up
10	129653425	rs4750921	GWAS Follow-Up
10	129660060	rs4590782	GWAS Follow-Up
10	129661686	rs11018367	GWAS Follow-Up
10	130675517	rs942528	Candidate
10	130679321	rs11016534	Candidate
10	130688400	rs10764827	Candidate
10	132384224	rs2397388	GWAS Follow-Up
10	133001451	rs10829946	GWAS Follow-Up
10	133002014	rs2918129	GWAS Follow-Up
11	840034	rs11246327	GWAS Follow-Up
11	5258162	rs4320977	GWAS Follow-Up
11	20293580	rs72927136	GWAS Follow-Up
11	31186536	rs61878246	GWAS Follow-Up
11	35161670	rs353558	GWAS Follow-Up
11	35163486	rs2553809	GWAS Follow-Up
11	35164108	rs2553808	GWAS Follow-Up
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11	44802602	rs1377330	GWAS Follow-Up
11	44807313	rs1670308	GWAS Follow-Up
11	44869167	rs835795	Candidate
11	44871323	rs755767	GWAS Follow-Up
11	46762142	rs6485688	GWAS Follow-Up
11	56575092	rs77235188	GWAS Follow-Up
11	62001414	rs12806663	Candidate
11	67186271	rs868167	GWAS Follow-Up
11	67200812	rs55987642	GWAS Follow-Up
11	67203442	rs60969594	GWAS Follow-Up
11	67235051	rs143199541	GWAS Follow-Up
11	67262411	rs144939807	GWAS Follow-Up
11	67266164	rs61755426	GWAS Follow-Up
11	67288594	rs2276118	GWAS Follow-Up
11	67291914	rs55657661	Candidate
11	67299586	rs118043292	Candidate
11	67339536	rs676653	Candidate
11	67344150	rs76835094	Candidate

11	67352689	rs1695	GWAS Follow-Up
11	67355797	rs79512139	Candidate
11	67385062	rs72934504	Candidate
11	67402362	rs3758938	GWAS Follow-Up
11	67405967	rs11820792	Candidate
11	67406829	rs1993839	Candidate
11	67414492	rs948445	GWAS Follow-Up
11	67430762	rs1551886	GWAS Follow-Up
11	67433869	rs1551888	GWAS Follow-Up
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11	67456775	rs72936320	Candidate
11	67461330	rs2514047	Candidate
11	67462549	rs11227881	Candidate
11	86165187	rs7108055	GWAS Follow-Up
11	86165814	rs6592296	GWAS Follow-Up
11	86165942	rs1563682	GWAS Follow-Up
11	96606436	rs72974940	GWAS Follow-Up
11	96617545	rs11214325	GWAS Follow-Up
11	96624349	rs56338927	GWAS Follow-Up
11	96653321	rs11215881	GWAS Follow-Up
11	100036291	rs12802629	GWAS Follow-Up
11	100051690	rs34562026	GWAS Follow-Up
11	100060325	rs34029128	GWAS Follow-Up
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11	100407990	rs947950	Candidate
11	101336544	rs12795728	GWAS Follow-Up
11	101462942	rs1938828	Candidate
11	101469434	rs2508736	Candidate
11	102562700	rs2509010	GWAS Follow-Up
11	102565820	rs35616217	GWAS Follow-Up
11	102571892	rs2846365	GWAS Follow-Up
11	102576358	rs2846707	GWAS Follow-Up
11	102576375	rs1939015	GWAS Follow-Up
11	102576382	rs12099177	GWAS Follow-Up
11	102576468	rs11225389	GWAS Follow-Up
11	102584104	rs35866072	GWAS Follow-Up
11	102593248	rs1940475	GWAS Follow-Up
11	102595492	rs3765620	GWAS Follow-Up
11	102595579	rs17099450	GWAS Follow-Up
11	102611332	rs117446737	Candidate
11	102647536	rs2276108	Candidate
11	102649482	rs17860955	GWAS Follow-Up
11	102650389	rs17293607	GWAS Follow-Up
11	102650424	rs486055	GWAS Follow-Up
11	102651313	rs17435959	GWAS Follow-Up

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11	102658807	rs11604098	Candidate
11	102660097	rs11600510	Candidate
11	102679052	rs1144396	GWAS Follow-Up
11	102682285	rs1144397	GWAS Follow-Up
11	102682503	rs502174	GWAS Follow-Up
11	102691482	rs11225434	GWAS Follow-Up
11	102695108	rs495366	GWAS Follow-Up
11	102710707	rs476762	Candidate
11	102711338	rs591058	GWAS Follow-Up
11	102713620	rs679620	Candidate
11	102714716	rs617819	GWAS Follow-Up
11	102716321	rs645419	Candidate
11	102717641	rs116187470	Candidate
11	102719534	rs114176245	Candidate
11	102720678	rs615098	Candidate
11	102720945	rs626750	Candidate
11	102721251	rs72981675	GWAS Follow-Up
11	102721859	rs72981680	GWAS Follow-Up
11	102724211	rs72981684	Candidate
11	102724730	rs586701	GWAS Follow-Up
11	102730033	rs72983521	Candidate
11	102735103	rs476185	Candidate
11	102736419	rs651159	Candidate
11	102736642	rs652438	GWAS Follow-Up
11	102738075	rs17368582	GWAS Follow-Up
11	102742761	rs17368659	Candidate
11	102748695	rs17368814	Candidate
11	102752600	rs17368890	Candidate
11	102754868	rs61493282	Candidate
11	102760015	rs10791599	Candidate
11	102760093	rs11225450	Candidate
11	102760103	rs76380544	GWAS Follow-Up
11	102761173	rs11607785	Candidate
11	102763750	rs1940936	Candidate
11	102764093	rs72983552	Candidate
11	102773998	rs72983568	GWAS Follow-Up
11	102785041	rs72983581	GWAS Follow-Up
11	102785262	rs11225478	GWAS Follow-Up
11	102791399	rs2096767	GWAS Follow-Up
11	102791442	rs2096768	Candidate
11	102795606	rs1892971	Candidate
11	102800278	rs72985562	Candidate
11	102804933	rs7115014	GWAS Follow-Up
11	102806458	rs66740390	Candidate
11	102814110	rs1042840	Candidate

11	102835040	rs72987535	Candidate
11	102835942	rs575188	Candidate
11	102836480	rs72987546	Candidate
11	102837559	rs4572101	Candidate
11	105921407	rs56351451	Candidate
11	105921935	rs17093811	Candidate
11	106272434	rs71486048	GWAS Follow-Up
11	106285669	rs17552029	GWAS Follow-Up
11	116334862	rs66899922	GWAS Follow-Up
11	116339980	rs66633871	GWAS Follow-Up
11	116347396	rs12295901	GWAS Follow-Up
11	116347944	rs59414734	GWAS Follow-Up
11	116348168	rs2102405	GWAS Follow-Up
11	116362654	rs61906588	Candidate
11	116362669	rs61904777	Candidate
11	121239165	rs34266697	GWAS Follow-Up
11	134019675	rs11223715	GWAS Follow-Up
12	3473418	rs7132636	Candidate
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12	3474645	rs887357	Candidate
12	3743248	rs73045289	Candidate
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12	5031590	rs4766312	GWAS Follow-Up
12	5039830	rs4766313	GWAS Follow-Up
12	13399602	rs77723079	GWAS Follow-Up
12	13400296	rs12306669	GWAS Follow-Up
12	13400843	rs4763331	GWAS Follow-Up
12	13406688	rs10845727	GWAS Follow-Up
12	13410141	rs879112	GWAS Follow-Up
12	13410267	rs879111	GWAS Follow-Up
12	13424324	rs11055327	GWAS Follow-Up
12	13449078	rs10772647	GWAS Follow-Up
12	13449850	rs7312507	GWAS Follow-Up
12	28499875	rs11049546	GWAS Follow-Up
12	28520621	rs10843161	GWAS Follow-Up
12	28525437	rs11049560	GWAS Follow-Up
12	28536817	rs1552760	GWAS Follow-Up
12	28660345	rs10843190	GWAS Follow-Up
12	28709700	rs2203088	GWAS Follow-Up
12	28714095	rs11049714	GWAS Follow-Up
12	28717991	rs7137119	GWAS Follow-Up
12	28752354	rs1398377	GWAS Follow-Up
12	28755517	rs1996042	GWAS Follow-Up
12	28757415	rs117476787	GWAS Follow-Up
12	28758275	rs1512568	GWAS Follow-Up

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12	30424221	rs12833560	Candidate
12	30451922	rs6487897	Candidate
12	30521245	rs1267323	GWAS Follow-Up
12	30526045	rs7974875	GWAS Follow-Up
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12	48410517	rs6580649	GWAS Follow-Up
12	48457385	rs3742074	GWAS Follow-Up
12	48477086	rs7963934	GWAS Follow-Up
12	48478664	rs4589362	GWAS Follow-Up
12	48592792	rs11168455	GWAS Follow-Up
12	48592872	rs4760698	GWAS Follow-Up
12	48686741	rs2732487	GWAS Follow-Up
12	48690177	rs2732446	GWAS Follow-Up
12	48690363	rs2258342	GWAS Follow-Up
12	48744897	rs2634674	GWAS Follow-Up
12	52343480	rs61914028	Candidate
12	52352745	rs813470	GWAS Follow-Up
12	52356892	rs772222	GWAS Follow-Up
12	52358168	rs771997	Candidate
12	52358195	rs771998	GWAS Follow-Up
12	52362479	rs10876222	GWAS Follow-Up
12	52362786	rs10783486	Candidate
12	52369300	rs2242106	GWAS Follow-Up
12	52371341	rs11169971	GWAS Follow-Up
12	52381026	rs2252518	GWAS Follow-Up
12	52381230	rs2252526	GWAS Follow-Up
12	52383641	rs2453069	GWAS Follow-Up
12	52384811	rs2641530	GWAS Follow-Up
12	52388891	rs2854464	GWAS Follow-Up
12	52391833	rs2359997	GWAS Follow-Up
12	52392200	rs877869	GWAS Follow-Up
12	57390038	rs35493121	GWAS Follow-Up
12	57397033	rs61752546	GWAS Follow-Up
12	57397876	rs117805856	GWAS Follow-Up
12	57422934	rs17119344	GWAS Follow-Up
12	57457959	rs17546579	GWAS Follow-Up
12	57503775	rs167769	GWAS Follow-Up
12	57510511	rs2122692	Candidate
12	57510661	rs324013	Candidate
12	57513866	rs12322902	Candidate
12	57515363	rs12298170	Candidate
12	57527283	rs11172113	Candidate
12	57567762	rs1800194	GWAS Follow-Up
12	57616013	rs10783815	GWAS Follow-Up
12	57624701	rs73338162	GWAS Follow-Up

12	57648644	rs78607331	GWAS Follow-Up
12	62260866	rs2359979	GWAS Follow-Up
12	62264022	rs1031579	GWAS Follow-Up
12	63179248	rs11174649	GWAS Follow-Up
12	63179929	rs11174650	GWAS Follow-Up
12	63196133	rs73130066	GWAS Follow-Up
12	63199004	rs73130069	GWAS Follow-Up
12	63200121	rs11615499	GWAS Follow-Up
12	68430172	rs12231190	Candidate
12	71639539	rs76062993	GWAS Follow-Up
12	77282680	rs78008978	Candidate
12	85421258	rs11609891	Candidate
12	85428374	rs13377881	Candidate
12	85511005	rs11612337	Candidate
12	90311971	rs11105462	GWAS Follow-Up
12	90360364	rs4503596	GWAS Follow-Up
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12	95491530	rs11107893	Candidate
12	95493912	rs4762172	GWAS Follow-Up
12	95494760	rs4762452	Candidate
12	96124901	rs11108222	GWAS Follow-Up
12	96131895	rs17288108	GWAS Follow-Up
12	96149288	rs4341610	GWAS Follow-Up
12	96237095	rs7306887	Candidate
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12	96249111	rs117885456	Candidate
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12	96292170	rs75959092	GWAS Follow-Up
12	96312686	rs12368787	GWAS Follow-Up
12	96316396	rs11108337	Candidate
12	96323344	rs10161346	Candidate
12	96332684	rs7964411	Candidate
12	96332825	rs7967282	Candidate
12	96337183	rs7955450	GWAS Follow-Up
12	96350254	rs4762651	Candidate
12	96355432	rs7485085	Candidate
12	96359301	rs4762657	Candidate
12	96365672	rs7976204	Candidate
12	96374614	rs7297245	GWAS Follow-Up
12	96813866	rs7304605	GWAS Follow-Up
12	97916472	rs7963257	GWAS Follow-Up
12	103553204	rs2271934	GWAS Follow-Up

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12	103555364	rs1520186	GWAS Follow-Up
12	103557292	rs10778216	GWAS Follow-Up
12	103916279	rs73187844	GWAS Follow-Up
12	116120720	rs1386030	GWAS Follow-Up
12	116123751	rs9788243	GWAS Follow-Up
12	116124357	rs872770	GWAS Follow-Up
12	116125734	rs74664232	GWAS Follow-Up
12	116227853	rs73212689	GWAS Follow-Up
12	116228016	rs12307483	GWAS Follow-Up
12	116601058	rs10444487	Candidate
12	116705604	rs17614779	Candidate
12	116711987	rs75639744	Candidate
12	118011133	rs845753	GWAS Follow-Up
12	118011284	rs816202	GWAS Follow-Up
12	118624641	rs696345	Candidate
12	123018475	rs11615433	Candidate
12	124171658	rs7309528	Candidate
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12	124194438	rs2222060	Candidate
12	125664357	rs3751178	Candidate
12	125681761	rs12578774	GWAS Follow-Up
12	125699977	rs12828711	GWAS Follow-Up
12	133140237	rs4992763	GWAS Follow-Up
12	133140262	rs67435543	GWAS Follow-Up
12	133140840	rs12809318	GWAS Follow-Up
12	133141973	rs5023077	GWAS Follow-Up
12	133151607	rs11146943	GWAS Follow-Up
13	24656545	rs7329133	GWAS Follow-Up
13	27134495	rs75932629	GWAS Follow-Up
13	35136291	rs928076	Candidate
13	36387563	rs4943339	GWAS Follow-Up
13	36388348	rs7995297	GWAS Follow-Up
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13	36401576	rs9531098	Candidate
13	36598404	rs1578809	GWAS Follow-Up
13	53441955	rs9596699	GWAS Follow-Up
13	53478771	rs75111298	GWAS Follow-Up
13	53479898	rs75574154	GWAS Follow-Up
13	54061825	rs9536431	Candidate
13	54087218	rs79571557	Candidate
13	54114469	rs9536454	Candidate
13	54117075	rs9536455	Candidate
13	54132247	rs9536463	Candidate
13	54192030	rs9536482	GWAS Follow-Up

13	54227768	rs4884605	GWAS Follow-Up
13	54277828	rs2785828	GWAS Follow-Up
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13	69109747	rs73200286	Candidate
13	69117890	rs11840657	Candidate
13	69126008	rs17557610	Candidate
13	69133985	rs12874564	Candidate
13	72439407	rs1325340	Candidate
13	72449211	rs6562684	Candidate
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13	78906075	rs80110846	GWAS Follow-Up
13	78907306	rs75058988	GWAS Follow-Up
13	90484030	rs7989426	GWAS Follow-Up
13	90487155	rs1932306	GWAS Follow-Up
13	98205979	rs190040278	GWAS Follow-Up
13	98948140	rs9517248	GWAS Follow-Up
13	98948788	rs9513394	GWAS Follow-Up
13	106760961	rs1550602	GWAS Follow-Up
13	106767807	rs9558679	GWAS Follow-Up
13	106775049	rs4772755	GWAS Follow-Up
13	107119360	rs9520081	GWAS Follow-Up
13	107120452	rs61965324	GWAS Follow-Up
13	107120760	rs9520084	GWAS Follow-Up
13	107122961	rs9558771	GWAS Follow-Up
13	107125157	rs9583089	GWAS Follow-Up
13	107125691	rs2391297	GWAS Follow-Up
14	25109648	rs1951596	GWAS Follow-Up
14	25126957	rs5002199	GWAS Follow-Up
14	25128141	rs2025211	GWAS Follow-Up
14	25128180	rs17257138	GWAS Follow-Up
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14	26807298	rs12887777	Candidate
14	26807731	rs12892878	Candidate
14	34441865	rs946630	GWAS Follow-Up
14	34442649	rs1628940	GWAS Follow-Up
14	34483149	rs75543768	GWAS Follow-Up
14	36638655	rs2774166	GWAS Follow-Up
14	36639206	rs1820604	GWAS Follow-Up
14	36640638	rs1834855	GWAS Follow-Up
14	36666488	rs1766123	GWAS Follow-Up
14	36670083	rs946068	GWAS Follow-Up
14	36671982	rs1114365	GWAS Follow-Up
14	36672026	rs1114852	GWAS Follow-Up
14	42353448	rs7159901	GWAS Follow-Up

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14	42547909	rs12888716	GWAS Follow-Up
14	42548912	rs1542668	GWAS Follow-Up
14	53349798	rs11157933	GWAS Follow-Up
14	53353454	rs6572869	GWAS Follow-Up
14	62740092	rs7492698	GWAS Follow-Up
14	62742003	rs12894069	GWAS Follow-Up
14	63799152	rs1609564	GWAS Follow-Up
14	63809172	rs10133798	GWAS Follow-Up
14	63811976	rs12433479	GWAS Follow-Up
14	63813414	rs1956250	GWAS Follow-Up
14	63815860	rs8015217	GWAS Follow-Up
14	63816662	rs11628882	GWAS Follow-Up
14	63817304	rs6573510	GWAS Follow-Up
14	63818672	rs8012319	GWAS Follow-Up
14	63820672	rs10498507	GWAS Follow-Up
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14	66211250	rs8003811	Candidate
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14	66272647	rs6573632	GWAS Follow-Up
14	66272664	rs6573633	GWAS Follow-Up
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14	86661632	rs9635280	GWAS Follow-Up
14	93064786	rs76725931	Candidate
14	93072317	rs35629566	GWAS Follow-Up
14	93077611	rs72699818	GWAS Follow-Up
14	93096391	rs11623779	Candidate
14	93099867	rs4904964	Candidate
14	93102251	rs17184313	Candidate
14	93104072	rs11627032	GWAS Follow-Up
14	93111715	rs78242330	GWAS Follow-Up
14	93114787	rs72699866	Candidate
14	93115410	rs754388	GWAS Follow-Up
14	93116351	rs72699870	Candidate
14	93118229	rs117068593	GWAS Follow-Up
14	93155696	rs12435559	GWAS Follow-Up
14	93157126	rs12895951	GWAS Follow-Up
14	93160522	rs11849228	GWAS Follow-Up
14	93195374	rs17736427	GWAS Follow-Up
14	94672731	rs112458284	Candidate
14	94844947	rs28929474	Candidate
14	101235455	rs76006621	GWAS Follow-Up
14	101237738	rs78437025	GWAS Follow-Up
14	101239299	rs76859673	GWAS Follow-Up
14	102382347	rs7157928	GWAS Follow-Up
14	102383175	rs60089041	GWAS Follow-Up

15	49582017	rs62009832	GWAS Follow-Up
15	49755019	rs34377746	GWAS Follow-Up
15	49766857	rs35224895	GWAS Follow-Up
15	49876773	rs34605270	GWAS Follow-Up
15	49888242	rs12900911	GWAS Follow-Up
15	49921464	rs16962673	GWAS Follow-Up
15	49947688	rs11854482	GWAS Follow-Up
15	49955738	rs12906970	GWAS Follow-Up
15	49974412	rs62022673	GWAS Follow-Up
15	49977187	rs1507617	GWAS Follow-Up
15	49999463	rs72731157	GWAS Follow-Up
15	50003084	rs1843147	GWAS Follow-Up
15	55944517	rs572531	GWAS Follow-Up
15	55949749	rs10851589	GWAS Follow-Up
15	62717563	rs7179091	GWAS Follow-Up
15	62720363	rs10519148	GWAS Follow-Up
15	62721768	rs4775500	GWAS Follow-Up
15	62752174	rs11637267	GWAS Follow-Up
15	71551640	rs76818896	Candidate
15	71571345	rs7174934	GWAS Follow-Up
15	71599643	rs12917206	Candidate
15	71604250	rs10851838	Candidate
15	71608127	rs8023818	Candidate
15	71608619	rs17786786	Candidate
15	71609306	rs4337253	Candidate
15	71609522	rs6494904	Candidate
15	71610835	rs11855326	GWAS Follow-Up
15	71612303	rs1837762	Candidate
15	71612397	rs1441357	Candidate
15	71612514	rs1441358	Candidate
15	71621524	rs11853359	Candidate
15	71621562	rs11856837	Candidate
15	71621878	rs16955436	Candidate
15	71622863	rs11854933	Candidate
15	71624368	rs56379569	Candidate
15	71631920	rs12916138	Candidate
15	71635928	rs10851840	GWAS Follow-Up
15	71637848	rs2028467	Candidate
15	71639634	rs12915616	Candidate
15	71640371	rs16955470	GWAS Follow-Up
15	71641551	rs3759830	GWAS Follow-Up
15	71643083	rs60193973	GWAS Follow-Up
15	71643787	rs4777372	GWAS Follow-Up
15	71645120	rs12899618	Candidate
15	71645334	rs10459646	Candidate

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15	71645663	rs11852640	GWAS Follow-Up
15	71648497	rs2415115	Candidate
15	71649544	rs1913768	Candidate
15	71666166	rs1561711	Candidate
15	71667478	rs11072277	Candidate
15	71668140	rs11632680	Candidate
15	71668512	rs1568010	Candidate
15	71669115	rs11858454	Candidate
15	71669872	rs56308303	Candidate
15	71674189	rs7181363	Candidate
15	71676939	rs55865815	Candidate
15	71678178	rs1441355	Candidate
15	71678480	rs10851842	GWAS Follow-Up
15	71678963	rs7167951	GWAS Follow-Up
15	71688979	rs4531689	Candidate
15	71689855	rs4238435	Candidate
15	71699681	rs1441363	Candidate
15	71703827	rs35270398	Candidate
15	71715312	rs12595821	Candidate
15	71717044	rs6494924	GWAS Follow-Up
15	71719084	rs920549	Candidate
15	71719382	rs36098907	Candidate
15	71720944	rs7177932	Candidate
15	71722819	rs4776552	GWAS Follow-Up
15	71727876	rs12593944	Candidate
15	71728529	rs8027920	Candidate
15	71729913	rs12902368	Candidate
15	71730079	rs1441353	Candidate
15	71730197	rs1441354	Candidate
15	71730403	rs13380076	GWAS Follow-Up
15	71731515	rs8025197	Candidate
15	71734158	rs28579204	Candidate
15	71739969	rs11632301	Candidate
15	71740069	rs11632349	Candidate
15	71741898	rs62015860	Candidate
15	71802020	rs4316710	Candidate
15	71802897	rs4349101	Candidate
15	71803046	rs56081634	Candidate
15	71805006	rs7183859	Candidate
15	71862739	rs11072301	GWAS Follow-Up
15	71888643	rs77984977	GWAS Follow-Up
15	76083019	rs2655133	Candidate
15	78712699	rs4887053	Candidate
15	78718899	rs2869045	Candidate
15	78724469	rs1394371	Candidate

15	78731808	rs924840	GWAS Follow-Up
15	78733390	rs17483686	Candidate
15	78733731	rs17483721	GWAS Follow-Up
15	78739471	rs2915695	Candidate
15	78740233	rs2568493	Candidate
15	78740932	rs2656052	Candidate
15	78740964	rs2568494	Candidate
15	78742376	rs17483929	Candidate
15	78745343	rs2656071	Candidate
15	78750549	rs2656065	Candidate
15	78752188	rs72738732	GWAS Follow-Up
15	78754102	rs2009746	Candidate
15	78757913	rs2938674	GWAS Follow-Up
15	78766250	rs1504550	GWAS Follow-Up
15	78766629	rs1504549	GWAS Follow-Up
15	78767850	rs12910910	GWAS Follow-Up
15	78768871	rs8043227	GWAS Follow-Up
15	78769130	rs12916801	GWAS Follow-Up
15	78772676	rs17484524	Candidate
15	78774271	rs8042238	Candidate
15	78778972	rs12903295	GWAS Follow-Up
15	78779384	rs12904234	GWAS Follow-Up
15	78783277	rs11858836	Candidate
15	78789223	rs965604	GWAS Follow-Up
15	78792527	rs1062980	Candidate
15	78796282	rs5019044	GWAS Follow-Up
15	78802586	rs9788682	GWAS Follow-Up
15	78802869	rs9788721	GWAS Follow-Up
15	78806023	rs8034191	GWAS Follow-Up
15	78814681	rs7163730	GWAS Follow-Up
15	78815298	rs61204066	GWAS Follow-Up
15	78816057	rs8031948	GWAS Follow-Up
15	78826180	rs931794	Candidate
15	78828086	rs72738786	Candidate
15	78832349	rs56117933	GWAS Follow-Up
15	78833036	rs57064725	GWAS Follow-Up
15	78837673	rs28498264	GWAS Follow-Up
15	78845110	rs905739	GWAS Follow-Up
15	78849918	rs7173514	GWAS Follow-Up
15	78857896	rs503464	GWAS Follow-Up
15	78858400	rs684513	Candidate
15	78863472	rs667282	GWAS Follow-Up
15	78865197	rs17486195	Candidate
15	78867482	rs17486278	Candidate
15	78869930	rs495956	GWAS Follow-Up

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15	78870003	rs495090	Candidate
15	78874555	rs116991229	Candidate
15	78875623	rs1700006	GWAS Follow-Up
15	78877150	rs11637635	Candidate
15	78878541	rs951266	GWAS Follow-Up
15	78882925	rs16969968	Candidate
15	78883813	rs518425	Candidate
15	78888400	rs578776	Candidate
15	78894339	rs1051730	Candidate
15	78896129	rs1317286	Candidate
15	78898723	rs12914385	Candidate
15	78898932	rs55676755	Candidate
15	78907656	rs6495308	Candidate
15	78909070	rs4887069	Candidate
15	78910258	rs3825845	Candidate
15	78911181	rs8040868	GWAS Follow-Up
15	78912472	rs117832812	GWAS Follow-Up
15	78914534	rs8039449	Candidate
15	78915864	rs10851907	Candidate
15	78915872	rs55958997	Candidate
15	78920935	rs12593950	GWAS Follow-Up
15	78923845	rs28534575	GWAS Follow-Up
15	78923987	rs17487223	GWAS Follow-Up
15	78925435	rs4887072	GWAS Follow-Up
15	78926726	rs12440014	Candidate
15	78928264	rs12441088	GWAS Follow-Up
15	78928878	rs11636605	GWAS Follow-Up
15	78929372	rs12441998	GWAS Follow-Up
15	78930510	rs1316971	GWAS Follow-Up
15	78931057	rs9920506	Candidate
15	78934318	rs67426328	GWAS Follow-Up
15	78934551	rs3813567	Candidate
15	78936168	rs55988292	Candidate
15	78946633	rs12594247	GWAS Follow-Up
15	78948152	rs7181405	Candidate
15	78948319	rs11638830	Candidate
15	78952697	rs11072774	GWAS Follow-Up
15	78953464	rs12595350	GWAS Follow-Up
15	78953740	rs7163204	GWAS Follow-Up
15	78953919	rs7164665	GWAS Follow-Up
15	78960529	rs6495314	Candidate
15	78964362	rs12905641	Candidate
15	78965254	rs7178007	GWAS Follow-Up
15	78966655	rs11639372	Candidate
15	78967401	rs12902602	GWAS Follow-Up

15	78968268	rs11857532	GWAS Follow-Up
15	78978364	rs4887077	Candidate
15	78995801	rs12324870	GWAS Follow-Up
15	78997076	rs11072791	Candidate
15	79019024	rs11629637	Candidate
15	79019610	rs3813565	GWAS Follow-Up
15	79024016	rs11639181	GWAS Follow-Up
15	79034276	rs8031513	GWAS Follow-Up
15	79067951	rs7171916	Candidate
15	79068328	rs12906691	Candidate
15	79070438	rs12907764	Candidate
15	79071095	rs12913260	GWAS Follow-Up
15	79083814	rs11639044	GWAS Follow-Up
15	79089111	rs3825807	GWAS Follow-Up
15	79089734	rs7177699	Candidate
15	79090606	rs28610385	Candidate
15	79092750	rs7173267	GWAS Follow-Up
15	79094325	rs11856536	GWAS Follow-Up
15	79105350	rs11634042	GWAS Follow-Up
15	79107355	rs12907065	GWAS Follow-Up
15	79110302	rs9806363	Candidate
15	79111093	rs4380028	GWAS Follow-Up
15	79122948	rs72749206	GWAS Follow-Up
15	79123753	rs7182716	Candidate
15	80695115	rs2278701	GWAS Follow-Up
15	86139866	rs16942046	GWAS Follow-Up
15	86141702	rs56657677	GWAS Follow-Up
15	86194209	rs72764205	GWAS Follow-Up
15	86226666	rs7165537	GWAS Follow-Up
15	94282614	rs7495918	GWAS Follow-Up
15	94283185	rs11857245	GWAS Follow-Up
15	94681150	rs10468110	GWAS Follow-Up
15	96758020	rs74702350	GWAS Follow-Up
15	96758441	rs7167152	GWAS Follow-Up
15	96758498	rs7171335	GWAS Follow-Up
15	101315569	rs34659386	GWAS Follow-Up
15	101320663	rs34023462	GWAS Follow-Up
15	101560504	rs59609022	GWAS Follow-Up
15	101561092	rs11633278	GWAS Follow-Up
15	101713301	rs11634552	GWAS Follow-Up
15	101714653	rs1975753	GWAS Follow-Up
15	101720143	rs1993338	GWAS Follow-Up
15	101742965	rs12443106	GWAS Follow-Up
16	392392	rs118100148	Candidate
16	927873	rs8043613	GWAS Follow-Up

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16	931686	rs4984954	Candidate
16	932087	rs13334877	Candidate
16	16260443	rs8057824	GWAS Follow-Up
16	16268230	rs4577106	GWAS Follow-Up
16	16271409	rs9924755	GWAS Follow-Up
16	16273374	rs150465	GWAS Follow-Up
16	17128503	rs149143200	GWAS Follow-Up
16	17558034	rs62030329	GWAS Follow-Up
16	24853115	rs7195553	Candidate
16	25208036	rs62034915	GWAS Follow-Up
16	25209195	rs12325483	GWAS Follow-Up
16	26352382	rs7202468	GWAS Follow-Up
16	26357471	rs17581662	GWAS Follow-Up
16	26357720	rs17503574	GWAS Follow-Up
16	28490517	rs151181	GWAS Follow-Up
16	28499291	rs34835	GWAS Follow-Up
16	28510393	rs40834	GWAS Follow-Up
16	28510537	rs40836	GWAS Follow-Up
16	28510845	rs40837	GWAS Follow-Up
16	28517709	rs26528	GWAS Follow-Up
16	28519096	rs153109	GWAS Follow-Up
16	28536473	rs62034323	GWAS Follow-Up
16	28549823	rs151226	GWAS Follow-Up
16	28563026	rs151228	GWAS Follow-Up
16	28574615	rs480400	GWAS Follow-Up
16	28587389	rs7186573	GWAS Follow-Up
16	28593347	rs17707300	GWAS Follow-Up
16	28595700	rs17640009	GWAS Follow-Up
16	53724970	rs13334070	GWAS Follow-Up
16	53816275	rs8050136	GWAS Follow-Up
16	53899008	rs2024471	GWAS Follow-Up
16	53901208	rs12918206	GWAS Follow-Up
16	53901293	rs12918363	GWAS Follow-Up
16	53906851	rs7206324	GWAS Follow-Up
16	53906852	rs7188378	GWAS Follow-Up
16	53907347	rs9673307	GWAS Follow-Up
16	53909185	rs10521303	GWAS Follow-Up
16	53910195	rs4784328	GWAS Follow-Up
16	53910261	rs4784329	GWAS Follow-Up
16	53911023	rs7191718	GWAS Follow-Up
16	53911770	rs1362571	GWAS Follow-Up
16	53912364	rs8061064	GWAS Follow-Up
16	53914302	rs67386617	GWAS Follow-Up
16	53926790	rs17820875	GWAS Follow-Up
16	53927323	rs11076008	GWAS Follow-Up

16	53930993	rs12933928	GWAS Follow-Up
16	53933547	rs1362570	GWAS Follow-Up
16	53937632	rs2111112	GWAS Follow-Up
16	53963063	rs11864972	GWAS Follow-Up
16	54234313	rs12445261	GWAS Follow-Up
16	54238008	rs10153048	GWAS Follow-Up
16	57935442	rs112002818	GWAS Follow-Up
16	57935470	rs79889567	GWAS Follow-Up
16	57937788	rs2303785	GWAS Follow-Up
16	57949224	rs10459809	GWAS Follow-Up
16	57954448	rs2161703	GWAS Follow-Up
16	57957216	rs12927214	GWAS Follow-Up
16	57993841	rs61745888	GWAS Follow-Up
16	57996960	rs13336595	GWAS Follow-Up
16	58019396	rs9934227	GWAS Follow-Up
16	58054099	rs16959641	GWAS Follow-Up
16	58075282	rs12447804	Candidate
16	58252843	rs2550370	Candidate
16	69191420	rs13332128	GWAS Follow-Up
16	69277073	rs12933098	GWAS Follow-Up
16	70690166	rs4985555	GWAS Follow-Up
16	70804743	rs1551528	GWAS Follow-Up
16	70804766	rs1551529	GWAS Follow-Up
16	70826868	rs713511	GWAS Follow-Up
16	71790812	rs11075901	GWAS Follow-Up
16	71804287	rs7204967	GWAS Follow-Up
16	75247245	rs7202877	GWAS Follow-Up
16	75281964	rs1862737	GWAS Follow-Up
16	75301838	rs148519476	GWAS Follow-Up
16	75306890	rs12919951	Candidate
16	75313258	rs8050367	Candidate
16	75318988	rs66885758	Candidate
16	75340231	rs4888379	Candidate
16	75342846	rs10871308	Candidate
16	75344476	rs10514393	Candidate
16	75346788	rs1862705	Candidate
16	75347690	rs4888380	Candidate
16	75477714	rs37586	Candidate
16	75478051	rs72787179	Candidate
16	75481215	rs451589	Candidate
16	75497840	rs116475745	Candidate
16	75513433	rs118144424	GWAS Follow-Up
16	75563330	rs3826107	GWAS Follow-Up
16	75590092	rs3743601	GWAS Follow-Up
16	76898620	rs118068599	GWAS Follow-Up

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16	80298569	rs62049540	GWAS Follow-Up
16	80299191	rs13336279	GWAS Follow-Up
16	80405292	rs2881978	GWAS Follow-Up
16	80408261	rs1484027	GWAS Follow-Up
16	80441136	rs1126264	GWAS Follow-Up
16	80442198	rs9935300	GWAS Follow-Up
16	80500455	rs72820465	GWAS Follow-Up
16	80501358	rs72820466	GWAS Follow-Up
16	86445086	rs56177656	GWAS Follow-Up
16	86446344	rs12929431	GWAS Follow-Up
16	86447328	rs12446923	GWAS Follow-Up
16	86447371	rs12448517	GWAS Follow-Up
16	86455653	rs34830546	GWAS Follow-Up
16	86463695	rs2178146	GWAS Follow-Up
16	87701433	rs13333847	GWAS Follow-Up
16	87701468	rs13330384	GWAS Follow-Up
17	701827	rs504607	Candidate
17	704042	rs655377	Candidate
17	7363088	rs9217	GWAS Follow-Up
17	7366348	rs78260319	GWAS Follow-Up
17	7366619	rs34914463	GWAS Follow-Up
17	7402600	rs2228129	GWAS Follow-Up
17	7417663	rs6761	GWAS Follow-Up
17	7462969	rs3803800	GWAS Follow-Up
17	7468277	rs35596387	GWAS Follow-Up
17	7484101	rs9901673	GWAS Follow-Up
17	7484782	rs17607	GWAS Follow-Up
17	7484812	rs9901675	GWAS Follow-Up
17	7490810	rs10852891	GWAS Follow-Up
17	7495219	rs190521854	GWAS Follow-Up
17	7529902	rs13894	GWAS Follow-Up
17	7534678	rs6258	GWAS Follow-Up
17	7536527	rs6259	GWAS Follow-Up
17	7557419	rs1642763	GWAS Follow-Up
17	7592168	rs2287499	GWAS Follow-Up
17	7606722	rs7640	GWAS Follow-Up
17	7633692	rs16956936	GWAS Follow-Up
17	7637789	rs3744255	GWAS Follow-Up
17	7669761	rs35788701	GWAS Follow-Up
17	7674784	rs73232344	GWAS Follow-Up
17	7698599	rs4233018	GWAS Follow-Up
17	7721542	rs1105813	Candidate
17	12326885	rs237322	GWAS Follow-Up
17	12327922	rs34321002	GWAS Follow-Up
17	12329031	rs10521196	GWAS Follow-Up

17	12339928	rs237279	GWAS Follow-Up
17	15224673	rs2610065	GWAS Follow-Up
17	15226933	rs397523	GWAS Follow-Up
17	15230379	rs230899	GWAS Follow-Up
17	29111368	rs11867457	Candidate
17	34330987	rs75456429	GWAS Follow-Up
17	34336633	rs76141508	GWAS Follow-Up
17	35270922	rs55955238	Candidate
17	35274282	rs12185265	Candidate
17	35282364	rs10048172	Candidate
17	39078825	rs2269862	GWAS Follow-Up
17	39083591	rs3785768	GWAS Follow-Up
17	39191533	rs147545279	GWAS Follow-Up
17	39525750	rs12450621	GWAS Follow-Up
17	39607035	rs12449652	GWAS Follow-Up
17	43549526	rs17631676	GWAS Follow-Up
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17	43903842	rs62057151	Candidate
17	43907896	rs16940665	Candidate
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17	44791643	rs199438	GWAS Follow-Up
17	44795234	rs142167	Candidate
17	44800046	rs7224296	Candidate
17	44800110	rs199454	GWAS Follow-Up
17	44824213	rs199534	GWAS Follow-Up
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17	44836302	rs9912530	Candidate
17	44837217	rs199529	Candidate
17	44847707	rs199526	Candidate
17	44847834	rs199525	GWAS Follow-Up
17	44848517	rs199523	Candidate
17	44853456	rs199521	GWAS Follow-Up
17	44853924	rs199519	GWAS Follow-Up
17	44862613	rs199501	Candidate
17	44863133	rs916888	GWAS Follow-Up
17	44865439	rs2074404	Candidate
17	44865498	rs199499	GWAS Follow-Up
17	44865603	rs199498	GWAS Follow-Up
17	47056753	rs72833620	Candidate
17	47065115	rs68106312	Candidate
17	58125948	rs59950371	GWAS Follow-Up
17	59358141	rs35886429	GWAS Follow-Up
17	68937753	rs35883109	Candidate
17	68950506	rs4793515	Candidate

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17	68962577	rs11077536	Candidate
17	68978215	rs72864792	Candidate
17	69007761	rs4793324	Candidate
17	69073192	rs9898686	GWAS Follow-Up
17	69073670	rs68193035	GWAS Follow-Up
17	69074779	rs9906150	GWAS Follow-Up
17	69108753	rs1859962	GWAS Follow-Up
17	69125606	rs11654749	Candidate
17	69198109	rs2215050	Candidate
17	69233083	rs8076167	GWAS Follow-Up
17	70025377	rs73352505	GWAS Follow-Up
17	74498585	rs4238992	GWAS Follow-Up
17	75096857	rs2585851	GWAS Follow-Up
17	75099917	rs11077889	GWAS Follow-Up
17	75114727	rs485018	GWAS Follow-Up
17	76700063	rs7220955	GWAS Follow-Up
17	76751234	rs77154538	Candidate
17	76799795	rs1057040	GWAS Follow-Up
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17	76802344	rs34121152	GWAS Follow-Up
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17	76817090	rs3744793	GWAS Follow-Up
17	76893671	rs3744787	Candidate
17	77078069	rs12937557	GWAS Follow-Up
17	77081788	rs4789879	GWAS Follow-Up
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18	2287899	rs12458161	GWAS Follow-Up
18	8799709	rs4797331	GWAS Follow-Up
18	10889678	rs10853191	Candidate
18	10908861	rs11080467	Candidate
18	13843246	rs12956045	GWAS Follow-Up
18	20727611	rs4800452	Candidate
18	20731930	rs4239436	Candidate
18	20732224	rs4239437	Candidate
18	20744658	rs10853502	Candidate
18	20746829	rs28589524	Candidate
18	20748733	rs4800455	Candidate
18	20758310	rs34302357	Candidate
18	20815612	rs117025081	Candidate
18	23915553	rs41306966	GWAS Follow-Up
18	24007303	rs80005603	GWAS Follow-Up
18	24024531	rs4800259	GWAS Follow-Up
18	33191702	rs8096745	Candidate
18	33199916	rs12959333	Candidate
18	35105203	rs12607040	GWAS Follow-Up

18	35106036	rs55927401	GWAS Follow-Up
18	39815648	rs2126258	Candidate
18	39815876	rs2169382	Candidate
18	58430041	rs76388103	GWAS Follow-Up
18	62112791	rs2959494	GWAS Follow-Up
18	77052242	rs7239390	GWAS Follow-Up
18	77138068	rs3591	GWAS Follow-Up
19	8540260	rs7507621	GWAS Follow-Up
19	8547457	rs6603083	GWAS Follow-Up
19	8552167	rs12608524	GWAS Follow-Up
19	8557966	rs58034536	GWAS Follow-Up
19	13710380	rs503084	GWAS Follow-Up
19	21383250	rs8111954	GWAS Follow-Up
19	21383587	rs12973927	GWAS Follow-Up
19	21384253	rs8101643	GWAS Follow-Up
19	21393187	rs7248088	GWAS Follow-Up
19	21394226	rs4609982	GWAS Follow-Up
19	21398889	rs6511215	GWAS Follow-Up
19	32535207	rs2240660	GWAS Follow-Up
19	32545548	rs1001377	GWAS Follow-Up
19	32545763	rs1005161	GWAS Follow-Up
19	40329178	rs117967160	GWAS Follow-Up
19	40890840	rs73046355	GWAS Follow-Up
19	40898209	rs73046364	GWAS Follow-Up
19	41208981	rs2288451	Candidate
19	41218611	rs2604913	GWAS Follow-Up
19	41221513	rs4802085	GWAS Follow-Up
19	41225299	rs1469427	GWAS Follow-Up
19	41227968	rs890934	Candidate
19	41244887	rs2607420	Candidate
19	41246378	rs2290692	GWAS Follow-Up
19	41255500	rs2254343	GWAS Follow-Up
19	41256131	rs1870087	Candidate
19	41256519	rs1870086	GWAS Follow-Up
19	41257176	rs1457141	GWAS Follow-Up
19	41257816	rs2604874	GWAS Follow-Up
19	41269076	rs2305797	Candidate
19	41269288	rs2279011	Candidate
19	41283693	rs2604869	Candidate
19	41289397	rs12973666	GWAS Follow-Up
19	41291119	rs17726276	GWAS Follow-Up
19	41292404	rs2604894	GWAS Follow-Up
19	41295859	rs7245595	GWAS Follow-Up
19	41299015	rs2644898	Candidate
19	41301115	rs7252227	Candidate

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19	41302706	rs7937	Candidate
19	41302949	rs2644899	Candidate
19	41309150	rs117391664	Candidate
19	41310571	rs3733829	Candidate
19	41311922	rs117139969	Candidate
19	41313202	rs3736329	GWAS Follow-Up
19	41315318	rs4802091	GWAS Follow-Up
19	41318899	rs12052092	Candidate
19	41333441	rs4803378	Candidate
19	41340573	rs10853742	Candidate
19	41341589	rs7251418	Candidate
19	41356310	rs8192720	GWAS Follow-Up
19	41363765	rs8102683	Candidate
19	41363898	rs8105704	Candidate
19	41366134	rs1496402	GWAS Follow-Up
19	41393760	rs5007415	Candidate
19	41414481	rs72480748	Candidate
19	41546992	rs55927443	GWAS Follow-Up
19	41559511	rs73039249	GWAS Follow-Up
19	41734560	rs4803448	GWAS Follow-Up
19	41847860	rs1800472	Candidate
19	41869392	rs2241714	GWAS Follow-Up
19	41903220	rs10853751	GWAS Follow-Up
19	41938222	rs2231943	GWAS Follow-Up
19	41939297	rs1043413	GWAS Follow-Up
19	41944237	rs2231940	GWAS Follow-Up
19	41947635	rs7260605	GWAS Follow-Up
19	42034033	rs62119375	Candidate
19	42035481	rs73933643	Candidate
19	50271924	rs10404868	GWAS Follow-Up
19	50275358	rs12971721	GWAS Follow-Up
19	53351869	rs59829511	GWAS Follow-Up
19	53358889	rs6509698	GWAS Follow-Up
19	53374032	rs4803017	GWAS Follow-Up
19	54781541	rs450937	Candidate
19	54792761	rs386000	GWAS Follow-Up
19	54792769	rs386003	GWAS Follow-Up
19	54796719	rs384116	GWAS Follow-Up
19	54797848	rs103294	GWAS Follow-Up
19	56498629	rs306458	GWAS Follow-Up
19	56509695	rs417952	GWAS Follow-Up
20	2258798	rs6075875	Candidate
20	2259016	rs6106447	Candidate
20	3541382	rs17782078	GWAS Follow-Up
20	3562866	rs118065662	GWAS Follow-Up

20	3577062	rs3886999	GWAS Follow-Up
20	3651472	rs2853209	Candidate
20	3651765	rs3918396	GWAS Follow-Up
20	3655219	rs3918392	GWAS Follow-Up
20	3660597	rs4987245	Candidate
20	3667081	rs6084436	Candidate
20	3672046	rs143489222	GWAS Follow-Up
20	3674309	rs61734522	GWAS Follow-Up
20	3675333	rs3746638	GWAS Follow-Up
20	3675498	rs709012	GWAS Follow-Up
20	3682126	rs34924243	GWAS Follow-Up
20	3684729	rs625372	GWAS Follow-Up
20	3685032	rs74553328	Candidate
20	3686307	rs76788623	Candidate
20	3686436	rs6037651	GWAS Follow-Up
20	3726565	rs6076550	GWAS Follow-Up
20	3776175	rs3761218	GWAS Follow-Up
20	3784110	rs1056720	GWAS Follow-Up
20	3803446	rs6052095	GWAS Follow-Up
20	3827309	rs4815617	GWAS Follow-Up
20	3838441	rs17857295	GWAS Follow-Up
20	3843027	rs7262903	GWAS Follow-Up
20	3844929	rs45437096	GWAS Follow-Up
20	3846397	rs7269320	GWAS Follow-Up
20	10456485	rs857011	GWAS Follow-Up
20	18214242	rs2144143	GWAS Follow-Up
20	20233939	rs6046759	GWAS Follow-Up
20	20236581	rs6046764	GWAS Follow-Up
20	21615147	rs4813436	GWAS Follow-Up
20	21619401	rs6047531	GWAS Follow-Up
20	21620667	rs2424386	GWAS Follow-Up
20	21623633	rs2424388	GWAS Follow-Up
20	30699632	rs6058526	GWAS Follow-Up
20	30701513	rs2295034	GWAS Follow-Up
20	30747080	rs6061196	GWAS Follow-Up
20	30782543	rs1056776	GWAS Follow-Up
20	30797628	rs11905172	GWAS Follow-Up
20	30863169	rs67208722	GWAS Follow-Up
20	30892996	rs66948641	GWAS Follow-Up
20	30922399	rs13111	GWAS Follow-Up
20	31087935	rs80061974	GWAS Follow-Up
20	32296681	rs6057884	Candidate
20	38555808	rs2208649	GWAS Follow-Up
20	38570656	rs62212405	GWAS Follow-Up
20	44470575	rs148674138	GWAS Follow-Up

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20	44505973	rs2903808	GWAS Follow-Up
20	44511257	rs35972756	GWAS Follow-Up
20	44511533	rs3746500	GWAS Follow-Up
20	44512082	rs45447691	GWAS Follow-Up
20	44576502	rs7679	GWAS Follow-Up
20	44582435	rs41280276	GWAS Follow-Up
20	44596207	rs6032606	GWAS Follow-Up
20	44637635	rs144023823	GWAS Follow-Up
20	44640225	rs17576	GWAS Follow-Up
20	44642406	rs2250889	GWAS Follow-Up
20	44643111	rs17577	GWAS Follow-Up
20	44653107	rs6094238	Candidate
20	44664493	rs77659338	GWAS Follow-Up
20	44740196	rs6074022	GWAS Follow-Up
20	44747947	rs4810485	GWAS Follow-Up
20	48851333	rs6122892	GWAS Follow-Up
20	48867761	rs4811014	GWAS Follow-Up
20	55454659	rs6099314	GWAS Follow-Up
20	58353445	rs1182499	GWAS Follow-Up
20	59569156	rs4810215	Candidate
20	59570371	rs6124047	Candidate
20	59572324	rs13044193	Candidate
20	59581209	rs13036423	Candidate
20	59597631	rs34306377	Candidate
20	59612913	rs6129015	Candidate
20	59621304	rs4812257	Candidate
20	61015611	rs2427345	Candidate
21	19487468	rs2824630	GWAS Follow-Up
21	19488183	rs2824632	GWAS Follow-Up
21	19488826	rs2824634	GWAS Follow-Up
21	19488983	rs1491773	GWAS Follow-Up
21	19489216	rs1491772	GWAS Follow-Up
21	26206434	rs76554345	GWAS Follow-Up
21	26209468	rs78747692	GWAS Follow-Up
21	35468605	rs35707420	GWAS Follow-Up
21	35514749	rs61910679	GWAS Follow-Up
21	35515333	rs3746864	GWAS Follow-Up
21	35596002	rs6517219	Candidate
21	35599128	rs9982601	GWAS Follow-Up
21	35641215	rs73205216	Candidate
21	35652239	rs9978142	Candidate
21	35656197	rs2834438	Candidate
21	35690786	rs2834442	GWAS Follow-Up
21	35690852	rs73205245	Candidate
21	35699797	rs73900502	Candidate

21	35699798	rs73902803	Candidate
21	35757915	rs34016792	GWAS Follow-Up
21	35820324	rs11909074	GWAS Follow-Up
21	35825266	rs1012944	Candidate
21	40488747	rs447988	GWAS Follow-Up
22	17760183	rs56893401	GWAS Follow-Up
22	17781035	rs8140080	GWAS Follow-Up
22	17781555	rs4819994	GWAS Follow-Up
22	30614437	rs2078856	GWAS Follow-Up
22	33549485	rs713697	GWAS Follow-Up
22	33558767	rs2227080	GWAS Follow-Up
22	33559508	rs987640	GWAS Follow-Up
22	34397453	rs243243	GWAS Follow-Up
22	34400253	rs20065	GWAS Follow-Up
22	34400330	rs739029	GWAS Follow-Up
22	34414616	rs1874353	GWAS Follow-Up
22	35660875	rs1053593	GWAS Follow-Up
22	35663523	rs2413338	GWAS Follow-Up
22	35702704	rs117971694	Candidate
22	35711098	rs138777	GWAS Follow-Up
22	35728466	rs138786	GWAS Follow-Up
22	35796652	rs743813	Candidate
22	35802661	rs2307340	GWAS Follow-Up
22	35968294	rs5750118	Candidate
22	42980678	rs2285137	GWAS Follow-Up
22	45072514	rs916400	GWAS Follow-Up
22	45073320	rs75655022	GWAS Follow-Up
22	47099954	rs16995604	GWAS Follow-Up

Supplemental Table 1. SNP Provenance

SNPs tested in the moderate-to-severe (GOLD spirometric stage 2-4) and severe (GOLD spirometric stage 3-4) association analysis are ordered by chromosome (CHR) and base-pair position (BP). The Source column indicates the SNPs provenance for consideration in our analysis. "GWAS Follow-Up" refers to SNPs in regions derived from regions of genome-wide or sub-genome wide significance ($p < 1x10^{-4}$) in previous association studies of COPD; "Candidate" refers to SNPs in regions derived from SNPs investigated by Castaldi et al(10);

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SUPPLEMENTAL TABLE 2

rs ID	Chromosome	Base Position	Effect Allele	p-value	Odds Ratio	Upper 95% CI	Lower 95% CI	Effect Allele Frequency	Nearest Gene
rs6604615	1	218634362	T	$7.62x10^{-9}$	1.19	1.26	1.12	0.72	*TGFB2*
rs4416442	4	89866713	T	$1.84x10^{-17}$	0.79	0.84	0.75	0.57	*FAM13A*
rs13141641	4	145506456	T	$1.26x10^{-18}$	1.29	1.36	1.22	0.61	*HHIP*
rs754388	14	93115410	C	$3.62x10^{-8}$	1.22	1.31	1.14	0.83	*RIN3*
rs12914385	15	78898723	T	$7.50x10^{-22}$	1.31	1.38	1.24	0.58	*CHRNA3*
rs40834	16	28510393	T	$1.90x10^{-8}$	1.17	1.24	1.11	0.45	*IL27*

Supplemental Table 2. Genome-wide Significant Moderate-to-Severe COPD Associations

Most significant associations for GOLD spirometric stage II-IV COPD, organized by chromosome. In each case, the lead SNP for the locus is presented. Effect alleles represent the allele that is associated with the stated odds ratio for COPD-risk. Base Position was calculated using hg19 coordinates.

SUPPLEMENTAL TABLE 3

MODERATE-TO-SEVERE		COPDGene NHW		COPDGene AA		GenKOLS		ECLIPSE		NETT/NAS		TCGS Poland		TCGS Korea		ICGN		EOCOPD	
SNP	Allele	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control
rs6604615	T	0.761	0.739	0.558	0.536	0.780	0.802	0.737	0.774	0.735	0.779	0.791	0.749	0.252	0.253	0.765	0.714	0.775	0.765
rs4416442	T	0.569	0.624	0.444	0.466	0.603	0.554	0.648	0.562	0.645	0.563	0.531	0.560	0.396	0.511	0.576	0.620	0.583	0.607
rs13141641	T	0.622	0.573	0.897	0.879	0.534	0.586	0.522	0.603	0.578	0.657	0.576	0.476	0.718	0.671	0.635	0.596	0.699	0.652
rs754388	C	0.834	0.802	0.872	0.845	0.831	0.839	0.793	0.830	0.794	0.847	0.824	0.824	1.000	1.000	0.838	0.835	0.842	0.854
rs12914385	T	0.559	0.617	0.780	0.823	0.626	0.563	0.563	0.538	0.627	0.528	0.465	0.311	0.322	0.304	0.500	0.432	0.471	0.432
rs40834	T	0.477	0.441	0.385	0.369	0.491	0.491	0.424	0.471	0.419	0.462	0.433	0.516	0.312	0.269	0.474	0.419	0.448	0.439

SEVERE		COPDGene NHW		COPDGene AA		GenKols		ECLIPSE		NETT/NAS		Poland		Korea		ICGN		EOCOPD	
SNP	Allele	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control
rs1890995	A	0.240	0.275	0.319	0.361	0.240	0.206	0.275	0.234	0.275	0.234	0.214	0.254	0.779	0.767	0.236	0.297	0.233	0.246
rs4416442	T	0.562	0.624	0.418	0.466	0.603	0.542	0.645	0.563	0.645	0.563	0.531	0.560	0.396	0.511	0.575	0.620	0.582	0.607
rs13141641	T	0.636	0.573	0.915	0.879	0.534	0.599	0.578	0.657	0.578	0.657	0.576	0.476	0.718	0.671	0.636	0.596	0.711	0.652
rs6860095	A	0.775	0.737	0.709	0.650	0.728	0.766	0.707	0.748	0.707	0.748	0.765	0.738	0.117	0.112	0.755	0.734	0.769	0.757
rs679620	T	0.458	0.500	0.606	0.660	0.522	0.551	0.507	0.571	0.507	0.571	0.508	0.480	0.315	0.311	0.539	0.515	0.522	0.487
rs112458284	T	0.956	0.966	0.983	0.994	0.972	0.948	0.962	0.959	0.962	0.959	0.936	0.958	1.000	1.000	0.966	0.968	0.948	0.966
rs17486278	A	0.587	0.658	0.666	0.719	0.689	0.599	0.667	0.573	0.667	0.573	0.574	0.718	0.681	0.694	0.523	0.614	0.558	0.619

Supplemental Table 3a. Effect Allele Frequencies in Cases and Controls

ICGN = International COPD Genetics Network; ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points, GenKOLS = Genetics of Chronic Obstructive Lung Disease, Norway, NETT = National Emphysema Treatment Trial, NAS = Normative Aging Study, EOCOPD = Boston Early-Onset COPD Study, TCGS = Transcontinental COPD Genetics Study. Significantly associated SNPs are listed along with the effect allele. Allele frequencies of the effect alleles are listed in cases and controls in each study.

SEVERE		COPDGene NHW		COPDGene AA		GenKols		ECLIPSE		NETT/NAS		Poland		Korea		ICGN		EOCOPD	
SNP	Allele	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control
rs28929474	T	0.028	0.018	0.012	0.003	0.016	0.034	0.031	0.034	0.024	0.037	0.030	0.005	0.000	0.000	0.020	0.017	0.034	0.022

Supplemental Table 3b. Alpha-1 Antitrypsin Deficiency Z-Allele Frequencies in Cases and Controls

ICGN = International COPD Genetics Network; ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points, GenKOLS = Genetics of Chronic Obstructive Lung Disease, Norway, NETT = National Emphysema Treatment Trial, NAS = Normative Aging Study, EOCOPD = Boston Early-Onset COPD Study, TCGS = Transcontinental COPD Genetics Study. Significantly associated SNPs are listed along with the effect allele. Allele frequencies of the effect alleles are listed in cases and controls in each study.

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SUPPLEMENTAL TABLE 4

Previously Reported Variant					Lead Variant in Meta-Analysis		Linkage Disequilibrium Between Previously Reported and Lead Variants	
Chromosome	rsID	Base Position	Nearest Gene	Meta-analysis p-value	rsID	Meta-analysis p-value	r^2	D'
1	rs12745189	110186563	*GSTM1*	0.29	rs11102001‡	0.06	0.01	0.35
1	rs1554286	206944233	*IL10*	0.23	rs4845140‡	0.02	0.01	1.00
1	rs3738037	225965803	*EPHX1*	0.12	rs3738037	0.12	N/A	N/A
2	rs17736515	85866118	*SFTPB*	0.32	rs2001593	0.01	0.01	1.00
2	rs3917386	113579866	*IL1B*	0.11	rs4849140‡	3.64×10^{-3}	0.03	1.00
2	rs16865545	224947170	*SERPINE2*	0.34	rs34078713	0.24	0.03	1.00
2	**rs7580152**	**229892748**	***PID1***	**0.03**	rs11903631‡	3.89×10^{-3}	0.00	0.21
4	rs17622933	24790680	*SOD3*	0.75	rs8192287	0.08	0.12	1.00
4	rs9291163	72699705	*GC*	0.23	rs72607837‡	0.06	0.07	1.00
5	rs11134242	7564015	*ADCY2*	0.10	rs6881726	1.97×10^{-3}	0.02	0.44
5	rs20541	131995964	*IL13*	0.62	rs17690923‡	0.05	0.02	0.41
5	**rs17108817**	**148215902**	***ADRB2***	**0.01**	rs17108817‡	0.01	N/A	N/A
6	rs2736172	31590898	*TNF*	0.28	rs2763977	0.01	0.17	0.94
6	rs12206691	39748040	*DAAM2*	0.33	rs2446651‡	2.77×10^{-3}	0.00	1.00
9	rs8176707	136135108	*ABO*	0.19	rs2285487‡	8.09×10^{-4}	0.01	0.82
11	rs676653	67339536	*GSTP1*	0.61	rs72936320‡	3.59×10^{-5}	0.00	0.12
11	**rs645419**	**102716321**	***MMP1/MMP12***	**1.36×10^{-5}**	rs679620‡	3.56×10^{-6}	1.00	1.00
17	rs6258	7534678	*TP53*	0.80	rs1105813‡	0.01	0.00	0.12
17	rs3744787	76893671	*TIMP2*	0.72	rs12937557	0.02	0.01	1.00
19	rs1800472	41847860	*TGFB1*	0.12	rs62119375‡	0.04	0.00	1.00
20	**rs2853209**	**3651472**	***ADAM33***	**2.06×10^{-3}**	rs2853209‡	2.06×10^{-3}	N/A	N/A
20	**rs6094238**	**44653107**	***MMP9***	**0.01**	rs6094238‡	0.01	N/A	N/A
22	rs743813	35796652	*HMOX1*	0.89	rs5750118‡	0.01	0.03	0.17

Supplemental Table 4. Additional Candidate Genes

For each previously reported variant and lead variant, the p-value refers to the association with moderate-to-severe COPD in our analysis. Nominally significant associations (p<0.05) among previously reported variants are shown in bold. Lead variants marked with ‡ had a smaller P-value than the top-ranked SNP in the analogous locus in the gene-based investigation by Castaldi et al(10).

SUPPLEMENTAL TABLE 5

rsID	Chromosome	Base Pair Position	Gene Locus	Allele1	Allele2	COPD7 Score
rs2284746	1	17306675	*MFAP2*	G	C	
rs4846480	1	218598469	*TGFB2*	A	T	**X**
rs993925	1	218860068	*TGFB2-LYPLAL1*	C	T	
rs7594321	2	230224031	*DNER*	C	T	
rs12477314	2	239877148	*HDAC4-FLJ43879*	C	T	
rs1529672	3	25520582	*RARB*	A	C	
rs1344555	3	169300219	*MECOM/EVI1*	T	C	
rs4416442	4	89866713	*FAM13A*	C	T	**X**
rs10516526	4	106688904	*GSTCD/INTS12/ NPNT*	A	G	
rs13141641	4	145506456	*HHIP*	C	T	**X**
rs153916	5	95036700	*SPATA9-RHOBTB3*	T	C	
rs11168048	5	147842353	*HTR4*	C	T	
rs6903823	6	28322296	*ZKSCAN3*	A	G	
rs2857595	6	31568469	*NCR3-AIF1*	G	A	
rs2070600	6	32151443	*AGER/PPT2*	T	C	
rs7765379	6	32680928	*HLA-DQB1*	G	T	
rs2798641	6	109268050	*ARMC2*	C	T	
rs3817928	6	142750516	*GPR126*	A	G	
rs16909898	9	98231008	*PTCH1*	A	G	
rs7068966	10	12277992	*CDC123*	C	T	
rs11001819	10	78315224	*C10orf11*	A	G	
rs626750	11	102720945	*MMP12*	G	A	**X**
rs11172113	12	57527283	*LRP1*	C	T	
rs754388	14	93115410	*RIN3*	C	G	**X**
rs12899618	15	71645120	*THSD4*	A	G	
rs12914385	15	78898723	*CHRNA3*	C	T	**X**
rs12447804	16	58075282	*MMP15*	C	T	
rs11654749	17	69125606	*KCNJ2/ CASC17*	G	T	
rs7937	19	41302706	*RAB4B/ EGLN2/ MIA/CYP2A6*	C	T	**X**
rs9978142	21	35652239	*KCNE2-LINC00310/ C21orf82*	A	T	

Supplemental Table 5. COPD7 and LUNG30 Risk Score Loci

rsID, chromosome, position, gene locus, and the two alleles for each risk score SNP in the LUNG30 score are shown in the table above. SNPs included in the COPD7 score are marked in the COPD7 Score column.

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SUPPLEMENTAL TABLE 6

	FEV_1 % per Risk Allele (adjusted)	p-value
COPD7	-2.40 (-2.02, -2.79)	$<2.0x10^{-16}$
LUNG30	-1.11 (-0.92,-1.29)	$<2.0x10^{-16}$

Supplemental Table 6a. Genetic Risk Scores: Lung Function in COPDGene NHW

For each risk score (COPD7, FX25, and LUNG30), the linear mixed model coefficient is presented with 95% confidence interval in parentheses and p-value. Final model included adjustment for age, pack years, and principal components for genetic ancestry. FEV_1 % represents the unit change in FEV_1 percent predicted.COPD7: 7 COPD risk SNPs (14 risk alleles); LUNG30: 30 COPD and lung function SNPs (60 risk alleles.)

		Moderate COPD	p-value	Severe COPD	p-value
COPD7	OR per Risk Allele	1.22 (1.17, 1.26)	$3.17x10^{-27}$	1.30 (1.24, 1.36)	$4.61x10^{-30}$
	AUC	0.61 (0.60, 0.63)		0.65 (0.63, 0.66)	
	NRI	0.094 (0.070-0.118)	$9.85x10^{-15}$	0.103 (0.073, 0.133)	$2.01x10^{-11}$
	Event NRI	4.34%		9.57%	
	Nonevent NRI	5.05%		0.75%	
LUNG30	OR per Risk Allele	1.09 (1.07, 1.11)	$3.70x10^{-24}$	1.12 (1.09, 1.14)	$9.19x10^{-24}$
	AUC	0.61 (0.59, 0.62)		0.64 (0.62, 0.65)	
	NRI	0.095 (0.071, 0.118)	$5.97x10^{-15}$	0.098 (0.068, 0.127)	$7.65x10^{-11}$
	Event NRI	4.48%		8.56%	
	Nonevent NRI	4.97%		1.18%	

Supplemental Table 6b. Genetic Risk Scores: Affection Status in COPDGene NHW

For each risk score (COPD7, FX25, and LUNG30), OR represents the odds ratio of each additional risk allele on the outcome of either Moderate COPD (GOLD II-IV) or Severe COPD (GOLD III-IV). AUC represents Area Under the Curve of a model including only the genetic data of risk score alleles adjusted for principal components of genetic ancestry. NRI represents the three-tiered net reclassification index value of the model combining genetic risk score, age, pack-years of smoking, and principal components of genetic ancestry compared to the model containing age and pack-years alone. Event NRI represents the percentage of subjects with the outcome of COPD adding correctly reclassified to a higher risk group after adding genetic data. Nonevent NRI represents the percentage of subjects without the outcome of COPD correctly reclassified to a lower risk group after genetic data. Data is presented with 95% confidence intervals in parentheses. COPD7: 14 COPD risk alleles; LUNG30: 60 COPD and lung function risk alleles

SUPPLEMENTAL TABLE 7

	FEV_1 % per Risk Allele (adjusted)	p-value
COPD7	-3.51 (-1.92,-5.09)	$1.65x10^{-7}$
LUNG30	-2.69 (-1.84, -3.54)	$8.56x10^{-10}$

Supplemental Table 7a. Genetic Risk Scores: Lung Function in TCGS Poland

For each risk score (COPD7 and LUNG30), the linear mixed model coefficient is presented with 95% confidence interval in parentheses and p-value. Final model included adjustment for age, pack years, and principal components for genetic ancestry. FEV_1 % represents the unit change in FEV_1 percent predicted.COPD7: 7 COPD risk SNPs (14 risk alleles); LUNG30: 30 COPD and lung function SNPs (60 risk alleles.)

		Severe COPD	p-value
COPD7	OR per Risk Allele	1.25 (1.13, 1.38)	$9.30x10^{-6}$
	AUC	0.62 (0.58, 0.67)	
	NRI	0.157 (0.080-0.233)	$6.20x10^{-5}$
	Event NRI	3.28%	
	Nonevent NRI	12.38%	
LUNG30	OR per Risk Allele	1.17 (1.11, 1.24)	$2.25x10^{-8}$
	AUC	0.64 (0.60, 0.68)	
	NRI	0.183 (0.095, 0.271)	$4.50x10^{-5}$
	Event NRI	3.95%	
	Nonevent NRI	14%	

Supplemental Table 7b. Genetic Risk Scores: Affection Status in TCGS Poland

For each risk score (COPD7 and LUNG30), OR represents the odds ratio of each additional risk allele on the outcome of either Moderate COPD (GOLD II-IV) or Severe COPD (GOLD III-IV). AUC represents Area Under the Curve of a model including only the genetic data of risk score alleles adjusted for principal components of genetic ancestry. NRI represents the three-tiered net reclassification index value of the model combining genetic risk score, age, pack-years of smoking, and principal components of genetic ancestry compared to the model containing age and pack-years alone. Event NRI represents the percentage of subjects with the outcome of COPD adding correctly reclassified to a higher risk group after adding genetic data. Nonevent NRI represents the percentage of subjects without the outcome of COPD correctly reclassified to a lower risk group after genetic data. Data is presented with 95% confidence intervals in parentheses. COPD7: 14 COPD risk alleles; LUNG30: 60 COPD and lung function risk alleles

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SUPPLEMENTAL TABLE 8

KEGG Pathway Name	p-value	FDR-corrected q-value
Pathways in cancer - Homo sapiens (human)	0.0004	0.0077
Malaria - Homo sapiens (human)	0.0066	0.0308
Hedgehog signaling pathway - Homo sapiens (human)	0.0071	0.0308
Basal cell carcinoma - Homo sapiens (human)	0.0083	0.0308

Supplemental Table 8a. LUNG30 Score KEGG Pathway Enrichment

Pathway enrichment among Kyoto Encyclopedia of Genes and Genomes pathways was performed using the online tool ConsensusPathDB. KEGG pathway name is presented with p-value and FDR-corrected q-value.

Reactome Pathway Name	p-value	FDR-corrected q-value
Ligand-receptor interactions	0.0002	0.0069
Molecules associated with elastic fibres	0.0025	0.0235
Collagen degradation	0.0030	0.0235
Elastic fibre formation	0.0034	0.0235
Extracellular matrix organization	0.0039	0.0235
Hedgehog ,on, state	0.0040	0.0235

Supplemental Table 8b. LUNG30 Score Reactome Pathway Enrichment

Pathway enrichment among Reactome pathways was performed using the online tool ConsensusPathDB. Reactome Pathway name is presented with p-value and FDR-corrected q-value.

GO Biological Process Ontology Term	p-value	FDR-corrected q-value	GO Identifier	GO Level
response to endogenous stimulus	9.04E-05	0.0028	GO:0009719	2
cell proliferation	0.0001	0.0028	GO:0008283	2
response to abiotic stimulus	0.0010	0.0143	GO:0009628	2
cellular component organization	0.0014	0.0143	GO:0016043	2
response to chemical	0.0016	0.0143	GO:0042221	2
cellular response to stimulus	0.0017	0.0143	GO:0051716	2
anatomical structure morphogenesis	0.0020	0.0143	GO:0009653	2
single organism signaling	0.0025	0.0153	GO:0044700	2
single-organism cellular process	0.0065	0.0334	GO:0044763	2
cell motility	0.0078	0.0334	GO:0048870	2
localization of cell	0.0078	0.0334	GO:0051674	2
regulation of molecular function	0.0082	0.0334	GO:0065009	2
muscle adaptation	0.0087	0.0334	GO:0043500	2

leukocyte homeostasis	0.0098	0.0352	GO:0001776	2
response to drug	8.47E-07	0.0001	GO:0042493	3
extracellular structure organization	7.66E-05	0.0050	GO:0043062	3
positive regulation of biological process	0.0001	0.0050	GO:0048518	3
muscle cell proliferation	0.0001	0.0050	GO:0033002	3
tissue development	0.0003	0.0086	GO:0009888	3
cellular response to chemical stimulus	0.0005	0.0124	GO:0070887	3
tube development	0.0008	0.0187	GO:0035295	3
response to organic substance	0.0009	0.0187	GO:0010033	3
response to hormone	0.0013	0.0227	GO:0009725	3
heart development	0.0016	0.0251	GO:0007507	3
multicellular organismal metabolic process	0.0022	0.0312	GO:0044236	3
regulation of localization	0.0024	0.0312	GO:0032879	3
appendage morphogenesis	0.0027	0.0329	GO:0035107	3
positive regulation of molecular function	0.0033	0.0329	GO:0044093	3
regulation of multicellular organismal process	0.0035	0.0329	GO:0051239	3
epithelial cell proliferation	0.0039	0.0329	GO:0050673	3
appendage development	0.0039	0.0329	GO:0048736	3
cell adhesion mediated by integrin	0.0041	0.0329	GO:0033627	3
cellular potassium ion transport	0.0042	0.0329	GO:0071804	3
embryonic morphogenesis	0.0046	0.0329	GO:0048598	3
ossification	0.0047	0.0329	GO:0001503	3
cellular response to endogenous stimulus	0.0047	0.0329	GO:0071495	3
cell migration	0.0050	0.0329	GO:0016477	3
regulation of developmental process	0.0050	0.0329	GO:0050793	3
tissue morphogenesis	0.0052	0.0329	GO:0048729	3
regulation of cell killing	0.0056	0.0345	GO:0031341	3
response to mechanical stimulus	0.0060	0.0353	GO:0009612	3
organ morphogenesis	0.0068	0.0382	GO:0009887	3
morphogenesis of a branching structure	0.0071	0.0382	GO:0001763	3
organ development	0.0072	0.0382	GO:0048513	3
cellular developmental process	0.0087	0.0400	GO:0048869	3
embryonic organ development	0.0087	0.0400	GO:0048568	3
nephron morphogenesis	0.0094	0.0400	GO:0072028	3
regulation of response to stimulus	0.0094	0.0400	GO:0048583	3
regulation of locomotion	0.0094	0.0400	GO:0040012	3
response to transforming growth factor beta	0.0097	0.0400	GO:0071559	3
head development	0.0097	0.0400	GO:0060322	3
reactive oxygen species metabolic process	0.0099	0.0400	GO:0072593	3
muscle cell migration	2.84E-06	0.0006	GO:0014812	4
regulation of system process	1.26E-05	0.0014	GO:0044057	4

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extracellular matrix organization	7.55E-05	0.0045	GO:0030198	4
response to steroid hormone	9.95E-05	0.0045	GO:0048545	4
response to organic cyclic compound	0.0001	0.0045	GO:0014070	4
neuron death	0.0001	0.0054	GO:0070997	4
regulation of cellular component movement	0.0003	0.0088	GO:0051270	4
regulation of ossification	0.0003	0.0088	GO:0030278	4
muscle system process	0.0005	0.0115	GO:0003012	4
smooth muscle cell proliferation	0.0006	0.0133	GO:0048659	4
mesonephric tubule development	0.0009	0.0154	GO:0072164	4
positive regulation of metabolic process	0.0009	0.0154	GO:0009893	4
mesonephros development	0.0010	0.0154	GO:0001823	4
negative regulation of developmental process	0.0010	0.0154	GO:0051093	4
regulation of heart rate by cardiac conduction	0.0012	0.0158	GO:0086091	4
regulation of membrane repolarization	0.0012	0.0158	GO:0060306	4
regulation of cell proliferation	0.0013	0.0167	GO:0042127	4
regulation of cell differentiation	0.0014	0.0171	GO:0045595	4
multicellular organismal macromolecule metabolic process	0.0016	0.0179	GO:0044259	4
morphogenesis of an epithelium	0.0018	0.0179	GO:0002009	4
embryonic appendage morphogenesis	0.0018	0.0179	GO:0035113	4
membrane repolarization	0.0018	0.0179	GO:0086009	4
renal system development	0.0019	0.0179	GO:0072001	4
membrane invagination	0.0022	0.0189	GO:0010324	4
embryonic digestive tract development	0.0022	0.0189	GO:0048566	4
limb morphogenesis	0.0027	0.0226	GO:0035108	4
urogenital system development	0.0030	0.0235	GO:0001655	4
vesicle-mediated transport	0.0031	0.0235	GO:0016192	4
response to lipid	0.0031	0.0235	GO:0033993	4
epithelium development	0.0034	0.0248	GO:0060429	4
branching morphogenesis of an epithelial tube	0.0035	0.0248	GO:0048754	4
limb development	0.0039	0.0255	GO:0060173	4
regulation of transport	0.0040	0.0255	GO:0051049	4
cellular response to organic substance	0.0041	0.0255	GO:0071310	4
potassium ion transmembrane transport	0.0042	0.0255	GO:0071805	4
muscle tissue development	0.0042	0.0255	GO:0060537	4
cell differentiation	0.0044	0.0256	GO:0030154	4
positive regulation of cellular process	0.0051	0.0261	GO:0048522	4
positive regulation of locomotion	0.0051	0.0261	GO:0040017	4
positive regulation of transport	0.0052	0.0261	GO:0051050	4
regulation of cell adhesion	0.0052	0.0261	GO:0030155	4
regulation of muscle adaptation	0.0053	0.0261	GO:0043502	4
nervous system development	0.0055	0.0261	GO:0007399	4

cellular response to drug	0.0056	0.0261	GO:0035690	4
inflammatory response	0.0058	0.0261	GO:0006954	4
cardiac conduction	0.0058	0.0261	GO:0061337	4
morphogenesis of a branching epithelium	0.0059	0.0261	GO:0061138	4
cardiovascular system development	0.0059	0.0261	GO:0072358	4
circulatory system development	0.0059	0.0261	GO:0072359	4
regulation of cell death	0.0060	0.0261	GO:0010941	4
regulation of cell motility	0.0063	0.0269	GO:2000145	4
signal transduction	0.0066	0.0276	GO:0007165	4
heart morphogenesis	0.0075	0.0306	GO:0003007	4
circulatory system process	0.0077	0.0306	GO:0003013	4
skeletal system morphogenesis	0.0078	0.0306	GO:0048705	4
cellular response to mechanical stimulus	0.0080	0.0306	GO:0071260	4
positive regulation of transporter activity	0.0080	0.0306	GO:0032411	4
negative regulation of multicellular organismal process	0.0082	0.0306	GO:0051241	4
phagocytosis	0.0084	0.0309	GO:0006909	4
collagen catabolic process	0.0091	0.0331	GO:0030574	4
negative regulation of locomotion	0.0096	0.0335	GO:0040013	4
cellular response to transforming growth factor beta stimulus	0.0096	0.0335	GO:0071560	4
negative regulation of response to stimulus	0.0100	0.0340	GO:0048585	4
regulation of muscle system process	1.71E-06	0.0002	GO:0090257	5
neuron apoptotic process	4.63E-05	0.0025	GO:0051402	5
hindlimb morphogenesis	5.26E-05	0.0025	GO:0035137	5
regulation of neuron death	7.97E-05	0.0029	GO:1901214	5
heart process	0.0004	0.0110	GO:0003015	5
macromolecule deacylation	0.0005	0.0112	GO:0098732	5
regulation of smooth muscle cell proliferation	0.0006	0.0112	GO:0048660	5
positive regulation of cell proliferation	0.0007	0.0112	GO:0008284	5
ureteric bud development	0.0008	0.0112	GO:0001657	5
regulation of blood circulation	0.0009	0.0112	GO:1903522	5
negative regulation of cartilage development	0.0010	0.0112	GO:0061037	5
negative regulation of cell proliferation	0.0010	0.0112	GO:0008285	5
regulation of osteoblast differentiation	0.0011	0.0112	GO:0045667	5
positive regulation of biosynthetic process	0.0011	0.0112	GO:0009891	5
phagocytosis, engulfment	0.0013	0.0124	GO:0006911	5
collagen metabolic process	0.0014	0.0124	GO:0032963	5
positive regulation of epidermis development	0.0016	0.0135	GO:0045684	5
potassium ion import	0.0017	0.0135	GO:0010107	5

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embryonic limb morphogenesis	0.0018	0.0135	GO:0030326	5
regulation of epithelial cell proliferation	0.0019	0.0138	GO:0050678	5
embryonic eye morphogenesis	0.0021	0.0138	GO:0048048	5
muscle contraction	0.0021	0.0138	GO:0006936	5
kidney epithelium development	0.0023	0.0144	GO:0072073	5
positive regulation of macromolecule metabolic process	0.0026	0.0149	GO:0010604	5
regulation of cell development	0.0027	0.0149	GO:0060284	5
regulation of reactive oxygen species metabolic process	0.0027	0.0149	GO:2000377	5
cardiac muscle cell action potential	0.0034	0.0173	GO:0086001	5
positive regulation of cell differentiation	0.0034	0.0173	GO:0045597	5
regulation of actin filament-based movement	0.0036	0.0175	GO:1903115	5
striated muscle tissue development	0.0037	0.0175	GO:0014706	5
positive regulation of nitrogen compound metabolic process	0.0040	0.0182	GO:0051173	5
regulation of programmed cell death	0.0042	0.0182	GO:0043067	5
positive regulation of cellular metabolic process	0.0043	0.0182	GO:0031325	5
muscle cell differentiation	0.0044	0.0182	GO:0042692	5
positive regulation of cell adhesion	0.0045	0.0182	GO:0045785	5
positive regulation of cellular component movement	0.0047	0.0182	GO:0051272	5
cellular response to organic cyclic compound	0.0047	0.0182	GO:0071407	5
neurogenesis	0.0055	0.0200	GO:0022008	5
regulation of epidermis development	0.0058	0.0200	GO:0045682	5
response to estrogen	0.0059	0.0200	GO:0043627	5
endocytosis	0.0059	0.0200	GO:0006897	5
regulation of reactive oxygen species biosynthetic process	0.0060	0.0200	GO:1903426	5
regulation of cartilage development	0.0060	0.0200	GO:0061035	5
osteoblast differentiation	0.0063	0.0206	GO:0001649	5
negative regulation of cellular component movement	0.0073	0.0218	GO:0051271	5
negative regulation of ossification	0.0074	0.0218	GO:0030279	5
regulation of smoothened signaling pathway	0.0074	0.0218	GO:0008589	5
blood circulation	0.0076	0.0218	GO:0008015	5
regulation of phosphorus metabolic process	0.0076	0.0218	GO:0051174	5
regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	0.0076	0.0218	GO:0090092	5
regulation of plasma membrane organization	0.0078	0.0219	GO:1903729	5

negative regulation of cell differentiation	0.0084	0.0232	GO:0045596	5
nephron epithelium morphogenesis	0.0089	0.0241	GO:0072088	5

Supplemental Table 8c. LUNG30 Score Gene Ontology Biological Process Enrichment

Enrichment among Gene Ontology (GO) terms within the Biological Processes ontology was performed using the online tool ConsensusPathDB. The GO term is presented with p-value, FDR-corrected q-value, GO identifier, and GO Level.

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SUPPLEMENTAL TABLE 9

Tissue Type	p-value
Appendix	0.0017
Trigeminal_Ganglion	0.0078
Superior_Cervical_Ganglion	0.0176
Fetal_Lung	0.0238
Cardiac_Myocytes	0.0241
Olfactory_Bulb	0.0287
Placenta	0.0484
Fetal_Thyroid	0.0545
Trachea	0.0548
Smooth_Muscle	0.0551
Skeletal_Muscle	0.0680
Lymphoma_Burkitts_Daudi	0.0746
Testis_Leydig_cell	0.0793
Salivary_Gland	0.0859

Supplemental Table 9. SNPsea tissue-specific enrichment of gene expression

Listed tissue types represent tissues enriched for gene expression of genes in linkage disequilibrium with LUNG30 risk SNPs. P-values were calculated against null distributions as per the SNPsea algorithm.

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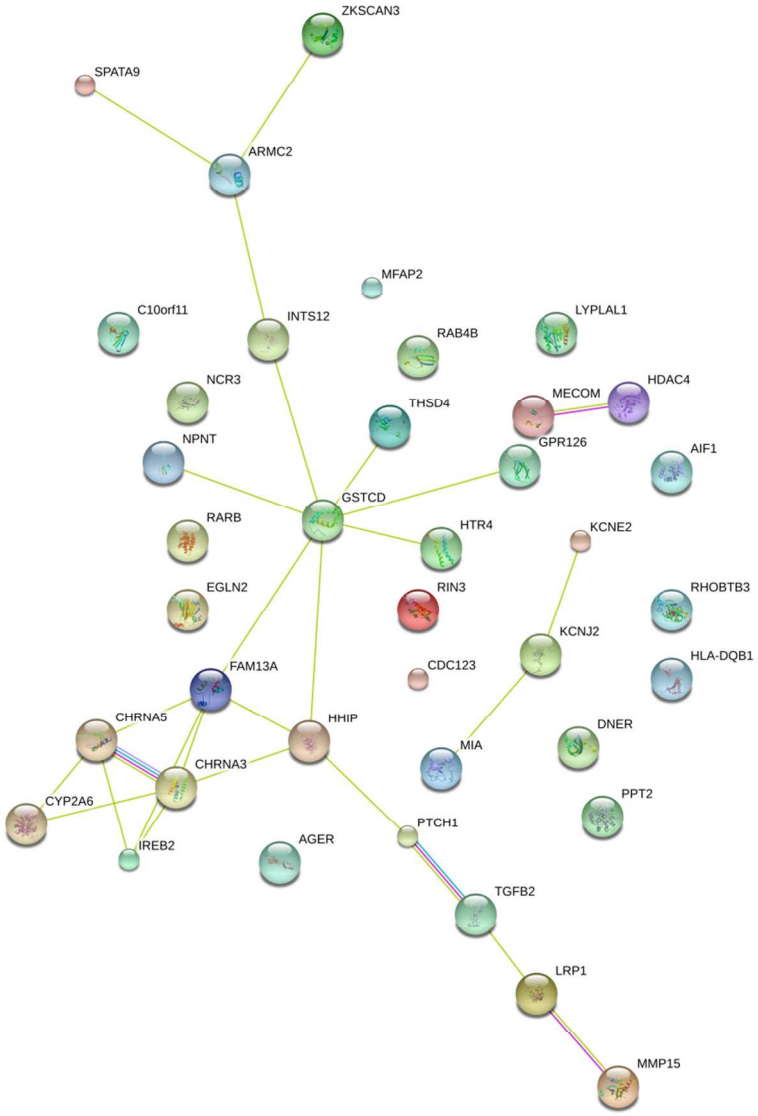

Supplemental Figure 1: Network Relationships of LUNG30 Score Loci

In the network diagram above (generated using string-db.org), each node represents a gene name of the nearest gene within the region of the LUNG30 SNPs or a gene from the first "shell" of proteins known to interact with this nearest gene, while edges represent protein-protein associations. Turquoise and magenta edges represent interactions from curated databases and experimentally determined interactions, respectively. Light green edges represent protein-protein associations from unsupervised textmining of relevant literature, while light purple edges represent protein homology.