The Genetic Architecture of Alopecia Areata

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ABSTRACT

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Alopecia areata (AA) is the most prevalent autoimmune disease in the US. With An estimated lifetime risk of 1.7%, it affects both genders with similar frequencies and people of all ages. AA affects more individuals than most other autoimmune diseases combined, and yet despite its prevalence, there is an enormous unmet medical need, in part due to the dearth of information about the underlying pathogenesis. In AA, autoimmunity arises against the hair follicles in the skin, which causes hair loss associated with an aberrant accumulation of immune-response cells around the affected hair follicles. Evidence supporting a genetic basis for AA stems from multiple lines of research, including increased risk of disease in first degree relatives, twin studies, and more recently, our initial family-based linkage study and genome wide association study (GWAS) in a cohort of unrelated individuals. Importantly, our GWAS identified a set of 16 statistically independent risk haplotypes across 8 loci, implicating specific genes that increase risk of AA, all of which have been validated. Genome wide genetic studies can provide critical insight into disease mechanisms, especially when little is known about the underlying causes of disease. In this study, I use complementary gene mapping methods, performing one study in a cohort of families and a second study in a cohort of unrelated cases and controls. Using these two approaches, I obtain new evidence about the genetic influences on AA. Our family cohort contains statistically significant evidence for linkage at a new locus, on chromosome 2q36.1-q37.3 (LOD=4.17) and family-based tests of association implicate 47 genes. I then conducted a GWAS that expanded our initial cohort with the addition of 800 cases and obtained statistically significant evidence for a new locus at chromosome 16p13.13 ($p=4.6x10^{-7}$). This region has been implicated in several other autoimmune diseases and

contains several genes that are known to be involved with immune processes. Taken together, these two studies demonstrate the presence of both rare and common variants are contributing to AA etiology and support emerging evidence that suggests the genetic architecture of common complex diseases involves both rare and common variants.

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Dedication

My dissertation is dedicated to my children, Kira Petukhova and Aleksandr Petukhov, for several reasons. First, they are the unsung heroes of this endeavor; enduring the ups and downs of graduate school with me, compromising schedules, and chipping in with chores so that we, as a family, could carve out time for my doctoral program. Second, because they were, and continue to be, an eternal source of inspiration; in an obvious way with their loud cheerleading and quiet prayers; and in a subtle way, the way children do, by providing an entirely new perspective on life's decisions. Finally, because there is an often iterated trepidation in science that children will be an impediment to success in research. While there is clearly a need for improved institutional infrastructure to support women in science, in dedicating this work to my children, I hope to highlight benefits of balancing motherhood with research. Children remind you to be curious and find awe in nature, they train you to be exceptionally organized, and they inspire you to be great. My children are the foundation to the success that I have achieved in my doctoral program.

Paper 1

Towards Defining the Causal Structure of Alopecia Areata

Introduction

Alopecia areata is an autoimmune disease that targets the hair follicles in the skin, causing disfiguring hair loss marked histologically by an accumulation of immune-response cells around the affected hair follicles. AA is the most prevalent autoimmune disease in the United States.[1,2] With a lifetime risk of 1.7%,[3] it targets both men and women and affects people of all ages.[4-6] AA affects more individuals than most other autoimmune diseases combined, yet despite its prevalence, there is an enormous unmet medical need[7] that arises primarily from the dearth of information about its underlying pathogenesis and is compounded by a lack of studies on its natural history, which presents challenges in designing robust and efficient clinical trials.

As an autoimmune disease, AA falls within a broader category of related disorders that are characterized by an aberrant targeted immune attack on cells, tissues or organs. Collectively autoimmune diseases carry a tremendous public health burden in the US and globally.[8-11] In the US, 5-8% of the population is affected by an autoimmune disease,[1] which results in annual direct health care costs of at least $100 billion,[2] and additional economic burden due to lost earnings. The chronic nature and unpredictable courses of these diseases impart severe physical and emotional burdens to the patients and their family members.

There are more than 100 autoimmune diseases when classified on the basis of the target of the immune attack.[2,11] Historically, treatment is based on organ involvement, and as a consequence, clinically distinct diseases have been studied as separate entities. However, emerging epidemiological[12-14] and genetic evidence[15-19] links sets of autoimmune diseases, revealing common mechanisms involving a discrete set of pathways that operate to dysregulate immune tolerance at different end organ sites. Importantly, such emerging evidence places AA within the larger context of autoimmune diseases, such that novel discoveries in AA may hold broader implications for disease mechanisms and therapeutic responses in related diseases, such as type 1 diabetes and rheumatoid arthritis. Additionally, since the target organ in AA (the

hair follicle) is readily observable and biopsied with minimal risk to the patient, AA is easier to study than other autoimmune diseases and more amenable to molecular investigations.

Understanding the causes of AA will allow us to redress the enormous unmet medical need of patients and may provide insight about other autoimmune diseases. Defining the causal structure of a disease begins by identifying a set of risk factors that exist within a given population. For an individual in that population, disease occurs when a particular configuration of risk factors converges. Thus, an important component of the causal structure is the relationship among risk factors. Identifying components of the causal structure will help to elucidate underlying pathogenesis and may reveal novel therapeutic interventions. Understanding how specific risk factors work together to promote disease can improve the management of AA, and may lead towards the development of effective and efficient prevention strategies.

In the field of human genetics, the term 'genetic architecture' is commonly used to describe the set of alleles that influences a disease or trait. It is defined as a catalogue of genes that contribute to trait variation and the characteristics of the alleles that reside at those loci, generally described in terms of their frequencies and effect sizes,[20,21] and sometimes expanded to include the interactions among environmental and genetic components of the variation.[22-25] Thus, its definition has come to capture not only the genomic structure that contributes to trait variation, but also all variables that influence the relationship between genetic and phenotypic variations. This current notion is somewhat removed from its original use, which was more narrowly focused only on the composition and organization of genetic material within populations of model organisms.[26] I have chosen to use the term 'causal structure' rather than genetic architecture, because it is more accurate and inclusive. Furthermore, it clarifies that environmental effects not only contribute to disease risk for common diseases, but also influence our estimates of genetic effects for risk alleles. I reserve

the use of genetic architecture to describe the genomic content that is capable of influencing disease. The intent of this review is describe what is known about causes of AA, both environmental and genetic; e.g. its causal structure.

As for other chronic diseases, etiological clues about the underlying biology that promotes and drives AA may be found in clinical manifestations of disease, treatment responses, epidemiological descriptions of population patterns of disease, and investigations into environmental and genetic sources of risk. However, of all of these avenues for research, gene mapping methods have proven to be most successful for gaining critical insight into disease mechanisms. The development of efficient technologies for scanning the genome has greatly accelerated the acquisition of knowledge about genetic risk factors, and certainly for AA, the insight we have gained from genetic studies has transformed both what we know about disease pathogenesis and how we think about therapeutic interventions. Genetic insight not only provides valuable information in and of itself, but also promises to resolve ambiguous or inconclusive evidence collected from more traditional epidemiological studies, and of particular importance, helps to clarify environmental influences on disease. For example, when genetic evidence implicates a physiological process that is known to respond to particular environmental stimuli, evidence for an etiological role of environmental factors is strengthened. Alternatively, genetic associations that have been established for environmental exposures can be used as instrumental variables in Mendelian randomization analyses. The power to detect the effect of an environmental exposure on AA would be enhanced by using a genetic instrumental variable as a proxy for the environmental exposure.[27]

In this review, I will provide a comprehensive description of what is either suggested or known about the causal structure of AA. In identifying critical gaps in the literature, I hope to lay out a roadmap for advancement of our understanding of AA pathogenesis and treatment and to

demonstrate that the integration of genetic studies into causal investigations can significantly enhance the strength of our conclusions.

Clinical Manifestations of Alopecia Areata

The current paradigm for AA is that an individual inherits a set of risk alleles that confers some level of disease susceptibility, and over the life-course, environmental factors are encountered that increase the probability of developing AA. At some point a particular configuration of risk alleles and environmental factors converges and disease onset occurs. Severity of disease and time course are highly variable within and across patients and are thus unpredictable (Figure 1a).

Although the immune attack can occur anywhere on the body, it is typically first brought to medical attention when it occurs as one or several patches of non-scarring hair loss on the scalp or face (Figure 1d). The initial regions of hair loss can appear either suddenly or more gradually over several days, and may regress as a result of spontaneous disease remission, or alternatively, the patches may grow (Figure 1c) and coalesce (Figure 1b), progressing to cover the entire scalp (alopecia totalis, AT) or eventually the entire body (alopecia universalis, AU). While some patients only ever experience a single episode of hair loss (transient AA- AAT), the disease can cycle through periods of spontaneous or therapeutically-induced remission, followed by relapse (patchy AA- AAP) (as in Figure 1a). These AAP patients experience bouts of hair loss and regrowth at several points throughout their lifetime, although the number and duration of relapse and remission have never been rigorously examined within a well-powered epidemiological study. The prognosis for AT and AU patients is generally poor, although there are reports of transient or permanent partial or full regrowth of hair. Furthermore, hair regrowth remains possible for all patients, because the immune attack targets the lower portion of the hair follicle, sparing the stem cell compartment of the organ. Nonetheless, it is difficult to estimate

how often complete remission occurs, as no study has prospectively followed patients. Currently, there are no biomarkers of prognosis and it is impossible to predict which patients will undergo spontaneous remission and which ones will experience relapsing/remitting hair loss or advancement to total hair loss.

Interestingly, the phenomenon of 'sudden whitening of the hair' is ascribed to the acute onset of AA at times of profound grief, stress or fear.[28] The immune attack preferentially targets pigmented hair follicles in the anagen (growth) phase of the hair cycle, and when regrowth occurs within lesions, the new hair is often white or colorless. When the disease occurs in individuals with a pre-existing blend of dark and white hair, so-called "salt and pepper" hair, the pigmented hair is selectively shed while the white hair is spared. In addition to the distinctive pattern of hair loss, short broken hairs known as 'exclamation mark' hairs may be found in active AA due to distal breakage of the hair shaft just above its exit from the scalp. Finally, AA is sometimes accompanied by nail changes in the form of pitting, brittleness and splitting.

Some of these clinical features may offer clues about underlying molecular pathology of AA. For example, the lack of pigment in hair follicles recovering from an autoimmune attack suggests that the synchronization of hair follicle stem cells and melanocyte stem cells, which occurs during normal hair cycling,[29] may become disrupted or uncoupled during AA pathogenesis.

In addition to providing etiological clues, distinctive and obvious clinical features allow for the simple, reliable diagnosis and robust phenotyping of patients. Stringent criteria for the classification of AA are published and have been incorporated into guidelines for the assessment of AA severity.[30,31] Thus, the ease of diagnosis and classification of AA confers a great advantage for epidemiologic studies of AA over other autoimmune diseases. Furthermore, as a dermatological disease, AA is particularly amenable to remote monitoring. When patients can transmit information and digital photographic images that document disease

status, it becomes possible to collect much more data than would be feasible with clinic visits, and greatly increases power, precision and sensitivity of both observational studies and randomized clinical trials (RCTs).[32-42] Patient reported outcomes can enable more frequent reporting at significantly lower cost, and mitigate recall bias by reducing the interval between occurrence and report and allowing the reporting to be done in the patient's natural environment. Finally, unambiguous classification of disease activity and minimal risk in performing skin biopsies greatly facilitate molecular investigation of disease mechanisms involved in autoimmunity. Thus, the study of AA is an ideal model for a multifaceted approach to studies of autoimmunity holds the potential to transform our understanding of the pathobiology and treatment of other autoimmune disorders that share disease mechanisms.

Treatment

An estimated 2.4 million dermatology office visits occur annually for the treatment of AA.[5] The repertoire of therapeutic options has not changed over the previous fifty years and remains limited. While some dermatologists advocate observation for mild cases, first-line treatment typically includes intralesional corticosteroids and topical immunotherapy for adults. Because of the extreme physical discomfort incurred from these therapies, first-line treatment for children is limited to topical corticosteroids and sometimes includes minoxidil.[43]

The exact mechanisms by which corticosteroids and topical immunotherapy ameliorate disease for some patients remain elusive. Corticosteroids have wide-ranging effects on a number of physiological responses, including the down-regulation of inflammatory and stress pathways. Topical immunotherapy involves the application of chemicals such as diphencyprone (DPCP), dinitrochlorobenzene (DNCB), or squaric acid dibutyl ester (SADBE) to the scalp to produce an allergic rash which resembles poison oak or ivy. It is thought that the induced allergic reaction shifts distributions of lymphocytes within the skin, and this either directly or

indirectly interferes with the autoimmune attack.[44] Despite the widespread use of both treatments, there is no evidence base for their effectiveness. No RCTs have been conducted for most of the drugs that are commonly used for AA treatment, and poor efficacy is demonstrated in the clinic. Approximately 20-30% of patients do not respond at all to standard treatments and complete recovery for 10–15 years is only achieved for one third of all cases.[45] Studies aimed at understanding the mechanisms that underlie therapeutic responses to these treatments could provide insight to the pathogenesis of disease and could assist with unraveling the genetic complexity of the disease. For example, the failure to respond to a particular treatment could reflect a particular mechanistic defect shared among nonresponders and distinct from disease mechanisms operating in patients that do have a therapeutic response.[46,47] Genetic analyses that are stratified for this subset of patients could increase the power to detect genetic effects that are specific to the underlying dysregulated physiological process.

There is a paucity of RCTs for the treatment of AA. A recent Cochrane analysis identified 17 RCTs involving a total of 540 participants and concluded that there is no proven treatment.[7] Each trial included from 6 to 85 participants and none of the assessed interventions showed significant treatment benefit in terms of hair growth when compared with placebo. Most trials have been poorly reported and/or are inadequately powered so that any important clinical benefits are inconclusive. The weak evidence-base for AA treatments contributes to the enormous unmet medical need for the 5.3 million people who live with AA in the United States.

Despite this precedent in RCTs for AA, the potential to evaluate the efficacy of treatments in AA is greatly enhanced by an unambiguous and easily observable treatment response. Hair regrowth can be objectively measured and remotely monitored, decreasing measurement error and trial cost, while greatly enhancing the power to detect a treatment effect. Currently, the main limitation in designing a well-powered RCT in AA is the lack of

information about the natural history of the disease, in particular, the rate of spontaneous remission.

It is challenging to design a well-powered trial and complicated to interpret treatment responses when naturally occurring remission in AA has never been rigorously evaluated. The few studies in the literature are not well-powered and arrive at highly variable rates, ranging from 20%-80%.[3,6,48-51] All of these studies ascertained patients through treatment centers and it was sometimes unclear whether remission was spontaneous or treatment induced. Finally, little attention was given to study design parameters that could contribute to the variability in estimates, such as length of observation and inclusion requirements. Spontaneous remission estimates in the placebo arms of published AA RCTs suffer from many of the same limitations as the epidemiological studies of remission, and also indicate high variability, ranging from 0%-80%.[52] Poor characterization of spontaneous remission in AA presents a major challenge in translational research for AA. Valid estimates would allow for more precise power estimates, insuring that sufficient numbers of controls without spontaneous remission would remain at the end of the trail. High placebo response rates in small studies could obscure effect estimates and mask the benefits of a truly efficacious treatment.[47] A natural history study of AA would be an invaluable addition to the literature and greatly facilitate translational research in AA.

Epidemiological Studies in Alopecia Areata

Descriptive Epidemiology

AA is estimated to be among the most prevalent autoimmune diseases, affecting 5.3 million people in the United States, and targeting both genders equally across all ethnic backgrounds. The disease affects people of all ages, with a median age of onset estimated to be in the second or third decade of life. It is the most common form of hair loss for children.

There is sparse literature on the epidemiology of AA. Only two studies have been published that characterize the distribution of AA in the US and only one of these has been population based.[3,53] The population-based study estimated the point prevalence of the disease. However, due to the episodic nature of AA, cumulative incidence better characterizes disease burden, as it estimates the probability of experiencing the disease over a lifetime. There has been one study of AA incidence the US[3], as well as several smaller studies conducted in other countries.[3,48,54-59] The main limitation of these studies is that patients were ascertained through treatment centers. Such studies underestimate the cumulative incidence because they exclude people without access to healthcare, people with less severe disease, and people who are not motivated to seek treatment because of prior knowledge of the inefficacy and physical discomfort of treatments that are currently available for AA.

The estimate of AA point prevalence in the US was obtained in the First National Health and Nutrition Examination study (NHANES-I).[53] In a probability sample of the US population, 20,794 people underwent a general dermatologic examination. While these exams identified 37 people with active AA, 11 cases were excluded from the estimate, as they were diagnosed in one center. The prevalence was then determined to be 122 per 100,000, 0.1%-0.2% of the population. Importantly, as noted by the study authors, this was likely to be an underestimate, primarily because the data collection method limited the number of dermatological diagnoses that could be recorded in the survey. Additionally, the variance in the number of cases ascertained across centers calls into question the validity of their estimate; inter-observer reliability was shown to be problematic with several data sets collected through NHANES-I.

The one incidence study that was conducted in the US utilized the medical records linkage system of the Rochester Epidemiology Project to obtain a population-based estimate. This study reviewed medical records over a 15 year period from 1975-1989 and identified 627 patients with any diagnosis related to AA, of whom 292 were Olmsted Country residents who

had received an initial diagnosis of AA within the study period. Incidence rates were determined by utilizing estimates of the total population of Olmsted County over the time period, assuming that the entire population was at risk. The overall age and gender-adjusted incidence was determined to be 20.2 per 100,000 person-years and the life-time cumulative incidence was estimated at 1.7%. Although this study did not find differences in the racial distribution of cases, the demographics of Olmsted county was 96% Caucasian, and so there is uncertainty in this estimate. Finally, the main limitation of the study is that it reflects only cases brought to medical attention and so is likely to underestimate the true cumulative incidence.

Comorbidities

The pathology of AA extends far beyond the physical aspects of hair loss, and the disease exerts a deeply disturbing impact on the psychological, emotional and social well-being of affected individuals.[60-62] Importantly, clinical severity is poorly correlated with impaired quality of life, such that even in patients with minimal hair loss in AA, the loss carries significant emotional and psychological meaning that pertains not only to hair, but also to quality of life, the ability to function in society, self-esteem, and psychological disturbances as profound as suicide. A number of studies have demonstrated high comorbidity of psychiatric disorders, in particular generalized anxiety, depression and phobic states.[63-74] Interestingly, a recent study that examined disease co-occurrences among a collection of 1.5 million patient records found statistically significant correlations between AA and a number of neuropsychological disorders, including migraines, depression, attention deficit, epilepsy, and bipolar disorder.[14] While this the size of the study provides good power to detect associations, the effect of medical utilization patterns on detected associations was not adequately explored. Furthermore, it remains unclear how neuropsychological comorbidities could relate to AA, for example developing as a consequence or being linked by shared dysregulated physiological processes. Temporal ordering of the onset of disorders within patients or analysis of cosegregation of neurological

disorders within large AA families are two study designs that could help to distinguish such hypotheses. To date, there are no such reports in the literature. Nonetheless, recommendations for the management of AA include attention to the psychosocial well-being of the patient.[75,76]

The public health burden imparted by AA thus encompasses not only people with active hair loss at a given point in time, but also people who suffer the psychological consequences of the disease, which may or may not correlate with actual hair loss. Because of the relapsing nature of AA, the highly unpredictable course of the disease, and the lack of prognostic biomarkers, even people who have only ever experienced a single resolved episode of hair loss continue to live in fear that their insidious condition could progress to total and irreversible hairlessness. Thus, the burden of disease for AA patients is heavily weighted with detrimental psychological ramifications that persist when hair loss is not evident.

AA patients have an increased risk of comorbid autoimmune disease.[77] Specific reported associations include AA with thyroid disease,[68,78-82] celiac disease (CeD),[83] rheumatoid arthritis (RA),[14,68,78] vitiligo[68,78-80,84,85] and type 1 diabetes (T1D).[14,68,81,86] Interestingly, in addition to reports of increased prevalence of T1D among AA patients, there are two family history studies that report a decreased prevalence of T1D among AA probands, but an increased prevalence of T1D among siblings of AA probands.[78,80] These studies surveyed a large number of AA patients (800 and 500 respectively) with a questionnaire about comorbidities in themselves and family members. However, the two largest and most recent studies to examine the joint distribution of AA and T1D in patients both found significant associations. The Denmark Patient Registry study also looked at co-occurrence of autoimmune diseases within individuals and found that T1D was the second most frequent autoimmune disease among AA patients with at least one comorbidity.[77] A study that explored pairwise disease correlations among a collection of 1.5 million patient records from Columbia University Medical Center found

statistically significant correlations between AA and T1D, RA, and Psoriasis.[14] Even though this study may be vulnerable to bias arising from medical service utilization, its findings are consistent with recent GWAS in AA and other autoimmune diseases have identified a number of alleles that increase risk for sets of autoimmune disorders, providing corroborating evidence for shared disease mechanisms.[87] Thus, discrepancies in the epidemiological literature could have arisen from the small sample sizes of the earlier studies, or limitations inherent to family history study designs. Consistencies among some of the epidemiological studies and genetic studies suggest biological validity. The rapid advancement in knowledge about the genetic architecture of autoimmune diseases and molecular studies that follow up on statistical associations will help to clarify mechanistic relationships among this class of diseases.

Etiology

Sources of risk for AA are both found within the genome and in the environment. The measurement of genetic risk factors has been greatly enhanced in recent years due to technological advances which make it cost effective to perform genome-wide analysis in large cohorts. As a consequence, our knowledge of the genome's influence on AA greatly exceeds our understanding of environmental risk.

Environmental Risk Factors

While the insight gained from genetic studies has transformed our understanding of AA pathogenesis, the first investigations into causes of AA focused on environmental causes. These studies were guided by findings in other autoimmune diseases, which had demonstrated associations with infectious and pharmaceutical agents, nutritional status, occupational exposures, sun exposure, smoking, and stress.[88] The scope of investigation into environmental causes of AA is much smaller, with only a few studies focused on nutritional factors, viral infection and stress.

There have been limited studies of the influence of nutrients. Two reports have found decreased serum levels of zinc in AA patients and one study demonstrated that zinc supplements shift the distribution of circulating lymphocytes in AA patients.[89-91] A recent study found decreased levels of zinc and copper in the hair of AA patients relative to controls.[92] Some physicians screen for iron or zinc deficiencies in AA patients.[93]

Cytomegalovirus (CMV) is a common viral infection that has been associated with a number of autoimmune diseases including systemic lupus erythomatosis (SLE), type 1 diabetes (T1D) and inflammatory bowel disease (IBD). CMV has been studied as a possible trigger for AA since it can infect the hair follicle matrix fibroblasts, and in mice, such infection leads to hair loss and expression of HLA-DR in thyroid epithelium.[94] An initial investigation in humans found CMV in AA lesions by PCR,[95] while a second study failed to find evidence for infection of viral members of the beta-herpes viridae family (CMV, EBV, HSV) in mRNA extracted from active lesions in patchy AA.[96] Finally, a third study investigated evidence for prior CMV infection in the blood, and found no correlation between CMV and AA.[94] These inconsistent findings may be attributed to small sample sizes, differences in experimental strategies across studies, and/or limitations inherent to study designs. For example, the prevalence of CMV is highly variable among geographic regions, ethnic populations and socioeconomic groups, requiring that association studies be well-powered and provide some means to control for these potential confounders. None of the published AA studies addressed these challenges. Despite the inconsistencies of these initial studies, it may be worthwhile to revisit the role of CMV in AA onset, given the validated finding of genetic associations of UL16 binding protein (ULBP) genes.[87,97] This gene family was initially discovered because the proteins transcribed from these loci are able to bind to a protein expressed by CMV-infected cells.[98] Thus, recent genetic evidence warrants reconsidering the possibility that CMV is capable of triggering AA onset.

Stress has been the most widely investigated potential environmental trigger to AA. The concept of stress has evolved since its original inception in 1950 and is in general recognized to be a broad construct encompassing a number of domains.[99] The ambiguity in its use has created confusion in the literature and may account for some of the inconsistencies in findings related to its influence on human physiology and health, and the scope of this problem extends to studies in AA. It is generally acknowledged that stress arises as a response to a stressor, which may be an event, encountered or conceived, *i.e.,* a stressor. In the autoimmune literature, stress is generally defined as an event or condition which is perceived as threatening to an individual's well-being and which adversely affects thoughts, emotions, behavior, and/or physiological functioning.[100] This definition includes both the stressors that are encountered, as well as the person's response to it. The vast majority of stress studies in AA examine the influence of stressors.

Many AA patients report the coincidence of stressful life events (SLE) or emotional trauma with the onset or exacerbation of AA, but the few formal epidemiological studies have produced inconsistent results. Four published case series reported elevated occurrences of emotional trauma at onset (12%, 23%, 23% and 30% of patients),[48,68,101,102] while one reported a decreased rate (6.7%).[103] Similarly, one case control study found a significant difference in reporting stressful events between cases and controls, (66% v. 22%),[104] while a second study found no difference between groups,[105] and a third study found an increase in SLEs only among patients with recurrent disease.[106] A more recent study in adolescents found an increase is stressful life events in AA patients relative to their healthy siblings and none relative to age matched epilepsy patients. Epilepsy patients were utilized as controls to account for possible secondary effects due to experiencing a chronic illness that is mechanistically unrelated to AA.[107] The fact that epilepsy was very recently identified as a possible comorbid feature of AA[14] suggests that there could be shared physiological features to these two disorders and

complicates the interpretation of their finding that SLEs were similar between the AA and epilepsy groups. Limitations of this study include a small sample size, with each group containing fewer than 30 participants, and the retrospective reporting of life events by mothers.[107] In conclusion, inconsistencies in the epidemiological literature with regard to the role of stress in the development of AA likely result from methodological limitations inherent to study designs, as small numbers of patients with retrospective reporting limit the power to detect effects. Importantly, there has never been a prospective epidemiological study that rigorously evaluated the relationship between stress encounters and AA.

There is experimental evidence to support a role of stress in AA onset and/or exacerbation, which arises from stress response. Stressors that are encountered in the environment exert physiological responses through activation of nervous system pathways, including activation of the sympathetic nervous system which results in the release of epinephrine and norepinephrine; upregulation of hormones such as prolactin, growth hormone, and nerve growth factor; and activation of the hypothalamic-pituitary-adrenal (HPA) axis, which results in the release of glucocorticoids from the adrenal gland through the intermediate hormones corticotropin releasing hormone (CRH), produced in the hypothalamus, and adrenocorticotropic hormone (ACTH) produced by the pituitary gland. The literature contains a number of studies that point to a physiological interaction between the hair follicle and nervous system, some of which have examined this within the context of AA. Interestingly, studies of hair follicle organ culture indicate that human hair follicles synthesize cortisol and respond to CRH and ACTH,[108-110] suggesting that the hair follicle has locally operating stress-response systems which may execute and coordinate peripheral stress responses. Furthermore, CRH significantly inhibits hair shaft production, induces apoptosis-driven hair follicle regression, and increases melanin production in the anagen hair bulb.[109] Additionally, there are a number of studies demonstrating that cortisol levels in hair provide a biomarker for stress.[111-120] A recent study in

an animal model for AA showed that disease is accompanied by altered stress responses in the animal.[121] Finally, the ability of corticosteroids to reverse disease for some patients suggests that stress response pathways contribute to disease. Cumulatively, these findings suggest that physiological interactions between the hair follicle and nervous system could contribute to the development of AA.[122,123]

While epidemiological evidence for the influence of environmental risk factors is limited and sometimes contradictory, our enhanced understanding of how genes influence AA and related physiological traits promises to resolve discrepancies and clarify etiological roles. For example, experiments to test the hypothesis that a dysregulated stress-response contributes to AA risk are facilitated by the recent identification of inherited genetic variants that correlate with levels of stress hormones and their receptors in humans[124,125] with the use Mendelian randomization methods. In such experiments, SNPs are used as instrumental variables, or proxy measures of stress response. Such variants account for individual differences in hormone levels and have fewer sources of measurement error and confounding relative to measurement of hormones in blood, saliva or urine. Similarly, SNPs associated with stress reactivity can be used to help clarify the role of stress in disease onset or progression.[126] Genomics offers a lens through which we can better understand the impact of environmental influences on chronic diseases, and understanding how the genome and the environment interact can help to clarify both the genetic and environmental influences on disease risk.

Genetic Risk Factors

By far, the greatest insights into disease mechanisms that operate in AA have been obtained from genetic studies. Initial evidence supporting a genetic basis for AA was obtained from multiple lines of research, including increased risk of disease in first degree relatives,[4,127] twin studies,[94,128] and studies in animal models.[129] The first genetic studies in AA were candidate-gene association studies, which investigated one or a few genes, chosen on the

basis of a prior hypothesis about its function, and typically based on the involvement of the gene in other autoimmune diseases. Although these initial genetic studies tended to be limited in terms of sample size and by definition, biased by choices of candidate genes, they nonetheless demonstrated associations with genes located within the human leukocyte antigen (HLA) complex: HLA-DQB1, HLA-DRB1, HLA-A, HLA-B, HLA-C, NOTCH4, MICA; as well as genes outside of the HLA: PTPN22, and AIRE (reviewed in [123]).

In contrast to candidate gene methods, genome-wide studies survey the entire genome for evidence of genetic contributions to disease without the *a priori* exclusion of any loci. Thus, these are particularly powerful methods for resolving disease mechanisms when much remains unknown about why or how the disease occurs. Currently, genome-wide methods can be categorized into marker-based or sequencing-based methods. Marker-based methods, such as linkage analysis and genome-wide association studies (GWAS), type genetic markers in families or cohorts of unrelated people to identify genomic regions with evidence for the presence of a proximal risk variant. In contrast, genome-wide sequencing-based methods generate whole-genome or whole-exome data, obviating the assumption that a risk variant is in physical proximity to a genetic marker and allow all variants to be directly tested. These methods have only recently become feasible, with the emergence of next generation sequencing technologies.[130,131] The pivotal challenge with these studies is to design a filtering strategy to prioritize a small number of variants from the massive lists generated by the experiment (reviewed in [132,133]).

To date, genome-wide studies in AA have employed marker-based methods and include a genome-wide linkage analysis, and two GWAS in AA.[87,134,135] Results from these studies confirm that: (1) there is a genetic basis to AA, (2) it is likely to be polygenic and (3) the genetic architecture is composed of both rare and common risk alleles. This last conclusion can be inferred from the success of both linkage and GWAS in AA.

The two marker-based approaches are complementary to each other, targeting different sets of disease alleles, because different sets of assumptions underlie each method.

Linkage methods identify genetic markers that cosegregate with disease in families and have the greatest power for detection of disease alleles that are rare in the population and have a strong correlation with disease expression (i.e., have large effect estimates in terms of ratio measures). Power to detect linkage is also influenced by the causal structure of the disease and will be weakened by etiologic heterogeneity and interaction among exposures, including gene-gene interaction (GxG) or gene-environment interaction (GxE). First, when there are many independent causes of a disease in the population, as is possible for common diseases, some families may have multiple independent causes of disease among family members, which would obscure co-segregation of any one locus with the disease. Some affected family members will not have disease alleles at the locus being analyzed. These independent causes could include either environmental exposures or genetic variants at different loci. Secondly, genetic variants that influence disease only when acting in concert with other variants or environmental factors will display reduced penetrance within families, and some family members who have the disease allele under investigation will not have the disease. Therefore, etiologic heterogeneity, as well as GxG and GxE, can generate inheritance patterns in pedigrees that are inconsistent with Mendel's Laws of Inheritance, reducing power to detect linkage. Linkage evidence is generally robust to biases that can influence association studies, such as population stratification. Genomic regions identified in linkage studies tend to be quite large, and so generally preclude the immediate identification of specific genes, but rather serve as a starting point for further positional mapping or sequencing of candidate genes within the linkage interval.

GWAS compares allele frequencies for large numbers of genetic markers across groups of unrelated cases and controls and is best suited for detecting disease alleles that are common

in the population. Power to detect linkage is reduced when there is a difference in allele frequency between the tagSNP and risk variant, even if the two alleles are in perfect linkage disequilibrium (LD=1).[136] Because most commercial genotyping arrays exclusively or predominantly type common alleles (p>0.01), GWAS have the greatest power to detect common risk variants. Furthermore, disease alleles that are common in the population are not likely to have strong phenotypic effects. GWAS tend to be more sensitive to confounding from ancestry, although there are analytic methods to test and correct for such biases. Finally, associated regions tend to be much smaller than linkage regions, therefore this method has the potential identify individual genes or small clusters of functionally related genes. In conclusion, linkage methods target rare disease alleles with strong effect estimates, while association methods target common disease alleles with weak effect estimates. Importantly, emerging empirical evidence, which is augmented by theoretical arguments, suggests that the genetic architecture of common diseases contains niches for both rare and common alleles.[137-149]

We conducted the first genome-wide linkage study in AA and identified several genomic regions that cosegregated in families.[150] Microsatellite markers were used to genotype a cohort of 20 US and Israeli families. We demonstrated strong evidence for linkage on chromosome 6q23.2 (Z=3.6) and suggestive evidence in several additional regions. Finemapping with microsatellite markers was then performed in an expanded cohort of 38 families for six regions. This analysis upheld evidence on chromosomes 6q23.3-q24.1 (Z=2.89) and 16q12.2 (Z=3.12), and strengthened evidence on chromosome 18p11.31-p11.21 (max multipoint LOD=3.93). This study provided robust evidence for a genetic component of AA, and because we identified at least four distinct regions in the genome, this study supports the notion that AA is a heterogeneous disease, with contributions to risk from several genes.

Next, we completed the first GWAS for AA, comparing allele frequencies across nearly 500,000 genetic markers, between a group of 1,054 unrelated AA patients and 3,278 unrelated

controls.[87] Our study identified 139 genotyped and more than 175 imputed SNPs with statistically significant association to AA ($p<5x10^{-7}$), which primarily cluster in eight regions of the genome, implicating genes of the immune system, as well as genes that are unique to the hair follicle: (1) 2q33.2 containing the CTLA4 gene; (2) 4q27 containing the IL2/IL21 locus; (3) 6p21.32 containing the HLA class II region; (4) 6q25.1 which harbors the ULBP gene cluster; (5) 9q31.1 containing syntaxin 17 (STX17); (6) 10p15.1 containing IL2RA; (7) 11q13 containing peroxiredoxin 5 (PRDX5); and (8) 12q13 containing Eos. Additionally, an imputed SNP in 18p11.21 exceeded our threshold for statistical significance and is located downstream of PTPN2. Each of these regions has been confirmed through independent studies.[87,97] The biological and therapeutic implications of these discoveries have been reviewed elsewhere.[151]

Because associated SNPs cluster within regions, statistical analysis was performed to identify independent association signals within each region, such that we were able to choose 16 SNPs that captured the majority of these associations. Further analysis revealed that the distribution of these risk alleles was significantly different between cases and controls ($p=1.1x10^{-107}$), such that on average, cases carried a greater genetic liability than controls.[87]

Importantly, the genes that have been implicated by our first GWAS align AA within the broader context of autoimmunity and suggest new therapeutic avenues to explore. For example, our GWAS revealed a number of risk loci in common with other forms of autoimmunity, such as type I diabetes, rheumatoid arthritis, and celiac disease, in particular, CTLA4, IL2/IL2RA, IL21 and genes critical to Treg maintenance. A gene cluster that our GWAS implicated for the first time in any human disease, containing ULBP3/ULBP6, further unites this set of autoimmune diseases, as the receptor for these genes, NKG2D, has been implicated by genetic and/or immunological evidence for each disease.[87,152,153] Finally, several of the genes implicated by our GWAS are targets for drugs that are in development or already available to treat other autoimmune diseases. For example, Abatacept is a form of recombinant CTLA4-Ig

used in the treatment of rheumatoid arthritis and currently in clinical trials for treatment of several other autoimmune diseases. Additionally, there is compelling preclinical data in AA demonstrating that CTLA4-Ig prevents disease onset in the mouse model for AA.[154] The findings from this initial GWAS in AA provide initial clues that are likely to transform the development of treatments for this disease.

Future Directions

Genetic studies in humans have proven to be a robust method for gaining insight into the pathogenesis of disease, implicating unanticipated biological pathways across a broad spectrum of human disorders. For AA, similar to other common diseases, our genetic studies suggest that there are risk alleles that are rare in the population and have a strong impact on disease,[134] as well as risk alleles that are common in the population and less strongly correlated with disease.[87] The identification of new risk genes for AA will help to clarify the biological pathways that underlie disease and substantially enhance our understanding of the causal structure of this prevalent and psychologically devastating disease.

Our linkage studies provide strong evidence for the existence of alleles cosegregating with disease, and also provide a critical starting point for methods that utilize next generation sequencing technologies to generate whole exome or whole genome sequence data. The integration of whole exome/genome sequencing data with linkage evidence is emerging as a powerful new means to identify disease alleles, providing an economical and efficient way to catalogue all linkage-interval variants, and a robust strategy for prioritizing the vast number of novel variants revealed by whole exome/genome sequencing.[155] The ongoing efforts of the National Alopecia Areata Registry have substantially expanded our family cohort since the completion of our first genome-wide linkage scan. Additionally, while our first linkage study utilized microsatellite markers, commercial genotyping arrays of SNPs offer increased

information content, which increases the power to detect linkage. Additionally, having both our family cohort and our GWAS cohort of unrelated individuals genotyped on a common platform will allow us to integrate the two data sets and better characterize the genetic architecture of AA. Therefore, we have begun SNP linkage analysis in this expanded cohort of AA families.

Importantly, emerging evidence from many different human disorders suggests that the genetic architecture of human disease comprises both rare and common disease alleles and thus argues for pursuit of both strategies when the goal is to comprehensively illuminate the genetic architecture of a disorder. As an illustrative example, GWAS have been tremendously successfully for identifying loci that contribute to inflammatory bowel disease (IBD), with more than 100 loci demonstrating statistically significant association,[156] and yet one gene with strong functional evidence for involvement has never exceeded the threshold for statistical significance in any GWAS or meta-analysis. X-box binding protein 1 (XBP1) was initially identified in a molecular screen for proteins that bind to X-box elements, a regulator of human major histocompatibility complex (MHC) genes. The selective knock out of this gene in mouse intestinal epithelium recapitulates many of the traits associated with IBD in humans, including spontaneous intestinal inflammations accompanied by lamina propria polymorphonuclear infiltrates, crypt abscesses and frank ulcerations, and an increase in intraepithelial lymphocyte numbers. Following phenotypic characterization of this mouse model, a candidate gene association study was performed in a cohort of 1100 IBD cases and 1100 controls identified a SNP with evidence for association that exceeded a candidate gene threshold (p=1.6x10-5), but would have not exceeded a genome-wide significance level.[157] Importantly, the region in the genome that harbors XBP1 was implicated with nominal evidence for linkage in three independent family-based studies,[158-160] and sequencing of the gene found a three-fold increase of rare SNPs in IBD patients relative to controls and identified five rare nonsynonomous variants that were not seen in control patients.[157] Cumulatively, this evidence suggests that pursuing

linkage studies in combination with deep sequencing will identify genes that contribute to common disease and escape detection with GWAS.

The trajectory for gene discoveries by GWAS in other autoimmune diseases suggests that there are many more risk alleles that are common in the population and await discovery from GWAS in larger cohorts. For example, the initial GWAS in Crohn's disease, which each analyzed less than 1000 patients increased the number of causal loci to approximately ten. When meta-analyses began to be performed across increasingly larger data sets, the number of loci increased dramatically, such that today, there are 79 bona fide disease loci (Figure 2). This sequence has been remarkably similar across a number of autoimmune diseases. Clearly, there is much more biological insight to be gained by continuing to conduct AA GWAS in independent samples and performing meta-analyses across studies.

Finally, the epidemiological and genetic evidence for shared disease mechanisms provides rationale for performing GWAS meta-analyses across aligned autoimmune diseases. For instance, thousands of samples have already been genotyped for GWAS in T1D and CeD, and these data sit in public repositories. A substantial number of loci implicated in our initial GWAS had previously been shown to increase risk of these diseases and suggests that a meta-analysis across diseases could provide greater resolution to AA disease mechanisms.

While pathophysiological insight is an important endpoint to genetic studies, there are additional promises that loom on the horizon. One of the earliest promises of the human genome project was that information contained within the genome could be used for the predictive assessment of health outcomes, including disease risk, prognosis and therapeutic response.[161-164] Furthermore, a more complete understanding of the genetic underpinnings of human disease could contribute to the development of innovative strategies to leverage genomics for the improvement of public health.[165] Correctly interpreting genomic data hinges on our understanding of the causal structure of a disease, which encompasses both

identification of a set of risk factors that exist within a given population, and an understanding of how specific factors act in concert to promote disease. Once this is understood, it becomes tractable to interpret a person's genomic information and to devise innovative and efficient strategies for integrating genomics into public health initiatives to reduce disease burden. A comprehensive understanding of the genetic architecture of a disease provides a robust starting point for evaluating relationships among all risk factors, both genetic and environmental. Moving forward, the prospective large-scale collection of data for environmental risk factors will significantly enhance our understanding of the causal structure of AA, and set the stage for analytic work that integrates genetic and non-genetic contributors to health, allowing us to rigorously evaluate how genomic information shapes environmental influences on health.

Figures and Legends

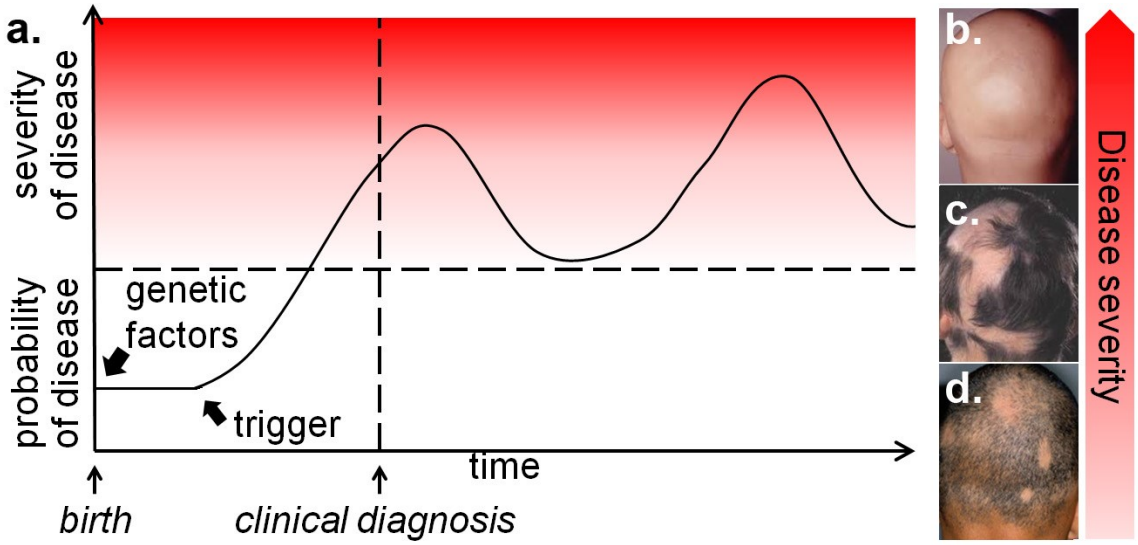

Figure 1. Trajectory of Disease (a) Model for AA disease trajectory in a patient. A person is born harboring a particular configuration of inherited risk alleles within his or her genome that sets a probability of developing disease. Over the life-course, that individual encounters risk factors in the environment that can alter the inborn liability for disease and at some point in time, a set of risk factors that is sufficient for disease converges on the individual and onset occurs. The severity of disease for AA is measured by surface area of hairloss, and is variable over time. **(b,c,d)** Clinical manifestation of disease varies greatly. **(b)** The most severe forms of disease involve loss of all scalp hair (alopecia totalis) or all scalp and body hair (alopecia universalis). **(c)** Patchy forms of AA involve relapsing/remitting hair loss. Disease can spontaneously remit in some regions while new patches develop elsewhere, or alternatively, patches can increase in size and coalesce. **(d)** Milder forms of AA present as one or a few small circumscribed regions of hair loss.

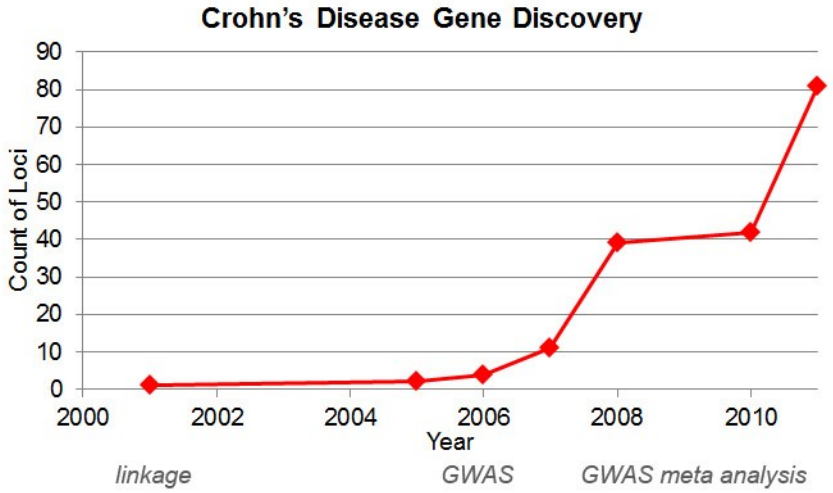

Figure 2. Trajectory for the discovery of Crohn's disease risk genes. The first gene implicated in Crohn's disease was identified by linkage analysis in 2001. The advent of genome-wide association studies greatly accelerated the acquisition of information about risk conferred by the genome, such that the first three GWAS increased the number of loci to ten. As the sample sizes increased and meta-analyses were performed across independent studies, the number of risk loci increased substantially, such that today, there are at least 79 bona fide Crohn's disease genes.

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Paper 2

SNP linkage scan in Alopecia Areata families confirms susceptibility loci and identifies two novel regions that harbor cosegregating disease variants.

Abstract

With a lifetime risk of approximately 2%, Alopecia Areata (AA) [MIM 104000] is one of the most common human autoimmune diseases, affecting approximately 5.3 million individuals in the US, including males and females of all ages and across ethnic groups. We previously found evidence for rare disease variants that cosegregate with AA in families by conducting a genome-wide linkage screen with microsatellite (ms) markers in 20 US and Israeli families. We demonstrated strong evidence for linkage on chromosome 6q (Z=3.6) and suggestive evidence (Z>1.5) on 6p near HLA and on an additional five chromosomes (1, 2, 9, 10, and 16). Fine mapping was then performed in an expanded cohort of 38 families for six regions with microsatellite markers, which upheld linkage evidence on chromosomes 6q (Z=2.89) and 16 (Z=3.12), and increased the strength of evidence on chromosome 18 (Z=3.93). Here we sought to increase linkage information by conducting a genome-wide linkage scan using 300,000 SNPs on a commercial genotyping array in 38 US families, consisting of 8 from the original scan, 18 which were added for the fine mapping project, and 12 new families. Linkage analysis identified eight regions with LOD scores >1.5, six of which coincide with regions identified in our first linkage scan, most notably on chromosomes 2 (Z=4.17), and two regions on chromosome 6q (Z=2.31 and 2.18). Two novel regions were identified, on chromosomes 5 (Z=1.71) and 20 (Z=1.52). Association analyses in these families implicate 47 genes, some of which map to biological processes implicated by our genome-wide association study (GWAS) which had been conducted in a cohort of unrelated AA patients and controls. Our data are consistent with emerging evidence in other complex diseases that the genetic architecture for common diseases consists of both rare mutations and common risk variants. These findings significantly advance our efforts to define the genetic architecture of AA systematically.

Introduction

Alopecia areata (AA; OMIM 10400) is one of the most common autoimmune diseases. It affects approximately 5.3 million people in the US and shows no predilection towards a particular gender. Although it can first strike at any age, the median age of onset is in the second or third decade of life, and it is the most common form of hair loss for children. Despite the prevalence of AA, there are no evidence based treatments, which creates an enormous unmet medical need.[1]

With AA, the autoimmune attack is targeted at the hair follicle and is characterized clinically by disfiguring hair loss and histologically by an accumulation of infiltrating lymphocytes at the base of the hair follicle. Because the stem cell compartment of the hair follicle is spared from the attack, hair regrowth remains possible. The disease is typically first identified as one or a few small circumscribed regions of hair loss on the scalp, although it can occur anywhere on the body. Prognosis is highly variable and unpredictable. For some patients, remission occurs and hair regrows within lesions and is never lost again (transient AA; AAT). For a subset of patients, the disease persists as a chronic relapsing remitting disorder, with regrowth occurring in some lesions, as new patches of hair loss arise (patchy alopecia areata; AAP). Finally, in severe forms of AA, the regions of hair loss increase in size and coalesce, eventually causing complete hair loss of the scalp (alopecia totalis; AT) or in extreme cases, the scalp and body (alopecia universalis; AU).

Initial evidence supporting a genetic basis for AA was obtained from multiple lines of research, including increased risk of disease in first degree relatives,[2,3] increased disease concordance among monozygotic twins relative to dizygotic twins,[4,5] studies in animal models,[6] and candidate gene studies that demonstrated associations between genes within the human leukocyte antigen complex (HLA): HLA-DQB1, HLA-DRB1, HLA-A, HLA-B, HLA-C, NOTCH4, MICA; as well as genes outside of the HLA: PTPN22, and AIRE (reviewed in [7]). The most

robust evidence for genetic contributions to AA was obtained from the first genome-wide linkage scan that we conducted by analyzing microsatellite markers in a small cohort of families. This study demonstrated significant evidence (LOD>3.0) for cosegregation of AA with at least three independent loci and thus firmly established a genetic basis and further supports a heterogeneous architecture, as the evidence is inconsistent with a single-gene disorder.[8] The sizes of the linkage intervals coupled with technological limitations precluded identification of particular genes in that study.

More recently, we conducted a genome-wide association study (GWAS), which implicated nine regions of the genome that contained 139 typed SNPs and 174 imputed SNPs with statistically significant association to AA ($p \leq 5x10^{-7}$).[9] Some of these regions only contained one or a small set of functionally related genes, which highlights the importance of T cell activation and maintenance of regulatory T cells in disease pathogenesis, in particular CTLA4, IL2/IL21, and IL2RA. This study also implicated ULBP3/ULBP6, PRDX5, STX17, Eos/ERBB3 and PTPN2, in addition to the HLA. The biological and therapeutic implications of these findings are extensively reviewed elsewhere.[10] Importantly, a number of identified genes had been previously shown to increase risk for other autoimmune diseases such as type 1 diabetes, rheumatoid arthritis and celiac disease, corroborating epidemiological evidence for an increased risk of these disorders among AA patients.[11-17] While these findings have transformed our understanding of the underlying pathology and suggest new therapeutic interventions for AA, they pertain to only a subset of components to the genetic architecture of the disease: those amenable to detection by GWAS.

Disease alleles that are amenable to detection by GWAS are common in the population and tend to have small effects on the distribution of disease. GWAS methods rely on an assumption that the typed or imputed markers, intended to serve as tagSNPs, will adequately capture the distribution of disease alleles within the study cohort. Power to detect association is

therefore greatest when high linkage disequilibrium (LD) exists between disease alleles and tagSNPs, and when the disease alleles are at similar frequencies to the tagSNPs.[18] Disease alleles that are rare in the population are less likely to demonstrate association via tagSNPs and are therefore not likely to be detected by this method. Such rare disease alleles are expected to have stronger phenotypic effects and thus to be more likely to demonstrate evidence for cosegregation with disease in families. So while our GWAS was successful in illuminating previously unsuspected and pathologically important biological pathways, the method is limited to detecting select components of the genetic architecture, i.e., disease alleles that are common in the population. Emerging empirical evidence, which is augmented by theoretical arguments, suggests that the genetic architecture of chronic diseases contains niches for both rare and common alleles.[19-32] Furthermore, while it is theoretically plausible that loci carrying common disease variants will also harbor rare disease variants, it is less likely that the reverse may be found. For example, if a locus is under strong purifying selection, disease alleles will be maintained at low frequencies. Therefore, although it remains unclear how these classes of alleles together influence the distribution of disease within populations, identifying a full spectrum of disease alleles will allow for a more complete illumination of the genetic architecture of disease, and in turn drive a more comprehensive understanding of the underlying pathophysiology.[33,34]

Our previous linkage analysis was small in scope, including only 20 families that were genotyped with 400 microsatellite markers. A number of independent groups have demonstrated that dense commercial genotyping arrays of SNP markers increase information content relative to panels of microsatellite markers.[35-39] Therefore, in this study, we expanded our linkage study by increasing the size of our cohort and utilizing a commercial genotyping array with 300,000 SNPs. While previous GWAS in AA have illuminated risk loci that harbor

common disease variants, this current study will utilize a complementary approach that will focus on identifying rare variants with stronger phenotypic effects.

Materials and Methods

Ascertainment of Families

Families were ascertained in the United States through the National Alopecia Areata Registry (NAAR) and recruited through a patient diagnosed with AA. NAAR inclusion criteria require that families have two or more affected relatives with confirmed diagnoses across at least two generations. All family members willing to participate were recruited for the study. All families that had completed enrollment at the time of genotyping were included in our study.

Clinical examiners diagnosed patients prior to the genetic studies in accordance with published criteria.[40,41] Unaffected family members are given the option to self-report disease status and so were not necessarily screened by a dermatologist. At the time of consultation, blood samples were drawn and written informed consent was obtained from all participants. The study was approved by the local IRB committees. Overall, a total of 38 families were included in this study, consisting of 121 affected and 98 unaffected/unknown individuals (Figure 1). Six of these families had been included in our previous linkage scan.[8] These are all the families from that study that had been ascertained in the US. On average, each family contained approximately 3 affected individuals. Ancestry information was obtained from 26 of the families: 18 self-report European descent and the remainder report race as African-American (n=2), Hispanic (n=3), mixed (n=2), or Pacific Islander (n=1).

Genotyping

Samples were genotyped on the Illumina HumanHap330V.2 genotyping Beadchip according to manufacturer's instructions at The Feinstein Institute for Medical Research as previously described.[42]

Statistical Analysis

Data Cleaning

Data cleaning was performed by Wei V. Chen and Christopher I. Amos at University of Texas MD Anderson Cancer Center, Houston, Texas. Mendelian inconsistencies were identified using a modified version of Pedcheck [43] that allows for the processing of more markers than the original version. Monozygotic (MZ) twins were identified using an in-house Perl script. Further relationship checking was performed using a version of Prest [44] that was modified to allow for more markers.

Merlin Cluster Non-parametric Linkage Analysis

Non-parametric analysis was performed by MD Anderson collaborators on cleaned data using Merlin.[45] Linkage analysis of markers in LD will increase the false positive rate. Our data set included over 300,000 genotyped SNPs. Therefore, to mitigate type I error, clusters of tightly linked markers were identified first, and then non-parametric linkage analysis was performed on the clusters. Marker position information was obtained from NCBI, genome build 36.

Tests of Association

I performed several tests of association on SNPs, as described below.

SNPs that were located within linkage regions were tested for evidence of allelic association by two methods. First, I performed a pedigree-based association test (PBAT).[46] This test is an extension of the transmission disequilibrium test (TDT) that allows for analysis of

extended families, and identifies alleles that are overtransmitted to affected offspring. It was run testing a null hypothesis of no association in the presence of linkage, under an assumption of an additive genetic model, as implemented in Helix Tree (Golden Helix). Details about this methodology can be found at http://www.goldenhelix.com/SNP_Variation/Manual/pbat_overview.html#x119-72800023.1.

Second, I evaluated evidence for joint and conditional linkage and LD with Pseudomarker[47]. This program uses a likelihood ratio test to perform five analyses: (1) test of linkage, (2) test of linkage in the presence of LD, (3) test of LD in the presence of linkage, (4) test of LD in the absence of linkage, and (5) joint test of linkage and LD. SNPs were analyzed under recessive and dominant models.

Finally, I ran PBAT on the full genome-wide data set, testing a null hypothesis of no association under the assumption of an additive genetic model.

For all analyses, marker position information was obtained from NCBI, genome build 36. The location of SNPs relative to genes was determined using Biomart in Ensembl (http://useast.ensembl.org/biomart).

Results

Data Cleaning

One pair of MZ twins was identified and subsequently confirmed; only one sib in the MZ twins was kept for subsequent analyses. Analyses of Mendelian inconsistencies identified two families causing 59% and 36% of errors, respectively. Further relationship checking was then performed and identified three sample switches in these two families. Switching back the samples reduced the number of Mendelian inconsistencies, removing more than 90% of the errors originally detected in both families. Genotypes involved in sporadic Mendelian

inconsistencies were recoded to missing to generate the clean data. 8567 SNPs of minor allele frequency (MAF) less than 0.05 were removed from all analyses.

Non-parametric Linkage Analysis

Non-parametric linkage analysis was performed on 26,473 clusters of correlated SNPs using MERLIN. Results are plotted for the whole genome in Figure 2. A maximum LOD score of 4.17 is observed on chromosome 2q36.1-q37.3. Two regions exceeded a LOD score of 2, both located on chromosome 6. At 6p12.2-q15 LOD=2.31 and at 6q22.31-q24.1 LOD=2.18. Five additional regions exceed a LOD score threshold of 1.5: 5q33.1-q34, 8p23.1, 12q21.33-q23.1, 9p24.3, and 20q13.12. An additional 12 regions on 8 chromosomes exceeded a LOD score threshold of 1. These 20 regions are listed in Table 1 with region boundaries that are provided by the most distal marker comprising the clusters that exceed a LOD score of 1.

We also examined the results for individual families, in order to identify families that could be used in future whole-exome sequencing studies. For the vast majority of families, linkage evidence did not permit prioritization of any reasonable number of regions in the genome. For example, on average for each family the maximum LOD score occurred for more than 3800 SNP clusters (14% of the genome). However, in seven families, the maximum LOD score was observed for a small number of clusters, less than 360, implicating relatively few regions (5-50 per family). This could allow a reasonable number of regions to be prioritized for follow-up sequencing (Figure 3). Thus, across these seven families, there were a total of 107 such regions, and 14 of these were shared by 2-4 of the families (Table 2). Only five of these shared regions achieved a LOD score ≥1.0 in the cohort (1p13.2, 1q23.3, 6q22.31-q24.1, 12q21.33-q23.1, 18p11.21). The identification of these regions will allow us to prioritize variants identified in future sequencing studies.

Pedigree-based Association Tests

We used PBAT to examine association, employing a null hypothesis no association in the presence of linkage. All 20 regions that contained at least one cluster for which LOD>1.00 were examined. In total, these intervals contained 11,272 SNPs that form 863 clusters of highly correlated markers, as determined from our analysis of LD structure within our dataset in preparation for linkage analysis. Therefore we used 5.8×10^{-5} as our threshold for statistical significance (0.05/863).

Of the 20 linkage intervals tested, eight contained at least one SNP with statistically significant association ($p<4.4 \times 10^{-6}$) (Figure 4). In total 71 SNPs demonstrated association, 25 of which fell within intergenic regions, 6 of which fell within five pseudogenes, and 40 of which fell within transcripts, implicating four noncoding RNAs and 26 genes (Table 3).

Pseudomarker

Pseudomarker was used to test individual SNPs within several regions, including all regions for which LOD>1.5 in this study, three genomic regions that demonstrated cosegregation in our previous linkage study but not in this study (10p14-p11.23, 10q23.31-q26.11, and 16p12.1-q13), and several additional regions that had weak to nominal evidence in this study. In total, I analyzed 30,440 SNPs, which clustered into approximately 2600 groups of highly correlated SNPs across 15 genomic regions. Because Pseudomarker runs five tests for each SNP, and I ran the program twice for each SNP, once under the assumption of a dominant mode of inheritance and once under the assumption of a recessive mode, I used a threshold for statistical significance of $p \leq 1.9 \times 10^{-6}$. Only two of the evaluated SNPs exceeded this threshold for statistical significance: one at 2q36.1-q37.3, and one SNP in 6q22.31-q24.1 (Figure 4). Neither of these SNPs is located within a gene.

A comparison of the results across the five hypotheses evaluated with Pseudomarker supports NPL analysis and suggests allelic heterogeneity underlies these loci. For the majority of SNPs tested, the strongest evidence was obtained for tests of linkage, while the tests for LD were consistently less significant (Figure 5). In order to display results, for each SNP, I report only the smallest p-value over all tests (Table 4).

Genome-wide Pedigree-based Association Test

A genome-wide search for evidence of pedigree-based association (PBAT) was conducted by testing 300,277 informative SNPs against a null hypothesis of no association. In estimating the LD structure for linkage analysis, we had determined that the genome-wide data set clustered into 26,473 independent sets of SNPs. Therefore I set a threshold of statistical significance at 1.89×10^{-6} (0.05/26,473). No evidence of association exceeded this threshold (min observed pvalue=2.78×10^{-6}). For the top 1% of scores (n=3003), $p<0.008$, 1232 SNPs fell within genes, including 53 genes that reside within loci that achieved at least nominal significance ($p<0.001$) in our GWAS (Table 5).

Integration of Association Results

The sample size and study design may contribute to a loss in power to detect association. I hypothesize that variants with evidence for cosegregation with disease in families will have a strong impact on disease and are likely to have low frequencies in the population. The SNPs that are in this data set are common in the population, with frequencies greater than 5%. Therefore, it is possible that there are differences in allele frequencies between disease variants and genotyped SNPs, which is reducing power to detect association.[18] Furthermore, linkage analysis identifies loci that cosegregate and is robust against allelic heterogeneity. Results from Pseudomarker suggest that there is allelic heterogeneity within the regions with

evidence for linkage, such that families are co-segregating different disease alleles within the linked loci. The association tests conducted in this study are based on the assumption that a disease allele will be shared among a proportion of affected individuals within the cohort from different families, and the results from Psuedomarker do not support this hypothesis. Therefore, I next sought to identify variants and genes that showed weak but consistent evidence for association.

For each of the three association analyses that I ran, I took the top 1% most significant associations and identified genes with evidence in more than one association statistic. Of the 3358 SNPs in the top 1% for at least one association analysis, 1470 are located within one of 864 protein coding genes. Thirty-nine genes are implicated by two or more of the association tests, 22 of which have at least one SNP that is significant for two different tests. For the remaining 17 genes, different SNPs demonstrate association across test statistics. In total, there are 111 SNPs that demonstrate association for these 39 genes, such that the majority of genes (n=30) are implicated by more than one SNP (Table 6).

Discussion

A cohort of 38 multiplex families, consisting of 121 affected and 98 unaffected/unknown individuals was genotyped with the Illumina 330v.2 genotyping chip. Statistically significant evidence for linkage is observed at 2q36.1-q37.3 (LOD=4.17) and nominal evidence is observed at 6p12.2-q15 (LOD=2.31) and 6q22.31-q24.1 (LOD=2.18). An additional 17 regions exceed a LOD score of 1 (Table 1). The cumulative size of all linkage regions that we identified with LOD≥1 is 114,440,871 bp. These regions contain 618 protein coding genes, whose transcripts account for 58,556,469 bp, or 51% of the regions. It is estimated that the 20,000 genes in the

human genome span about 30Mb of DNA, or account for 1% of the genome. Thus the linkage regions contain a much greater density of genes than expected, which suggests that variation in protein coding genes is driving evidence for linkage.

Of the 618 protein coding genes within the linkage intervals, 14 are located within regions that achieved at least nominal significance ($p \leq 0.001$) in our previously published GWAS, 18 have been annotated as involved in an immune process in the Gene Ontology database, and 161 have been previously identified in a hair follicle gene expression experiment.

Comparison with Microsatellite Scan

Of the 8 regions that exceeded a LOD score of 1.5 in this current study, six regions had at least suggestive evidence (LOD>1.0) in our initial microsatellite scan (2q36.1-q37.3, 6p12.2-q15, 6q22.31-q24.1, 8p23.1, 9p24.3, and 12q21.33-q23.1) and two are completely novel (5q33.1-q34, and 20q13.12). The three regions with the strongest evidence for linkage in this study, had different estimates in our previous study (Figure 7). In this study, the maximum LOD score is observed at 2q36.1-q37.3 (LOD=4.18). In our previous linkage study, the maximimum LOD score observed in this region was 0.93. Linkewise, region 6p12.1-q15 achieved a LOD score of 2.31 in this study, and 1.17 in our previous study. Finally, region 6q22.31-q24.1 demonstrated a LOD score of 2.18 in this study and 3.55 in our previous study. For three of the previously identified regions, SNP linkage evidence reduces the size of the linked interval from that implicated by the microsatellite data (6q22.31-q24.1, 9p24.3, 12q21.33-q23.1).

Evidence of Association

When I examined evidence for association with three analytic methods, only one provided statistically significant evidence. Pedigree-based association tests (PBAT) within linkage intervals, employing a null hypothesis of no association in the presence of linkage, identified 71 SNPs for which $p<5.8 \times 10^{-5}$, 40 of which fell within a protein coding transcript,

implicating a total of 26 genes. When I next searched for nominal but consistent evidence for association by integrating the top 1% most significant SNPs for each of the three methods, 39 genes were implicated by more than one association statistic, some of which were implicated by at least one statistically significant SNP with PBAT in linkage intervals. Therefore, this study identifies a total of 47 genes that contain SNPs with evidence for association within our cohort of AA families (Table 7).

Three of these genes are annotated as immune response genes in the Gene Ontology Database. Sec61 alpha form 2 isoform a (SEC61A2) is involved with antigen processing and presentation of peptide antigen via MHC class I (GO:0002474). Integrin, alpha M (ITGAM) is involved with activated T cell proliferation (GO:0050798). Pantetheinase (VNN1) is implicated in innate immune responses (GO:0045087), and T cell differentiation (GO:0033089), in addition to response to oxidative stress (GO:0006979), and anti-apoptosis (GO:0006916). A third gene, methionine sulfoxide reductase A isoform a (MSRA), is also annotated as a gene that responds to oxidative stress. Finally, Abelson helper integration site 1 (AHI1), deleted in colorectal carcinoma (DCC), and collagen, type IV, alpha 3 (COL4A3) are all annotated as apoptosis genes (respectively GO:0043066, GO:0042981, and GO:0006917).

It is interesting to note that all five of these pathways have been implicated by loci identified in our GWAS. For example, MICA ($p=1.2x10-7$) and TAP2 ($p=3.9x10-7$) are both involved with MHC class I presentation of antigen; PRDX5 ($p=4.1x10-7$), MICB ($1.7x10-5$), and PARK2 ($p=8.8x10-5$) are oxidative stress response genes; lymphocyte differentiation genes include IL2RA ($p=1.7x10-12$), CTLA4 ($3.6x10-13$), and IL21 ($p=4.27x10-8$); innate immune response genes include CFB ($p=3.2x10-8$) and C2 ($p=7.4x10-7$); and anti-apoptosis genes include IL2 ($p=2.7x10-6$) and IER3 ($p=2.8x10-7$).

Six of the genes implicated by association analyses are located with LD blocks that achieved nominal significance in our GWAS ($p<0.001$): AHI1, KN motif and ankyrin repeat

domains 1 (KANK1); eyes shut homolog (EYS); GLIS family zinc finger 3 (GLIS3), KIAA1217, and sarcoglycan, zeta (SGCZ). GLIS3 is a particularly interesting candidate gene. Rare mutations in this loci have been implicated in neonatal diabetes [48], while common variants confer risk to type 1 diabletes [49]. Our GWAS in AA identified several loci that increase risk for both type 1 diabetes and AA.[9,10]

Comparison with GWAS

We published the first GWAS in AA, identifying statistically significant association to nine regions in the genome, some of which contain only one or a few functionally related genes. This study confirmed association with the HLA region and additionally implicated IL2/IL21, CTLA4, ULBP3/ULBP6, IL2RA, STX17, PRDX5 and Eos/ERBB3. Each of these regions has since been confirmed through independent studies.[9,50,51] Of these genes, only IL2RA came up as nominally significant in our genome-wide PBAT. This is consistent with the notion that GWAS and linkage are complementary methods, targeting fundamentally different types of disease alleles. GWAS alleles will be common in the population and have weak correlations with disease and so are not likely to demonstrate cosegregation in families. Tests of association within families identify disease alleles that cosegregate with disease and are more strongly correlated with disease. When I examined the distribution of GWAS risk alleles in our cohort of families, I found that the frequency of risk alleles was greater than what we found in a sample of unrelated unaffected people, but did not differ within families between affected and unaffected family members (Table 7). This suggests that GWAS risk alleles are not sufficient for disease within these families and exemplifies the necessity of pursing both methods, GWAS and linkage, when seeking to illuminate the genetic architecture of a common disease.

In conclusion, by conducting this second genome-wide linkage study, we have found significant evidence for a disease locus that cosegregates with AA, located within a genomic region that only achieved suggestive evidence in our previous linkage scan, chromosome 2q36.1-q37.3. Association analyses within all regions of at least suggestive linkage evidence implicates 22 protein coding genes. Furthermore, by identifying SNPs with nominal but consistent association evidence in at least two different analytic methods increases the total number of genes identified in this study to 47. While there is very little overlap in the genes identified in this study and genes identified in our AA GWAS, there are extensive similarities in the biological processes implicated by each set of genes. Both studies identified genes involved with antigen presentation, lymphocyte differentiation, immune response, oxidative stress response, and apoptosis. This is consistent with emerging evidence that suggests both common and rare risk alleles underlie common diseases. It is interesting that while the the first three pathways predominate GWAS findings, association in families more strongly implicate the latter two pathways. This suggests that different biological pathways may be more compatible with assumptions in one or the other genetic method and further supports pursuit of both methods moving forward.

Figures and Legends

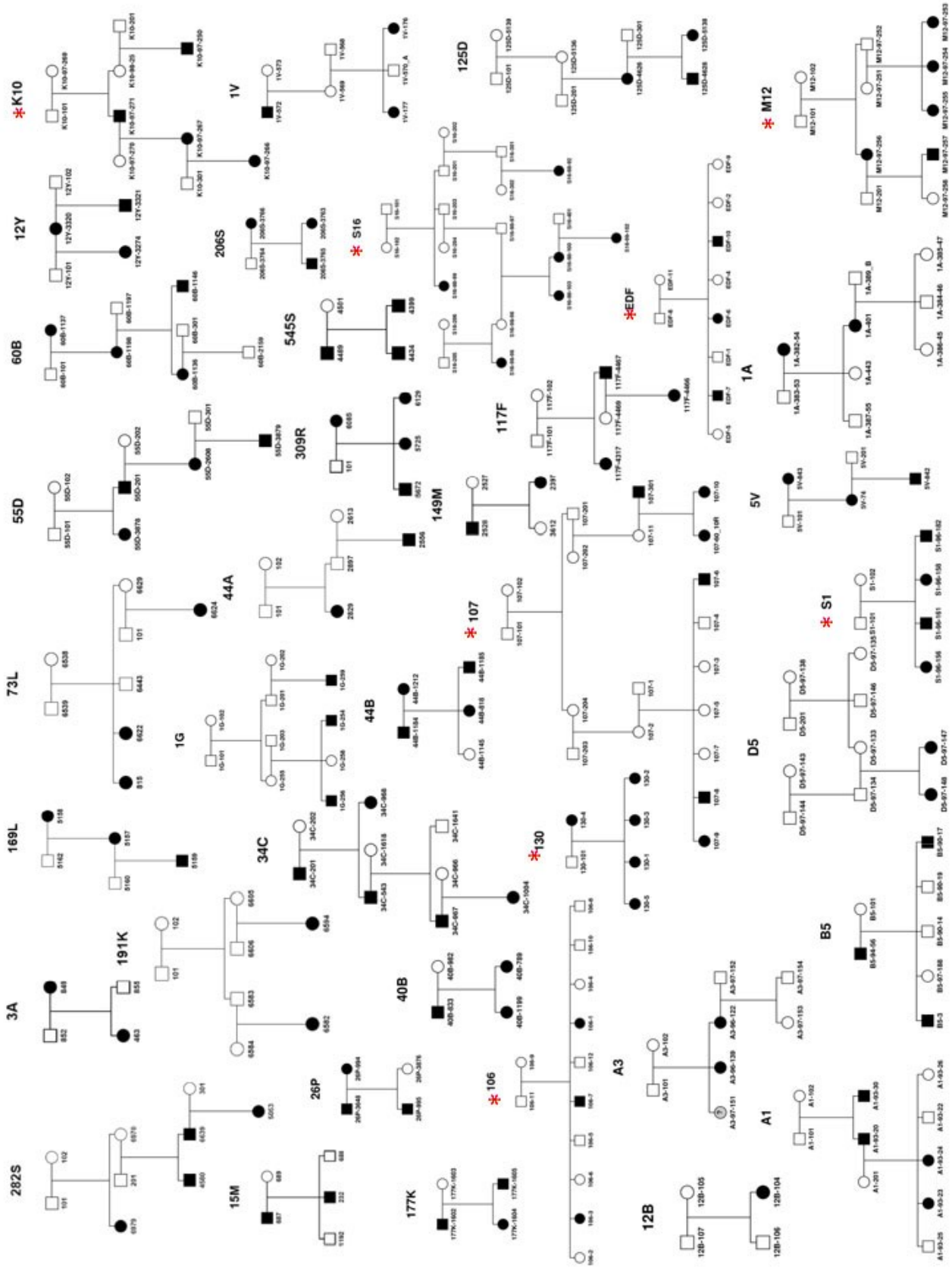
*K10
12Y
60B
55D
73L
169L
3A
282S
1V
206S
S16
545S
309R
44A
1G
191K
15M
26P
*106
177K
40B
44B
34C
*130
*107
149M
117F
*EDF
125D
1A
5V
*M12
*S1
D5
B5
A1
A3
12B

Figure 1. Pedigrees of Family-based Cohort. Families with two or more affected individuals across three generations were ascertained in the United States through the National Alopecia Areata Registry. Eight of these families had been included in our previously reported microsatellite scan (red asterisk).

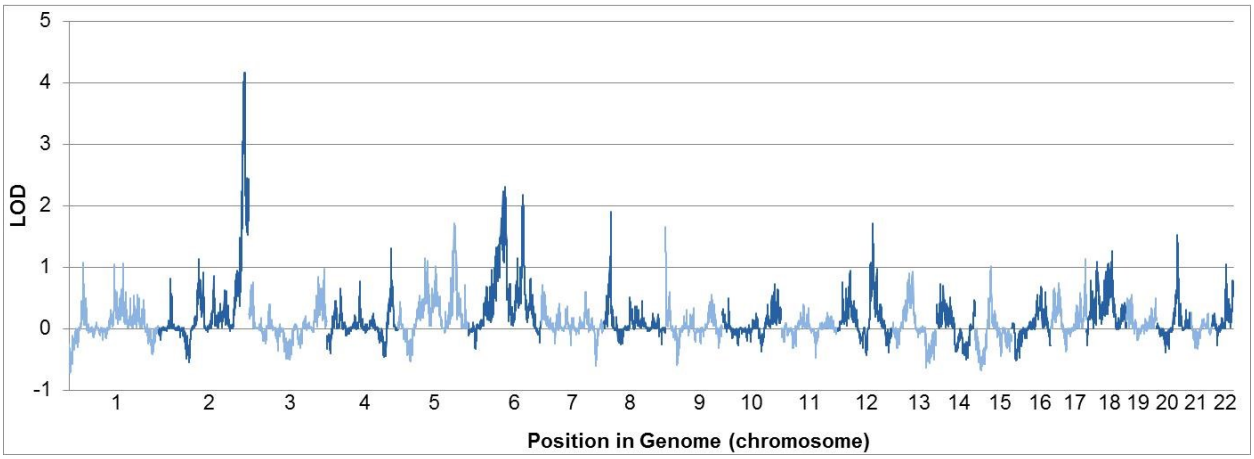

Figure 2. Whole genome plot of nonparametric linkage analysis. A maximum LOD score of 4.17 occurred on chromosome 2q36.1-q37.3. Two regions exceeded a LOD score of 2, both located on chromosome 6. A LOD score of 2.31 was observed at 6p12.2-q15, and a LOD score of 2.18 was observed at 6q22.31-q24.1. Five additional regions exceed a LOD score threshold of 1.5: 5q33.1-q34, 8p23.1, 12q21.33-q23.1, 9p24.3, and 20q13.12. An additional 12 regions on 8 chromosomes exceeded a LOD score threshold of 1.

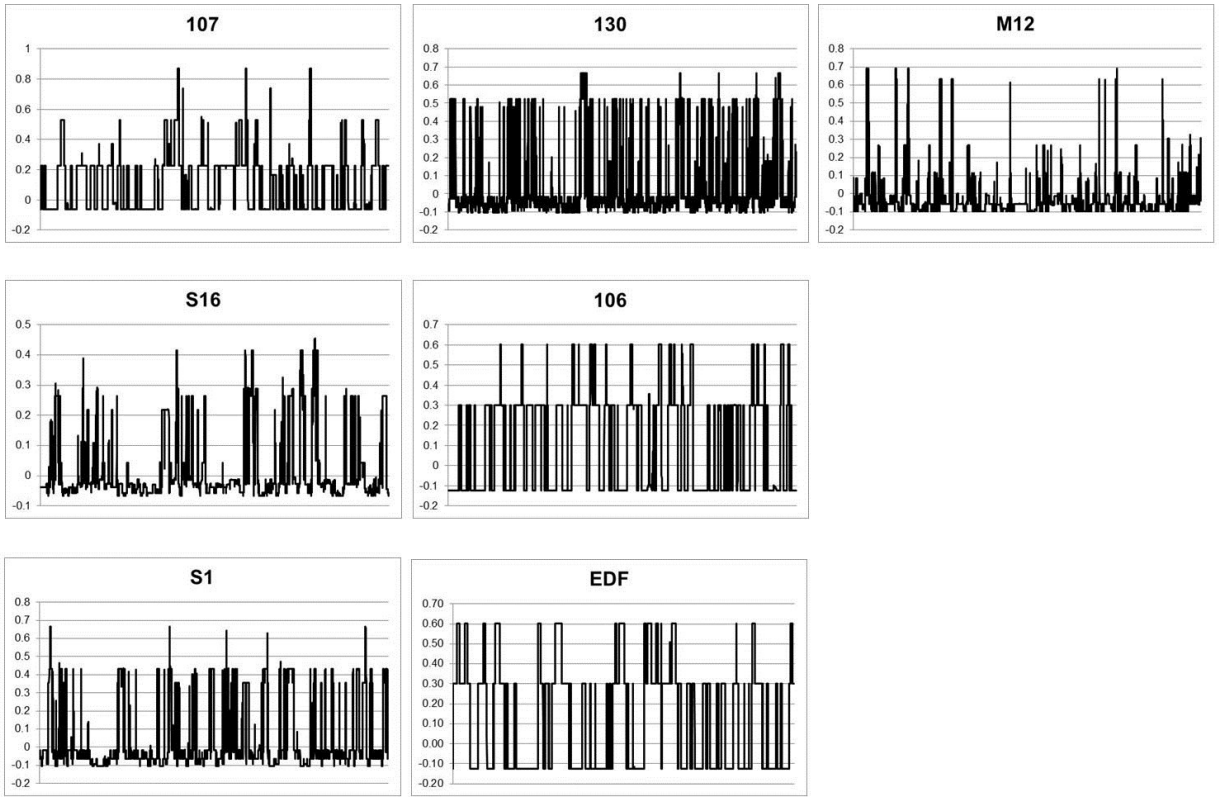

Figure 3. Whole genome plot of nonparametric linkage analysis for seven families. For seven families, the maximum LOD score occurred at a small number of regions (5-50 per family), allowing regions to be prioritized for follow-up sequencing. Across these seven families, there are a total of 107 such regions, 14 of which are shared by 2-4 of the families. The y-axis display LOD scores and are not consistent across the seven plots. The x-axis represents position in the genome and is consistent across the plots.

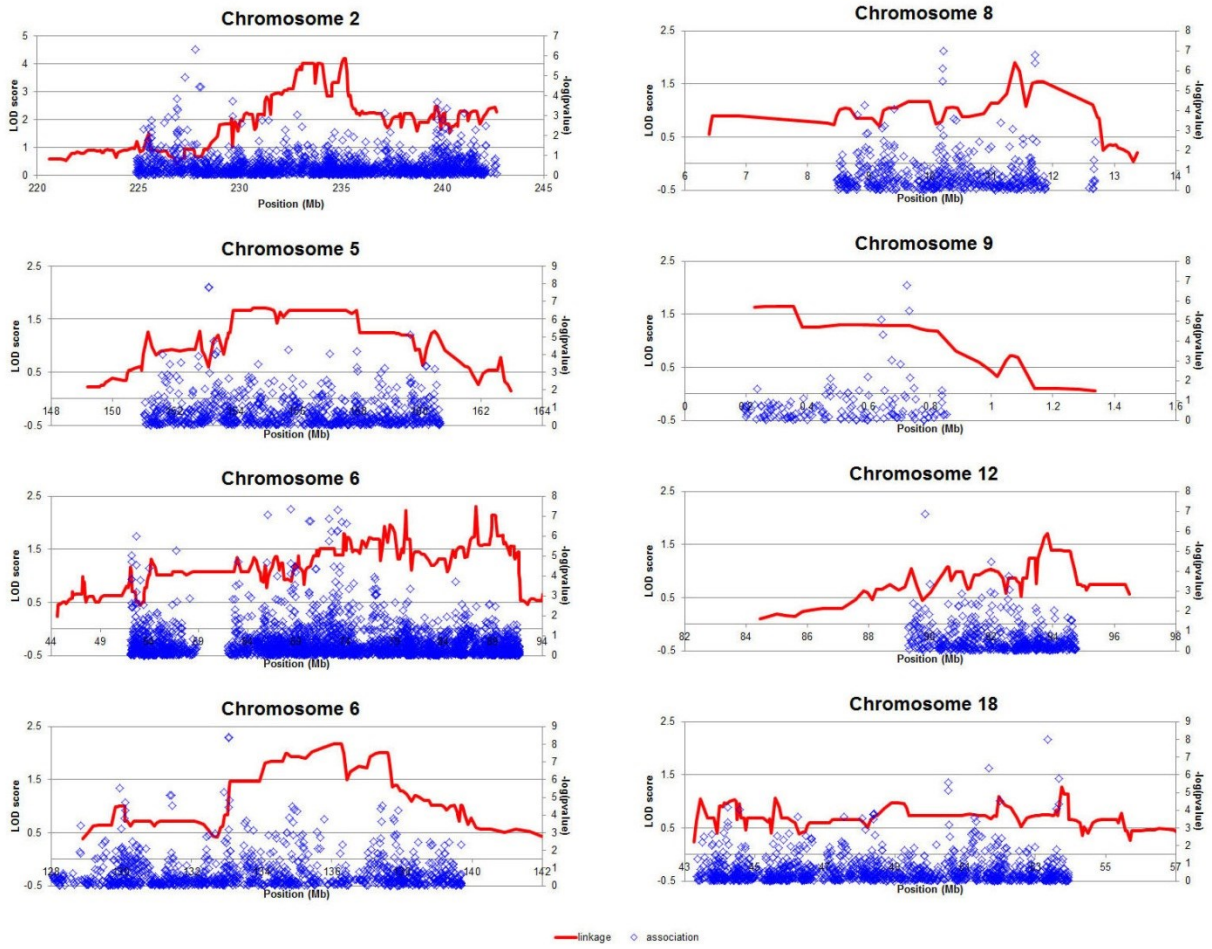

Figure 4. Pedigree-based association tests identified significant associations within eight linkage intervals. NPL results are plotted on the first Y-axis in red. Association results are plotted on the second Y-axis in blue. Y-axis values are consistent for all plots except for chromosome 2, which is plotted on a different scale to accommodate the larger score.

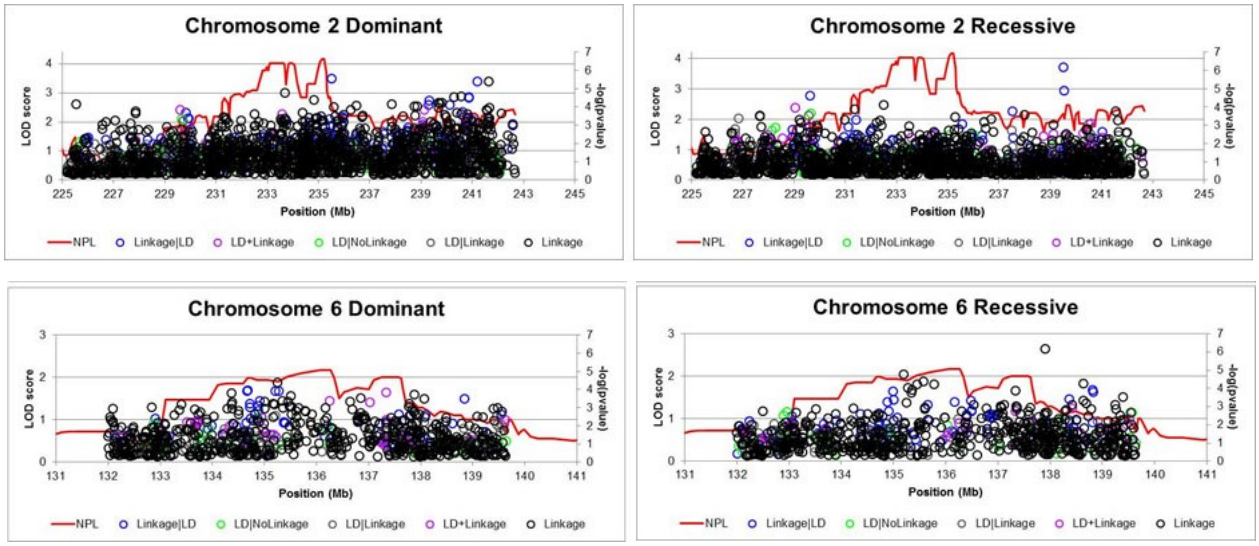

Figure 5. Pseudomarker identified significant associations within three linkage intervals. NPL results are plotted on the first Y-axis in red. Association results are plotted on the second Y-axis and color coded by the test with the minimum pvalue. The scale for the LOD score axis varies between the plots for chromosome 2 and 6.

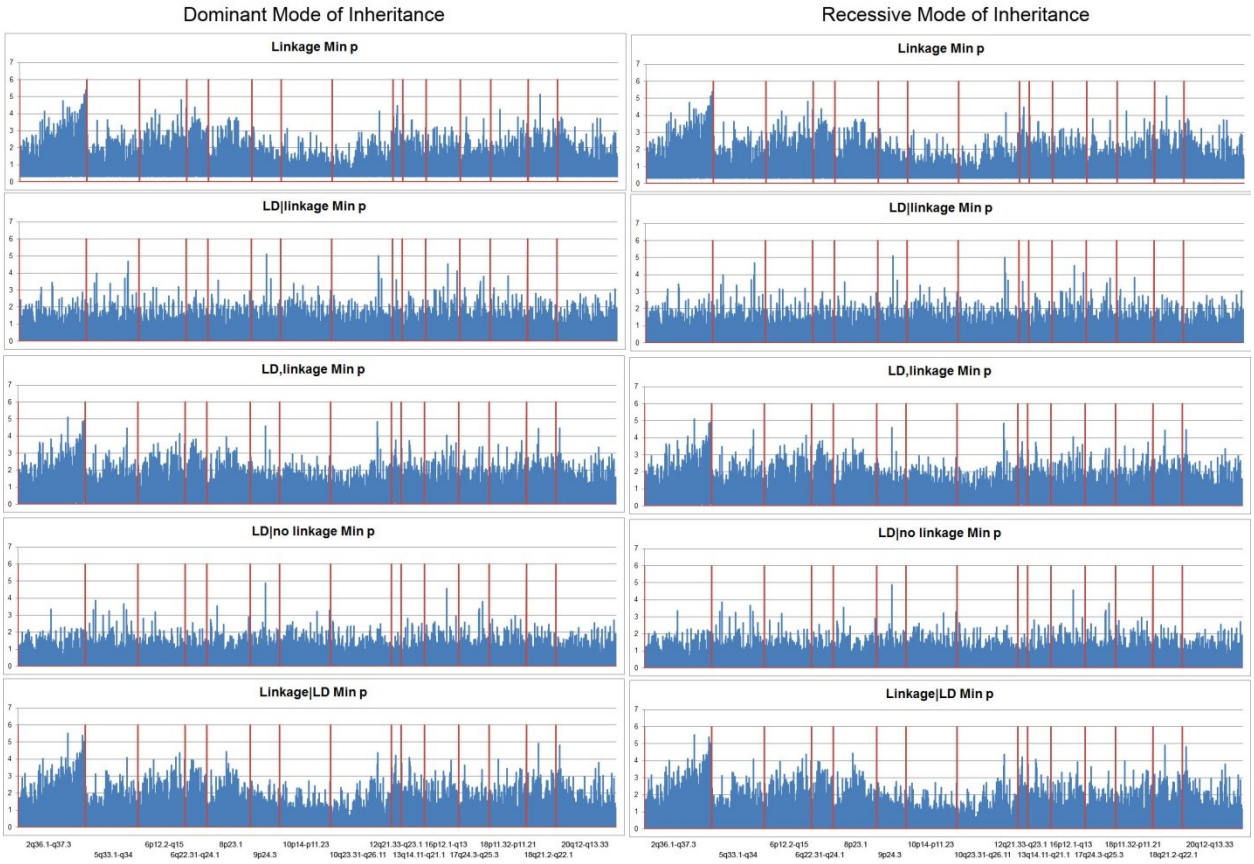

Figure 6. Pseudomarker Results across all regions tested. 30,440 SNPs, which clustered into approximately 2600 groups of highly correlated SNPs within 15 genomic regions were analyzed. Results are plotted as –log(pvalue), regions are delimited by red lines and labelled along the s-axis.

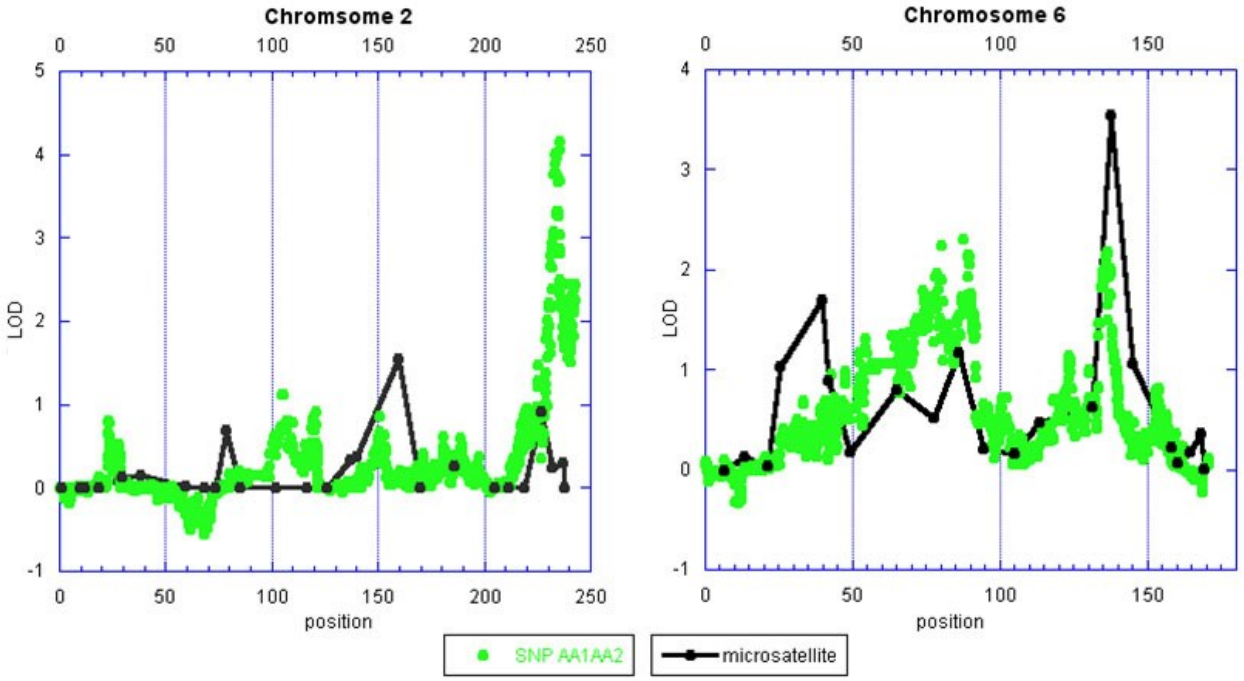

Figure 7. A comparison of SNP linkage scan with microsatellite linkage scan. Linkage analysis in this study identified three genomic regions on two different chromosomes with at least nominal evidence. Results from both studies for these two chromosomes are presents. Results of NPL analysis from this study is shown in green, while results from the first linkage study conducted with microsatellites is plotted in black. The Y-axis scales are different between the two graphs to accommodate the LOD scores.

Tables

chr	Cytoband	snp start	position start	snp stop	position stop	region size	max NPL LOD
1	1p36.1	rs10794531	26,694,245	rs9438620	26,716,136	21,891	1.08
1	1p13.2	rs155646	112,688,022	rs3128373	112,858,294	170,272	1.04
1	1q23.3	rs4657210	162,587,423	rs1704745	162,693,795	106,372	1.06
2	2q12.1	rs7571700	105,189,937	rs2679852	105,797,790	607,853	1.13
2	2q36.1-q37.3	rs2098533	225,182,419	rs12469535	243,044,147	17,861,728	4.17
4	4q34.3	rs1991983	182,454,723	rs6821430	182,499,174	44,451	1.31
5	5q13.1-q13.3	rs2047588	71,578,902	rs2114950	76,726,202	5,147,300	1.15
5	5q21.2	rs11955569	103,472,789	rs2034227	103,647,014	174,225	1.01
5	5q33.1-q34	rs4958486	151,058,334	rs10515827	160,754,957	9,696,623	1.71
6	6p12.2-q15	rs4715280	51,974,289	rs1504292	91,637,689	39,663,400	2.31
6	6q22.31-q24.1	rs9385268	123,041,722	rs7744152	139,663,885	16,622,163	2.18
8	8p23.1	rs7843504	8,439,068	rs7463440	12,652,105	4,213,037	1.9
9	9p24.3	rs10964134	204,201	rs755383	863,635	659,434	1.65
12	12q21.33-q23.1	rs2897852	90,768,440	rs11612901	96,221,318	5,452,878	1.71
15	15q22.2	rs11630244	60,021,637	rs7174483	60,123,836	102,199	1.02
17	17q25.3	rs1869932	77,318,565	rs2241886	78,113,832	795,267	1.13
18	18p11.21	rs1149360	13,540,713	rs3760534	13,874,975	334,262	1.09
18	18q21.2-q21.31	rs1105471	45,086,502	rs554192	55,784,763	10,698,261	1.27
20	20q13.11-q13.12	rs6065582	41,771,701	rs2179069	43,507,254	1,735,553	1.52
22	22q13.2	rs2072884	43,436,169	rs695537	43,769,871	333,702	1.05

Table 1. Nonparametric linkage results. Regions with the top 20 highest LOD scores are shown.

Chr	Linkage Evidence	Min of Region Start	Max of Region Stop	Family Count	Family1	Family2	Family3	Family4
1	1p13.2	40.344	120.112	**3**	EDF	M12	S1	
1	1q23.3	144.184	178.478	**2**	EDF	M12		
2		140.385	222.478	**4**	EDF	M12	S16	S1
3		149.192	182.782	**2**	106	EDF		
4		60.75	149.882	**2**	EDF	M12		
5		0.126	4.661	**3**	106	EDF	M12	
6		25.281	41.449	**2**	106	EDF		
6	6q22.31-q24.1	106.549	141.653	**3**	130	EDF	S16	
6		145.188	156.341	**3**	107	130	EDF	
7		4.443	30.475	**3**	106	107	EDF	
7		149.164	158.812	**2**	106	EDF		
10		72.394	75.425	**2**	S16	EDF		
10		79.666	85.406	**2**	107	EDF		
10		125.152	135.241	**2**	106	S16		
11		62.773	111.852	**2**	106	EDF		
12	12q21.33-q23.1	84.993	126.472	**2**	106	EDF		
13		40.656	93.521	**2**	EDF	M12		
14		19.745	32.632	**2**	S16	EDF		
14		41.511	55.661	**2**	EDF	M12		
14		94.976	106.285	**2**	107	130		
18	18p11.21	7.873	48.008	**4**	106	130	EDF	M12
20		5.491	15.991	**2**	130	EDF		
20		49.624	62.375	**2**	106	EDF		

Table 2. Linkage evidence within families. For each family, a list of regions with maximum LOD score was compiled. Comparison across families identified a set of regions shared across families that achieved a LOD score greater than 1 for the entire cohort.

Marker	chr	position	MinP	Gene	Gene Type
rs2262438	6	133,058,735	3.9E-09	CCNG1P1	pseudogene
rs2745443	6	133,063,075	4.2E-09	CCNG1P1	pseudogene
rs473728	18	53,348,005	1.1E-08		
rs4958676	5	153,132,470	1.4E-08	GRIA1	protein_coding
rs1381119	5	153,138,879	1.6E-08	GRIA1	protein_coding
rs11964693	6	68,425,331	4.5E-08		
rs985564	6	73,225,898	4.8E-08		
rs17496685	6	66,063,541	8.8E-08	RP11-74E24.2	pseudogene
rs11249987	8	10,218,116	1.0E-07	MSRA	protein_coding
rs4523751	12	89,842,084	1.3E-07	RP11-916O13.1	lincRNA

rs185634	6	72,293,749	1.4E-07		
rs10815567	9	723,049	1.6E-07	KANK1	protein_coding
rs1534863	8	11,705,562	1.6E-07	FDFT1	protein_coding
rs1000468	6	70,402,661	1.7E-07		
rs1293044	6	70,290,602	1.8E-07		
rs17742423	6	73,588,333	2.0E-07	KCNQ5	protein_coding
rs9360664	6	74,098,145	2.3E-07	PAICSP3	pseudogene
rs10871622	18	51,677,998	4.2E-07		
rs1736058	8	11,708,450	4.3E-07	FDFT1	protein_coding
rs4430946	2	227,786,952	4.7E-07	COL4A3	protein_coding
rs9342947	6	73,222,052	5.5E-07		
rs10737976	6	72,572,001	5.7E-07		
rs9342944	6	73,131,044	5.9E-07	RIMS1	protein_coding
rs4307347	8	10,205,504	8.1E-07	MSRA	protein_coding
rs2670153	6	52,648,456	1.0E-06	TMEM14A	protein_coding
rs8094024	18	53,667,211	1.5E-06		
rs199635	6	72,282,724	1.8E-06		
rs2198229	18	50,520,401	2.8E-06		
rs10758863	9	732,642	3.1E-06	KANK1	protein_coding
rs10499162	6	129,960,703	3.1E-06	ARHGAP18	protein_coding
rs6601431	8	10,207,955	3.5E-06	MSRA	protein_coding
rs8192624	6	132,933,946	5.1E-06	TAAR6	protein_coding
rs13200559	6	56,750,279	5.6E-06	DST	protein_coding
rs9216	5	159,708,625	7.5E-06	C1QTNF2	protein_coding
rs9375796	6	131,382,691	7.8E-06	EPB41L2	protein_coding
rs1037391	18	50,518,821	7.9E-06		
rs951251	6	131,432,905	8.0E-06		

rs10491593	9	640,373	8.2E-06	KANK1	protein_coding
rs12199650	6	52,232,503	9.3E-06	MCM3	protein_coding
rs2178704	2	227,287,451	1.3E-05		
rs2294757	6	133,076,791	1.4E-05	VNN1	protein_coding
rs1461241	5	153,285,631	1.8E-05		
rs1781011	6	52,230,899	1.9E-05		
rs9354868	6	63,043,165	2.0E-05	KHDRBS2	protein_coding
rs4897336	6	130,123,754	2.0E-05	RP3-341I10.1	pseudogene
rs12209342	6	65,936,970	2.2E-05	EYS	protein_coding
rs2493383	6	68,418,391	2.4E-05		
rs7746344	6	52,646,130	2.8E-05	TMEM14A	protein_coding
rs276550	6	137,443,470	2.9E-05		
rs9398976	6	131,446,361	3.0E-05		
rs9960795	18	51,983,082	3.0E-05	AC006305.1	protein_coding
rs1542481	12	91,982,962	3.3E-05	RP11-511B23.2	antisense
rs2219188	6	68,816,458	3.3E-05		
rs1328857	6	73,414,549	3.3E-05	KCNQ5-IT1	sense_intronic
rs4896067	6	134,873,179	3.4E-05	RP11-557H15.3	lincRNA
rs9342910	6	72,753,745	3.5E-05	RIMS1	protein_coding
rs4707479	6	68,787,830	3.6E-05		
rs2300077	6	133,072,185	3.7E-05	VNN1	protein_coding
rs4643531	2	227,993,717	3.9E-05		
rs6705042	2	228,088,692	3.9E-05	AGFG1	protein_coding
rs10080737	6	53,997,540	3.9E-05	MLIP	protein_coding
rs6908735	6	70,953,236	4.4E-05	COL19A1	protein_coding
rs4346276	18	53,668,370	4.5E-05		
rs276504	6	137,394,212	4.6E-05	IL20RA	protein_coding

rs3806065	6	70,966,500	4.7E-05	COL19A1	protein_coding
rs228433	6	134,936,515	4.8E-05	RP11-557H15.4	processed_transcript
rs912170	9	646,736	4.9E-05	RP11-130C19.1	pseudogene
rs6570174	6	137,888,424	5.3E-05		
rs140616	5	155,743,532	5.3E-05	SGCD	protein_coding
rs9402168	6	130,108,429	5.3E-05	RP11-73O6.4	protein_coding
rs2979269	8	8,938,550	5.3E-05	ERI1	protein_coding
rs6936034	6	135,013,187	5.9E-05	RP11-557H15.4	processed_transcript
rs897405	6	68,867,259	6.6E-05		
rs824872	5	157,971,509	6.9E-05		
rs1202100	6	73,363,249	6.9E-05	RP3-474G15.1	pseudogene
rs7704562	5	153,387,590	6.9E-05	FAM114A2	protein_coding
rs1565247	18	44,223,758	6.9E-05		
rs10503019	18	53,605,375	7.9E-05	ATP8B1	protein_coding
rs2816903	6	68,436,846	8.1E-05		
rs10503381	8	9,411,916	8.2E-05		
rs2270820	5	157,090,950	9.1E-05	THG1L	protein_coding
rs11877669	18	44,568,382	9.1E-05	CTIF	protein_coding
rs11750592	5	151,627,960	9.8E-05	CTB-12O2.1	lincRNA
rs1898659	5	153,336,611	1.0E-04		
rs1011503	5	153,336,759	1.0E-04		
rs2106553	6	67,065,007	1.1E-04		
rs9360979	6	76,900,873	1.1E-04		
rs4246043	5	152,796,682	1.2E-04		
rs9321445	6	134,794,917	1.4E-04	RP11-557H15.3	lincRNA
rs524207	6	52,194,855	1.5E-04		
rs2894593	2	226,898,561	1.5E-04		

rs9321599	6	137,760,226	1.5E-04		
rs9398918	6	130,087,370	1.5E-04	RP11-73O6.4	protein_coding
rs7231528	18	48,412,118	1.5E-04	DCC	protein_coding
rs1825651	6	76,983,174	1.5E-04		
rs2039523	6	52,174,886	1.5E-04		
rs332022	8	8,820,875	1.6E-04		
rs4077047	6	53,097,965	1.7E-04	RP11-506E9.3	sense_overlapping
rs11830104	12	92,554,610	1.7E-04	RP11-887P2.3	pseudogene
rs1221872	18	48,384,335	1.8E-04	DCC	protein_coding
rs1221874	18	48,385,108	1.8E-04	DCC	protein_coding
rs1221877	18	48,387,824	1.8E-04	DCC	protein_coding
rs1221884	18	48,389,344	1.8E-04	DCC	protein_coding
rs11154801	6	135,781,048	1.8E-04	AHI1	protein_coding
rs7595911	2	104,621,738	1.8E-04		
rs6749383	2	104,626,334	1.8E-04		
rs2249751	6	72,963,918	1.9E-04	RIMS1	protein_coding
rs6937168	6	85,187,128	2.0E-04	RP1-90L14.1	processed_transcript
rs4608504	2	229,640,616	2.0E-04	PID1	protein_coding
rs489806	2	239,764,393	2.2E-04	HDAC4	protein_coding
rs477094	6	133,565,482	2.2E-04		
rs9494759	6	137,786,779	2.2E-04		
rs11877776	18	47,550,493	2.3E-04		
rs2119547	18	46,217,962	2.4E-04		
rs7761494	6	74,782,377	2.4E-04		
rs276585	6	137,418,306	2.4E-04		
rs10503002	18	51,260,200	2.5E-04	TCF4	protein_coding
rs754151	6	134,894,887	2.6E-04	RP11-557H15.4	processed_transcript

rs4392859	8	10,382,432	2.6E-04	RP11-981G7.4	antisense

Table 3. Results of PBAT|Linkage. Pedigree based association tests were performed across regions with evidence for linkage. Significant results are displayed. If the SNP falls within a transcript, it is annotated with a gene name and transcript type.

Marker	chr	position	MinP	MinTest	MinMOI	Gene
rs203691	6	137,909,141	7.0E-07	Linkage	rec	BTF3L4P3
rs4073751	2	239,543,016	7.1E-07	Linkage|LD	rec	
rs10203538	2	235,514,778	3.0E-06	Linkage|LD	dom	
rs2975785	2	241,218,002	4.0E-06	Linkage|LD	dom	GPR35
rs12694993	2	241,663,037	4.0E-06	Linkage	dom	SNED1
rs11783751	8	13,474,949	6.0E-06	Linkage	rec	RP11-145O15.3
rs4940732	18	54,436,031	7.0E-06	Linkage	dom	ALPK2
rs1535260	6	88,950,229	8.0E-06	Linkage	rec	
rs10511454	9	3,733,938	8.0E-06	LD|Linkage	dom	
rs11776120	8	6,877,045	9.0E-06	LD+Linkage	rec	DEFA11P
rs1395608	18	11,008,926	9.0E-06	Linkage	rec	PIEZO2
rs4573621	10	113,977,538	1.0E-05	LD|Linkage	dom	
rs7447732	5	158,461,713	1.1E-05	Linkage|LD	rec	EBF1
rs4591363	2	239,560,574	1.3E-05	Linkage|LD	rec	AC114788.1
rs2474619	6	90,936,756	1.5E-05	Linkage	dom	BACH2
rs4740731	9	3,737,376	1.5E-05	LD|Linkage	dom	
rs4450678	20	41,152,010	1.5E-05	Linkage|LD	dom	PTPRT
rs11693862	2	233,707,325	1.7E-05	Linkage	dom	INPP5D
rs11752655	6	135,202,002	1.8E-05	Linkage	rec	
rs1790994	18	2,903,431	2.0E-05	Linkage|LD	rec	LPIN2

rs3910253	5	162,993,830	2.1E-05	LD|Linkage	dom	
rs31278	2	229,630,498	2.5E-05	Linkage|LD	rec	PID1
rs10193614	2	240,589,309	2.7E-05	Linkage	dom	NDUFA10
rs4672907	2	219,529,413	2.8E-05	LD+Linkage	rec	KRT8P30
rs2720430	16	50,126,959	2.8E-05	LD|NoLinkage	dom	
rs7597153	2	240,875,489	2.9E-05	Linkage|LD	dom	
rs1437731	2	240,297,565	3.0E-05	Linkage	dom	
rs7589895	2	240,873,613	3.2E-05	Linkage|LD	dom	
rs10507058	12	94,622,878	3.5E-05	Linkage	dom	RP11-410A13.3
rs3088186	8	10,263,765	3.6E-05	Linkage|LD	dom	MSRA
rs4747964	10	12,217,003	3.8E-05	Linkage|LD	rec	SEC61A2
rs7239592	18	5,763,584	3.8E-05	Linkage|LD	rec	RP11-945C19.1
rs8083777	18	5,759,552	4.1E-05	Linkage|LD	rec	RP11-945C19.1
rs7368976	2	234,821,858	4.1E-05	Linkage	dom	
rs10885330	10	114,062,134	4.3E-05	Linkage|LD	dom	GUCY2GP
rs7760247	6	135,582,862	4.4E-05	Linkage	rec	MYB
rs962189	6	135,251,875	4.4E-05	Linkage	dom	
rs4446534	6	92,886,209	4.7E-05	Linkage	dom	U3
rs4643485	2	239,336,345	4.7E-05	Linkage|LD	dom	
rs9633625	10	21,406,784	5.1E-05	LD|Linkage	rec	NEBL
rs203136	6	138,647,945	5.4E-05	Linkage	rec	KIAA1244
rs7234567	18	3,410,806	5.7E-05	Linkage	dom	TGIF1
rs9494139	6	135,456,486	5.9E-05	Linkage	rec	HBS1L
rs1343484	6	78,291,084	5.9E-05	Linkage	dom	
rs7595357	2	239,845,273	5.9E-05	Linkage	dom	HDAC4
rs3791426	2	239,704,338	6.0E-05	Linkage	dom	HDAC4
rs11154801	6	135,781,048	6.1E-05	Linkage	rec	AHI1

rs4628288	8	17,995,037	6.1E-05	LD|Linkage	rec	CTD-2547L16.1
rs10099571	8	8,322,712	6.6E-05	Linkage	rec	CTA-398F10.1
rs4890008	17	75,920,214	6.7E-05	Linkage|LD	rec	RNF213
rs3791500	2	239,740,482	6.8E-05	Linkage	dom	HDAC4
rs921281	2	225,562,364	7.1E-05	Linkage	dom	DOCK10
rs9965626	18	5,757,540	7.2E-05	LD+Linkage	rec	RP11-945C19.1
rs4663712	2	237,873,814	7.5E-05	Linkage	dom	
rs967411	8	15,080,072	7.7E-05	Linkage	rec	SGCZ
rs893265	16	53,864,590	7.8E-05	LD|Linkage	dom	RP11-26L20.3
rs2757732	6	89,327,343	7.9E-05	Linkage|LD	dom	
rs4942767	13	48,029,770	8.0E-05	Linkage|LD	dom	
rs10084197	2	232,518,427	8.1E-05	Linkage	rec	0
rs7571643	2	240,132,491	8.1E-05	Linkage|LD	dom	
rs2660278	18	10,999,337	8.2E-05	Linkage	rec	PIEZO2
rs3849745	5	162,991,179	8.2E-05	Linkage|LD	dom	
rs4128254	2	239,310,782	8.3E-05	Linkage|LD	dom	AC113618.2
rs943265	10	114,037,385	8.4E-05	LD|Linkage	dom	TECTB
rs10211191	2	236,503,077	8.8E-05	Linkage	dom	AGAP1
rs2798509	6	78,267,482	8.8E-05	Linkage	dom	RPS6P7
rs7594825	2	210,106,477	9.1E-05	Linkage	rec	MAP2
rs12472274	2	238,760,161	9.2E-05	Linkage	dom	ILKAP
rs7579382	2	238,880,147	9.2E-05	Linkage	dom	
rs9494115	6	135,277,227	9.9E-05	Linkage	rec	ALDH8A1
rs1984191	13	44,269,573	1.0E-04	Linkage	dom	LINC00330
rs869385	20	55,972,383	1.0E-04	Linkage	rec	RP13-379L11.2
rs693405	18	8,728,849	1.0E-04	Linkage	rec	SOGA2
rs12163992	5	148,889,270	1.0E-04	LD|Linkage	dom	CSNK1A1

rs3812813	12	94,451,893	1.1E-04	Linkage	dom	USP44
rs1469375	2	235,614,926	1.1E-04	Linkage	dom	SH3BP4
rs238135	18	3,438,979	1.1E-04	Linkage	rec	TGIF1
rs9937837	16	31,206,440	1.1E-04	Linkage|LD	rec	ITGAM
rs6923743	6	134,679,540	1.1E-04	Linkage|LD	dom	SGK1
rs427056	5	162,782,337	1.1E-04	LD|Linkage	dom	RP11-541P9.3
rs3791399	2	239,690,698	1.1E-04	Linkage	dom	HDAC4
rs3815291	2	241,681,213	1.2E-04	Linkage	dom	MTERFD2
rs10189030	2	229,074,427	1.2E-04	LD+Linkage	rec	AC009410.1
rs7086845	10	91,733,609	1.2E-04	LD|Linkage	rec	SNRPD2P1
rs4543320	6	80,572,696	1.2E-04	Linkage	dom	RP1-159G19.1
rs7195219	16	27,184,557	1.2E-04	Linkage	rec	NSMCE1
rs7193898	16	52,142,422	1.2E-04	Linkage|LD	dom	
rs1040806	6	135,217,869	1.2E-04	Linkage|LD	dom	
rs9376080	6	135,357,091	1.2E-04	Linkage	rec	HBS1L
rs9493897	6	134,672,476	1.2E-04	Linkage|LD	dom	SGK1
rs693845	5	163,000,520	1.2E-04	LD|Linkage	dom	
rs10499200	6	138,813,645	1.3E-04	Linkage|LD	rec	NHSL1
rs13439657	8	14,855,604	1.3E-04	Linkage	rec	SGCZ
rs6914810	6	137,348,212	1.3E-04	Linkage	rec	RP11-55K22.5
rs4942780	13	48,214,742	1.3E-04	Linkage|LD	dom	
rs2865387	20	55,500,243	1.4E-04	LD|NoLinkage	rec	CTCFL
rs359980	2	219,537,450	1.4E-04	LD|Linkage	rec	AC097468.7
rs3792069	2	231,380,816	1.4E-04	Linkage	rec	CAB39
rs2109818	2	229,614,496	1.4E-04	LD+Linkage	dom	PID1
rs17302436	12	93,217,382	1.5E-04	Linkage	dom	PLXNC1
rs11756594	6	134,994,990	1.5E-04	Linkage|LD	rec	CTA-31J9.2

rs4797233	18	5,822,773	1.5E-04	Linkage	rec	
rs1891487	6	137,343,274	1.5E-04	LD+Linkage	dom	RP11-55K22.5
rs1881191	2	236,272,663	1.5E-04	Linkage	dom	AGAP1
rs4238922	16	25,694,112	1.5E-04	Linkage	rec	HS3ST4
rs11081236	18	6,433,601	1.5E-04	LD|Linkage	dom	
rs10205276	2	241,578,294	1.5E-04	Linkage	dom	AC104809.2
rs4663910	2	239,152,081	1.5E-04	LD+Linkage	dom	
rs10466280	10	12,231,939	1.6E-04	Linkage|LD	rec	SEC61A2
rs2289529	17	75,636,840	1.6E-04	LD|NoLinkage	dom	CCDC40
rs4497870	2	241,606,350	1.6E-04	Linkage	dom	AC005237.4
rs47137	6	134,367,799	1.6E-04	Linkage	dom	SLC2A12
rs13184089	5	148,912,761	1.6E-04	Linkage	rec	CSNK1A1
rs4381835	20	56,052,150	1.6E-04	Linkage|LD	dom	
rs12201016	6	90,205,994	1.6E-04	Linkage	rec	ANKRD6
rs1037257	17	68,662,948	1.6E-04	Linkage	dom	
rs683278	18	9,633,749	1.6E-04	Linkage	dom	
rs2183147	6	138,826,610	1.7E-04	Linkage|LD	rec	NHSL1
rs6918870	6	76,334,016	1.7E-04	Linkage	dom	
rs646967	6	76,377,566	1.7E-04	Linkage	dom	RP11-474L11.5
rs11906	8	8,678,669	1.7E-04	Linkage	rec	RP11-211C9.1
rs3848999	8	13,219,316	1.7E-04	Linkage	dom	DLC1
rs4390761	2	227,865,213	1.7E-04	Linkage	dom	AC097662.2
rs4404876	8	10,440,498	1.8E-04	Linkage	dom	RP11-981G7.4
rs7600637	2	237,538,697	1.8E-04	Linkage|LD	rec	
rs12526072	6	135,345,049	1.8E-04	Linkage	rec	HBS1L
rs925100	18	9,347,786	1.8E-04	Linkage|LD	rec	TWSG1
rs8083237	18	11,586,076	1.8E-04	LD+Linkage	dom	

rs7350066	8	10,898,795	1.8E-04	Linkage|LD	dom	XKR6
rs969997	20	55,069,845	1.8E-04	Linkage	dom	
rs3798461	6	76,473,375	1.8E-04	Linkage	dom	SENP6
rs7008575	8	13,732,274	1.9E-04	Linkage	rec	
rs209348	5	161,441,306	1.9E-04	LD|Linkage	dom	GABRG2
rs4889940	17	75,553,402	1.9E-04	Linkage	dom	TBC1D16
rs6723140	2	219,482,944	2.0E-04	LD+Linkage	rec	AC073128.10
rs9321616	6	137,882,761	2.0E-04	Linkage	dom	
rs607127	18	58,737,929	2.0E-04	Linkage	dom	PHLPP1
rs6437268	2	240,649,535	2.0E-04	Linkage|LD	dom	
rs12230722	12	94,480,909	2.0E-04	Linkage	dom	
rs1227005	2	229,830,629	2.1E-04	Linkage|LD	dom	PID1
rs6030998	20	41,692,374	2.1E-04	Linkage	dom	IFT52
rs4546368	5	148,519,293	2.1E-04	Linkage	rec	ABLIM3
rs10974470	9	4,318,940	2.1E-04	Linkage	rec	GLIS3
rs3888260	8	14,056,650	2.1E-04	Linkage	rec	SGCZ
rs4241236	2	240,405,549	2.1E-04	Linkage	dom	
rs10509976	10	115,170,888	2.1E-04	LD|Linkage	dom	
rs10803663	2	234,382,408	2.2E-04	Linkage	dom	HEATR7B1
rs6538505	12	93,453,691	2.2E-04	Linkage	rec	
rs6476878	9	4,553,316	2.2E-04	LD|Linkage	dom	SLC1A1
rs7074995	10	100,965,619	2.2E-04	Linkage	rec	HPSE2
rs12455606	18	2,511,602	2.2E-04	Linkage	rec	
rs4800960	18	52,914,826	2.3E-04	Linkage	dom	
rs1371552	2	224,074,704	2.3E-04	LD+Linkage	dom	AC013448.2
rs7074881	10	21,409,713	2.3E-04	LD|Linkage	rec	NEBL
rs1529370	13	48,376,029	2.3E-04	Linkage	dom	

rs4271760	2	227,875,788	2.3E-04	Linkage	dom	AC097662.2
rs2963998	5	153,157,246	2.3E-04	Linkage	dom	GRIA1
rs3795877	2	224,574,421	2.3E-04	Linkage	dom	SERPINE2
rs9494155	6	135,510,584	2.3E-04	Linkage	dom	
rs10944237	6	87,282,208	2.4E-04	Linkage|LD	dom	
rs880769	5	149,135,070	2.4E-04	Linkage	rec	PPARGC1B
rs1014174	2	229,660,208	2.4E-04	LD|NoLinkage	rec	PID1
rs10883766	10	104,454,753	2.4E-04	Linkage	rec	ARL3
rs7558942	2	242,157,685	2.4E-04	Linkage	dom	BOK
rs8082554	17	75,654,462	2.5E-04	LD|Linkage	rec	CCDC40
rs1009283	2	240,842,754	2.5E-04	Linkage	dom	AC124861.1
rs1427167	13	48,357,698	2.5E-04	Linkage	dom	
rs353237	5	148,812,043	2.5E-04	Linkage	dom	
rs4310018	5	152,266,397	2.5E-04	Linkage	rec	AC091969.1
rs1528628	8	13,157,347	2.5E-04	Linkage	rec	DLC1
rs7830329	8	12,879,139	2.5E-04	Linkage	dom	KIAA1456
rs27788	16	47,921,013	2.5E-04	Linkage|LD	rec	
rs10039868	5	148,849,420	2.5E-04	Linkage	dom	CSNK1A1
rs2027704	18	52,856,704	2.5E-04	Linkage	rec	
rs4463219	5	152,268,750	2.6E-04	Linkage	rec	AC091969.1
rs10859888	12	94,412,553	2.6E-04	LD|Linkage	dom	METAP2
rs4831486	8	13,766,365	2.6E-04	Linkage	dom	
rs578026	18	587,751	2.6E-04	Linkage|LD	rec	CLUL1
rs11250154	8	11,534,095	2.6E-04	Linkage	rec	
rs2078155	10	21,411,538	2.6E-04	LD|Linkage	rec	NEBL
rs6718480	2	233,587,310	2.6E-04	LD+Linkage	dom	AC106876.2
rs2964027	5	153,221,840	2.6E-04	Linkage	dom	

rs4478599	8	6,389,774	2.7E-04	LD|Linkage	dom	ANGPT2
rs4149549	2	240,579,939	2.7E-04	Linkage	dom	NDUFA10
rs3802554	10	114,455,760	2.7E-04	Linkage	rec	RP11-25C19.1
rs11787063	8	9,483,710	2.8E-04	Linkage	rec	TNKS
rs13163929	5	148,882,531	2.8E-04	LD|Linkage	dom	CSNK1A1
rs7590833	2	239,948,271	2.8E-04	Linkage	dom	HDAC4
rs11691754	2	236,004,806	2.8E-04	Linkage	dom	
rs11776235	8	8,987,303	2.8E-04	Linkage|LD	rec	ERI1
rs2032165	18	8,978,701	2.8E-04	LD|NoLinkage	rec	
rs2324934	6	87,293,586	2.8E-04	Linkage|LD	dom	
rs334384	18	7,127,068	2.9E-04	Linkage|LD	rec	
rs2425483	20	40,451,346	2.9E-04	Linkage	dom	PTPRT
rs7185824	16	51,604,183	2.9E-04	Linkage	rec	RP11-467J12.3
rs6719451	2	238,001,541	2.9E-04	Linkage	rec	AC112721.2
rs6506440	18	6,771,016	2.9E-04	Linkage	rec	ARHGAP28
rs10490035	2	229,593,322	3.0E-04	LD|Linkage	rec	PID1
rs2341697	2	238,785,391	3.0E-04	Linkage	dom	
rs1922020	2	227,688,019	3.0E-04	Linkage	rec	COL4A4
rs2504377	6	139,403,630	3.0E-04	Linkage	rec	ABRACL
rs6501243	17	74,256,150	3.1E-04	LD|Linkage	dom	CYTH1
rs10799	2	219,793,182	3.1E-04	Linkage	dom	ABCB6
rs7232823	18	54,106,201	3.1E-04	LD+Linkage	dom	NEDD4L
rs2181096	6	136,854,008	3.1E-04	Linkage	dom	MAP7
rs4742608	9	959,044	3.2E-04	Linkage|LD	rec	DMRT1
rs6752442	2	236,738,515	3.2E-04	Linkage	dom	GBX2
rs9450463	6	87,243,160	3.2E-04	Linkage	dom	AL391417.1
rs1036853	6	90,556,223	3.2E-04	Linkage	rec	MDN1

rs1402331	8	13,834,445	3.3E-04	Linkage|LD	rec	
rs7445323	5	153,116,978	3.3E-04	Linkage	dom	GRIA1
rs7565690	2	224,105,705	3.3E-04	LD+Linkage	dom	
rs10484885	6	90,451,737	3.3E-04	Linkage	rec	MDN1
rs1414684	10	24,676,562	3.3E-04	LD|Linkage	rec	KIAA1217
rs7592582	2	235,110,992	3.3E-04	Linkage	dom	
rs7588391	2	235,665,894	3.3E-04	Linkage	dom	AC114814.4
rs4273649	5	153,100,241	3.4E-04	Linkage	dom	GRIA1
rs6889794	5	153,103,648	3.4E-04	Linkage	dom	GRIA1
rs8180663	6	138,068,047	3.4E-04	Linkage	dom	RP11-95M15.2
rs10105588	8	11,291,289	3.4E-04	Linkage	rec	C8orf12
rs6937832	6	138,849,270	3.4E-04	Linkage|LD	dom	NHSL1
rs11675161	2	227,686,723	3.5E-04	Linkage	rec	COL4A4
rs10498886	6	73,678,955	3.5E-04	Linkage	dom	KCNQ5
rs4797245	18	6,487,116	3.5E-04	Linkage|LD	dom	
rs3820809	2	238,309,774	3.5E-04	Linkage	dom	LRRFIP1
rs11662751	18	6,078,451	3.5E-04	LD|Linkage	rec	L3MBTL4
rs4377285	2	236,726,693	3.5E-04	Linkage	dom	Y_RNA
rs958358	8	13,570,617	3.5E-04	LD+Linkage	rec	
rs7573905	2	213,799,751	3.6E-04	LD|NoLinkage	rec	
rs1918674	18	10,719,880	3.6E-04	Linkage|LD	dom	PIEZO2
rs12386051	17	68,922,486	3.6E-04	LD+Linkage	rec	SDK2
rs4256890	10	26,068,819	3.6E-04	LD|Linkage	rec	
rs1020694	18	59,415,278	3.6E-04	Linkage|LD	rec	SERPINB13
rs10190128	2	235,952,005	3.6E-04	Linkage|LD	dom	0
rs7586477	2	235,303,819	3.7E-04	Linkage	rec	
rs2059125	5	166,131,339	3.7E-04	Linkage	rec	

rs11203996	8	12,878,691	3.7E-04	Linkage	dom	KIAA1456
rs2043358	8	16,476,834	3.7E-04	Linkage|LD	rec	
rs975137	20	53,673,356	3.7E-04	Linkage	dom	
rs2542145	18	12,762,318	3.7E-04	Linkage|LD	rec	RP11-973H7.1
rs4851975	2	240,008,450	3.8E-04	Linkage	dom	
rs7604147	2	231,306,107	3.8E-04	Linkage	dom	CAB39
rs353222	5	148,842,039	3.8E-04	Linkage	dom	
rs666336	8	16,758,689	3.8E-04	Linkage	rec	RP11-13N12.1
rs2910288	5	160,747,917	3.8E-04	Linkage	rec	GABRB2
rs2887401	2	240,685,626	3.8E-04	LD+Linkage	dom	
rs3792074	2	231,374,190	3.9E-04	Linkage	dom	CAB39
rs9960998	18	13,292,602	3.9E-04	Linkage	dom	C18orf1
rs2902991	20	55,500,962	3.9E-04	LD|NoLinkage	rec	CTCFL
rs9376314	6	138,376,730	4.0E-04	Linkage|LD	rec	
rs1833710	5	147,947,939	4.0E-04	LD|Linkage	dom	HTR4
rs1495922	2	240,865,032	4.0E-04	Linkage	dom	
rs439115	20	41,704,335	4.0E-04	Linkage	dom	IFT52
rs3748085	6	90,372,508	4.1E-04	Linkage	rec	ANKRD6
rs861136	10	13,358,066	4.1E-04	LD|Linkage	rec	PHYH
rs250973	2	234,647,740	4.1E-04	Linkage	dom	SPP2
rs6454046	6	78,920,318	4.1E-04	LD+Linkage	rec	
rs11616524	13	50,446,356	4.1E-04	LD|Linkage	rec	RNASEH2B
rs12958345	18	5,756,006	4.2E-04	LD+Linkage	rec	RP11-945C19.1
rs10183172	2	241,643,687	4.2E-04	Linkage	dom	AC005237.4
rs3900638	2	234,985,938	4.2E-04	Linkage|LD	dom	
rs753943	5	154,552,621	4.2E-04	LD|Linkage	dom	
rs1026580	10	14,021,168	4.2E-04	LD|Linkage	dom	FRMD4A

rs13254942	8	10,295,088	4.3E-04	Linkage|LD	dom	MSRA
rs964818	2	226,840,024	4.3E-04	LD|Linkage	rec	
rs6570053	6	136,258,992	4.3E-04	LD+Linkage	dom	PDE7B
rs1062748	2	241,677,414	4.3E-04	Linkage	dom	MTERFD2
rs10209413	2	234,884,275	4.3E-04	Linkage	dom	
rs6936034	6	135,013,187	4.3E-04	Linkage|LD	rec	RP11-557H15.4
rs6436860	2	229,932,713	4.3E-04	Linkage|LD	dom	DNER
rs9294143	6	80,167,823	4.3E-04	Linkage	dom	RP1-232L24.4
rs4973189	2	229,917,200	4.3E-04	Linkage|LD	dom	
rs918149	8	5,113,756	4.4E-04	Linkage|LD	dom	
rs867294	2	234,937,428	4.4E-04	Linkage	dom	
rs11968144	6	88,875,684	4.4E-04	Linkage|LD	dom	
rs2144218	6	134,912,743	4.4E-04	Linkage|LD	dom	RP11-557H15.4
rs2102795	2	235,965,246	4.4E-04	Linkage|LD	dom	
rs7197521	16	47,031,763	4.4E-04	LD|Linkage	rec	SIAH1
rs7235478	18	9,447,066	4.4E-04	Linkage|LD	rec	
rs13282358	8	13,587,566	4.5E-04	Linkage|LD	dom	
rs761011	20	40,749,905	4.5E-04	Linkage|LD	dom	RP1-232N11.2
rs12959212	18	60,327,866	4.5E-04	LD|Linkage	dom	
rs10193128	2	233,695,966	4.5E-04	Linkage	dom	INPP5D
rs6935503	6	85,291,123	4.6E-04	Linkage	rec	RP1-90L14.1
rs6707071	2	233,526,575	4.6E-04	Linkage	dom	NGEF
rs203138	6	138,640,978	4.7E-04	Linkage	rec	KIAA1244
rs1174741	10	106,748,224	4.7E-04	Linkage|LD	rec	SORCS3
rs205355	16	28,012,030	4.7E-04	Linkage|LD	dom	XPO6
rs3799386	6	136,491,840	4.8E-04	Linkage|LD	rec	RP13-143G15.4
rs4921515	5	159,024,995	4.8E-04	Linkage	rec	

rs6903961	6	140,195,104	4.8E-04	Linkage|LD	rec	
rs8084667	18	6,549,076	4.9E-04	LD|Linkage	dom	
rs10515629	5	148,875,068	4.9E-04	LD|NoLinkage	dom	CSNK1A1
rs903748	2	240,817,894	4.9E-04	Linkage|LD	dom	AC124861.1
rs1692821	8	11,737,397	4.9E-04	Linkage	rec	FDFT1
rs7585293	2	235,433,921	4.9E-04	Linkage|LD	dom	AC010148.1
rs9342002	6	85,591,301	4.9E-04	Linkage|LD	dom	
rs754111	5	159,654,250	5.0E-04	Linkage	dom	CCNJL
rs797566	6	136,657,205	5.0E-04	Linkage	dom	BCLAF1
rs4785201	16	48,646,693	5.0E-04	Linkage|LD	dom	RP11-429P3.3
rs3765259	6	137,031,976	5.0E-04	LD+Linkage	dom	MAP3K5
rs2492303	6	134,388,701	5.1E-04	Linkage	dom	SLC2A12
rs495005	18	58,748,488	5.1E-04	Linkage|LD	dom	PHLPP1
rs3751812	16	52,375,961	5.1E-04	LD|NoLinkage	rec	FTO

Table 4. Psuedomarker results. Top 1% most significant results across all five tests performed by pseudomarker are organized by significance and annotated by gene name if the SNP falls within a gene. The test and mode of inheritance for the test is also indicated.

SNP	Chr	Position	pvalue	Gene	GWAS min p for Gene
rs1247096	10	30,078,618	2.8E-06		
rs2761743	9	9,806,955	5.4E-06	PTPRD	
rs1434478	9	26,739,094	6.0E-06	RP11-18A15.1	
rs923076	11	129,723,793	7.2E-06	RP11-121M22.1	
rs10738342	9	13,748,505	1.3E-05		
rs1322133	9	10,195,835	1.4E-05	PTPRD	4.7E-03
rs2948068	2	128,461,050	1.7E-05	SAP130	
rs10222358	3	171,982,775	1.7E-05	CLDN11	
rs3783281	14	50,311,239	2.1E-05	NIN	
rs6530650	8	13,496,360	2.2E-05	RP11-145O15.3	

rs1022538	1	165,892,276	2.5E-05	RCSD1	
rs1926050	10	25,458,413	2.9E-05		
rs10906652	10	14,431,720	3.7E-05	FRMD4A	
rs4725084	7	8,343,391	3.7E-05	AC007128.1	
rs9380700	6	12,099,225	3.8E-05	RP11-456H18.1	
rs1077734	13	105,926,360	4.7E-05		
rs16874	9	9,850,735	4.9E-05	PTPRD	4.7E-03
rs3901866	8	18,089,629	5.4E-05	NAT1	5.2E-03
rs1409288	6	12,082,826	5.5E-05		
rs1411872	9	32,248,600	5.7E-05		
rs1328238	13	108,866,662	5.7E-05		
rs2498399	6	26,814,523	5.9E-05		
rs7012951	8	18,084,041	5.9E-05	NAT1	5.2E-03
rs10514569	16	82,033,605	6.0E-05	CDH13	1.9E-03
rs10977327	9	8,855,925	6.0E-05	RP11-75C9.1	4.7E-03
rs10815567	9	723,049	6.2E-05	KANK1	4.4E-04
rs2229869	14	49,686,628	6.3E-05	SOS2	
rs11104516	12	86,398,520	6.3E-05		
rs2360192	9	29,979,597	6.6E-05		
rs2451741	6	26,737,383	6.8E-05	VN1R14P	
rs4397737	10	30,130,754	7.1E-05		
rs1408118	9	9,848,060	7.2E-05	PTPRD	4.7E-03
rs6545031	2	48,411,764	7.6E-05	FOXN2	
rs3242	8	41,238,711	8.0E-05	SFRP1	
rs458664	6	25,163,144	8.1E-05	RP3-425P12.1	
rs6022196	20	51,031,721	9.1E-05	TSHZ2	6.7E-04
rs4749487	10	30,074,383	9.2E-05		
rs12646389	4	14,536,106	9.3E-05	AC006296.3	
rs4772174	13	98,565,578	9.5E-05		
rs4363255	9	9,259,284	9.9E-05	PTPRD	4.7E-03
rs2451731	6	26,732,801	1.0E-04		
rs4978101	9	26,741,101	1.0E-04	RP11-18A15.1	
rs7857851	9	28,499,969	1.1E-04	LINGO2	2.2E-03
rs6733871	2	80,383,467	1.1E-04	CTNNA2	
rs1867551	10	60,274,889	1.2E-04		
rs11104481	12	86,353,732	1.2E-04		
rs10756511	9	13,780,202	1.2E-04		
rs11774662	8	41,256,599	1.2E-04	CTD-3080F16.3	
rs4942965			1.3E-04	RPL5P31	
rs7611945	3	127,160,204	1.3E-04	RP11-666A20.3	
rs1956621	14	25,531,905	1.3E-04	RP11-314P15.2	

rs12590252	14	56,082,358	1.5E-04	RP11-624J12.1	
rs288956	6	156,935,240	1.5E-04		
rs2183825	9	28,402,375	1.5E-04	LINGO2	2.2E-03
rs7096525	10	120,538,129	1.6E-04	U3	
rs3904501	9	9,354,637	1.6E-04	PTPRD	4.7E-03
rs6027571	20	58,395,771	1.7E-04	RP5-1043L13.1	
rs10758863	9	732,642	1.7E-04	KANK1	4.4E-04
rs3904537	10	85,435,487	1.8E-04		
rs2521230	7	24,500,595	1.8E-04		
rs4503787	16	80,182,340	1.8E-04	CMIP	
rs10483610	14	50,295,474	1.9E-04	NIN	
rs1184626	1	76,865,768	1.9E-04	ST6GALNAC3	4.7E-03
rs1902409	10	33,980,802	1.9E-04		
rs1684617	16	4,696,545	1.9E-04	ANKS3	
rs7200613	16	49,681,302	2.1E-04		
rs1913291	3	132,964,347	2.1E-04	CPNE4	1.5E-03
rs6104663	20	10,721,298	2.1E-04		
rs9873588	3	110,293,726	2.2E-04	MORC1	3.6E-03
rs8083237	18	11,586,076	2.2E-04		
rs33350	16	50,608,803	2.2E-04	RP11-152O14.5	
rs900768	16	83,987,411	2.2E-04	#N/A	
rs9348467	6	21,446,588	2.2E-04		
rs10521087	9	109,749,408	2.2E-04		
rs10031277	4	14,540,933	2.3E-04	AC006296.3	
rs4650112	1	69,370,007	2.3E-04	RP11-424D14.1	
rs12932558	16	54,600,670	2.3E-04		
rs10104990	8	136,202,757	2.3E-04		
rs10891611	11	113,356,623	2.4E-04	HTR3A	
rs9301233	13	107,025,880	2.4E-04	FAM155A	5.4E-04
rs10756657	9	15,330,686	2.4E-04		
rs1564961	10	72,334,003	2.5E-04		
rs4492438	9	9,272,982	2.5E-04	PTPRD	4.7E-03
rs4725047	7	7,912,925	2.5E-04	AC006465.4	
rs7147228	14	49,922,978	2.5E-04	CDKL1	
rs10486972	7	82,035,405	2.6E-04		
rs633596	6	153,107,180	2.6E-04		
rs10871622	18	51,677,998	2.6E-04		
rs4785239	16	49,758,032	2.6E-04		
rs2323624	4	22,164,415	2.6E-04		
rs2296170	9	9,793,954	2.6E-04	RP11-527D15.1	4.7E-03
rs4711507	6	12,090,447	2.7E-04		

rs6943258	7	8,299,180	2.7E-04	AC007128.1	
rs10817700	9	116,815,624	2.7E-04		
rs4909885	8	136,203,239	2.8E-04		
rs9364599	6	161,826,097	2.8E-04	PARK2	8.8E-05
rs2881483	16	77,512,176	2.9E-04	WWOX	3.1E-03
rs10919620	1	187,952,120	3.2E-04		
rs914987	10	10,318,853	3.2E-04	Y_RNA	
rs6015739	20	58,388,925	3.2E-04	RP5-1043L13.1	
rs12702671	7	7,909,920	3.2E-04	AC006465.3	
rs2438039	2	128,423,160	3.2E-04	SAP130	
rs7994366	13	110,474,921	3.2E-04		
rs2761752	9	9,809,028	3.3E-04	PTPRD	4.7E-03
rs4949857	1	75,153,767	3.3E-04		
rs1927450	10	30,114,806	3.3E-04		
rs1545217	6	158,930,367	3.3E-04	TMEM181	
rs2761748	9	9,807,514	3.3E-04	PTPRD	4.7E-03
rs7875247	9	16,232,088	3.4E-04	C9orf92	
rs4747064	10	72,018,762	3.4E-04		
rs10733060	1	187,990,113	3.4E-04		
rs10498662	6	3,356,110	3.4E-04	SLC22A23	
rs4915627	1	63,229,847	3.4E-04		
rs9884246	4	134,440,559	3.4E-04		
rs4779939	15	29,985,165	3.4E-04		
rs1921752	7	40,763,143	3.4E-04	C7orf10	
rs10517003	4	40,963,950	3.4E-04	UCHL1	
rs4356557	18	73,477,767	3.5E-04		
rs1247330	6	161,246,640	3.5E-04	RP11-235G24.1	
rs1008132	7	20,927,491	3.5E-04	AC006481.1	
rs2588209	8	17,428,639	3.6E-04	SLC7A2	
rs11257877	10	12,622,719	3.6E-04	CAMK1D	2.1E-03
rs10997044	10	67,727,449	3.7E-04	CTNNA3	8.7E-04
rs2125952	8	3,032,594	3.7E-04	CSMD1	8.6E-05
rs10503019	18	53,605,375	3.7E-04	ATP8B1	
rs3736781	6	26,613,341	3.7E-04	BTN1A1	
rs2323982	12	131,652,594	3.8E-04	FBRSL1	
rs6572667	14	49,917,611	3.9E-04	CDKL1	
rs2155369	11	120,544,020	3.9E-04	TECTA	
rs1339287	9	8,223,804	3.9E-04		
rs8056477	16	86,156,751	3.9E-04		
rs7856322	9	9,821,142	4.0E-04	PTPRD	4.7E-03
rs856003	10	119,393,553	4.0E-04		

rs3014864	1	151,588,208	4.0E-04	PGLYRP4	
rs6122372	20	61,209,792	4.0E-04	HAR1A	
rs6026872	20	57,420,894	4.1E-04		
rs395371	4	72,791,238	4.1E-04		
rs9356895	6	23,883,847	4.1E-04		
rs942659	6	23,892,972	4.1E-04		
rs377687			4.2E-04		
rs185925	2	31,463,497	4.2E-04	XDH	
rs10513441	3	154,522,958	4.2E-04		
rs2906801	16	80,906,745	4.2E-04		
rs2794251	13	80,229,654	4.3E-04		
rs819571	5	72,863,969	4.3E-04		
rs3811992	5	161,049,520	4.4E-04	GABRA6	6.5E-03
rs4953713	2	43,100,719	4.4E-04		
rs12447774	16	80,183,738	4.4E-04	CMIP	
rs2262438	6	133,058,735	4.5E-04	CCNG1P1	
rs4542003	9	109,962,839	4.5E-04		
rs954811	16	77,499,272	4.5E-04	WWOX	3.1E-03
rs1432536	11	90,969,219	4.5E-04		
rs11249987	8	10,218,116	4.5E-04	MSRA	8.7E-03
rs2745443	6	133,063,075	4.5E-04	CCNG1P1	
rs6659974			4.5E-04		
rs9348547	6	23,268,267	4.7E-04	RP1-209A6.1	
rs4142313	13	42,995,658	4.7E-04	ENOX1	
rs11014425	10	25,473,731	4.7E-04		
rs573946	11	125,968,781	4.7E-04	KIRREL3-AS1	1.6E-03
rs1510218	16	77,515,978	4.7E-04	WWOX	3.1E-03
rs598832	6	154,314,311	4.8E-04		
rs1523635	7	16,982,220	4.8E-04		
rs10217611	9	14,801,009	4.8E-04	FREM1	
rs1333108	9	9,449,099	4.8E-04	PTPRD	4.7E-03
rs3006448	1	151,580,777	4.8E-04	PGLYRP4	6.5E-03
rs4601425	9	27,142,292	4.9E-04	TEK	7.4E-03
rs3858042	9	4,370,422	4.9E-04	AL162419.1	
rs912174	9	702,156	4.9E-04	KANK1	4.4E-04
rs7752854	6	162,714,014	5.0E-04	PARK2	8.8E-05
rs10498581	14	84,806,621	5.0E-04	RNU3P3	
rs2145997	10	80,828,991	5.0E-04	ZCCHC24	
rs16949651	17	43,374,600	5.0E-04	AC003665.1	
rs10946999	6	29,679,588	5.0E-04	GABBR1	
rs7211832	17	29,393,973	5.0E-04	TLK2P1	3.3E-03

rs646707	12	5,115,044	5.0E-04		
rs13253111	8	28,117,893	5.1E-04		
rs9342944	6	73,131,044	5.1E-04	RIMS1	
rs2501917	9	74,505,943	5.1E-04	TMC1	
rs901151	3	56,262,564	5.2E-04	ERC2	
rs484299	1	76,871,317	5.2E-04	ST6GALNAC3	
rs4818219	21	41,469,764	5.2E-04	BACE2-IT1	
rs2720492	8	17,428,016	5.2E-04	SLC7A2	
rs4541976	8	73,958,102	5.2E-04	RP11-1145L24.1	
rs2758767	6	153,027,201	5.3E-04		
rs13074670	3	151,911,821	5.3E-04	RP11-103G8.2	
rs9323505	14	67,856,540	5.3E-04	RAD51B	4.6E-04
rs10814755	9	38,743,508	5.3E-04		
rs2720586	8	17,419,158	5.3E-04	SLC7A2	
rs10945816	6	162,699,141	5.3E-04	PARK2	8.8E-05
rs2279830	3	148,588,480	5.3E-04	ZIC4-AS1	
rs7603997	2	24,378,462	5.4E-04	ITSN2	
rs17289605	3	171,930,731	5.4E-04	CLDN11	
rs12546427	8	6,592,314	5.4E-04	AGPAT5	7.3E-03
rs7954341	12	79,943,528	5.4E-04	ACSS3	
rs12666612	7	18,341,770	5.4E-04	HDAC9	
rs538257	18	53,932,365	5.5E-04	NEDD4L	
rs13279789	8	17,420,156	5.5E-04	SLC7A2	
rs6900805	6	154,329,725	5.5E-04		
rs7322914	13	105,938,911	5.5E-04	EFNB2	
rs10511761	9	25,602,704	5.5E-04		
rs7098831	10	30,057,054	5.5E-04	SVIL	
rs11255096	10	7,458,399	5.5E-04	SFMBT2	6.1E-03
rs3819340	3	150,097,977	5.6E-04	RP11-680B3.2	
rs10935734	3	150,108,496	5.6E-04	RP11-680B3.2	
rs318572	7	34,243,290	5.6E-04	AC009262.2	
rs1020138	4	41,398,145	5.7E-04	LIMCH1	
rs2749592	10	38,298,848	5.7E-04	ZNF25	
rs11962266	6	159,818,380	5.7E-04		
rs9378109	6	30,882,453	5.9E-04	LINC00243	
rs4797559	18	11,573,447	5.9E-04		
rs7123583	11	116,105,231	5.9E-04		
rs9393366	6	23,185,290	5.9E-04	RP1-209A6.1	
rs34198	7	31,722,195	6.0E-04		
rs9348465	6	21,438,787	6.0E-04		
rs7655641	4	60,203,770	6.0E-04		

rs7913550	10	44,885,296	6.1E-04	RP11-445N18.3	
rs7819785	8	140,962,053	6.1E-04	TRAPPC9	
rs639790	12	51,194,521	6.1E-04	KRT5	
rs4775758	15	46,457,597	6.1E-04		
rs4376547	9	104,090,485	6.1E-04	RP11-402M4.1	
rs7023878	9	20,055,113	6.1E-04		
rs4908803	1	8,982,757	6.1E-04	SLC2A7	
rs2883739	14	49,649,885	6.2E-04	METTL21D	
rs9469003	6	31,515,807	6.2E-04	XXbac-BPG181B23.4	
rs4237860	12	70,922,902	6.2E-04	TRHDE	
rs426361	9	36,515,772	6.3E-04		
rs10980412	9	112,305,681	6.3E-04	SVEP1	5.0E-03
rs12650313	4	41,401,850	6.3E-04		
rs277351	1	75,081,601	6.5E-04		
rs1006087	9	38,225,659	6.5E-04		
rs4937306	11	127,610,247	6.6E-04		
rs10510099	10	123,421,836	6.6E-04		
rs5759157	22	41,817,204	6.6E-04	AL022237.3	
rs2097585	8	18,063,184	6.7E-04		
rs10962912	9	17,209,242	6.7E-04	CNTLN	
rs4307347	8	10,205,504	6.7E-04	MSRA	8.7E-03
rs9348260	6	170,358,048	6.7E-04	RP11-302L19.2	
rs11069780			6.7E-04		
rs969015	7	82,195,220	6.7E-04		
rs908978	16	84,558,240	6.8E-04		
rs2420382	2	60,750,244	6.8E-04		
rs12445310	16	61,444,459	6.8E-04		
rs228840	20	49,504,665	6.8E-04	NFATC2	
rs2918217	3	117,029,070	6.9E-04	LSAMP	
rs2064112	6	11,447,755	6.9E-04	NEDD9	
rs1376405	2	46,622,047	6.9E-04	ATP6V1E2	
rs11129896	3	41,270,771	6.9E-04	CTNNB1	3.9E-03
rs2405748	3	163,565,423	6.9E-04		
rs12351299	9	30,144,925	6.9E-04		
rs10810013	9	13,736,595	7.0E-04		
rs761523	14	25,752,869	7.0E-04		
rs9847681	3	145,187,206	7.0E-04	C3orf58	
rs8141749	22	41,813,186	7.1E-04	AL022237.3	
rs3213881	16	47,930,306	7.2E-04	RP11-491F9.6	
rs471364			7.2E-04	TTC39B	
rs2788381	6	152,653,569	7.2E-04	SYNE1	4.8E-03

rs7350390	10	73,268,910	7.2E-04	PSAP	2.2E-03
rs6027561	20	58,386,602	7.3E-04	RP5-1043L13.1	
rs1529482	19	17,302,488	7.3E-04	ANO8	
rs1369491	7	12,178,552	7.3E-04		
rs10971103	9	32,715,278	7.3E-04	RP11-462B18.1	
rs10512052	9	77,773,007	7.4E-04	PCSK5	9.0E-03
rs1866657	2	127,157,628	7.4E-04	AC013474.4	
rs6923240	6	164,105,374	7.5E-04	RP1-230L10.1	
rs6494039	15	29,979,194	7.5E-04		
rs920818	2	80,410,180	7.5E-04	CTNNA2	6.0E-03
rs6715376	2	149,780,195	7.5E-04	LYPD6B	
rs2627468	8	3,812,607	7.5E-04	CSMD1	8.6E-05
rs4142055	6	152,592,176	7.5E-04	SYNE1	4.8E-03
rs921070	2	43,060,347	7.5E-04		
rs484809	3	120,849,573	7.5E-04	POPDC2	
rs12420554	11	127,094,570	7.5E-04		
rs7613643	3	173,509,404	7.5E-04	FNDC3B	2.5E-03
rs11969972	6	161,794,001	7.5E-04	PARK2	8.8E-05
rs17405238	7	36,738,917	7.5E-04		
rs10484501	6	162,720,146	7.5E-04	PARK2	8.8E-05
rs6942109	6	161,706,684	7.6E-04	PARK2	8.8E-05
rs8118732	20	54,356,605	7.6E-04		
rs4952621	2	40,495,927	7.7E-04	SLC8A1	8.9E-04
rs1909668	10	123,401,335	7.7E-04		
rs2670153	6	52,648,456	7.7E-04	TMEM14A	
rs2471544	12	86,994,149	7.7E-04	CEP290	
rs175238	2	161,314,813	7.8E-04		
rs689423	1	76,911,492	7.8E-04		
rs3786916	19	38,679,802	7.8E-04	PEPD	
rs10492892	16	79,611,798	7.8E-04	RP11-303E16.3	
rs17496685	6	66,063,541	7.8E-04	RP11-74E24.2	4.5E-04
rs359980	2	219,537,450	7.9E-04	AC097468.7	
rs12770890	10	16,585,949	7.9E-04	PTER	
rs11198993	10	85,244,450	7.9E-04		
rs7746447	6	158,976,564	8.0E-04	DYNLT1	
rs12547387	8	136,206,752	8.0E-04		
rs1145536	1	161,888,649	8.0E-04		
rs11125238	2	49,496,567	8.0E-04		
rs10509258	10	67,453,443	8.1E-04	CTNNA3	8.7E-04
rs855987	10	119,401,433	8.1E-04		
rs940120	9	14,896,868	8.1E-04	FREM1	

rs914605	9	20,732,963	8.2E-04	KIAA1797	
rs10935735	3	150,115,954	8.2E-04	RP11-680B3.2	
rs6870053	5	74,312,322	8.2E-04	CTD-2503O16.4	
rs10115218	9	30,135,864	8.2E-04		
rs10498580	14	84,690,252	8.2E-04		
rs4760381	12	91,972,190	8.3E-04	RP11-511B23.2	
rs4076746	10	1,820,848	8.3E-04		
rs1472834	8	18,972,720	8.4E-04	PSD3	
rs10503303	8	5,312,389	8.4E-04		
rs11642029	16	84,922,333	8.4E-04	AC092327.1	
rs894520	9	38,179,527	8.4E-04	snoU13	
rs11166679	8	138,038,252	8.4E-04	RP11-30J20.1	
rs12675992	8	28,120,336	8.4E-04		
rs9935462	16	80,924,587	8.5E-04		
rs12286609	11	90,946,180	8.5E-04		
rs4840374	8	8,823,160	8.5E-04		
rs9940922	16	82,293,571	8.5E-04	CDH13	1.9E-03
rs9541407	13	67,978,683	8.6E-04		
rs1229655	7	26,399,449	8.6E-04		
rs10483853	14	72,826,052	8.7E-04	NUMB	
rs11917772	3	145,149,515	8.8E-04		
rs4429143	12	86,933,325	8.8E-04	C12orf50	7.5E-03
rs7624504	3	144,436,867	8.8E-04		
rs11205275	1	151,591,780	8.9E-04	PGLYRP4	
rs427048	3	42,494,564	9.0E-04		
rs11865624	16	82,878,275	9.0E-04		
rs1327793	9	111,574,677	9.1E-04	PALM2	5.6E-03
rs4937504	11	129,752,910	9.1E-04	RP11-121M22.1	
rs2802490	10	43,919,019	9.2E-04		
rs12831250	12	87,097,672	9.2E-04	TMTC3	
rs1261234	2	79,036,329	9.3E-04		
rs1358863	10	89,416,488	9.3E-04	PAPSS2	
rs4688023	3	120,861,876	9.3E-04	POPDC2	
rs2283491	16	3,939,585	9.3E-04	RP11-462G12.1	
rs36982	5	1,556,205	9.3E-04	LPCAT1	
rs1366119	5	5,435,695	9.4E-04		
rs12000040	9	77,809,649	9.4E-04	PCSK5	9.0E-03
rs17771443	10	49,595,617	9.4E-04	WDFY4	1.0E-03
rs17153021	8	11,133,645	9.4E-04		
rs4398831	7	96,594,993	9.4E-04	ACN9	
rs7778021	7	40,753,457	9.5E-04	C7orf10	

rs285480	1	163,670,527	9.6E-04	RXRG	
rs3803651	16	79,876,383	9.7E-04	BCMO1	
rs7645524	3	198,610,700	9.7E-04		
rs7742171	6	838,848	9.7E-04		
rs6476179	9	29,975,815	9.7E-04		
rs2387595	10	6,767,544	9.8E-04		
rs11996662	8	18,080,684	9.8E-04	NAT1	5.2E-03
rs2793150	9	74,509,273	9.8E-04	TMC1	
rs7421353	2	29,495,378	9.8E-04	ALK	1.7E-03
rs2759243	13	80,195,640	9.8E-04		
rs11880217	19	12,279,795	9.9E-04		
rs618541			9.9E-04		
rs17692472			9.9E-04		
rs983596	14	40,420,142	9.9E-04		
rs1393784	3	106,373,405	9.9E-04		
rs11964693	6	68,425,331	1.0E-03		
rs7212512	17	4,660,945	1.0E-03	RP11-81A22.5	
rs561168	13	109,682,209	1.0E-03	COL4A1	3.1E-03
rs985564	6	73,225,898	1.0E-03		
rs1000198	3	120,596,510	1.0E-03	ARHGAP31	
rs4592392	11	39,560,586	1.0E-03		
rs1599796	3	120,726,624	1.0E-03	TIMMDC1	2.0E-03
rs1509197	9	1,009,473	1.0E-03		
rs7843177	8	2,466,863	1.0E-03	RP11-378A12.1	
rs2188023	8	18,083,511	1.0E-03	NAT1	5.2E-03
rs7188426	16	83,538,351	1.0E-03		
rs2584548	9	17,399,012	1.0E-03	CNTLN	
rs976796	14	40,380,655	1.0E-03		
rs7714420	5	74,376,083	1.0E-03	RP11-229C3.2	
rs587639	8	132,794,913	1.0E-03	CTD-2008O4.1	
rs2958492	8	145,889,935	1.0E-03	AF186192.1	
rs11974778	7	101,343,083	1.0E-03	CUX1	6.7E-03
rs9283723	5	30,823,028	1.0E-03		
rs9695393	9	29,339,856	1.1E-03		
rs10756505	9	13,770,058	1.1E-03		
rs4740993	9	9,841,382	1.1E-03	PTPRD	4.7E-03
rs12701134	7	31,739,647	1.1E-03		
rs2073001	6	21,440,915	1.1E-03		
rs10095543	8	23,187,341	1.1E-03	R3HCC1	
rs16941783	16	85,233,851	1.1E-03	RP11-58A18.1	
rs4577393	22	31,315,687	1.1E-03	SYN3	

rs862456	19	44,030,503	1.1E-03	HNRNPL	
rs220723	6	160,246,557	1.1E-03	RP1-249F5.3	
rs636398	9	22,670,915	1.1E-03	RP11-399D6.2	
rs1161110	12	66,125,429	1.1E-03	RP11-473M14.3	
rs6030812	20	41,434,425	1.1E-03		
rs1000531	2	46,365,443	1.1E-03		
rs3759324	12	6,355,922	1.1E-03	SCNN1A	
rs2247278	2	37,957,293	1.1E-03	LINC00211	
rs4850933			1.1E-03		
rs4843628	16	86,141,814	1.1E-03		
rs883438	14	56,050,922	1.1E-03	RP11-624J12.1	
rs1938164	6	6,750,058	1.1E-03		
rs6040669	20	11,360,024	1.1E-03		
rs11647427	16	54,622,772	1.1E-03		
rs4852163	2	79,875,554	1.1E-03	CTNNA2	6.0E-03
rs10962397	9	16,354,925	1.1E-03		
rs7170390	15	57,407,382	1.1E-03	MYO1E	4.2E-03
rs6139948	20	622,962	1.1E-03		
rs2045812	4	22,152,992	1.1E-03		
rs7405014	16	86,643,348	1.1E-03	BANP	
rs2059098	5	163,340,393	1.1E-03		
rs10757817	9	29,182,125	1.1E-03		
rs1983764	14	50,262,409	1.1E-03	NIN	
rs602227	1	64,029,576	1.1E-03	RP4-597J3.1	
rs1445210	9	9,182,961	1.1E-03	PTPRD	4.7E-03
rs11623335	14	56,102,829	1.1E-03	C14orf101	
rs3792298	3	169,024,676	1.1E-03	SERPINI1	5.2E-04
rs4466762	10	47,167,032	1.1E-03	ANTXRL	
rs563850	13	50,325,146	1.1E-03	DLEU7-AS1	
rs244972	5	155,258,116	1.1E-03	SGCD	
rs7027471	9	29,954,976	1.1E-03		
rs1410351	13	105,217,814	1.2E-03		
rs17774360	9	30,004,366	1.2E-03		
rs3815571	12	15,154,326	1.2E-03	RERG	
rs6945523	7	114,314,605	1.2E-03		
rs4555301	2	29,493,183	1.2E-03	ALK	1.7E-03
rs10511905	9	32,338,024	1.2E-03		
rs276550	6	137,443,470	1.2E-03		
rs11008423	10	19,415,497	1.2E-03		
rs4955755	3	171,977,103	1.2E-03	CLDN11	
rs10064872	5	125,021,832	1.2E-03		

rs427896			1.2E-03	AL589825.1	
rs2109313	2	128,292,394	1.2E-03		
rs1436434	16	45,141,599	1.2E-03	ANKRD26P1	
rs7118508	11	124,478,042	1.2E-03	TMEM218	
rs2115925	11	120,687,058	1.2E-03	SC5DL	
rs1327080	1	75,083,945	1.2E-03		
rs10142258	14	72,879,970	1.2E-03	NUMB	
rs3747868	10	73,190,834	1.2E-03	CDH23	
rs3755579	3	120,697,239	1.2E-03	POGLUT1	
rs2723520	7	17,780,202	1.2E-03		
rs253155	12	9,902,102	1.2E-03	CLEC2B	9.0E-04
rs11779707	8	41,247,867	1.2E-03	SFRP1	
rs10862220	12	79,954,730	1.2E-03	ACSS3	
rs1887866	9	7,253,702	1.2E-03		
rs7161541	14	49,670,230	1.2E-03	SOS2	
rs8060701	16	71,630,790	1.2E-03	ZFHX3	3.4E-03
rs10959161	9	10,533,899	1.2E-03	PTPRD	4.7E-03
rs6863278	5	72,727,144	1.2E-03	RP11-79P5.8	
rs3778333	6	7,254,149	1.2E-03	SSR1	
rs7746261	6	7,255,258	1.2E-03	#N/A	
rs7863381	9	30,862,374	1.2E-03		
rs2849576	6	162,506,056	1.2E-03	PARK2	8.8E-05
rs4354369			1.2E-03		
rs12184535	13	110,890,000	1.2E-03		
rs742487	6	2,392,698	1.2E-03		
rs6026395	20	56,611,417	1.2E-03	RP5-907D15.3	
rs12189965	6	153,350,005	1.3E-03	RP1-101K10.6	
rs991335	3	56,209,972	1.3E-03	ERC2	
rs854771	17	18,000,917	1.3E-03	MYO15A	
rs10507539	13	45,732,707	1.3E-03	LRRC63	
rs12670250	7	27,543,628	1.3E-03	HIBADH	
rs1531228	12	13,520,648	1.3E-03		
rs489049	1	57,347,657	1.3E-03	DAB1	6.9E-03
rs6530746	8	14,179,648	1.3E-03	SGCZ	5.9E-04
rs575242	3	171,934,775	1.3E-03	CLDN11	
rs9405561	6	2,412,474	1.3E-03		
rs12316831	12	87,189,927	1.3E-03		
rs4843549	16	85,795,364	1.3E-03	C16orf95	
rs791589	10	6,129,577	1.3E-03	IL2RA	1.7E-12
rs12423283	12	72,878,975	1.3E-03	RP11-81H3.2	
rs10996895	10	67,529,571	1.3E-03	CTNNA3	8.7E-04

rs6789549	3	40,996,267	1.3E-03		
rs2653330	3	188,751,659	1.3E-03		
rs2328472	20	19,894,076	1.3E-03	RIN2	
rs1018159	16	77,512,959	1.3E-03	WWOX	3.1E-03
rs2367214	5	38,322,363	1.3E-03	EGFLAM-AS4	
rs11196905	10	116,518,284	1.3E-03	RP11-106M7.1	
rs289073	4	31,061,064	1.3E-03		
rs11988651	8	145,789,590	1.3E-03	ARHGAP39	
rs4879543			1.3E-03		
rs36987	5	1,552,175	1.3E-03	LPCAT1	
rs7617219			1.3E-03	CPHL1P	
rs250157	16	78,146,121	1.3E-03		
rs6480128	10	67,453,139	1.3E-03	CTNNA3	8.7E-04
rs215006	6	152,797,321	1.3E-03	SYNE1	4.8E-03
rs2283149	11	2,500,006	1.3E-03	KCNQ1	3.8E-03
rs9368297	6	21,445,003	1.3E-03		
rs505480	8	12,923,214	1.3E-03	KIAA1456	6.9E-03
rs474588	3	171,945,283	1.3E-03	RP11-373E16.4	
rs1915280	12	72,042,402	1.3E-03	RP11-314D7.4	
rs10763176	10	56,478,812	1.3E-03	PCDH15	
rs162870	3	78,959,907	1.3E-03	ROBO1	
rs7866438	9	33,954,118	1.3E-03	OSTCP8	
rs1922166	10	56,465,084	1.3E-03	PCDH15	
rs2112979	5	55,327,793	1.3E-03	IL6ST	
rs9693804	8	126,954,773	1.3E-03		
rs564598	3	171,940,031	1.3E-03	RP11-373E16.4	
rs16906775	8	80,409,145	1.3E-03		
rs7916379	10	4,764,610	1.3E-03		
rs16932846	12	28,487,596	1.3E-03	CCDC91	
rs4997129	6	856,832	1.3E-03	RP5-1077H22.2	
rs10242866	7	17,887,138	1.3E-03	SNX13	
rs708860	12	116,494,692	1.3E-03	KSR2	2.6E-04
rs1485187	9	7,624,720	1.3E-03		
rs7011529	8	102,261,354	1.3E-03	ZNF706	
rs10249530	7	90,830,257	1.3E-03	RP11-115N4.1	
rs6664881	1	169,072,251	1.3E-03		
rs3016774	11	128,240,876	1.4E-03	KCNJ1	
rs7862217	9	27,141,645	1.4E-03	TEK	7.4E-03
rs2064813	2	32,066,439	1.4E-03	DPY30	
rs559135	9	119,342,663	1.4E-03		
rs4672667	2	213,506,125	1.4E-03	AC093865.1	

rs10502249	11	122,009,461	1.4E-03		
rs4839620	3	144,404,654	1.4E-03		
rs1796993	9	74,505,258	1.4E-03	TMC1	
rs9808084	2	80,396,255	1.4E-03	CTNNA2	6.0E-03
rs900369	2	213,484,594	1.4E-03	AC108066.1	
rs7021584	9	3,358,111	1.4E-03	RP11-62E14.2	
rs2825663	21	19,877,775	1.4E-03		
rs6439099	3	129,114,251	1.4E-03	KBTBD12	
rs1356768	3	168,229,302	1.4E-03	AC092965.1	
rs1558905	12	14,112,158	1.4E-03		
rs12536822	7	12,162,916	1.4E-03		
rs4933782	10	83,179,160	1.4E-03		
rs1962503	18	30,360,416	1.4E-03	DTNA	
rs2656620	16	77,470,888	1.4E-03	WWOX	3.1E-03
rs3922817	2	109,390,585	1.4E-03	SH3RF3	
rs1383852	3	100,598,897	1.4E-03		
rs9365324	6	162,107,902	1.4E-03	PARK2	8.8E-05
rs11146960	12	131,532,533	1.4E-03		
rs7614661	3	169,619,384	1.4E-03	EGFEM1P	
rs7797908	7	142,351,329	1.4E-03	KEL	
rs4683806	3	141,327,360	1.4E-03	CLSTN2	1.3E-03
rs534080	1	57,357,309	1.4E-03	DAB1	6.9E-03
rs1360585	9	7,759,626	1.4E-03		
rs4502539	3	127,259,128	1.4E-03	SLC41A3	
rs6997118	8	17,415,784	1.4E-03	SLC7A2	
rs1009221	2	26,748,093	1.4E-03	AC015977.6	
rs4144431	14	50,820,213	1.4E-03		
rs9831023	3	120,594,452	1.4E-03	ARHGAP31	
rs4325703	2	128,512,647	1.4E-03		
rs702279	9	6,959,634	1.4E-03	RP11-403H13.1	
rs9315681	13	38,881,671	1.4E-03	LHFP	1.5E-03
rs719804	11	112,739,985	1.4E-03	TTC12	
rs7635829	3	148,576,912	1.4E-03		
rs1942007	10	67,456,130	1.4E-03	CTNNA3	8.7E-04
rs7234618	18	22,563,606	1.5E-03		
rs2795380	9	103,718,706	1.5E-03		
rs6934511	6	2,406,202	1.5E-03		
rs8099150	18	11,568,474	1.5E-03		
rs7857376	9	111,140,779	1.5E-03		
rs1460537	18	39,760,015	1.5E-03		
rs7250408	19	45,025,811	1.5E-03	FBL	

rs2210539	9	17,158,867	1.5E-03	CNTLN	
rs10964182	9	19,484,098	1.5E-03	AL158206.1	
rs8012887	14	83,268,846	1.5E-03		
rs8045161	16	53,160,653	1.5E-03		
rs7780032	7	20,199,797	1.5E-03	MACC1	7.0E-03
rs17780143	14	49,971,518	1.5E-03	MAP4K5	
rs3933328			1.5E-03		
rs328114	18	42,527,784	1.5E-03	ST8SIA5	
rs7633016	3	46,703,663	1.5E-03	ALS2CL	
rs7667847	4	7,389,753	1.5E-03	SORCS2	
rs1383453	8	136,143,126	1.5E-03		
rs10869675	9	77,779,855	1.5E-03	PCSK5	9.0E-03
rs10756088	9	10,651,370	1.5E-03		
rs823918	9	103,703,117	1.5E-03		
rs1247336	6	161,297,547	1.5E-03	RP3-428L16.1	
rs10428541	5	52,760,915	1.5E-03		
rs4921804	8	17,594,903	1.5E-03	MTUS1	
rs2830927	21	27,712,794	1.5E-03	RPL10P1	
rs10937088	3	183,639,928	1.5E-03		
rs1645060	5	41,427,106	1.5E-03	PLCXD3	
rs2756916	9	103,717,772	1.5E-03		
rs5021764	13	23,496,757	1.5E-03	RP11-309I15.1	
rs2484918	9	26,354,526	1.5E-03		
rs2758774			1.5E-03		
rs7516390	1	160,957,563	1.6E-03	DDR2	6.8E-03
rs1768575	9	8,225,513	1.6E-03		
rs7068134	10	67,450,904	1.6E-03	CTNNA3	8.7E-04
rs11775938	8	40,053,601	1.6E-03		
rs4885145	13	73,497,210	1.6E-03	KLF12	
rs10928942	2	130,399,814	1.6E-03	AC079776.2	
rs2272571	17	17,987,914	1.6E-03	MYO15A	
rs823920	9	103,702,406	1.6E-03		
rs1038268	9	31,967,623	1.6E-03		
rs4364720	9	26,332,947	1.6E-03		
rs750669	16	84,470,371	1.6E-03		
rs2133886	3	56,917,110	1.6E-03	ARHGEF3	
rs1503161	3	106,288,374	1.6E-03		
rs951016	3	194,576,396	1.6E-03	ATP13A5	
rs10886432	10	85,217,844	1.6E-03		
rs2700586	3	100,577,480	1.6E-03		
rs697471	6	166,299,886	1.6E-03	LINC00473	

rs7092223	10	56,556,926	1.6E-03	PCDH15	
rs1947223	2	225,654,301	1.6E-03		
rs2688647	3	120,813,592	1.6E-03	PLA1A	
rs2358657	10	20,344,631	1.6E-03	PLXDC2	6.4E-03
rs1915762	2	79,000,216	1.6E-03		
rs713054	6	162,491,345	1.6E-03	PARK2	8.8E-05
rs6547363	2	81,408,438	1.6E-03		
rs256845	5	155,852,825	1.6E-03	SGCD	
rs9458397	6	162,176,278	1.6E-03	PARK2	8.8E-05
rs11785590	8	22,792,914	1.6E-03	RP11-87E22.2	1.7E-03
rs13138213	4	30,424,187	1.6E-03	PCDH7	
rs9299090	9	9,254,932	1.6E-03	PTPRD	4.7E-03
rs1320546	9	95,759,720	1.6E-03	BARX1	
rs1728171	17	39,028,855	1.7E-03		
rs625852	18	8,448,190	1.7E-03	AP001793.1	
rs975037	8	122,421,236	1.7E-03		
rs1855217	9	9,353,616	1.7E-03	PTPRD	4.7E-03
rs4937626	11	130,844,247	1.7E-03	NTM	
rs3770306	2	80,473,746	1.7E-03	CTNNA2	6.0E-03
rs792746	3	158,857,927	1.7E-03	C3orf55	
rs12493995	3	175,885,280	1.7E-03	NAALADL2	
rs2191041	7	13,152,407	1.7E-03	AC011288.2	
rs1951346	14	43,270,925	1.7E-03		
rs30425	16	78,159,425	1.7E-03		
rs915508	9	26,349,485	1.7E-03		
rs2756318			1.7E-03		
rs10737558	1	187,956,641	1.7E-03		
rs218769	4	14,037,640	1.7E-03		
rs17680996	7	12,823,244	1.7E-03		
rs17389100	2	18,361,324	1.7E-03	KCNS3	
rs10810127	9	14,284,350	1.7E-03	NFIB	
rs12887744	14	83,173,812	1.7E-03		
rs7895709	10	18,945,941	1.7E-03	NSUN6	3.7E-03
rs10940495	5	55,298,417	1.7E-03	IL6ST	
rs1011427	5	147,968,170	1.7E-03	HTR4	
rs1331226	9	32,282,317	1.7E-03	RN5S281	
rs7076094	10	67,456,054	1.7E-03	CTNNA3	8.7E-04
rs12548717	8	13,583,929	1.7E-03		
rs3736495	15	66,400,544	1.7E-03	ITGA11	
rs6779258	3	71,632,329	1.7E-03	FOXP1	2.2E-03
rs1779	7	873,265	1.7E-03	SUN1	

rs2118891	2	212,387,888	1.7E-03	ERBB4	1.1E-03
rs1037459	15	22,549,328	1.7E-03		
rs2893978	10	67,452,838	1.7E-03	CTNNA3	8.7E-04
rs10737976	6	72,572,001	1.7E-03		
rs1534863	8	11,705,562	1.7E-03	FDFT1	
rs1671078	11	129,662,255	1.7E-03	ZBTB44	
rs1929831	9	29,353,582	1.7E-03		
rs2740902	8	3,889,960	1.7E-03	CSMD1	8.6E-05
rs9322304	6	151,537,080	1.7E-03	RP1-292B18.4	
rs354731	20	58,384,823	1.7E-03	RP5-1043L13.1	
rs1925191	6	23,943,322	1.7E-03		
rs1496248	11	133,057,322	1.7E-03		
rs156007	5	95,862,056	1.7E-03	CTD-2337A12.1	
rs7829474	8	73,957,878	1.7E-03	RP11-1145L24.1	
rs737590	9	30,217,140	1.7E-03		
rs1442514	9	17,409,319	1.7E-03	CNTLN	
rs2242310	4	53,518,828	1.7E-03	RP11-752D24.2	7.6E-03
rs12637387	3	110,095,943	1.7E-03		
rs10861063	12	102,555,541	1.8E-03	STAB2	1.7E-03
rs7778616	7	13,043,590	1.8E-03		
rs17444315	9	38,345,790	1.8E-03	RP11-113O24.3	
rs9814525	3	67,177,665	1.8E-03		
rs7159343			1.8E-03		
rs1333652	6	10,381,949	1.8E-03		
rs1877589	3	132,969,848	1.8E-03	CPNE4	1.5E-03
rs2190935	7	7,249,542	1.8E-03	C1GALT1	5.7E-03
rs2023073	6	162,552,161	1.8E-03	PARK2	8.8E-05
rs912196	13	112,781,336	1.8E-03	MCF2L	
rs9789477	2	51,576,611	1.8E-03	AC007682.1	
rs1718861	4	57,644,456	1.8E-03	IGFBP7	
rs7977726	12	87,142,283	1.8E-03		
rs1753415	10	27,435,108	1.8E-03	YME1L1	
rs2101201	4	53,537,471	1.8E-03	SCFD2	7.6E-03
rs1519654	2	100,463,392	1.8E-03	NMS	
rs2413975	15	47,976,595	1.8E-03	ATP8B4	
rs10937003	3	180,598,074	1.8E-03	MFN1	
rs12360468	10	43,618,874	1.8E-03		
rs1215130	9	15,333,709	1.8E-03		
rs4868825	5	163,313,622	1.8E-03		
rs2442863	10	26,073,064	1.8E-03		
rs3774332	3	37,049,672	1.8E-03	MLH1	

rs7015700	8	9,565,117	1.8E-03	TNKS	
rs2105606	11	131,337,414	1.8E-03	NTM	
rs7624807	3	169,420,582	1.8E-03		
rs1667087	9	22,686,345	1.8E-03	RP11-399D6.2	
rs1138714	11	815,110	1.8E-03	AP006621.8	
rs1178118	7	18,718,523	1.8E-03	HDAC9	6.5E-03
rs2037719	7	96,557,076	1.8E-03		
rs736707	7	102,917,639	1.8E-03	RELN	
rs2383154	9	20,857,809	1.8E-03	KIAA1797	
rs2001688	9	30,018,022	1.8E-03		
rs276585	6	137,418,306	1.8E-03		
rs2194657	7	7,825,773	1.8E-03	AC006465.3	
rs7684626	4	134,416,918	1.8E-03		
rs3119848	9	17,166,955	1.8E-03	CNTLN	
rs2960920	7	71,721,683	1.8E-03	TYW1B	3.2E-04
rs10800319	1	165,820,273	1.8E-03		
rs973174	3	59,562,526	1.8E-03		
rs11779064	8	22,810,244	1.8E-03	RP11-87E22.1	1.7E-03
rs12329577	20	4,795,010	1.8E-03	SLC23A2	2.8E-03
rs10199869	2	36,187,574	1.8E-03		
rs11868497	17	42,820,734	1.8E-03	C17orf57	
rs10514929	17	42,859,869	1.8E-03	CTD-2026D20.2	
rs1407297	9	35,837,756	1.9E-03	TMEM8B	
rs9360664	6	74,098,145	1.9E-03	PAICSP3	
rs481297	18	42,533,661	1.9E-03	ST8SIA5	
rs4238558	15	29,933,027	1.9E-03	OTUD7A	
rs9440550	1	109,194,424	1.9E-03	AKNAD1	
rs1422429	5	149,146,627	1.9E-03	PPARGC1B	
rs6505669	18	11,649,501	1.9E-03		
rs4798428	18	6,012,319	1.9E-03	L3MBTL4	8.6E-03
rs1796518	6	26,496,651	1.9E-03	BTN2A2	
rs1901548	6	159,818,518	1.9E-03		
rs4297265	1	67,624,923	1.9E-03	IL12RB2	
rs4856985	3	67,187,792	1.9E-03		
rs7632299	3	144,539,157	1.9E-03	SLC9A9-AS1	1.6E-04
rs10425564	19	62,004,792	1.9E-03	ZIM2	
rs4238055			1.9E-03		
rs9939954	16	80,210,594	1.9E-03	CMIP	
rs1113401	9	21,002,170	1.9E-03	PTPLAD2	
rs2843157	1	2,230,243	1.9E-03	SKI	
rs1374650	4	30,429,864	1.9E-03	PCDH7	

rs2761763	9	9,822,245	1.9E-03	PTPRD	4.7E-03
rs7552405	1	104,915,372	1.9E-03		
rs2500286	1	3,265,998	1.9E-03	PRDM16	
rs7322524	13	75,638,199	1.9E-03		
rs6957548	7	20,106,813	1.9E-03	AC005062.2	
rs2054956	3	67,433,729	1.9E-03	RP11-85I21.1	
rs2270614	1	67,628,609	1.9E-03	IL12RB2	
rs1011531	9	13,745,192	1.9E-03		
rs4411234	10	85,211,638	1.9E-03		
rs10852172	15	90,526,504	1.9E-03	RP11-152L20.3	
rs4839805	6	102,746,163	1.9E-03		
rs1368686	9	8,858,684	2.0E-03	PTPRD	4.7E-03
rs4679705	3	154,526,910	2.0E-03		
rs10890800	11	107,409,856	2.0E-03	CUL5	
rs6905741	6	152,601,496	2.0E-03	SYNE1	4.8E-03
rs140616	5	155,743,532	2.0E-03	SGCD	
rs479137	1	187,919,867	2.0E-03		
rs11861610	16	25,715,369	2.0E-03	HS3ST4	4.3E-03
rs11098778	4	80,758,025	2.0E-03		
rs4742630	9	9,853,227	2.0E-03	PTPRD	4.7E-03
rs962319	11	131,638,578	2.0E-03	NTM	
rs1510716	4	28,138,936	2.0E-03	RP11-123O22.1	
rs1921467	3	177,348,511	2.0E-03		
rs4937917	11	133,960,488	2.0E-03		
rs673733	4	28,128,457	2.0E-03	RP11-123O22.1	
rs855314	1	63,867,699	2.0E-03	PGM1	
rs534795	1	187,911,942	2.0E-03		
rs842767	2	60,722,118	2.0E-03	AC012498.1	
rs842764	2	60,726,355	2.0E-03	AC012498.1	
rs3746228	19	62,496,174	2.0E-03	ZNF460	
rs9599855	13	71,023,642	2.0E-03	DACH1	1.7E-03
rs30743	5	135,360,470	2.0E-03		
rs11586980	1	48,988,958	2.0E-03	BEND5	
rs1926937	10	7,816,837	2.0E-03	ITIH2	2.2E-03
rs12003093	9	32,578,258	2.0E-03		
rs2128001	8	51,624,066	2.0E-03	SNTG1	
rs4960248	6	6,753,207	2.0E-03		
rs4261746	2	100,588,062	2.0E-03	AC068538.4	
rs2375811	9	31,979,998	2.0E-03		
rs2044726	11	131,644,038	2.0E-03	NTM	
rs1329851	9	24,616,089	2.0E-03		

rs9815702	3	165,217,908	2.0E-03		
rs4747194	10	73,228,892	2.0E-03	CDH23	4.7E-03
rs473728	18	53,348,005	2.0E-03		
rs1491099	9	108,548,141	2.0E-03		
rs6040638	20	11,338,446	2.0E-03		
rs1501157	4	14,206,930	2.0E-03	LINC00504	
rs244496	12	31,101,381	2.0E-03	RP11-551L14.5	
rs1428079	5	163,915,592	2.0E-03	CTC-340A15.2	
rs823907	9	103,734,745	2.0E-03		
rs7032682	9	35,199,763	2.0E-03	UNC13B	
rs10491775	9	14,433,784	2.0E-03		
rs4723018	7	30,809,187	2.0E-03	INMT-FAM188B	
rs2389411	7	15,504,962	2.1E-03	AGMO	1.6E-03
rs17794012	2	128,756,194	2.1E-03	HS6ST1	
rs1500218	5	36,348,269	2.1E-03		
rs1257180	2	134,694,811	2.1E-03	MGAT5	
rs12357256	10	38,399,507	2.1E-03	ZNF33A	
rs2054894	3	178,025,981	2.1E-03	RP11-644C3.1	
rs12503047	4	80,793,266	2.1E-03		
rs12476995	2	127,512,490	2.1E-03		
rs10496978	2	145,806,644	2.1E-03	AC064865.2	
rs13031843	2	40,518,225	2.1E-03	SLC8A1	8.9E-04
rs1891385	9	6,209,845	2.1E-03	IL33	
rs7695536	4	57,649,991	2.1E-03	IGFBP7	
rs10499305	6	155,450,109	2.1E-03	TIAM2	
rs2827308	21	22,545,897	2.1E-03	AP000705.7	
rs1888171	9	27,677,159	2.1E-03		
rs4977786	9	20,863,224	2.1E-03	KIAA1797	
rs4306251	10	34,050,796	2.1E-03		
rs2391333	13	105,964,695	2.1E-03	EFNB2	5.1E-03
rs627222	7	6,094,981	2.1E-03	AC004895.4	
rs6441075	3	157,724,000	2.1E-03	KCNAB1	
rs7320401	13	71,051,569	2.1E-03	DACH1	1.7E-03
rs1529252	7	53,913,754	2.1E-03		
rs9842314	3	163,261,159	2.1E-03		
rs10498611	14	86,598,814	2.1E-03		
rs4950949	1	201,077,185	2.1E-03		
rs7903907	10	67,541,780	2.1E-03	CTNNA3	8.7E-04
rs206811	2	31,490,419	2.1E-03	XDH	
rs1417614	9	74,485,413	2.1E-03	TMC1	
rs9577637	13	111,876,415	2.1E-03		

rs2815851	1	239,464,285	2.1E-03	RGS7	
rs719802	11	112,739,889	2.1E-03	TTC12	
rs11991859	8	145,809,866	2.1E-03	ARHGAP39	
rs2832877	21	30,738,594	2.1E-03	KRTAP15-1	
rs4777039	15	66,408,502	2.1E-03	ITGA11	
rs9993663	4	142,529,192	2.1E-03	#N/A	
rs454387			2.1E-03	KRT6A	
rs7336364	13	43,064,351	2.1E-03	ENOX1	
rs2995211	9	103,748,841	2.1E-03		
rs1830775	9	9,791,907	2.1E-03	RP11-527D15.1	4.7E-03
rs610634			2.1E-03		
rs2842043	1	69,291,359	2.1E-03	RP11-424D14.1	
rs1009748	20	11,338,766	2.1E-03		
rs7557190	2	46,605,081	2.1E-03	ATP6V1E2	
rs4557782	9	38,694,680	2.1E-03		
rs1752582	10	30,031,941	2.1E-03	RP11-192N10.2	
rs2350277	3	141,326,327	2.2E-03	CLSTN2	1.3E-03
rs1105314	16	77,130,043	2.2E-03	RP11-264L1.3	3.1E-03
rs9563011	13	50,371,905	2.2E-03	RNASEH2B-AS1	
rs6099115	20	54,374,547	2.2E-03	AURKA	8.4E-03
rs2011688	1	110,530,927	2.2E-03	SLC6A17	
rs1324568	6	18,604,350	2.2E-03		
rs9702737	10	1,743,194	2.2E-03	ADARB2	4.2E-03
rs1859040	7	25,654,099	2.2E-03	AC003090.1	
rs1355782	3	132,970,356	2.2E-03	CPNE4	1.5E-03
rs10889011	1	56,955,736	2.2E-03	C1orf168	
rs1247343	6	161,291,611	2.2E-03	RP3-428L16.1	
rs661891	10	6,567,350	2.2E-03	PRKCQ	2.1E-03
rs2101634			2.2E-03		
rs593909	9	22,720,877	2.2E-03	RP11-399D6.2	
rs2959799	8	6,461,123	2.2E-03	CTD-2541M15.1	2.0E-03
rs12551069	9	37,343,252	2.2E-03	ZCCHC7	
rs6928084	6	143,006,732	2.2E-03		
rs263125			2.2E-03	RP11-440G9.1	
rs2493383	6	68,418,391	2.2E-03		
rs1511476	6	23,959,285	2.2E-03		
rs8012283	14	50,303,910	2.2E-03	NIN	
rs3766186	1	1,152,298	2.2E-03	SDF4	
rs3742467	14	49,709,284	2.2E-03	SOS2	
rs4636555	10	18,943,611	2.2E-03	NSUN6	3.7E-03
rs17241017	16	54,043,258	2.2E-03	RP11-212I21.2	

rs1927430	6	167,120,803	2.2E-03	RPS6KA2	
rs4670230	2	38,099,220	2.2E-03	AC016689.1	8.4E-04
rs1534154	3	120,793,720	2.2E-03	ADPRH	
rs1352671	9	32,033,985	2.2E-03		
rs17583618	10	122,496,218	2.2E-03		
rs1983208	3	163,236,803	2.2E-03		
rs1924353	13	107,923,485	2.2E-03		
rs10516278	4	14,129,536	2.2E-03	LINC00504	
rs11159412	14	79,235,135	2.2E-03	RP11-242P2.1	3.0E-03
rs7036061	9	35,203,538	2.2E-03	UNC13B	
rs386574	19	6,600,564	2.2E-03		
rs2291382	3	132,671,218	2.2E-03	MRPL3	
rs10101045	8	3,055,131	2.2E-03	CSMD1	8.6E-05
rs7647153	3	150,764,922	2.2E-03	WWTR1	
rs6601431	8	10,207,955	2.2E-03	MSRA	8.7E-03
rs11137281	9	139,880,482	2.2E-03	EHMT1	
rs8018889	14	37,353,342	2.2E-03	TTC6	
rs955093	1	69,360,781	2.2E-03	RP11-424D14.1	
rs1336158	1	69,368,055	2.2E-03	RP11-424D14.1	
rs2720518	8	17,379,232	2.2E-03		
rs5762528	22	26,953,364	2.2E-03	TTC28	
rs10501120	11	29,853,673	2.2E-03	CTD-3138F19.1	
rs11864884	16	84,458,540	2.2E-03		
rs1110339	16	85,807,520	2.3E-03	RP11-899L11.3	
rs3813199	1	1,148,140	2.3E-03	SDF4	
rs1043469	12	102,690,890	2.3E-03	RP11-341G23.4	
rs12933937	16	86,306,049	2.3E-03	KLHDC4	
rs11714671	3	79,952,602	2.3E-03		
rs922306	1	238,240,914	2.3E-03	RPS7P5	
rs2973675	5	177,695,031	2.3E-03	COL23A1	
rs11110532	12	99,727,666	2.3E-03	ANO4	
rs2294757	6	133,076,791	2.3E-03	VNN1	
rs2744728	1	22,413,505	2.3E-03		
rs6908425	6	20,836,710	2.3E-03	CDKAL1	3.6E-03
rs7002959	8	145,656,204	2.3E-03	CYHR1	
rs7783229	7	20,175,526	2.3E-03	MACC1	7.0E-03
rs13177348	5	36,373,050	2.3E-03		
rs277576	9	34,796,065	2.3E-03		
rs4719495	7	17,289,208	2.3E-03	AC003075.4	
rs1364196	16	58,761,704	2.3E-03		
rs4872012	8	22,702,726	2.3E-03	RP11-459E5.1	1.7E-03

rs2236483	21	45,750,482	2.3E-03	COL18A1	2.6E-03
rs6916705	6	15,135,265	2.3E-03	RP11-146I2.1	
rs1354298	10	111,195,892	2.3E-03		
rs10816129	9	9,445,711	2.3E-03	PTPRD	4.7E-03
rs6451273	5	36,389,507	2.3E-03		
rs2888853	2	43,077,288	2.3E-03	AC016735.1	
rs7766508	6	161,713,309	2.3E-03	PARK2	8.8E-05
rs3935137	12	89,833,922	2.3E-03	RP11-916O13.1	
rs4745127	9	70,386,196	2.3E-03	RP11-274B18.4	
rs4879956	9	36,136,652	2.3E-03	GLIPR2	
rs9852917	3	174,819,412	2.3E-03	NLGN1	1.9E-04
rs12662891	6	22,683,075	2.3E-03	HDGFL1	
rs10732328	9	11,825,471	2.3E-03		
rs2862482	2	81,407,215	2.3E-03		
rs1420566	16	54,623,261	2.3E-03		
rs11720121	3	71,677,948	2.3E-03	FOXP1	2.2E-03
rs4971588	2	49,408,487	2.3E-03		
rs7910208	10	15,362,323	2.3E-03	FAM171A1	
rs9423346	10	125,181,102	2.3E-03	RP11-338O1.2	
rs8024396	15	57,435,925	2.3E-03	RP11-356M20.3	4.2E-03
rs944638	9	25,558,851	2.3E-03		
rs2189103	7	82,753,366	2.3E-03		
rs7248389	19	38,624,155	2.3E-03	PEPD	
rs288579	16	61,135,127	2.3E-03		
rs7040048	9	35,243,676	2.3E-03	UNC13B	
rs1543677	9	20,844,449	2.4E-03	KIAA1797	
rs10772682	12	13,516,717	2.4E-03		
rs1224147	13	107,754,759	2.4E-03	TNFSF13B	
rs1551411	9	2,621,932	2.4E-03	VLDLR	
rs1424223	16	26,216,163	2.4E-03		
rs9558743	13	105,793,586	2.4E-03		
rs391734	14	44,038,745	2.4E-03	FSCB	
rs1006146	17	66,872,466	2.4E-03		
rs964691	15	66,413,596	2.4E-03	ITGA11	
rs12057561	1	84,357,482	2.4E-03	PRKACB	
rs3771254	2	20,269,726	2.4E-03	SDC1	
rs3818532	6	33,787,785	2.4E-03	MNF1	
rs7089181	10	91,699,103	2.4E-03	RP11-478K7.2	
rs8001719	13	98,572,725	2.4E-03		
rs1451386	7	25,875,733	2.4E-03		
rs13090251	3	146,805,632	2.4E-03		

rs1002154	20	36,511,034	2.4E-03	SNHG11	
rs1340721	13	68,498,950	2.4E-03		
rs1609516	16	78,843,385	2.4E-03	#N/A	
rs10505470	8	127,433,877	2.4E-03		
rs7674006	4	41,394,864	2.4E-03	LIMCH1	
rs3732568	3	135,998,026	2.4E-03	EPHB1	3.6E-03
rs4843792	16	86,673,631	2.4E-03	RP11-863P13.5	
rs4746391	10	77,847,540	2.4E-03	C10orf11	
rs614705	4	31,051,457	2.4E-03		
rs517543	18	73,496,612	2.4E-03		
rs2383802	9	29,340,711	2.4E-03		
rs9873887	3	77,518,313	2.4E-03	ROBO2	2.5E-03
rs7330144	13	48,154,504	2.4E-03		
rs225263	17	30,983,950	2.4E-03	AP2B1	
rs9925917	16	14,006,322	2.4E-03	CTD-2135D7.5	
rs921172	3	110,253,080	2.4E-03	MORC1	3.6E-03
rs1105244	2	66,165,727	2.4E-03		
rs7645827	3	148,479,699	2.4E-03	RP11-635I10.1	
rs6590725	11	133,039,413	2.4E-03		
rs2396327	2	226,912,248	2.4E-03		
rs10971020	9	32,536,117	2.4E-03	AL353671.2	
rs4820001	22	16,207,684	2.4E-03		
rs4075049	16	28,150,790	2.5E-03		
rs10828834	10	18,852,440	2.5E-03	RP11-499P20.2	1.7E-03
rs10518531	1	76,871,826	2.5E-03	ST6GALNAC3	
rs972246	7	8,551,314	2.5E-03	NXPH1	2.6E-03
rs1452353	9	28,030,937	2.5E-03	LINGO2	2.2E-03
rs1333657	6	10,404,322	2.5E-03		
rs632023			2.5E-03	KIRREL3-AS1	
rs12701401	7	4,099,925	2.5E-03	SDK1	
rs7593862	2	23,123,501	2.5E-03	AC016768.1	
rs12765658	10	65,214,873	2.5E-03	RP11-170M17.1	
rs10886106	10	119,382,644	2.5E-03		
rs10817039	9	112,349,358	2.5E-03	SVEP1	5.0E-03
rs4366594	13	93,203,337	2.5E-03	GPC6	1.0E-03
rs1384491	2	13,155,099	2.5E-03		
rs6100805	20	58,242,908	2.5E-03	RP5-1043L13.1	
rs8009813	14	67,896,272	2.5E-03	RAD51B	4.6E-04
rs446149	4	31,099,803	2.5E-03		
rs2217843	12	70,431,403	2.5E-03	RAB21	
rs11790297	9	30,964,923	2.5E-03		

rs7660498	4	2,214,663	2.5E-03	POLN	
rs2451255	6	159,430,804	2.5E-03		
rs185634	6	72,293,749	2.5E-03		
rs11011284	10	37,945,854	2.5E-03		
rs9564573	13	69,018,508	2.5E-03		
rs2893666	10	57,413,194	2.5E-03		
rs485028			2.5E-03		
rs10964759	9	20,915,921	2.5E-03	KIAA1797	
rs10758338	9	35,958,663	2.5E-03	YBX1P10	
rs9299057	9	7,819,623	2.5E-03	C9orf123	
rs1860394	12	3,309,312	2.5E-03	RP5-1063M23.2	
rs473773	1	187,893,806	2.5E-03		
rs6849536	4	20,049,574	2.5E-03	SLIT2	
rs2284757	1	166,629,786	2.6E-03		
rs11924144	3	187,328,277	2.6E-03	DGKG	
rs6539986	16	85,526,711	2.6E-03		
rs10483899	14	77,910,936	2.6E-03	NRXN3	
rs6414023	2	131,793,849	2.6E-03	PLEKHB2	
rs10773558	12	127,643,363	2.6E-03	TMEM132C	
rs2593943	3	110,172,911	2.6E-03	MORC1	3.6E-03
rs7314616	12	97,280,155	2.6E-03		
rs288740	13	106,299,212	2.6E-03		
rs9559574	13	108,834,331	2.6E-03		
rs205185	16	25,484,728	2.6E-03		
rs7744253	6	31,131,503	2.6E-03	HCG22	7.4E-05
rs1157392	3	117,997,607	2.6E-03	LSAMP	
rs1810807	9	32,774,838	2.6E-03	TMEM215	
rs4662808	2	128,895,709	2.6E-03		
rs8061866	16	25,713,267	2.6E-03	HS3ST4	4.3E-03
rs17124656	14	51,395,835	2.6E-03	GNG2	
rs12220980	10	80,902,453	2.6E-03		
rs12454396	18	62,299,667	2.6E-03		
rs11843565	13	58,191,289	2.6E-03		
rs6122383	20	61,256,104	2.6E-03		
rs2902583	1	187,944,854	2.6E-03		
rs3827494	3	46,577,235	2.6E-03	LRRC2	
rs4132141	5	97,626,217	2.6E-03		
rs3904561	9	34,049,287	2.6E-03		
rs287548	13	72,803,784	2.6E-03		
rs7867247	9	8,695,964	2.6E-03	RP11-134K1.3	4.7E-03
rs7838051	8	10,934,272	2.6E-03	XKR6	

rs12116575	1	67,684,847	2.6E-03		
rs7527726	1	104,537,534	2.6E-03		
rs2585655	9	38,156,392	2.6E-03		
rs10919607	1	187,942,039	2.6E-03		
rs7638530	3	116,924,298	2.6E-03	GAP43	
rs7322238	13	107,355,800	2.6E-03		
rs4235137	4	43,411,555	2.6E-03		
rs813945	3	130,143,627	2.6E-03	KIAA1257	
rs1901744	8	27,990,118	2.6E-03	C8orf80	
rs9890721	17	45,958,502	2.6E-03	MYCBPAP	
rs4591550	4	162,223,074	2.6E-03		
rs10125105	9	110,266,009	2.6E-03		
rs328131	18	42,518,576	2.6E-03	ST8SIA5	
rs1330362	9	116,819,489	2.6E-03	TNC	
rs9322396	6	153,097,247	2.6E-03		
rs4854585	3	134,619,974	2.6E-03	BFSP2	
rs10810035	9	13,777,648	2.6E-03		
rs7865357			2.6E-03		
rs3012677	9	3,343,579	2.6E-03	RFX3	
rs1476081	7	17,245,819	2.6E-03		
rs3802217	8	141,177,159	2.6E-03	TRAPPC9	
rs1463230	3	151,517,246	2.6E-03		
rs10494624	1	188,004,012	2.6E-03		
rs945464	9	9,176,346	2.6E-03	PTPRD	4.7E-03
rs9301099	13	105,483,574	2.6E-03		
rs11767557	7	142,819,261	2.6E-03	EPHA1	
rs1999603	13	70,881,342	2.7E-03		
rs6870249	5	145,652,624	2.7E-03	RBM27	
rs7922927	10	21,635,297	2.7E-03		
rs2740885	8	3,898,685	2.7E-03	CSMD1	8.6E-05
rs4752360	10	121,732,421	2.7E-03		
rs1258094	9	77,863,413	2.7E-03	PCSK5	9.0E-03
rs1521381	12	77,392,088	2.7E-03	RP11-171L9.1	
rs2767699	10	7,447,340	2.7E-03	SFMBT2	6.1E-03
rs6064832	20	36,718,407	2.7E-03		
rs10486459	7	25,492,292	2.7E-03		
rs4337169	13	93,214,002	2.7E-03	GPC6	1.0E-03
rs940222	15	59,156,777	2.7E-03	RORA	5.4E-04
rs4866655	5	2,211,719	2.7E-03		
rs7511842	1	165,909,808	2.7E-03	RCSD1	
rs4466848	11	130,077,198	2.7E-03	C11orf44	

rs10486725	7	41,839,234	2.7E-03		
rs12750699	1	165,540,384	2.7E-03	POU2F1	
rs1411418	9	10,978,308	2.7E-03		
rs7746344	6	52,646,130	2.7E-03	TMEM14A	
rs6075164	20	16,985,876	2.7E-03		
rs10494011	1	104,691,609	2.7E-03		
rs2999394	14	50,629,779	2.7E-03	RP11-1140I5.1	4.5E-03
rs1337088	1	238,214,126	2.7E-03		
rs1829975	2	161,493,415	2.7E-03		
rs4463175	5	134,967,023	2.7E-03	CTC-321K16.1	
rs4937316	11	127,706,360	2.7E-03		
rs9877183	3	169,414,149	2.7E-03		
rs844030	12	100,209,553	2.7E-03	UTP20	
rs7635904	3	190,543,782	2.7E-03		
rs4574773	7	128,956,719	2.7E-03		
rs1202100	6	73,363,249	2.7E-03	RP3-474G15.1	
rs8017415	14	55,274,324	2.7E-03		
rs7045753	9	10,658,198	2.7E-03		
rs10869715	9	77,970,295	2.7E-03	PCSK5	9.0E-03
rs2275612	1	95,140,004	2.7E-03	CNN3	1.8E-03
rs2494711	6	26,757,400	2.7E-03	ZNF322	
rs359311	10	17,420,810	2.7E-03	ST8SIA6	
rs11733193	4	15,655,673	2.7E-03	PROM1	
rs7557891	2	77,623,499	2.8E-03	LRRTM4	
rs9625422	22	19,734,113	2.8E-03	P2RX6P	
rs181663	10	119,373,203	2.8E-03		
rs6958161	7	3,121,336	2.8E-03		
rs1833288	18	50,668,904	2.8E-03	RAB27B	
rs283832	2	79,090,597	2.8E-03		
rs2474589	10	38,461,927	2.8E-03		
rs9324756	5	153,044,424	2.8E-03	GRIA1	1.8E-03
rs1057090	8	6,466,450	2.8E-03	CTD-2541M15.1	2.0E-03
rs721936	9	89,472,969	2.8E-03	DAPK1	
rs4838650	10	49,664,276	2.8E-03	WDFY4	1.0E-03
rs10904629	10	15,894,758	2.8E-03	FAM188A	
rs949664	12	69,368,222	2.8E-03	PTPRR	
rs2798616	10	91,661,625	2.8E-03	RP11-478K7.2	
rs625165	9	9,528,589	2.8E-03	PTPRD	4.7E-03
rs6589938	11	122,011,218	2.8E-03		
rs4233734	2	29,490,544	2.8E-03	ALK	1.7E-03
rs7805607	7	142,222,926	2.8E-03	TRBV30	

rs3825644	14	64,481,252	2.8E-03	CHURC1	
rs294829	9	10,187,122	2.8E-03	PTPRD	4.7E-03
rs2226409	21	19,390,523	2.8E-03		
rs6790188	3	26,612,410	2.8E-03		
rs4750334	10	13,339,929	2.8E-03		
rs2272631	8	144,406,670	2.8E-03	ZFP41	
rs1240891	13	67,980,008	2.8E-03		
rs2324805	13	40,740,546	2.8E-03	MTRF1	
rs4887794	16	73,521,965	2.8E-03	WDR59	
rs6571820	14	37,291,743	2.8E-03	TTC6	
rs2481556	9	30,253,627	2.8E-03		
rs1897499	3	14,726,880	2.8E-03	C3orf20	2.6E-03
rs2014729	7	26,346,635	2.8E-03	SNX10	
rs8059958	16	63,780,673	2.8E-03	RP11-256I9.2	
rs1446109	2	80,391,930	2.8E-03	CTNNA2	6.0E-03
rs364331	9	32,039,631	2.8E-03		
rs456699	16	82,391,190	2.8E-03	RP11-483P21.2	
rs815846	9	83,412,725	2.8E-03	TLE1	8.9E-03
rs10488578	7	20,708,193	2.8E-03	ABCB5	1.0E-03
rs4645956	8	128,819,394	2.8E-03	RP11-1136L8.1	
rs748445	4	6,006,173	2.8E-03	C4orf50	
rs7845577	8	80,063,146	2.8E-03		
rs4697205	4	20,733,627	2.8E-03	KCNIP4	5.5E-04
rs1536761	13	46,485,423	2.8E-03		
rs1654658	19	59,886,493	2.9E-03		
rs2201554			2.9E-03		
rs1324751	13	104,784,307	2.9E-03		
rs4408557	16	77,920,300	2.9E-03		
rs7564226	2	129,017,050	2.9E-03		
rs2893386	13	110,456,068	2.9E-03		
rs732010	17	64,554,335	2.9E-03	ABCA9	
rs630973	9	14,370,945	2.9E-03	NFIB	
rs9826966	3	18,712,800	2.9E-03	AC105750.1	
rs2955195			2.9E-03		
rs6542824	2	109,411,568	2.9E-03	SH3RF3	
rs762625	1	201,411,924	2.9E-03	CHI3L1	
rs3988342	8	17,010,348	2.9E-03	EFHA2	
rs1422673	5	150,419,181	2.9E-03	TNIP1	
rs6788677	3	60,111,967	2.9E-03	FHIT	6.4E-04
rs9378384	6	3,753,854	2.9E-03		
rs10513361	3	151,328,079	2.9E-03	RP11-167H9.4	

rs6742210	2	40,469,024	2.9E-03	SLC8A1	8.9E-04
rs2018728	10	44,837,353	2.9E-03	RP11-285G1.8	
rs6571907	14	38,752,236	2.9E-03	RP11-407N17.2	
rs12533743	7	24,435,064	2.9E-03		
rs560227	1	187,902,915	2.9E-03	RN5S73	
rs2971007	2	100,549,959	2.9E-03	PDCL3	
rs7098143	10	83,329,037	2.9E-03		
rs7515377	1	75,215,414	2.9E-03		
rs2216588	5	170,214,294	2.9E-03		
rs2383716	9	26,767,330	2.9E-03	RP11-18A15.1	
rs9503867	6	3,927,524	2.9E-03	RP3-406P24.1	
rs7557980	2	222,422,055	2.9E-03		
rs642722	6	74,327,295	2.9E-03	RP11-505P4.7	
rs16900289	6	157,926,844	3.0E-03	RP11-193H22.2	
rs10929183	2	237,293,840	3.0E-03		
rs7682973	4	5,996,007	3.0E-03		
rs174313	22	16,381,375	3.0E-03	DNAJA1P6	
rs897405	6	68,867,259	3.0E-03		
rs40184	5	1,448,077	3.0E-03	SLC6A3	
rs7656054	4	28,089,513	3.0E-03	RP11-123O22.1	
rs2380902	9	3,807,537	3.0E-03		
rs30882			3.0E-03		
rs1361636	10	25,757,917	3.0E-03	GPR158	3.5E-03
rs7045369	9	19,444,906	3.0E-03	RP11-363E7.4	
rs1860447	17	64,543,052	3.0E-03	ABCA9	
rs6830109	4	21,101,543	3.0E-03	KCNIP4	5.5E-04
rs1975802	16	66,843,348	3.0E-03	RP11-96D1.7	
rs6539999	16	85,636,503	3.0E-03		
rs7025945	9	31,960,850	3.0E-03		
rs9652250	13	82,059,194	3.0E-03		
rs1970288	10	24,334,617	3.0E-03	KIAA1217	1.4E-04
rs4238915	16	25,643,984	3.0E-03	HS3ST4	4.3E-03
rs6775393	3	189,987,692	3.0E-03	LPP	9.8E-04
rs7098268	10	6,944,186	3.0E-03		
rs1122059	16	77,920,325	3.0E-03		
rs1769463	14	86,581,817	3.0E-03		
rs4755819	11	44,336,365	3.0E-03		
rs214950	6	152,750,003	3.0E-03	SYNE1	4.8E-03
rs874838	2	85,275,202	3.0E-03	TCF7L1	6.2E-03
rs449851	9	70,174,192	3.0E-03	PGM5	
rs17348854	8	4,811,985	3.0E-03	CSMD1	8.6E-05

rs162297	6	167,375,129	3.0E-03	FGFR1OP	
rs1998517	9	8,502,133	3.0E-03	PTPRD	4.7E-03
rs7131752	12	79,999,969	3.0E-03	ACSS3	
rs12116744	1	160,447,080	3.0E-03	NOS1AP	
rs4274995	5	162,331,039	3.1E-03		
rs12675592			3.1E-03	RP11-134O21.1	
rs870427	10	133,889,881	3.1E-03	STK32C	
rs10112327	8	41,152,710	3.1E-03		
rs12962998	18	40,094,447	3.1E-03		
rs7205107	16	48,138,708	3.1E-03	ZNF423	8.5E-03
rs7631529	3	39,261,829	3.1E-03		
rs2810442	13	75,639,902	3.1E-03		
rs13353497	3	46,573,381	3.1E-03	LRRC2	
rs3780354	9	36,198,626	3.1E-03	CLTA	
rs2127355	10	62,204,222	3.1E-03	CDK1	
rs4752744	11	1,674,842	3.1E-03	KRTAP5-6	
rs7704562	5	153,387,590	3.1E-03	FAM114A2	
rs8046811	16	8,385,232	3.1E-03		
rs958309	16	83,324,471	3.1E-03	USP10	
rs2753338	1	86,707,624	3.1E-03	CLCA1	
rs4493419	3	5,453,865	3.1E-03		
rs704649	1	243,667,431	3.1E-03	KIF26B	1.9E-03
rs661827	13	68,322,752	3.1E-03		
rs13188129	5	180,052,650	3.1E-03	OR2AI1P	
rs517315	3	171,948,066	3.1E-03	CLDN11	
rs198178	16	24,128,125	3.1E-03	PRKCB	
rs7836666	8	143,257,639	3.1E-03		
rs4260187	2	213,397,743	3.1E-03	AC093865.1	
rs2088170	12	65,068,679	3.1E-03	GRIP1	1.0E-03
rs10104977	8	119,793,078	3.1E-03		
rs1254722	6	2,524,404	3.1E-03		
rs7752020	6	164,924,604	3.1E-03		
rs13219162	6	15,124,166	3.1E-03	RP11-146I2.1	
rs1558308	7	23,703,035	3.1E-03	C7orf46	
rs4921416	5	161,109,151	3.1E-03	GLRXP3	
rs8071475	17	55,328,702	3.1E-03	RPS6KB1	
rs1877447	9	8,711,943	3.1E-03	PTPRD	4.7E-03
rs6717256	2	77,625,651	3.1E-03	LRRTM4	
rs1859275	7	8,552,281	3.1E-03	NXPH1	2.6E-03
rs1993802	3	112,078,092	3.1E-03		
rs2124209	9	3,809,902	3.1E-03	GLIS3	

rs6073045	20	41,375,700	3.1E-03		
rs9288037	2	180,078,538	3.1E-03	ZNF385B	7.5E-03
rs11968578	6	162,122,933	3.1E-03	PARK2	8.8E-05
rs2553578	14	35,794,358	3.1E-03		
rs4746209	10	76,042,043	3.1E-03	ADK	
rs2812661	10	34,159,820	3.1E-03		
rs1452425	2	18,265,913	3.1E-03	KCNS3	
rs10515241	5	95,988,347	3.1E-03	CTD-2337A12.1	
rs299098	5	68,755,507	3.1E-03	MARVELD2	
rs245883	7	29,154,471	3.2E-03	CPVL	
rs884432	3	133,414,672	3.2E-03	CPNE4	
rs1000810	6	52,642,890	3.2E-03	RP1-152L7.5	
rs9838734	3	173,485,649	3.2E-03	FNDC3B	2.5E-03
rs2391298	13	105,923,806	3.2E-03		
rs9321599	6	137,760,226	3.2E-03		
rs4933300	10	85,446,164	3.2E-03		
rs2110398	2	60,353,988	3.2E-03		
rs628957	11	75,509,963	3.2E-03	UVRAG	
rs4752161	10	120,203,154	3.2E-03		
rs3789867	9	116,915,509	3.2E-03	TNC	7.3E-03
rs328753	12	70,472,924	3.2E-03	RP11-2H8.2	
rs10781655	12	131,554,987	3.2E-03		
rs10521320	16	54,133,662	3.2E-03	RP11-212I21.4	2.2E-03
rs4605746	5	54,248,473	3.2E-03		
rs2921449	10	74,161,815	3.2E-03	MCU	
rs9379840	6	10,964,087	3.2E-03	TMEM14B	
rs663319	11	120,512,584	3.2E-03	TECTA	
rs318961	11	130,869,705	3.2E-03	NTM	
rs10919649	1	187,969,811	3.2E-03		
rs4362766	3	180,163,136	3.2E-03		
rs978716	20	58,928,466	3.2E-03		
rs17742423	6	73,588,333	3.2E-03	KCNQ5	
rs7104942	11	107,443,788	3.2E-03	CUL5	
rs12639674	4	14,171,117	3.2E-03	LINC00504	
rs1164624	5	74,178,621	3.2E-03	FAM169A	
rs8059056	16	76,324,079	3.2E-03	NUDT7	
rs1473822	9	8,716,153	3.2E-03	PTPRD	4.7E-03
rs17329096	19	39,159,672	3.3E-03		
rs10513812	3	188,388,188	3.3E-03		
rs16842042	3	135,975,279	3.3E-03	EPHB1	
rs2756109	10	101,548,736	3.3E-03	ABCC2	

rs431370	4	31,056,923	3.3E-03		
rs2271716	11	113,820,182	3.3E-03	REXO2	
rs4410448	3	110,295,956	3.3E-03	MORC1	3.6E-03
rs7806681	7	17,194,647	3.3E-03		
rs430072	9	26,407,714	3.3E-03		
rs11130760	3	60,171,577	3.3E-03	FHIT	6.4E-04
rs1028308	6	27,237,736	3.3E-03		
rs2817458	6	156,990,541	3.3E-03		
rs4540845			3.3E-03	AP005135.2	
rs2716454	11	24,710,115	3.3E-03	LUZP2	2.5E-03
rs2064175	6	18,689,151	3.3E-03		
rs4431442	6	100,320,236	3.3E-03		
rs2049819	7	142,236,056	3.3E-03		
rs13118771	4	3,735,553	3.3E-03	AC141928.1	
rs597131	9	32,527,141	3.3E-03	TOPORS	
rs13223065	7	3,606,138	3.3E-03	SDK1	
rs150385	18	54,063,403	3.3E-03	NEDD4L	
rs7564926	2	212,670,237	3.3E-03	ERBB4	1.1E-03
rs1462845	3	118,425,700	3.3E-03	LSAMP	
rs659406	1	64,028,606	3.3E-03	RP4-597J3.1	
rs731710	16	86,442,048	3.3E-03	SLC7A5	
rs9394708	6	40,708,020	3.3E-03		
rs2121053	1	66,761,087	3.3E-03		
rs1328857	6	73,414,549	3.3E-03	KCNQ5-IT1	
rs1372117	2	129,719,058	3.3E-03	AC079586.1	
rs9342947	6	73,222,052	3.3E-03		
rs2274512	14	32,899,031	3.3E-03	NPAS3	3.2E-04
rs1925054	13	54,473,384	3.3E-03		
rs1407376	9	76,952,269	3.3E-03	OSTF1	
rs10418296	19	58,594,425	3.3E-03	ZNF765	
rs2029046	14	40,319,704	3.3E-03		
rs7333151	13	72,517,230	3.3E-03		
rs1108029	16	27,123,267	3.3E-03	JMJD5	
rs2252268	20	59,419,864	3.3E-03	CDH4	4.6E-04
rs1406	19	35,006,952	3.3E-03	CCNE1	
rs7595482	2	38,106,517	3.3E-03	AC016689.1	8.4E-04
rs8013122	14	35,500,214	3.3E-03	RP11-116N8.1	
rs7395920	11	1,920,888	3.3E-03	TNNT3	
rs3176774	12	9,808,373	3.3E-03	CD69	
rs7656798	4	75,606,837	3.3E-03		
rs672046	1	96,650,333	3.4E-03		

rs7527078	1	4,590,753	3.4E-03		
rs9354868	6	63,043,165	3.4E-03	KHDRBS2	
rs2259969	9	78,132,776	3.4E-03	PCSK5	9.0E-03
rs2906649	7	101,363,758	3.4E-03	CUX1	6.7E-03
rs7149088	14	26,690,636	3.4E-03	RP11-384J4.2	
rs1344375	2	80,508,405	3.4E-03	CTNNA2	6.0E-03
rs7198494	16	79,652,592	3.4E-03	RP11-303E16.8	
rs11738161	5	180,052,616	3.4E-03	OR2AI1P	
rs12992095	2	32,515,047	3.4E-03	BIRC6	
rs2543016	18	41,217,724	3.4E-03		
rs868421	8	138,668,249	3.4E-03		
rs6544336	2	40,481,216	3.4E-03	SLC8A1	8.9E-04
rs8051651	16	58,280,250	3.4E-03		
rs6869332	5	60,165,118	3.4E-03	ELOVL7	
rs2368251	10	28,014,785	3.4E-03	MKX	6.8E-03
rs943043	10	25,434,343	3.4E-03		
rs9973235	19	4,798,713	3.4E-03	PLIN3	
rs329076			3.4E-03	EGFEM1P	
rs2839798	12	61,552,251	3.4E-03	PPM1H	5.0E-03
rs2381609	9	7,462,661	3.4E-03	RP11-87M1.1	
rs1000468			3.4E-03		
rs702718	5	57,794,308	3.4E-03	PLK2	
rs2705044	8	17,366,532	3.4E-03	ADAM24P	
rs1293044	6	70,290,602	3.4E-03		
rs34186	7	31,716,818	3.4E-03	PPP1R17	
rs1530439	10	63,315,965	3.4E-03		
rs15677	11	107,482,699	3.4E-03	RP11-144G7.2	
rs2289221	15	90,925,162	3.4E-03	RP11-386M24.3	
rs10085000	4	156,186,681	3.4E-03		
rs2959802	8	6,459,403	3.4E-03	CTD-2541M15.1	2.0E-03
rs1702161	15	88,281,590	3.4E-03	RP11-493E3.2	
rs4688021	3	120,846,256	3.4E-03	POPDC2	
rs1981522	7	25,655,960	3.4E-03	AC003090.1	
rs2735246	3	126,961,752	3.4E-03	GS1-388B5.8	
rs1022909	13	107,468,774	3.4E-03		
rs2110699	14	88,974,191	3.4E-03	RP11-33N16.3	
rs3793179	7	158,152,317	3.4E-03	NCAPG2	
rs6064592	20	55,788,953	3.4E-03		
rs954197	9	2,473,942	3.4E-03	RP11-125B21.2	
rs1917286	7	51,536,912	3.4E-03		
rs577876	6	161,843,145	3.4E-03	PARK2	8.8E-05

rs2135488	13	70,515,776	3.4E-03	LINC00348	
rs9295730	6	27,236,785	3.4E-03		
rs890125	11	29,972,772	3.4E-03		
rs2862079	3	154,694,531	3.5E-03	RP11-23D24.2	
rs9909324	17	55,401,538	3.5E-03	RNFT1	
rs3778229	6	161,564,530	3.5E-03	AGPAT4	3.3E-03
rs1111367	10	20,313,589	3.5E-03	PLXDC2	6.4E-03
rs1955985	14	43,649,706	3.5E-03	RP11-305B6.3	
rs183376	4	13,910,107	3.5E-03		
rs6937168	6	85,187,128	3.5E-03	RP1-90L14.1	
rs2950	6	11,458,251	3.5E-03	NEDD9	
rs11114788	12	80,123,692	3.5E-03	ACSS3	
rs213207	6	33,349,147	3.5E-03	VPS52	
rs10055973	5	180,052,524	3.5E-03	OR2AI1P	
rs9862715	3	61,011,332	3.5E-03	FHIT	6.4E-04
rs11185546	3	197,787,935	3.5E-03	FBXO45	
rs1078373	19	36,492,970	3.5E-03	TSHZ3	
rs3111643	5	53,722,645	3.5E-03	RP11-461C13.1	
rs1152944	12	68,684,239	3.5E-03	RP11-611E13.2	
rs2168358	15	90,875,894	3.5E-03		
rs4968318	17	42,806,893	3.5E-03	C17orf57	
rs11257622	10	12,335,345	3.5E-03	CDC123	
rs1889380	14	56,055,419	3.5E-03	RP11-624J12.1	
rs2220602	5	29,131,883	3.5E-03		
rs4945876	6	111,522,333	3.5E-03	SLC16A10	
rs2177308	17	44,564,860	3.5E-03	B4GALNT2	
rs3733397	4	4,900,303	3.5E-03		
rs234853	11	2,807,404	3.5E-03	KCNQ1	3.8E-03
rs533045	1	187,929,464	3.5E-03		
rs747417	8	41,277,161	3.5E-03	SFRP1	
rs928195	13	111,913,111	3.5E-03		
rs1528430	2	151,042,707	3.5E-03	RND3	
rs6564744	16	78,765,658	3.5E-03	RP11-525K10.3	
rs842304	9	7,672,601	3.5E-03		
rs1674815	7	16,714,742	3.5E-03	BZW2	
rs4515870	10	21,791,617	3.5E-03		
rs754048	11	132,520,788	3.6E-03	OPCML	2.4E-04
rs2812234	13	50,185,815	3.6E-03	DLEU7	7.8E-03
rs7082368	10	20,290,116	3.6E-03	PLXDC2	6.4E-03
rs2355597	5	22,439,701	3.6E-03	CDH12	5.3E-03
rs7091304	10	21,597,792	3.6E-03		

rs4558864			3.6E-03		
rs7629257	3	165,959,187	3.6E-03	RP11-71H9.1	
rs2163050	2	41,680,242	3.6E-03	AC010739.1	
rs1407045	6	26,584,134	3.6E-03	BTN2A1	
rs1471239	12	83,524,053	3.6E-03		
rs6904395	6	2,388,180	3.6E-03		
rs872288	2	45,968,529	3.6E-03	PRKCE	
rs4979816	10	79,901,867	3.6E-03	RP11-90J7.3	
rs7770766	6	5,330,325	3.6E-03	FARS2	
rs720651	13	25,129,946	3.6E-03	ATP8A2	
rs17663979	5	72,865,786	3.6E-03		
rs6789646	3	129,698,465	3.6E-03	RP11-475N22.4	
rs4927600	2	1,340,999	3.6E-03	SNTG2	7.5E-03
rs2566758	1	68,405,071	3.6E-03	RP11-518D3.3	
rs12756859	1	68,781,782	3.6E-03	RP4-694A7.4	
rs12463274	19	14,819,042	3.6E-03		
rs12955031	18	62,401,259	3.6E-03	CDH19	1.7E-04
rs918498	5	150,439,981	3.6E-03	TNIP1	
rs10470540	3	193,152,780	3.6E-03	RP11-655G22.2	
rs11646219	16	85,654,078	3.6E-03	RP11-134D3.1	
rs2549513	16	78,108,228	3.6E-03	RP11-467I17.1	
rs12585282	13	108,857,114	3.6E-03		
rs1057091	8	6,487,952	3.6E-03	CTD-2541M15.1	2.0E-03
rs979525	9	28,470,661	3.6E-03	LINGO2	2.2E-03
rs7120230	11	70,617,976	3.6E-03	SHANK2	
rs7577867	2	128,609,678	3.6E-03	AC108059.4	
rs7544722	1	72,179,997	3.6E-03	NEGR1	
rs1503673	3	115,430,553	3.6E-03	RP11-553L6.3	
rs2818849	10	58,347,388	3.7E-03		
rs1053230	1	239,821,971	3.7E-03	OPN3	
rs2485945	1	2,873,792	3.7E-03		
rs3106818	3	170,458,317	3.7E-03	MECOM	
rs6979475	7	24,884,499	3.7E-03	OSBPL3	
rs277344	1	75,092,849	3.7E-03		
rs7795793	7	17,192,132	3.7E-03		
rs12741316	1	238,672,355	3.7E-03	FMN2	2.3E-03
rs12199650			3.7E-03	MCM3	
rs7680019	4	22,165,683	3.7E-03		
rs1435192	18	39,314,102	3.7E-03		
rs611652	12	5,110,030	3.7E-03		
rs7917682	10	73,845,889	3.7E-03	MICU1	

rs4334286	16	80,270,325	3.7E-03	CMIP	
rs4771519	13	105,495,523	3.7E-03		
rs7143959	14	50,315,416	3.7E-03	NIN	
rs276504	6	137,394,212	3.7E-03	IL20RA	
rs11720523	3	71,627,860	3.7E-03	FOXP1	2.2E-03
rs251069	5	29,116,075	3.7E-03		
rs9381218	6	42,846,727	3.7E-03	KIAA0240	
rs1386866	3	164,154,735	3.7E-03		
rs2305862	12	100,281,661	3.7E-03	UTP20	
rs7339421	13	101,576,026	3.7E-03	FGF14	2.6E-03
rs2342845	14	55,424,344	3.7E-03		
rs1073644	10	77,705,677	3.7E-03	C10orf11	
rs7077721	10	91,739,092	3.7E-03		
rs1527757	2	156,475,079	3.7E-03		
rs796985	6	24,556,040	3.7E-03	GPLD1	
rs8050142	16	78,651,415	3.7E-03		
rs1157067	9	9,187,812	3.7E-03	PTPRD	4.7E-03
rs3828712	6	158,847,639	3.7E-03	TULP4	
rs11756366	6	153,893,287	3.7E-03		
rs7020545			3.7E-03		
rs2827641	21	22,917,993	3.7E-03		
rs11116190	12	75,837,346	3.7E-03		
rs9567204	13	42,970,438	3.7E-03	ENOX1	
rs157350	5	156,072,147	3.7E-03	SGCD	
rs9521239	13	108,684,428	3.8E-03		
rs181662	10	119,372,445	3.8E-03		
rs12340535	9	3,400,838	3.8E-03	RFX3	
rs8061885	16	48,143,565	3.8E-03	ZNF423	8.5E-03
rs9342910	6	72,753,745	3.8E-03	RIMS1	
rs6861772	5	55,307,378	3.8E-03	IL6ST	
rs471377	18	39,265,343	3.8E-03		
rs10789262	1	41,210,004	3.8E-03		
rs7589480	2	81,311,990	3.8E-03		
rs1598997	3	39,960,397	3.8E-03	MYRIP	
rs12633941	3	39,967,978	3.8E-03	MYRIP	
rs7459662	8	29,802,177	3.8E-03	RP11-94H18.1	
rs10892301	11	118,240,686	3.8E-03		
rs1017002	7	8,717,957	3.8E-03	NXPH1	2.6E-03
rs1750836	1	7,443,514	3.8E-03	CAMTA1	8.8E-06
rs1009671	2	37,946,350	3.8E-03	LINC00211	
rs8127595	21	37,271,110	3.8E-03	HLCS	

rs2078527	6	25,382,624	3.8E-03	LRRC16A	
rs11678304	2	81,362,633	3.8E-03		
rs984119	9	10,630,526	3.8E-03		
rs9564466	13	67,936,455	3.8E-03		
rs16939801	18	12,737,129	3.8E-03		
rs4683428	3	140,951,811	3.8E-03		
rs1035533	16	82,208,011	3.8E-03	CDH13	1.9E-03
rs2768395	1	72,174,618	3.8E-03	NEGR1	
rs1535564	13	25,165,518	3.8E-03	ATP8A2	
rs3808864	9	35,805,613	3.8E-03	SPAG8	
rs2214976	7	25,688,838	3.8E-03	AC003090.1	
rs654894	6	153,885,996	3.8E-03		
rs1930386	9	80,756,308	3.8E-03		
rs12131051	1	187,931,480	3.8E-03		
rs1218486	10	14,425,271	3.8E-03	FRMD4A	
rs704014	10	80,502,780	3.8E-03	ZMIZ1	1.7E-03
rs886836	7	25,695,009	3.8E-03	CTA-242H14.1	
rs6033079	20	11,201,554	3.8E-03	RP4-734C18.1	
rs277606	9	34,775,308	3.8E-03		
rs7581641	2	8,543,557	3.8E-03		
rs1386288	3	151,326,866	3.8E-03	RP11-167H9.4	
rs1976437	1	187,905,803	3.9E-03	RN5S73	
rs7150477	14	97,738,741	3.9E-03	RP11-61O1.1	
rs267339	6	104,985,242	3.9E-03		
rs10951092	7	25,705,885	3.9E-03	AC003090.1	
rs996139	6	115,695,172	3.9E-03		
rs2724785	10	12,493,038	3.9E-03	CAMK1D	2.1E-03
rs3112586	16	51,241,545	3.9E-03	RP11-297L17.1	
rs6030188	20	34,987,036	3.9E-03	SAMHD1	
rs6761200	2	18,189,686	3.9E-03	KCNS3	
rs1126644	1	158,915,173	3.9E-03	RP11-404F10.2	
rs7851558	9	3,361,304	3.9E-03	RFX3	
rs849923	7	29,455,521	3.9E-03	CHN2	3.9E-04
rs4747964	10	12,217,003	3.9E-03	SEC61A2	
rs556808	4	75,290,591	3.9E-03	MTHFD2L	5.0E-04
rs10046843	9	34,621,159	3.9E-03	ARID3C	
rs1353005	4	54,940,654	3.9E-03	RP11-231C18.2	
rs1477018	16	50,615,390	3.9E-03	RP11-152O14.5	
rs11116589	12	83,676,432	3.9E-03		
rs4841511	8	11,116,669	3.9E-03		
rs10020207	4	58,401,219	3.9E-03		

rs7764728	6	14,776,436	3.9E-03		
rs946808	9	81,309,730	3.9E-03	RP11-375O18.2	
rs11620185	13	107,215,219	3.9E-03	FAM155A	5.4E-04
rs11104713	12	86,918,902	3.9E-03	C12orf50	7.5E-03
rs955738	2	179,483,397	3.9E-03	CCDC141	
rs7603075	2	41,686,382	3.9E-03		
rs1296513	10	91,671,324	3.9E-03	RP11-478K7.2	
rs7629791	3	129,701,100	3.9E-03	RP11-475N22.4	
rs9385517	6	99,357,637	3.9E-03		
rs8049837	16	29,996,939	3.9E-03	PPP4C	
rs470039	22	45,951,921	3.9E-03	TBC1D22A	
rs929873	16	72,014,878	3.9E-03	RP11-140I24.1	
rs960908	9	19,448,939	3.9E-03	RP11-363E7.3	
rs7639810	3	169,526,023	3.9E-03	EGFEM1P	
rs2413979	15	48,008,638	3.9E-03	ATP8B4	
rs7635505	3	64,624,234	3.9E-03	ADAMTS9	1.2E-03
rs12191536	6	49,335,964	3.9E-03		
rs1022034	12	87,442,874	3.9E-03	KITLG	
rs2036535	17	28,775,126	4.0E-03	ASIC2	3.3E-03
rs6951428	7	142,305,806	4.0E-03		
rs7193701	16	66,742,661	4.0E-03	NFATC3	
rs10827831	10	38,150,819	4.0E-03	RP11-162G10.1	
rs4690912	4	159,891,509	4.0E-03		
rs1001396	7	4,685,157	4.0E-03	FOXK1	
rs199635	6	72,282,724	4.0E-03		
rs6118746	20	9,749,670	4.0E-03	PAK7	
rs10759371	9	111,626,418	4.0E-03	PALM2	
rs2976290	8	26,098,961	4.0E-03		
rs1990602	7	12,088,321	4.0E-03		
rs1020265	4	4,378,813	4.0E-03	RP11-265O12.1	
rs7602256	2	150,741,717	4.0E-03	AC016682.1	
rs7515865	1	169,648,370	4.0E-03		
rs7865406	9	35,167,345	4.0E-03	UNC13B	
rs2151779	14	56,077,176	4.0E-03	RP11-624J12.1	
rs10508415	10	10,747,950	4.0E-03		
rs1914609	4	18,429,784	4.0E-03		
rs10818289	9	121,033,329	4.0E-03	DBC1	9.3E-03
rs1530793	16	53,005,467	4.0E-03		
rs10498688	6	17,930,753	4.0E-03	KIF13A	1.1E-03
rs263315	2	157,747,471	4.0E-03		
rs7662460	4	28,090,156	4.0E-03	RP11-123O22.1	

rs11717776	3	199,053,956	4.0E-03	LRCH3	
rs1171627	10	61,130,981	4.0E-03	SLC16A9	
rs1862504	16	26,429,776	4.0E-03		
rs17722373	6	49,271,152	4.0E-03		
rs11190578	10	102,228,943	4.0E-03	WNT8B	
rs2298075	10	102,237,398	4.0E-03	WNT8B	
rs10249873	7	91,663,104	4.0E-03	AC000120.7	
rs8004799	14	50,853,500	4.0E-03	LINC00519	
rs2033348	1	68,347,517	4.0E-03	RP11-518D3.1	
rs9511692	13	24,679,352	4.0E-03	RPL23AP69	
rs6914262	6	154,356,609	4.0E-03		
rs6708183	2	78,238,254	4.0E-03		
rs904510	13	67,986,542	4.0E-03		
rs4725029	7	7,796,040	4.0E-03	AC006465.3	
rs7027828	9	20,214,476	4.0E-03		
rs658230	10	6,548,569	4.1E-03	PRKCQ	2.1E-03
rs10905785	10	10,765,693	4.1E-03		
rs2909277	18	26,352,432	4.1E-03		
rs742019	22	47,094,527	4.1E-03		
rs396648	1	30,765,592	4.1E-03		
rs4632572	3	106,314,295	4.1E-03		
rs10250643	7	24,502,175	4.1E-03		
rs2913788	5	177,690,370	4.1E-03	COL23A1	
rs10783046	1	96,688,425	4.1E-03	EEF1A1P11	
rs4376154	4	134,044,421	4.1E-03	RP11-404I7.2	
rs2287270	2	15,568,019	4.1E-03	NBAS	
rs1959936	14	40,578,949	4.1E-03		
rs9930956	16	2,025,296	4.1E-03	SLC9A3R2	
rs176127	18	60,951,384	4.1E-03		
rs4937333	11	127,835,730	4.1E-03	ETS1	8.7E-03
rs1434477	9	26,744,019	4.1E-03	RP11-18A15.1	
rs1854042	13	21,269,252	4.1E-03		
rs2585833	17	53,379,612	4.1E-03	CUEDC1	
rs6887452	5	148,763,960	4.1E-03	IL17B	
rs6795768	3	173,500,799	4.1E-03	FNDC3B	2.5E-03
rs4471130	9	29,743,415	4.1E-03		
rs4627208	13	70,909,008	4.1E-03	DACH1	
rs528001	1	187,961,920	4.1E-03		
rs7761494	6	74,782,377	4.1E-03		
rs1499570	6	119,871,818	4.1E-03		
rs6662147	1	91,839,182	4.1E-03	RP11-91I11.1	

rs8060494	16	78,808,972	4.1E-03	RP11-525K10.3	
rs859548	7	39,025,282	4.1E-03	POU6F2	5.4E-03
rs6938648	6	3,954,503	4.1E-03		
rs4300522	13	67,007,248	4.2E-03		
rs983121	9	12,479,681	4.2E-03		
rs17087900	13	63,972,138	4.2E-03		
rs12205310	6	26,713,843	4.2E-03		
rs1624281	10	30,029,188	4.2E-03	RP11-192N10.2	
rs7662456	4	63,897,510	4.2E-03	RP11-553E5.1	
rs4959569	6	1,478,446	4.2E-03		
rs2189460	7	8,549,029	4.2E-03	NXPH1	2.6E-03
rs453585	3	18,609,876	4.2E-03		
rs604168	12	67,957,425	4.2E-03	CPSF6	
rs9930698	16	77,892,824	4.2E-03		
rs1736058	8	11,708,450	4.2E-03	FDFT1	
rs7664704	4	160,085,626	4.2E-03	C4orf45	3.1E-03
rs11644803	16	58,771,222	4.2E-03		
rs9521936	13	110,234,390	4.2E-03		
rs2070844	5	149,803,978	4.2E-03	RPS14	
rs1446372	13	68,673,098	4.2E-03		
rs6003620	22	21,995,356	4.2E-03	AP000343.2	
rs1355781	3	133,083,145	4.2E-03	CPNE4	1.5E-03
rs712332	14	36,336,400	4.2E-03	RP11-81F13.1	5.5E-03
rs4626584	8	52,824,649	4.2E-03	PXDNL	3.0E-03
rs1351518	11	107,119,468	4.2E-03	CTD-2651C21.3	
rs2155945	18	27,537,143	4.2E-03		
rs6086103	20	7,489,572	4.2E-03		
rs7821932	8	124,699,533	4.2E-03	CTD-2552K11.2	
rs10486076	7	13,721,999	4.2E-03		
rs7159869	14	50,390,000	4.2E-03	RP11-218E20.2	
rs1890854	13	68,285,687	4.2E-03		
rs11647213	16	85,228,015	4.2E-03	RP11-463O9.6	
rs9326078	1	68,224,976	4.2E-03	RP11-518D3.1	
rs4584211	9	77,746,957	4.2E-03	PCSK5	9.0E-03
rs1959930	14	40,565,658	4.2E-03		
rs4687833	3	120,159,182	4.2E-03	IGSF11	2.0E-05
rs6118062	20	8,035,581	4.2E-03		
rs917526	5	134,954,974	4.2E-03	CTC-321K16.1	
rs1959730	14	82,471,511	4.2E-03		
rs10460872	3	168,232,433	4.2E-03		
rs10771180	12	8,940,500	4.2E-03		

rs11679483	2	161,232,395	4.2E-03		
rs2138599	11	21,070,884	4.2E-03	NELL1	1.2E-03
rs382854	6	8,960,568	4.2E-03		
rs1507160	3	154,600,394	4.3E-03	RP11-23D24.2	
rs7919387	10	85,427,803	4.3E-03	RP11-344L13.2	
rs4948491	10	63,366,895	4.3E-03	ARID5B	1.7E-03
rs2494928	1	69,342,987	4.3E-03	RP11-424D14.1	
rs9859634	3	65,599,769	4.3E-03	MAGI1	7.6E-03
rs11816696	10	25,402,896	4.3E-03		
rs2300077	6	133,072,185	4.3E-03	VNN1	
rs1158541	12	13,737,940	4.3E-03	GRIN2B	8.6E-03
rs2765440	10	90,259,547	4.3E-03	RNLS	
rs12586346	14	57,536,347	4.3E-03	C14orf37	
rs4694691	4	75,602,196	4.3E-03		
rs650329	18	42,533,890	4.3E-03	ST8SIA5	
rs2077820	2	79,007,802	4.3E-03		
rs1447522	2	30,145,982	4.3E-03	AC016907.3	
rs11877408	18	62,399,126	4.3E-03	CDH19	1.7E-04
rs7951076	11	3,847,429	4.3E-03	STIM1	
rs9325808	8	17,257,500	4.3E-03	MTMR7	
rs2169641	3	82,823,888	4.3E-03		
rs10827292	10	34,145,360	4.3E-03		
rs7207403	17	44,565,505	4.3E-03	B4GALNT2	
rs7568281	2	192,452,056	4.3E-03	DNAJB1P1	
rs1327504	9	18,893,330	4.3E-03	ADAMTSL1	1.1E-03
rs2067678	3	169,423,008	4.3E-03		
rs9874286	3	169,425,673	4.3E-03		
rs12414710	10	33,995,752	4.3E-03		
rs4407257	2	117,540,267	4.3E-03		
rs9925302	16	85,223,804	4.3E-03	RP11-463O9.6	
rs10920503	1	201,082,609	4.3E-03	RP11-480I12.5	
rs9341423	6	74,224,127	4.3E-03	MTO1	
rs10485541	20	15,646,025	4.3E-03	MACROD2	4.1E-03
rs9818534	3	185,960,449	4.3E-03	RP11-329B9.1	
rs7122702	11	120,013,510	4.4E-03	GRIK4	
rs2948286	8	8,167,570	4.4E-03		
rs12495947	3	127,254,388	4.4E-03	SLC41A3	
rs9458257	6	161,783,940	4.4E-03	PARK2	8.8E-05
rs1361115	1	235,388,592	4.4E-03	RYR2	5.4E-04
rs6736347	2	125,214,817	4.4E-03	CNTNAP5	
rs719721	20	50,408,904	4.4E-03	RP4-723E3.1	

rs7223092	17	28,355,538	4.4E-03		
rs2070454	22	22,426,674	4.4E-03	VPREB3	
rs1327510	9	13,743,249	4.4E-03		
rs1330351	9	116,880,743	4.4E-03	TNC	7.3E-03
rs10505836	12	19,179,775	4.4E-03	PLEKHA5	
rs8180086	3	152,520,570	4.4E-03	MED12L	
rs1915282	12	72,153,974	4.4E-03	RP11-314D7.4	
rs632177	6	7,852,138	4.4E-03	TXNDC5	
rs2156283	18	48,684,273	4.4E-03	DCC	7.6E-03
rs2576542			4.4E-03	RP11-212I21.2	
rs874952	2	65,462,029	4.4E-03	SPRED2	
rs11664283	18	640,968	4.4E-03	C18orf56	
rs10982926	9	117,608,644	4.4E-03		
rs2382688	7	102,891,644	4.4E-03	CTB-107G13.1	
rs2881068	2	45,955,890	4.4E-03	PRKCE	
rs10497193	2	158,417,924	4.4E-03	ACVR1	
rs9498701	6	102,336,911	4.4E-03	GRIK2	9.7E-04
rs10870381	10	39,098,677	4.4E-03	RP11-453N3.1	
rs13196989	6	184,373	4.4E-03		
rs1582029	9	17,233,746	4.4E-03	CNTLN	
rs1056984	20	60,989,487	4.4E-03	DIDO1	
rs12261792	10	11,949,902	4.4E-03	RP11-401F24.4	
rs2049581	2	156,738,975	4.4E-03		
rs2039803	9	109,751,762	4.4E-03		
rs2271058	19	4,803,106	4.4E-03	PLIN3	
rs791881	10	89,398,226	4.4E-03	RP11-57C13.6	
rs4772933	13	107,458,063	4.5E-03		
rs7961199	12	13,515,616	4.5E-03		
rs633719	9	9,516,138	4.5E-03	PTPRD	4.7E-03
rs2787136			4.5E-03		
rs1158542	14	40,443,450	4.5E-03		
rs2967436	19	41,739,312	4.5E-03	ZNF529	
rs830605	3	71,691,966	4.5E-03	FOXP1	2.2E-03
rs2654417	3	106,285,277	4.5E-03		
rs17678470	13	100,639,945	4.5E-03	NALCN	2.2E-03
rs850509	12	109,726,744	4.5E-03		
rs9810554	3	82,076,783	4.5E-03		
rs10778943	12	82,062,811	4.5E-03		
rs1539089	10	102,211,414	4.5E-03	WNT8B	
rs181649	10	119,366,617	4.5E-03		
rs2887041	10	25,477,868	4.5E-03		

rs11001617	10	77,549,112	4.5E-03	C10orf11	
rs12141361	1	14,599,072	4.5E-03		
rs4787367	16	26,255,281	4.5E-03	AC009158.1	
rs316	8	19,862,716	4.5E-03	LPL	
rs1012775	7	24,815,354	4.5E-03	OSBPL3	
rs6466523	7	114,748,659	4.5E-03		
rs1949880	7	39,062,913	4.5E-03	POU6F2	5.4E-03
rs7100857	10	44,918,561	4.5E-03	RP11-445N18.4	
rs631871	2	165,028,234	4.5E-03		
rs7324781	13	95,032,754	4.5E-03	DZIP1	
rs6783997	3	110,179,807	4.5E-03	MORC1	3.6E-03
rs2246219	3	110,141,846	4.5E-03	GUCA1C	
rs10791048	11	129,162,426	4.5E-03	RP11-507F16.1	
rs886834	7	28,987,861	4.5E-03		
rs6976396	7	28,789,977	4.5E-03	CREB5	2.4E-04
rs17319192	8	3,032,637	4.5E-03	CSMD1	8.6E-05
rs4473785	5	172,918,217	4.6E-03	CTB-33O18.1	
rs1483632	3	177,516,393	4.6E-03		
rs12209342	6	65,936,970	4.6E-03	EYS	4.5E-04
rs4371513	3	64,609,618	4.6E-03	ADAMTS9	1.2E-03
rs10099847	8	3,030,072	4.6E-03	CSMD1	8.6E-05
rs721590	8	134,599,750	4.6E-03	ST3GAL1	
rs9868350	3	146,840,283	4.6E-03		
rs951043	12	79,725,769	4.6E-03	LIN7A	
rs1016126	1	72,208,991	4.6E-03	NEGR1	
rs331702	5	124,854,142	4.6E-03	RP11-756H20.1	
rs10503002	18	51,260,200	4.6E-03	TCF4	6.1E-03
rs1862560	5	28,769,666	4.6E-03		
rs980798	1	187,938,851	4.6E-03		
rs3752864	17	42,826,227	4.6E-03	C17orf57	
rs1324188	9	13,597,227	4.6E-03		
rs697199	12	102,566,866	4.6E-03	STAB2	1.7E-03
rs1359712	9	87,506,706	4.6E-03	AGTPBP1	
rs955619	14	83,206,531	4.6E-03		
rs17598689	2	63,088,057	4.6E-03	EHBP1	
rs10757753	9	28,506,764	4.6E-03	LINGO2	2.2E-03
rs1494913	8	108,957,826	4.6E-03		
rs2049974	22	35,272,269	4.6E-03		
rs1425316	4	58,210,076	4.6E-03	RP11-4O3.1	
rs734584	14	39,744,190	4.6E-03		
rs724291	7	33,765,662	4.6E-03		

rs1993853	10	67,443,315	4.6E-03	CTNNA3	8.7E-04
rs2723891	12	89,482,389	4.6E-03		
rs17044607	12	76,878,115	4.6E-03	NAV3	1.2E-03
rs1465727	12	127,972,538	4.6E-03	GLT1D1	
rs7219526	17	9,236,034	4.6E-03	STX8	8.5E-04
rs1340363	10	72,849,622	4.6E-03	CDH23	4.7E-03
rs891943	5	149,667,306	4.6E-03	ARSI	
rs1328413	9	81,011,093	4.6E-03		
rs1927432	6	167,121,023	4.6E-03	RPS6KA2	
rs4679302	3	128,110,471	4.6E-03	CHCHD6	
rs702045	3	126,332,460	4.6E-03	SLC12A8	
rs328847	9	7,674,244	4.6E-03		
rs6945120	7	46,981,927	4.6E-03	AC004870.4	
rs17751083	12	96,037,531	4.6E-03	RP11-541G9.1	
rs1995892	11	75,323,598	4.7E-03	UVRAG	
rs3887078	8	41,047,280	4.7E-03		
rs7861296	9	28,616,095	4.7E-03	LINGO2	2.2E-03
rs7893862	10	126,733,086	4.7E-03	CTBP2	3.7E-03
rs1074282	2	117,711,193	4.7E-03		
rs9465985	6	21,293,569	4.7E-03	CDKAL1	3.6E-03
rs9881418	3	144,954,522	4.7E-03	SLC9A9	1.6E-04
rs923757	10	25,397,590	4.7E-03		
rs7107024	11	108,408,545	4.7E-03	RP11-25I9.2	
rs310282			4.7E-03	RP11-175E9.1	
rs1561	17	8,204,059	4.7E-03	AC135178.1	
rs3861699	1	84,303,705	4.7E-03		
rs6796074	3	103,316,740	4.7E-03	ZPLD1	
rs9985400	3	141,329,869	4.7E-03	CLSTN2	1.3E-03
rs2776932	10	33,632,412	4.7E-03	NRP1	2.9E-04
rs2832861	21	30,716,253	4.7E-03	KRTAP13-3	
rs901363	6	159,098,333	4.7E-03	SYTL3	
rs13387889	2	128,604,678	4.7E-03	UGGT1	
rs10946673	6	24,231,293	4.7E-03	NRSN1	
rs512384	21	39,909,757	4.7E-03	C21orf88	
rs884540	9	8,250,902	4.7E-03		
rs11861057	16	81,065,551	4.7E-03		
rs1346860	2	82,181,397	4.7E-03		
rs7028831	9	80,703,417	4.7E-03		
rs2230805	9	106,663,850	4.7E-03	ABCA1	6.8E-03
rs4745511	9	77,952,115	4.7E-03	PCSK5	9.0E-03
rs788219	10	27,513,241	4.7E-03	MASTL	

rs2858223	22	31,349,789	4.7E-03	SYN3	
rs6589804	11	119,666,851	4.8E-03	POU2F3	
rs242965	10	119,240,201	4.8E-03	EMX2OS	
rs7853898	9	26,757,510	4.8E-03	RP11-18A15.1	
rs11218544	11	121,544,262	4.8E-03	RP11-820L6.1	
rs9364622	6	162,236,323	4.8E-03	PARK2	8.8E-05
rs10483709	14	58,522,894	4.8E-03	RP11-112J1.2	
rs2720016	3	165,145,085	4.8E-03		
rs10483222	22	42,880,277	4.8E-03	PARVB	
rs4627206	13	67,959,686	4.8E-03		
rs6606825	15	20,614,243	4.8E-03	NIPA1	
rs4272631	1	105,056,444	4.8E-03		
rs2110328	7	20,114,240	4.8E-03	AC005062.2	
rs4846689	1	219,444,058	4.8E-03		
rs949365	11	78,208,368	4.8E-03	ODZ4	6.5E-03
rs4777882	15	91,785,205	4.8E-03	RP11-266O8.1	
rs2894593	2	226,898,561	4.8E-03		
rs2275516	9	1,043,910	4.8E-03	DMRT2	
rs4692196	4	26,949,002	4.8E-03		
rs10801655	1	187,866,774	4.8E-03		
rs480113	9	109,791,503	4.8E-03		
rs1929129	9	111,352,337	4.8E-03		
rs2288403	11	129,243,199	4.8E-03	NFRKB	
rs4675431	2	204,814,338	4.8E-03		
rs9461448	6	28,371,700	4.8E-03	PGBD1	
rs6895622	5	72,660,292	4.8E-03		
rs7539465	1	96,452,588	4.8E-03		
rs1898866	4	161,529,827	4.8E-03		
rs10858677	12	86,909,653	4.8E-03	C12orf50	7.5E-03
rs956187	1	96,679,097	4.8E-03		
rs1929408	9	11,942,796	4.8E-03		
rs1018654	9	7,226,712	4.8E-03		
rs6476920	9	4,885,947	4.8E-03		
rs1621211	11	120,378,286	4.8E-03		
rs12570033	10	133,984,693	4.8E-03	STK32C	
rs6737959			4.8E-03	AC018682.6	
rs3783113	13	109,632,747	4.8E-03	COL4A1	3.1E-03
rs196034	6	22,151,788	4.8E-03		
rs7498882	16	28,124,106	4.8E-03	XPO6	
rs4408788	20	4,143,591	4.8E-03		
rs754819	9	21,616,573	4.8E-03		

rs9505900	6	169,448,612	4.8E-03		
rs9456490	6	160,318,320	4.8E-03	IGF2R	
rs9833473	3	80,174,096	4.8E-03		
rs6061612	20	59,540,967	4.8E-03	CDH4	4.6E-04
rs10508096	13	102,258,865	4.8E-03	BIVM	
rs6020739	20	48,828,918	4.8E-03		
rs8079768	17	65,626,554	4.8E-03	AC002539.1	1.5E-03
rs9984655	21	35,803,301	4.8E-03	RUNX1	
rs1376983	3	56,189,120	4.8E-03	ERC2	
rs7942029	11	113,329,075	4.8E-03		
rs2459067	10	123,785,063	4.8E-03	TACC2	
rs2198935	2	81,257,733	4.8E-03		
rs1997634	22	25,839,769	4.8E-03		
rs4921165	5	160,212,958	4.8E-03	ATP10B	
rs8058389	16	86,488,782	4.9E-03	GS1-21A4.1	
rs6481032	10	55,162,168	4.9E-03		
rs10048789	2	128,775,665	4.9E-03	HS6ST1	
rs1528799	2	51,536,268	4.9E-03	AC007682.1	
rs10864479	1	10,891,317	4.9E-03		
rs9927943	16	59,131,895	4.9E-03		
rs1483622	3	177,490,277	4.9E-03		
rs10509475	10	85,203,345	4.9E-03		
rs1577665	9	26,336,141	4.9E-03		
rs756913	7	24,506,297	4.9E-03		
rs1814370	9	18,843,257	4.9E-03	ADAMTSL1	1.1E-03
rs2847254	18	12,717,224	4.9E-03	PSMG2	
rs9309819	3	78,930,722	4.9E-03	ROBO1	
rs4599384	4	48,013,147	4.9E-03		
rs11176179	12	65,118,988	4.9E-03	GRIP1	1.0E-03
rs7080655	10	44,823,480	4.9E-03	RP11-285G1.8	
rs712322	14	21,059,681	4.9E-03	AE000658.22	
rs10810738	9	17,213,492	4.9E-03	CNTLN	
rs138646	22	26,719,012	4.9E-03	TTC28	
rs2006902	16	77,595,532	4.9E-03	RP11-319G9.5	3.1E-03
rs1413336	9	82,133,946	4.9E-03		
rs1843786	3	78,967,414	4.9E-03	ROBO1	
rs7356656	5	2,717,214	4.9E-03		
rs9033	16	65,739,500	4.9E-03	B3GNT9	
rs931401	2	36,138,443	4.9E-03		
rs733918	18	6,932,295	4.9E-03	LAMA1	
rs11631489	15	85,042,215	4.9E-03	AGBL1	1.8E-03

rs2890856	9	9,190,590	4.9E-03	PTPRD	4.7E-03
rs321225	9	20,210,838	4.9E-03		
rs2106503	7	103,763,225	4.9E-03	LHFPL3	8.7E-04
rs3778135	6	129,549,602	4.9E-03	RP11-73O6.4	2.4E-03
rs288637	16	61,248,592	4.9E-03		
rs8126757	21	45,672,710	4.9E-03	COL18A1	2.6E-03
rs12119007	1	245,284,850	4.9E-03	ZNF670	
rs6954232	7	9,674,747	4.9E-03		
rs569230	4	20,098,122	4.9E-03	SLIT2	
rs13073410	3	134,704,642	4.9E-03		
rs2748220	5	149,744,486	5.0E-03	TCOF1	
rs4559036	5	160,209,255	5.0E-03	ATP10B	3.7E-03
rs10112963	8	102,231,893	5.0E-03		
rs1866168	10	60,031,568	5.0E-03	BICC1	7.8E-03
rs10785024	12	72,056,061	5.0E-03	RP11-314D7.4	
rs9371769	6	154,349,428	5.0E-03		
rs7086661	10	130,495,599	5.0E-03		
rs1554277	12	75,098,696	5.0E-03		
rs840418	13	72,775,303	5.0E-03		
rs501957	17	27,338,617	5.0E-03	SUZ12	
rs4401960	9	20,028,477	5.0E-03		
rs936960	15	56,539,169	5.0E-03	RP11-355N15.1	
rs655937	18	61,108,446	5.0E-03		
rs906065	18	61,141,520	5.0E-03		
rs9882054	3	169,414,907	5.0E-03		
rs41348	7	28,683,373	5.0E-03	CREB5	2.4E-04
rs1780138	10	38,541,660	5.0E-03	RP11-508N22.8	
rs11751802	6	5,355,151	5.0E-03	FARS2	
rs12234501	7	8,738,675	5.0E-03	NXPH1	2.6E-03
rs4662763	2	128,469,956	5.0E-03	SAP130	
rs1339249	9	77,818,018	5.0E-03	PCSK5	9.0E-03
rs254870	5	171,000,864	5.0E-03		
rs7032583	9	85,380,931	5.0E-03		
rs766455	8	82,040,988	5.0E-03	PAG1	
rs4870821	8	123,950,371	5.0E-03	ZHX2	
rs7937715	11	129,818,391	5.0E-03		
rs2399786	10	12,255,186	5.0E-03	SEC61A2	
rs2016588	6	159,345,695	5.0E-03	RSPH3	
rs1545909	9	7,645,364	5.0E-03		
rs2275886	9	21,007,743	5.0E-03	PTPLAD2	
rs9524260	13	93,311,791	5.0E-03	GPC6	1.0E-03

rs1295107	1	6,001,979	5.1E-03	KCNAB2	
rs10224816	7	9,678,184	5.1E-03		
rs7002825	8	101,740,397	5.1E-03	SNX31	
rs2241954	16	54,936,479	5.1E-03	GNAO1	
rs2066219	13	68,428,665	5.1E-03		
rs9257694	6	29,382,465	5.1E-03	OR14J1	
rs7044578	9	20,876,882	5.1E-03	KIAA1797	
rs10900213	10	45,224,720	5.1E-03	ALOX5	
rs2428158	5	135,341,751	5.1E-03		
rs2539669	2	59,648,113	5.1E-03	AC007131.2	
rs4131051	5	97,537,826	5.1E-03		
rs7910211	10	80,898,384	5.1E-03		
rs11216360	11	116,718,399	5.1E-03	CEP164	
rs524207	6	52,194,855	5.1E-03		
rs1962674	3	155,356,264	5.1E-03	ARHGEF26	
rs1769465	14	86,587,947	5.1E-03		
rs929544	7	9,819,192	5.1E-03		
rs2986267	9	7,463,692	5.1E-03	RP11-87M1.1	
rs12349982	9	90,128,943	5.1E-03	RP11-350G13.1	
rs1971830	2	35,172,516	5.1E-03	AC012593.1	
rs6131768	20	15,975,036	5.1E-03	MACROD2	4.1E-03
rs6672784	1	238,274,416	5.1E-03	FMN2	
rs4925145	17	18,038,743	5.1E-03	ALKBH5	
rs11001742	10	77,777,156	5.1E-03	C10orf11	
rs4884906	13	70,279,527	5.1E-03		
rs6439474	3	135,483,237	5.1E-03		
rs1876868	15	58,344,233	5.1E-03		
rs1929403	9	11,880,199	5.1E-03		
rs13437290	6	167,131,680	5.1E-03	RPS6KA2	
rs2399422	3	113,554,624	5.1E-03	CD200	2.6E-03
rs13146316	4	4,406,675	5.1E-03	NSG1	
rs622173	11	1,842,723	5.1E-03	AC051649.12	1.1E-03
rs6480643	10	74,204,180	5.1E-03	MCU	
rs10817781	9	99,369,961	5.1E-03	TMOD1	
rs210179	6	33,593,214	5.1E-03		
rs6925772	6	12,128,227	5.1E-03	HIVEP1	
rs2831178	21	28,135,194	5.1E-03		
rs2898501	8	20,354,398	5.1E-03		
rs1115219	3	134,977,707	5.1E-03	TF	
rs7145106			5.1E-03		
rs2293286	6	161,470,989	5.1E-03	AGPAT4	

rs10519010	15	58,339,218	5.1E-03		
rs758951	4	24,363,205	5.1E-03		
rs4936050	11	127,826,464	5.1E-03		
rs228832	20	49,493,555	5.1E-03	NFATC2	
rs404284	7	101,396,787	5.1E-03	CUX1	6.7E-03
rs10485540	20	15,645,748	5.1E-03	MACROD2	4.1E-03
rs13086288	3	142,031,775	5.2E-03		
rs11036814	11	5,301,168	5.2E-03	AC104389.28	
rs6414353	3	144,459,441	5.2E-03		
rs9315500	13	37,006,472	5.2E-03		
rs11011294	10	37,961,076	5.2E-03		
rs12727900	1	186,768,771	5.2E-03	RP11-669M2.1	
rs2829949	21	26,144,693	5.2E-03		
rs1033871	13	108,629,670	5.2E-03	MYO16-AS1	3.3E-03
rs3817077	7	25,556,981	5.2E-03	AC091705.1	
rs9324220	13	112,790,596	5.2E-03	MCF2L	
rs974179	4	14,784,134	5.2E-03	RP11-665G4.1	
rs10466280	10	12,231,939	5.2E-03	SEC61A2	
rs10102337	8	22,704,701	5.2E-03	RP11-459E5.1	1.7E-03
rs324519	9	9,028,430	5.2E-03	PTPRD	4.7E-03
rs6024783	20	54,317,745	5.2E-03		
rs12433087	14	25,659,936	5.2E-03	RP11-314P15.2	
rs2144676	20	59,964,839	5.2E-03	TAF4	
rs12921771	16	80,722,684	5.2E-03	RP11-510J16.5	
rs4374305	19	14,815,503	5.2E-03	OR7A10	
rs2780894	1	65,081,964	5.2E-03	JAK1	
rs9837084	3	152,221,445	5.2E-03	CLRN1-AS1	
rs4842610	12	87,335,820	5.2E-03		
rs6839295	4	6,017,702	5.2E-03	C4orf50	
rs1970331	13	111,876,993	5.2E-03		
rs13057591	22	41,745,525	5.2E-03	PACSIN2	
rs1232597	20	10,553,631	5.2E-03	C20orf94	
rs1825651	6	76,983,174	5.2E-03		
rs2039523	6	52,174,886	5.2E-03		
rs6798107	3	198,639,494	5.2E-03		
rs11757721	6	169,164,340	5.2E-03		
rs12528760	6	66,900,502	5.2E-03		
rs10753848	1	197,542,817	5.2E-03	RP11-382E9.1	
rs7086222	10	77,768,797	5.2E-03	C10orf11	
rs1247488	10	77,675,236	5.2E-03	C10orf11	
rs1889326	9	112,301,821	5.3E-03	SVEP1	5.0E-03

rs2744734	1	22,422,316	5.3E-03		
rs2534795	6	29,619,320	5.3E-03	GPR53P	
rs2816323	1	224,250,217	5.3E-03	C1orf55	
rs2102956	12	117,615,105	5.3E-03		
rs13100658			5.3E-03		
rs206816	2	31,498,487	5.3E-03		
rs4262613	1	232,165,075	5.3E-03	SLC35F3	
rs3738226	1	165,878,450	5.3E-03	RCSD1	
rs4491677	2	128,505,674	5.3E-03	SAP130	
rs1161901	6	891,665	5.3E-03		
rs283838	2	79,117,211	5.3E-03		
rs11163016	1	80,680,736	5.3E-03		
rs2306706	4	186,664,865	5.3E-03	PDLIM3	
rs10149335	14	49,937,222	5.3E-03	RP11-247L20.3	
rs1809889	12	123,367,179	5.3E-03	RP11-522N14.1	
rs2554506	8	3,806,491	5.3E-03	CSMD1	8.6E-05
rs11376	14	50,274,746	5.3E-03	NIN	
rs1509177	1	95,771,870	5.3E-03	RP11-286B14.1	
rs1443002	18	26,230,812	5.3E-03		
rs1343660	12	80,215,275	5.3E-03	RP11-121G22.3	4.0E-03
rs2150855	9	28,402,544	5.3E-03	LINGO2	2.2E-03
rs741192	22	19,316,010	5.3E-03	SMPD4P1	
rs2170614	6	2,589,629	5.3E-03	RP11-145H9.3	
rs2882825	6	67,084,250	5.3E-03		
rs2388050	10	7,455,780	5.3E-03	SFMBT2	6.1E-03
rs11896903	2	104,081,758	5.3E-03		
rs6830266	4	178,479,392	5.3E-03	NEIL3	
rs9295089	6	159,383,952	5.3E-03	TAGAP	
rs1112573	14	77,915,081	5.3E-03	NRXN3	
rs4467099	16	11,450,395	5.3E-03	CTD-3088G3.5	
rs2489686	10	42,189,775	5.3E-03		
rs978993	7	15,642,160	5.3E-03	MEOX2	
rs7618160	3	89,718,321	5.3E-03	RP11-91A15.1	
rs859068	1	95,124,503	5.3E-03	SLC44A3	
rs4463269	6	151,903,921	5.3E-03	C6orf97	1.8E-03
rs4488795	3	29,355,715	5.3E-03	RBMS3	5.9E-04
rs10506885	12	81,873,327	5.3E-03	TMTC2	
rs4319778	16	77,110,455	5.4E-03	WWOX	3.1E-03
rs330676	5	123,232,291	5.4E-03		
rs330679	5	123,233,993	5.4E-03		
rs7863087	9	71,619,570	5.4E-03	RP11-109D9.3	

rs8128258	21	19,370,336	5.4E-03		
rs476663	3	151,932,573	5.4E-03		
rs4959338	6	5,345,657	5.4E-03	FARS2	
rs1624390	6	162,296,972	5.4E-03	PARK2	8.8E-05
rs7985622	13	65,243,299	5.4E-03		
rs1942418	18	45,637,241	5.4E-03	MYO5B	6.6E-03
rs355321	18	31,319,287	5.4E-03	INO80C	
rs17692544	9	26,587,540	5.4E-03		
rs9511834	13	25,092,059	5.4E-03	ATP8A2	
rs6872806	5	41,371,807	5.4E-03	PLCXD3	
rs331679	19	6,799,220	5.4E-03	VAV1	2.4E-03
rs2275895	1	201,047,153	5.4E-03	KDM5B-AS1	
rs3943166	6	76,986,284	5.4E-03		
rs4238264	13	108,060,380	5.4E-03	MYO16	3.3E-03
rs2622781	18	39,335,330	5.4E-03		
rs1554279	9	109,769,058	5.4E-03	RP11-272G11.1	
rs17546413	13	88,080,427	5.4E-03	RP11-360A9.2	
rs177773	4	3,631,009	5.4E-03		
rs4744188	9	94,990,282	5.4E-03	WNK2	5.9E-03
rs753687	11	44,317,366	5.4E-03		
rs10878946	12	67,928,582	5.4E-03	CPSF6	
rs10501575	11	84,245,672	5.4E-03	DLG2	4.9E-03
rs9368002	6	18,646,024	5.4E-03		
rs4805994	19	39,333,496	5.4E-03		
rs9505109	6	7,219,353	5.4E-03	RP11-69L16.4	
rs2771994	9	134,714,722	5.4E-03	AK8	
rs10496654	2	126,519,270	5.4E-03		
rs2480933	9	116,904,430	5.4E-03	TNC	7.3E-03
rs3789868	9	116,915,502	5.4E-03	TNC	7.3E-03
rs2132082	4	14,564,496	5.4E-03	AC006296.3	
rs2240090	7	51,064,468	5.4E-03	COBL	4.1E-03
rs10438342	15	30,189,338	5.4E-03	CHRNA7	
rs419473	2	225,637,345	5.4E-03		
rs1885927	9	746,415	5.4E-03		
rs10109281	8	55,568,620	5.5E-03		
rs4731330	7	126,234,800	5.5E-03	GRM8	1.6E-03
rs13092591	3	163,937,546	5.5E-03		
rs859088	1	95,114,753	5.5E-03	SLC44A3	
rs11152120	18	54,919,779	5.5E-03		
rs1488171	3	164,186,242	5.5E-03		
rs7989455	13	21,279,204	5.5E-03		

rs6930033	6	29,431,884	5.5E-03	OR5V1	
rs1077773	7	17,409,204	5.5E-03	AC019117.1	
rs707104	2	155,030,329	5.5E-03	AC009227.3	
rs6029495	20	39,047,713	5.5E-03		
rs4264315	14	50,798,106	5.5E-03		
rs1535618	9	110,215,428	5.5E-03		
rs7086311	10	27,432,015	5.5E-03	ANKRD26	
rs2274634	10	27,474,489	5.5E-03	YME1L1	
rs768505	10	71,224,480	5.5E-03		
rs7485624	12	20,508,680	5.5E-03	PDE3A	
rs10895193	11	101,137,143	5.5E-03	RP11-748H22.2	
rs1492506	4	40,067,757	5.5E-03		
rs7543449	1	187,984,282	5.5E-03		
rs9295924			5.5E-03	LINC00243	
rs12760768	1	165,885,957	5.5E-03	RCSD1	
rs6801757	3	110,291,677	5.5E-03	MORC1	3.6E-03
rs837550	16	54,119,967	5.5E-03	LPCAT2	2.2E-03
rs1650	10	18,942,808	5.5E-03	NSUN6	3.7E-03
rs7903919	10	67,440,952	5.5E-03	CTNNA3	8.7E-04
rs6775137	3	193,649,843	5.5E-03	FGF12	6.3E-03
rs1547960	7	120,732,453	5.5E-03		
rs2274352	10	13,741,677	5.5E-03	RP11-295P9.3	
rs638501	6	10,488,442	5.5E-03		
rs12253574	10	83,310,878	5.5E-03		
rs4128664	10	47,173,619	5.5E-03	CTGLF11P	
rs10902882	10	124,894,601	5.5E-03	HMX3	
rs7034380	9	14,898,056	5.5E-03	FREM1	
rs13284716	9	111,372,846	5.6E-03		
rs7168069	15	66,411,450	5.6E-03	ITGA11	
rs902633	10	133,793,790	5.6E-03	JAKMIP3	7.0E-03
rs6583830	10	94,388,098	5.6E-03	KIF11	
rs480774	6	6,968,671	5.6E-03		
rs2837156	21	40,048,557	5.6E-03	IGSF5	
rs2451576	6	77,180,387	5.6E-03		
rs7961978	12	8,594,842	5.6E-03	RP11-561P12.5	
rs10510165	3	1,225,310	5.6E-03	CNTN6	3.9E-03
rs7517671	1	207,185,511	5.6E-03		
rs7968026	12	83,754,187	5.6E-03		
rs960761	4	187,884,344	5.6E-03	FAT1	
rs3796139	3	99,861,391	5.6E-03	RP11-569H14.1	
rs7635103	3	187,316,453	5.6E-03	DGKG	

rs1032757	5	81,975,074	5.6E-03		
rs1907348	10	77,854,822	5.6E-03	C10orf11	
rs745034	9	13,776,493	5.6E-03		
rs3801306	7	36,447,372	5.6E-03	ANLN	
rs480958			5.6E-03	AP002954.4	
rs4655059	1	22,608,493	5.6E-03		
rs10975175	9	5,534,405	5.6E-03	PDCD1LG2	
rs7921016	10	20,341,676	5.6E-03	PLXDC2	6.4E-03
rs6886199	5	112,927,149	5.6E-03	YTHDC2	4.0E-03
rs4597272	15	35,712,784	5.6E-03		
rs6093416	20	39,048,197	5.6E-03		
rs7999900	13	107,795,019	5.6E-03		
rs7732831	5	32,697,591	5.6E-03		
rs3732191	2	47,893,789	5.6E-03	FBXO11	
rs1336336	9	26,798,023	5.6E-03	RP11-337A23.6	
rs162005	18	22,701,784	5.6E-03	AQP4	
rs4764997	12	99,733,862	5.6E-03	ANO4	
rs10275615	7	18,062,346	5.6E-03		
rs4679786	3	151,918,374	5.6E-03	RP11-103G8.1	
rs2029001	3	110,211,360	5.6E-03	MORC1	3.6E-03
rs7653651	3	110,263,521	5.6E-03	MORC1	3.6E-03
rs1456767	8	40,999,658	5.6E-03		
rs2076706	22	24,504,168	5.6E-03	MYO18B	
rs618751	1	4,562,392	5.6E-03		
rs1528805	2	51,591,897	5.6E-03	AC080091.1	
rs649526	15	40,223,294	5.6E-03	PLA2G4F	
rs8005104	14	49,950,227	5.7E-03	MAP4K5	
rs11734695	4	6,473,961	5.7E-03	PPP2R2C	
rs884025	17	74,965,704	5.7E-03	RBFOX3	
rs708486	14	51,810,721	5.7E-03	PTGDR	
rs6706062	2	120,650,568	5.7E-03	AC012363.4	
rs825191	1	64,480,599	5.7E-03	UBE2U	6.6E-03
rs9845043	3	118,393,014	5.7E-03	LSAMP	
rs27223	5	59,788,397	5.7E-03	PDE4D	
rs11645312	16	25,458,337	5.7E-03		
rs2958522	8	145,995,756	5.7E-03	ZNF517	
rs7914814	10	94,372,930	5.7E-03	KIF11	
rs1761285	9	71,270,137	5.7E-03	APBA1	
rs9597069	13	54,461,091	5.7E-03		
rs4809258	20	62,256,817	5.7E-03	MYT1	
rs16914086	9	100,028,298	5.7E-03	TBC1D2	

rs1411060	9	37,036,091	5.7E-03	RP11-297B17.2	
rs4610795	8	145,852,141	5.7E-03	ARHGAP39	
rs11583257	1	3,904,110	5.7E-03	RP13-614K11.2	
rs704308	1	184,509,298	5.7E-03		
rs8018219	14	93,555,707	5.7E-03		
rs7939158	11	130,672,353	5.7E-03	AP002856.5	
rs10162514	14	47,105,557	5.7E-03	MDGA2	
rs12401392	1	101,668,533	5.7E-03		
rs10493972	1	102,075,419	5.7E-03	OLFM3	2.6E-04
rs649649	9	9,564,336	5.7E-03	PTPRD	4.7E-03
rs10283145	8	10,278,821	5.7E-03	MSRA	8.7E-03
rs549427	11	113,590,069	5.7E-03	ZBTB16	
rs10498286	14	25,957,294	5.7E-03		
rs370534	22	21,587,051	5.7E-03	IGLC6	
rs321739			5.7E-03		
rs2302442			5.7E-03	MAGI2	
rs12414156	10	56,612,592	5.7E-03	PCDH15	
rs2605242	4	48,605,727	5.7E-03	OCIAD2	
rs6564738	16	78,727,594	5.7E-03	RP11-525K10.1	
rs1861739	22	45,510,714	5.7E-03	CERK	
rs9606282	22	18,580,513	5.7E-03		
rs7763526	6	155,849,971	5.7E-03		
rs1806760	9	71,247,826	5.7E-03	APBA1	
rs7023148	9	10,674,803	5.8E-03		
rs889764	16	87,360,910	5.8E-03	PIEZO1	
rs10945799	6	162,512,797	5.8E-03	PARK2	8.8E-05
rs1888420	21	22,501,004	5.8E-03	AP000705.7	
rs464805	22	21,581,857	5.8E-03	IGLC4	
rs9965494	18	6,082,174	5.8E-03	L3MBTL4	8.6E-03
rs1007266	1	60,006,335	5.8E-03	RP4-782L23.1	
rs2246083	1	201,047,787	5.8E-03	KDM5B-AS1	
rs2203919	3	168,222,279	5.8E-03	AC092965.1	
rs6434026	2	184,015,156	5.8E-03		
rs2572349	4	48,606,785	5.8E-03	OCIAD2	
rs9398918	6	130,087,370	5.8E-03	RP11-73O6.4	
rs2057588	13	71,363,953	5.8E-03		
rs7774958	6	107,600,111	5.8E-03	PDSS2	
rs732803	8	141,039,000	5.8E-03	TRAPPC9	
rs17010281	2	124,056,775	5.8E-03		
rs17723697	9	1,625,184	5.8E-03		
rs4877706	9	84,565,274	5.8E-03		

rs873224	8	142,600,146	5.8E-03	AC138647.1	
rs9565596	13	80,115,492	5.8E-03		
rs4823617	22	46,003,908	5.8E-03		
rs2175075	13	75,656,049	5.8E-03		
rs1870105	2	160,846,898	5.8E-03	RBMS1	6.1E-04
rs1000989	13	109,625,304	5.8E-03	COL4A1	3.1E-03
rs12596308	16	29,598,697	5.8E-03	QPRT	
rs761076	1	165,886,606	5.8E-03	RCSD1	
rs272110	2	131,262,790	5.8E-03		
rs7615318	3	49,962,479	5.8E-03	RBM6	
rs1832312	10	24,335,334	5.8E-03	KIAA1217	1.4E-04
rs2820899	9	7,198,342	5.8E-03		
rs7157202	14	58,945,345	5.8E-03		
rs4901055	14	50,296,750	5.8E-03	NIN	
rs7653603	3	152,472,732	5.8E-03	SETP11	
rs389694	9	20,184,147	5.8E-03		
rs7300317	12	50,918,840	5.8E-03	KRT7	
rs1507864	4	48,300,385	5.9E-03	FRYL	
rs7834389	8	23,621,823	5.9E-03	RP11-175E9.1	
rs12293101	11	5,292,175	5.9E-03	OR51B3P	
rs205117	16	25,473,468	5.9E-03		
rs1994575	10	55,163,697	5.9E-03		
rs12541335	8	22,144,377	5.9E-03	PHYHIP	
rs10512395	9	111,283,142	5.9E-03	PTPN3	
rs9320730	6	120,354,028	5.9E-03		
rs4683870	3	103,316,759	5.9E-03	ZPLD1	
rs4539216			5.9E-03	RP11-108B14.4	
rs312462	17	6,854,376	5.9E-03	RNASEK	
rs6773689	3	173,514,057	5.9E-03	FNDC3B	2.5E-03
rs4977545	9	19,502,746	5.9E-03	SLC24A2	3.7E-03
rs827297	10	72,370,659	5.9E-03	RP11-432J9.6	
rs13200559	6	56,750,279	5.9E-03	DST	
rs9442813	6	73,301,649	5.9E-03	AL445568.1	
rs389177			5.9E-03		
rs10027212	4	30,585,306	5.9E-03	PCDH7	
rs13241564	7	9,016,318	5.9E-03		
rs9304028	18	9,007,786	5.9E-03	RP11-143J12.1	
rs10828906	10	18,881,801	5.9E-03	NSUN6	3.7E-03
rs2654247	3	106,287,891	5.9E-03		
rs2883423	2	51,586,377	5.9E-03	AC007682.1	
rs9283872	6	22,033,470	5.9E-03		

rs2415439	14	37,647,766	5.9E-03	CTD-2058B24.2	
rs9316020	13	42,892,291	5.9E-03	ENOX1	
rs1074201	13	87,815,648	5.9E-03		
rs2963154	5	142,722,730	5.9E-03	NR3C1	4.3E-03
rs1037855	4	43,622,591	5.9E-03		
rs10882091	10	94,364,357	5.9E-03	KIF11	
rs4640872	6	165,195,024	5.9E-03		
rs9360979	6	76,900,873	5.9E-03		
rs7871216	9	36,235,759	5.9E-03	CLTA	
rs179083	14	29,880,418	6.0E-03		
rs1433825	9	18,786,886	6.0E-03	ADAMTSL1	1.1E-03
rs10490851	3	145,606,091	6.0E-03		
rs1707469	3	147,343,995	6.0E-03	PLOD2	8.3E-03
rs12988659	2	40,496,130	6.0E-03	SLC8A1	8.9E-04
rs7718156	5	172,028,971	6.0E-03	NEURL1B	
rs7117189	11	122,054,424	6.0E-03	UBASH3B	
rs4132589	13	25,122,025	6.0E-03	ATP8A2	
rs11090233	22	22,020,325	6.0E-03		
rs7901348	10	63,349,287	6.0E-03	ARID5B	1.7E-03
rs7341836	9	115,543,671	6.0E-03		
rs7114211	11	44,404,498	6.0E-03		
rs6786617	3	155,336,359	6.0E-03	ARHGEF26	
rs7095243	10	24,640,924	6.0E-03	RP11-429A24.4	1.4E-04
rs199169	5	8,639,300	6.0E-03		
rs7380706	5	178,894,478	6.0E-03		
rs923926	9	14,755,030	6.0E-03	FREM1	
rs3760372	17	42,735,001	6.0E-03	RP11-290H9.4	
rs1217745	5	71,281,720	6.0E-03		
rs13296976	9	9,347,444	6.0E-03	PTPRD	4.7E-03
rs533810	6	167,109,679	6.0E-03	RPS6KA2	
rs480025	1	187,897,346	6.0E-03	RN5S73	
rs4490947	9	15,088,969	6.0E-03		
rs2237848	8	17,918,884	6.0E-03	PCM1	
rs13068081	3	56,267,869	6.0E-03	ERC2	
rs1447563	2	46,490,868	6.0E-03		
rs1377095	15	85,061,729	6.0E-03	AGBL1	1.8E-03
rs6471171	8	134,991,862	6.1E-03		
rs3015480	14	50,269,942	6.1E-03	NIN	
rs4741304	9	13,478,608	6.1E-03	RP11-536O18.1	
rs7102167	11	1,394,679	6.1E-03	BRSK2	
rs4506892	16	80,196,410	6.1E-03	CMIP	

rs721087	2	4,942,340	6.1E-03		
rs896771	7	157,788,887	6.1E-03	PTPRN2	1.7E-03
rs2292609	2	166,104,049	6.1E-03	CSRNP3	
rs612183	9	15,272,158	6.1E-03	TTC39B	
rs11761859	7	24,825,775	6.1E-03	OSBPL3	
rs2369105	4	4,403,987	6.1E-03	NSG1	
rs7645818	3	36,505,422	6.1E-03	STAC	
rs7734427	5	74,363,824	6.1E-03	GCNT4	
rs1934775	6	9,939,516	6.1E-03	OFCC1	
rs1962543	9	29,999,444	6.1E-03		
rs3936194	4	1,589,489	6.1E-03	FAM53A	
rs10890809	11	107,462,687	6.1E-03	CUL5	
rs4571789	9	77,007,222	6.1E-03	U6	
rs2474606	10	38,491,647	6.1E-03	RP11-508N22.6	
rs10958672	8	41,274,498	6.1E-03	SFRP1	
rs4911287	20	31,090,952	6.1E-03	BPIFB6	
rs2111110	16	54,634,636	6.1E-03		
rs948138	11	102,006,875	6.1E-03	RP11-817J15.2	
rs310602	20	61,579,614	6.1E-03		
rs1341740	9	15,840,604	6.1E-03	C9orf93	
rs2354391	6	156,436,700	6.1E-03		
rs10505545	8	130,646,449	6.1E-03	CCDC26	
rs12033458	1	18,330,155	6.1E-03	IGSF21	7.1E-03
rs10510305	3	5,437,347	6.1E-03		
rs7089809	10	57,398,714	6.1E-03		
rs451664	9	26,360,564	6.1E-03		
rs17017378	2	79,717,878	6.1E-03	CTNNA2	6.0E-03
rs1931371	9	95,178,378	6.1E-03	U6	
rs4261301	11	57,871,560	6.1E-03	OR5B10P	
rs17761890	12	72,647,245	6.1E-03		
rs2028211	2	127,618,127	6.1E-03		
rs2294998	20	60,994,578	6.1E-03	DIDO1	
rs7092964	10	128,737,210	6.1E-03	DOCK1	5.5E-04
rs9325388	3	198,586,306	6.1E-03		
rs1074894	22	33,310,085	6.1E-03	RP1-101G11.2	
rs7813807	8	41,033,884	6.1E-03		
rs592398	13	108,677,223	6.2E-03		
rs2125566	22	33,108,009	6.2E-03		
rs6824576			6.2E-03		
rs9503013	6	1,652,398	6.2E-03	GMDS	
rs6494223	15	30,183,749	6.2E-03	CHRNA7	

rs2700592	3	100,614,099	6.2E-03		
rs7561383	2	40,427,711	6.2E-03	SLC8A1	8.9E-04
rs4950025	1	97,489,867	6.2E-03	DPYD-AS1	
rs767478	4	30,239,480	6.2E-03		
rs1446271	9	12,036,260	6.2E-03		
rs8047113	16	83,867,391	6.2E-03		
rs491106	1	187,950,736	6.2E-03		
rs7994590	13	60,945,769	6.2E-03		
rs10509845			6.2E-03		
rs2220182	9	7,609,121	6.2E-03		
rs42386	16	8,354,976	6.2E-03	RP11-568A19.1	
rs10958409	8	55,489,644	6.2E-03		
rs34736	5	96,193,646	6.2E-03	CTD-2260A17.2	
rs2057374	9	38,271,314	6.2E-03		
rs10487590	7	7,243,788	6.2E-03	C1GALT1	5.7E-03
rs10762795	10	80,075,943	6.2E-03	RP11-90J7.3	
rs3117148	6	159,373,801	6.2E-03	TAGAP	
rs11898149	2	98,019,838	6.2E-03		
rs10493669	1	80,727,323	6.2E-03		
rs11821606	11	94,836,868	6.2E-03		
rs7853954	9	38,389,721	6.2E-03	ALDH1B1	
rs17798906	2	117,555,176	6.2E-03		
rs916954	20	51,292,709	6.2E-03	TSHZ2	6.7E-04
rs8043658	16	85,521,537	6.2E-03		
rs1340589	1	67,696,979	6.2E-03		
rs2770712	9	7,239,055	6.2E-03		
rs9603096	13	36,238,240	6.2E-03		
rs1983011	3	178,859,580	6.2E-03	LINC00578	
rs6972852	7	2,424,235	6.2E-03	CHST12	
rs4841154	8	9,352,928	6.2E-03	RP11-375N15.1	
rs10937705	4	6,234,085	6.2E-03	JAKMIP1	
rs6985907	8	13,638,013	6.2E-03		
rs3759589	14	50,122,718	6.2E-03	ATL1	
rs400345	16	82,885,995	6.2E-03	RP11-558A11.2	7.6E-03
rs4432683	3	54,255,177	6.2E-03	CACNA2D3	7.3E-05
rs2760217	1	161,907,797	6.2E-03		
rs881950	3	150,628,104	6.3E-03		
rs6590598	11	131,173,745	6.3E-03	NTM	
rs9867793	3	67,243,323	6.3E-03		
rs1000016	2	235,355,721	6.3E-03		
rs727422	11	120,673,388	6.3E-03	SC5DL	

rs2577098	18	4,499,325	6.3E-03		
rs9573095	13	72,545,361	6.3E-03	KLF5	
rs7995886	13	50,266,987	6.3E-03	DLEU7	7.8E-03
rs4525696	2	85,791,511	6.3E-03		
rs1532010	18	20,182,039	6.3E-03	OSBPL1A	
rs914405	9	137,311,515	6.3E-03		
rs2509961	11	62,067,485	6.3E-03	RP11-864I4.4	
rs3823267	6	1,722,853	6.3E-03	GMDS	
rs1371091	3	60,988,473	6.3E-03	FHIT	6.4E-04
rs902856	4	40,075,664	6.3E-03	RNU7-74P	
rs9533481	13	42,887,185	6.3E-03	ENOX1	
rs6921388	6	27,188,184	6.3E-03	U2	
rs797810	7	83,434,619	6.3E-03	SEMA3A	4.1E-03
rs7904837	10	128,222,450	6.3E-03	C10orf90	
rs1461917	11	37,513,473	6.3E-03		
rs3009559	10	74,120,325	6.3E-03	MCU	
rs6480640	10	74,200,213	6.3E-03	MCU	
rs1722791	15	21,503,831	6.3E-03		
rs1972947	2	183,878,598	6.3E-03		
rs1405969	2	49,529,832	6.3E-03		
rs2905503	11	60,607,228	6.3E-03		
rs4704166			6.3E-03	GCNT4	
rs2665272	16	52,684,118	6.3E-03	FTO	
rs12578013	11	122,525,441	6.3E-03	CLMP	
rs9521198	13	108,636,331	6.3E-03	MYO16-AS1	3.3E-03
rs3813135	19	15,448,345	6.3E-03	PGLYRP2	
rs7759626	6	1,304,689	6.3E-03		
rs727345	10	31,939,079	6.3E-03	RP11-472N13.2	
rs9812681	3	173,481,044	6.3E-03	FNDC3B	2.5E-03
rs789239	3	130,116,498	6.3E-03	ACAD9	
rs6722778	2	128,475,570	6.3E-03	SAP130	
rs10486608	7	29,178,576	6.3E-03	CPVL	
rs6959914	7	57,834,528	6.3E-03	RP11-548K12.7	
rs522409	3	167,766,851	6.3E-03	RP11-450H5.1	
rs2422173	2	75,631,476	6.3E-03	FAM176A	2.6E-03
rs9572198	13	69,075,552	6.4E-03		
rs12525751	6	109,444,416	6.4E-03	SESN1	
rs885821	10	72,028,661	6.4E-03	PRF1	
rs506380	10	83,439,664	6.4E-03		
rs983093	10	83,477,461	6.4E-03		
rs2947658			6.4E-03	RP11-379B18.5	

rs7941030	11	122,027,585	6.4E-03	UBASH3B	
rs12446940	16	3,902,621	6.4E-03		
rs328845			6.4E-03		
rs7147755	14	47,248,356	6.4E-03		
rs9543561	13	73,769,467	6.4E-03		
rs13105217	4	65,064,629	6.4E-03		
rs729424	6	33,752,011	6.4E-03	ITPR3	
rs8049156	16	25,370,548	6.4E-03	CYCSP39	
rs6919391	6	26,716,304	6.4E-03		
rs4732529	7	83,473,522	6.4E-03	SEMA3A	4.1E-03
rs9851203	3	56,017,268	6.4E-03	ERC2	
rs12811136	12	131,603,653	6.4E-03	FBRSL1	
rs4689381	4	6,308,089	6.4E-03		
rs4972052	2	88,359,658	6.4E-03		
rs2029413	6	152,715,782	6.4E-03	SYNE1	4.8E-03
rs666134	3	120,816,966	6.4E-03	PLA1A	
rs9784675	5	132,097,638	6.4E-03	KIF3A	4.0E-05
rs1017266	7	8,912,697	6.4E-03		
rs2030592	15	35,102,817	6.4E-03	RP11-29M5.1	
rs4090570	19	46,807,966	6.4E-03	CEACAMP3	
rs2581578	8	2,111,101	6.4E-03	RP11-1049H7.1	
rs1972844	8	23,685,197	6.4E-03	RP11-175E9.1	
rs3862560	10	85,573,223	6.4E-03		
rs4676286	2	109,377,918	6.4E-03	SH3RF3	
rs41261	7	105,399,068	6.4E-03	CDHR3	
rs11879005	19	44,402,743	6.4E-03		
rs13317946	3	80,226,508	6.4E-03		
rs1883959	11	34,190,721	6.4E-03	ABTB2	1.2E-03
rs2540554	7	91,063,578	6.4E-03		
rs2389049	13	93,260,101	6.4E-03	GPC6	1.0E-03
rs12048529	1	90,859,695	6.4E-03		
rs4654465	1	4,854,635	6.5E-03		
rs17653196	13	68,422,613	6.5E-03		
rs2866712	16	74,946,942	6.5E-03	CNTNAP4	
rs1869156	3	56,318,391	6.5E-03	ERC2	
rs7086916			6.5E-03		
rs7124057	11	62,090,672	6.5E-03	EEF1G	
rs1781011	6	52,230,899	6.5E-03		
rs4242698	9	27,114,745	6.5E-03	TEK	7.4E-03
rs3885388	1	167,280,052	6.5E-03	RP11-375F2.2	
rs7624567	3	149,044,993	6.5E-03	RP11-78O22.1	

rs9828150	3	2,518,302	6.5E-03	CNTN4	
rs2616752	9	15,300,704	6.5E-03	TTC39B	
rs10142203	14	50,774,540	6.5E-03	TMX1	
rs12442329	15	85,056,724	6.5E-03	AGBL1	1.8E-03
rs2789891	1	187,946,162	6.5E-03		
rs11642377	16	20,017,154	6.5E-03		
rs10425066	19	35,018,134	6.5E-03		
rs9612814	22	23,657,959	6.5E-03	TMEM211	
rs1750770	10	22,966,999	6.5E-03	PIP4K2A	7.1E-03
rs7710178	5	155,946,409	6.5E-03	SGCD	
rs1777112	10	86,251,786	6.5E-03	FAM190B	
rs622200	11	113,533,984	6.5E-03	ZBTB16	
rs2390252	7	20,110,194	6.5E-03	AC005062.2	
rs2129446	10	3,723,386	6.5E-03		
rs830510	8	73,487,211	6.5E-03		
rs1276430	20	54,930,012	6.5E-03		
rs13267240	8	122,399,652	6.5E-03		
rs697216	12	100,178,691	6.5E-03		
rs4473985	7	49,609,214	6.5E-03		
rs9972695	16	80,268,484	6.5E-03	CMIP	
rs1393001	2	105,691,340	6.5E-03		
rs9965599	18	75,021,193	6.5E-03	ATP9B	
rs17768434	14	37,111,621	6.5E-03	RP11-356O9.1	
rs853256	3	64,290,504	6.5E-03	PRICKLE2	
rs2762699	1	42,809,287	6.5E-03	RP11-163G10.4	
rs1389976	8	108,959,180	6.5E-03		
rs7315833	12	125,459,435	6.6E-03	RP5-944M2.1	
rs2194295	16	74,798,976	6.6E-03		
rs4686799	3	187,933,930	6.6E-03	KNG1	
rs323689			6.6E-03		
rs1903595	8	14,433,852	6.6E-03	SGCZ	5.9E-04
rs10799329	1	224,181,122	6.6E-03	PYCR2	
rs4624521	3	128,157,844	6.6E-03	CHCHD6	
rs10996824	10	67,437,424	6.6E-03	CTNNA3	8.7E-04
rs12782894	10	34,006,326	6.6E-03		
rs4885065	13	72,547,636	6.6E-03	KLF5	
rs13032261	2	226,976,835	6.6E-03		
rs504384	1	187,954,827	6.6E-03		
rs2216974	7	24,021,536	6.6E-03		
rs1935286	1	165,820,854	6.6E-03		
rs2504011	10	33,177,557	6.6E-03	C10orf68	

rs1355784			6.6E-03	CPNE4	
rs7996418	13	111,930,016	6.6E-03		
rs1842636	9	32,100,777	6.6E-03		
rs4240725	12	80,039,177	6.6E-03	RP11-543H12.1	
rs10936485	3	167,547,230	6.6E-03		
rs554653	6	6,492,486	6.6E-03	LY86-AS1	
rs4783095	16	81,073,474	6.6E-03		
rs27813	16	47,970,032	6.6E-03	C16orf78	8.5E-03
rs6912202	6	77,005,395	6.6E-03		
rs923553	6	77,109,051	6.6E-03		
rs9289675	3	145,608,722	6.6E-03		
rs2170176	8	20,357,815	6.6E-03		
rs4822857	22	25,832,567	6.6E-03		
rs996062	7	124,154,815	6.6E-03		
rs9301679	13	89,938,730	6.6E-03	RP11-158A8.1	
rs6925813	6	160,221,348	6.6E-03		
rs8069696	17	62,004,935	6.6E-03	PRKCA	9.3E-03
rs7101509	11	130,487,858	6.6E-03	AP002806.1	
rs984903	2	81,212,504	6.6E-03		
rs10485518	20	15,061,008	6.6E-03	MACROD2	4.1E-03
rs4299072	14	64,775,011	6.6E-03	CTD-2509G16.3	
rs3006664	10	32,472,024	6.6E-03		
rs3736964	10	7,824,930	6.7E-03	ITIH2	2.2E-03
rs1519662	2	100,510,050	6.7E-03		
rs1667783			6.7E-03		
rs1501281	3	160,260,909	6.7E-03	IQCJ-SCHIP1	
rs10496117	2	64,541,169	6.7E-03	LGALSL	
rs6475372	9	1,984,204	6.7E-03		
rs7049103	9	3,814,004	6.7E-03	GLIS3	
rs9347479	6	161,422,084	6.7E-03	MAP3K4	9.1E-03
rs615545	7	18,358,396	6.7E-03	HDAC9	
rs816203	12	116,495,371	6.7E-03	KSR2	2.6E-04
rs1381251	3	138,429,828	6.7E-03		
rs10813878	9	32,849,234	6.7E-03	RP11-462B18.3	
rs501878	10	6,566,503	6.7E-03	PRKCQ	2.1E-03
rs10893370	11	124,697,053	6.7E-03	PKNOX2	
rs2505024	6	77,153,728	6.7E-03		
rs7664215	4	95,548,180	6.7E-03		
rs10492428	13	25,179,281	6.7E-03	ATP8A2	
rs10777276	12	89,815,815	6.7E-03		
rs1562045	9	13,764,329	6.7E-03		

rs1026900	6	149,288,218	6.7E-03	UST	
rs17590608	6	167,106,014	6.7E-03	RPS6KA2	
rs7587138	2	46,510,593	6.7E-03	AC018682.6	
rs6040486	20	11,187,118	6.7E-03	RP4-734C18.1	
rs2182667	13	73,314,882	6.7E-03	KLF12	
rs6489016	12	124,862,044	6.7E-03		
rs877616			6.7E-03		
rs9365729	6	164,910,428	6.7E-03		
rs6569585	6	129,516,639	6.7E-03	BMPR1APS1	2.4E-03
rs4719607	7	2,626,477	6.7E-03		
rs6717876	2	81,216,889	6.7E-03		
rs11784810	8	24,482,929	6.7E-03	RP11-624C23.1	
rs1858886	12	109,744,939	6.7E-03		
rs10052431	5	13,886,009	6.8E-03	DNAH5	9.3E-04
rs7760528	6	20,550,333	6.8E-03	E2F3	9.3E-03
rs2858729	22	31,325,281	6.8E-03	SYN3	
rs1986466	9	30,008,156	6.8E-03		
rs9399121	6	135,145,917	6.8E-03		
rs872606	13	97,690,672	6.8E-03	FARP1	
rs12554063	9	111,357,283	6.8E-03		
rs7544426	1	109,977,503	6.8E-03	RP5-1160K1.6	
rs741664	7	131,720,594	6.8E-03	PLXNA4	6.4E-03
rs12938678	17	24,734,553	6.8E-03		
rs10800783	1	199,718,475	6.8E-03	CSRP1	
rs10011689	4	11,184,945	6.8E-03		
rs219176	2	33,083,590	6.8E-03	LTBP1	
rs4076553	1	41,665,843	6.8E-03		
rs9879974	3	80,966,560	6.8E-03		
rs17179281	14	37,118,858	6.8E-03	RP11-356O9.1	
rs4753826	11	107,363,852	6.8E-03		
rs896253	16	84,377,703	6.8E-03	COX4NB	
rs3786944	19	3,129,372	6.8E-03	S1PR4	
rs40277	5	135,359,799	6.8E-03		
rs4823882	22	45,629,789	6.8E-03	TBC1D22A	
rs4743992	9	92,259,388	6.8E-03		
rs4408145	1	41,682,317	6.8E-03		
rs2280580	3	120,830,090	6.8E-03	PLA1A	
rs946646	1	179,421,458	6.8E-03	RP11-540K16.2	
rs638230	9	9,562,790	6.8E-03	PTPRD	4.7E-03
rs4296182	14	50,731,917	6.8E-03		
rs2900964	19	13,413,763	6.8E-03	CACNA1A	8.5E-03

rs2210455	20	9,867,383	6.8E-03		
rs4847368	1	95,149,626	6.8E-03	CNN3	1.8E-03
rs2375256	9	1,159,485	6.8E-03	RP11-341G2.1	
rs703712	12	100,205,204	6.8E-03	UTP20	
rs9344826	6	89,283,373	6.8E-03		
rs7194648	16	72,284,372	6.9E-03		
rs9300636	13	100,362,458	6.9E-03	NALCN-AS1	
rs867744	6	85,878,413	6.9E-03		
rs936769	9	7,671,711	6.9E-03		
rs4521641	6	8,872,893	6.9E-03		
rs11860152	16	84,374,825	6.9E-03	COX4NB	
rs1886237	6	161,804,620	6.9E-03	PARK2	8.8E-05
rs90192	11	116,564,557	6.9E-03	SIDT2	
rs6869617	5	124,389,487	6.9E-03		
rs1876869	15	58,344,343	6.9E-03		
rs11989071	8	25,853,544	6.9E-03	AC090103.1	
rs1532122	5	66,833,479	6.9E-03	RP11-434D9.1	
rs12669134	7	23,755,075	6.9E-03	STK31	3.0E-03
rs2561143	5	38,307,208	6.9E-03	EGFLAM	
rs2594499	2	46,287,756	6.9E-03		
rs10496653	2	126,486,008	6.9E-03		
rs9301495	13	88,214,498	6.9E-03		
rs10484153	14	82,734,864	6.9E-03		
rs17406451	2	43,485,980	6.9E-03	THADA	1.1E-03
rs2333562	17	55,188,728	6.9E-03	VMP1	
rs877885	18	44,495,161	6.9E-03	CTIF	
rs1381640	14	46,197,769	6.9E-03		
rs4801332	19	61,749,068	6.9E-03	ZFP28	3.5E-03
rs1125825	4	27,625,465	6.9E-03		
rs10496347	2	100,431,642	6.9E-03		
rs7939247	11	127,831,260	6.9E-03	ETS1	
rs7020007	9	14,525,343	6.9E-03	RP11-408A13.2	
rs4075798	5	2,176,985	6.9E-03		
rs10812643	9	27,680,090	6.9E-03		
rs2341264	1	73,956,997	6.9E-03	RP11-275A6.2	
rs7760923	6	77,000,235	6.9E-03		
rs2695109	2	178,509,996	6.9E-03	PDE11A	
rs12314621	12	44,134,997	6.9E-03		
rs371346	18	42,504,953	6.9E-03		
rs6441449	3	163,557,476	6.9E-03		
rs1008746	5	167,591,276	6.9E-03	ODZ2	2.5E-03

rs4922665	11	23,680,342	6.9E-03		
rs12677076	8	20,328,401	6.9E-03		
rs12130139	1	245,608,675	6.9E-03		
rs6797432	3	190,108,582	6.9E-03		
rs10243603	7	31,554,143	6.9E-03	CCDC129	5.4E-03
rs1339446	1	188,000,602	6.9E-03		
rs4796915	18	11,218,713	6.9E-03		
rs2282457	10	5,767,329	6.9E-03	FAM208B	
rs10815044	9	4,630,712	6.9E-03	SPATA6L	7.4E-04
rs4950392	1	145,203,172	6.9E-03	CHD1L	
rs4771031	13	26,289,249	6.9E-03		
rs6071491	20	59,117,976	6.9E-03		
rs2870477	19	62,036,725	6.9E-03	PEG3	
rs10485205	6	157,238,666	7.0E-03	ARID1B	4.8E-03
rs10901042	7	154,697,319	7.0E-03		
rs1601360	2	151,555,468	7.0E-03	AC023469.2	
rs1168292	12	65,018,927	7.0E-03	HELB	
rs6456735	6	26,682,128	7.0E-03		
rs2107785	7	80,802,211	7.0E-03	AC004866.1	
rs1341626	10	119,160,671	7.0E-03		
rs804267	8	11,666,650	7.0E-03	NEIL2	
rs2035987	9	14,744,010	7.0E-03	FREM1	
rs1962044	8	35,009,528	7.0E-03		
rs7867067	9	8,880,946	7.0E-03	PTPRD	4.7E-03
rs770457	12	76,641,418	7.0E-03		
rs998022	12	67,955,492	7.0E-03	CPSF6	
rs6039459	20	940,713	7.0E-03		
rs4389424	3	23,652,529	7.0E-03		
rs850942	12	13,039,758	7.0E-03	HEBP1	
rs6133869	20	10,268,196	7.0E-03	HIGD1AP15	
rs1713434	14	19,951,367	7.0E-03	TEP1	
rs3759704			7.0E-03		
rs10164749	2	20,336,328	7.0E-03	PUM2	
rs1233492	6	29,566,456	7.0E-03	RPS17P1	
rs32056	5	156,006,717	7.0E-03	SGCD	
rs383815	3	192,657,909	7.0E-03	PYDC2	
rs7335635	13	35,814,985	7.0E-03	SPG20	
rs7010127	8	3,115,425	7.0E-03	CSMD1	8.6E-05
rs2035481	16	87,947,857	7.0E-03	ANKRD11	
rs6953890	7	46,960,870	7.0E-03	AC004901.1	
rs2143725	20	50,346,145	7.0E-03	RP4-723E3.1	

rs13178332	5	57,865,837	7.0E-03		
rs1420686	16	48,785,487	7.0E-03	PAPD5	
rs1327990	6	4,259,879	7.0E-03		
rs1776503	14	51,757,619	7.0E-03		
rs1995549	16	77,541,637	7.0E-03	WWOX	3.1E-03
rs2153445	6	102,425,032	7.0E-03	GRIK2	9.7E-04
rs12001341	9	85,393,066	7.0E-03		
rs910425	6	170,494,116	7.0E-03	FAM120B	
rs4948235	10	61,055,737	7.1E-03		
rs11640609	16	21,596,245	7.1E-03	OTOA	
rs1354719	1	63,940,620	7.1E-03		
rs2249871	17	67,252,248	7.1E-03		
rs40512	5	59,841,224	7.1E-03	PDE4D	
rs1018155	6	39,840,410	7.1E-03		
rs535176	10	44,067,065	7.1E-03		
rs10273448	7	35,738,028	7.1E-03	AC018647.3	
rs1144949	12	67,547,311	7.1E-03	CPM	
rs8048539	16	78,261,653	7.1E-03	AC009159.1	
rs911087	14	25,882,608	7.1E-03		
rs4286772	6	22,830,587	7.1E-03		
rs4782742	16	81,573,151	7.1E-03	CTD-3253I12.1	1.9E-03
rs10247874	7	30,842,648	7.1E-03	INMT-FAM188B	
rs6991834	8	3,115,506	7.1E-03	CSMD1	8.6E-05
rs1464500	12	24,280,927	7.1E-03	RP11-444D3.1	7.7E-04
rs11645023	16	78,483,635	7.1E-03		
rs2394180	6	29,913,178	7.1E-03		
rs12699725	7	15,500,240	7.1E-03	AGMO	1.6E-03
rs9950834	18	42,548,720	7.1E-03	ST8SIA5	
rs534286	9	110,840,055	7.1E-03	TMEM245	
rs7703727	5	176,990,043	7.1E-03	RP11-1277A3.2	
rs7960860	12	117,532,673	7.1E-03		
rs2930732	9	7,648,953	7.1E-03		
rs6476322	9	32,031,861	7.1E-03		
rs9785096	8	41,212,307	7.1E-03		
rs762066	14	50,374,445	7.1E-03		
rs12004815	9	98,353,833	7.1E-03	CDC14B	
rs10018304	4	83,120,969	7.1E-03	RP11-689K5.3	
rs11082399	18	40,364,087	7.1E-03		
rs6077004	20	6,390,961	7.1E-03	RP11-199O14.1	
rs1468263	17	27,171,997	7.1E-03		
rs6505423	17	30,032,439	7.1E-03		

rs4681901	3	58,680,914	7.1E-03	C3orf67	
rs12619539	2	169,958,048	7.1E-03		
rs2273697	10	101,553,805	7.1E-03	ABCC2	
rs2838956	21	45,769,452	7.1E-03	SLC19A1	
rs2855736	12	11,872,565	7.1E-03	ETV6	1.0E-03
rs7958091	12	117,579,622	7.1E-03		
rs10818896	9	100,214,009	7.1E-03	GABBR2	
rs1359480	13	107,413,961	7.1E-03		
rs17291274	13	81,065,943	7.2E-03		
rs218204	2	33,204,540	7.2E-03	LTBP1	
rs2581965	4	22,244,178	7.2E-03		
rs1857649	9	20,998,725	7.2E-03	PTPLAD2	
rs995030	12	87,414,802	7.2E-03	KITLG	
rs3751834	16	77,573,909	7.2E-03	WWOX	3.1E-03
rs10497310	2	167,717,651	7.2E-03	XIRP2	6.8E-03
rs4881403			7.2E-03	RP11-499O7.5	
rs7873669	9	9,876,403	7.2E-03	PTPRD	4.7E-03
rs218203	2	33,204,034	7.2E-03	LTBP1	
rs1833710	5	147,947,939	7.2E-03	HTR4	
rs4838594	10	49,339,148	7.2E-03	ARHGAP22	
rs2065585	1	63,186,989	7.2E-03		
rs9901648	17	76,650,303	7.2E-03	BAIAP2	
rs10486748	7	50,993,431	7.2E-03	RP4-724E13.2	
rs234146	14	97,224,265	7.2E-03	RP11-76E12.1	
rs1010984	7	24,864,529	7.2E-03	OSBPL3	
rs4332113	8	132,925,828	7.2E-03		
rs1997885	22	41,513,706	7.2E-03	GOLGA2P4	
rs3759614	14	22,906,941	7.2E-03	EFS	
rs1457788	8	133,389,718	7.2E-03	KCNQ3	2.0E-03
rs1873164	2	179,461,794	7.2E-03	CCDC141	
rs11790439	9	108,764,188	7.2E-03	ZNF462	
rs4281084	8	31,614,916	7.2E-03	NRG1	
rs1471745	15	57,361,535	7.2E-03	MYO1E	4.2E-03
rs2359536	10	20,939,614	7.2E-03		
rs1953478	14	43,735,132	7.2E-03	RP11-305B6.3	
rs7783211	7	82,609,331	7.2E-03	PCLO	6.2E-03
rs2802487	10	43,984,530	7.2E-03		
rs7767396	6	44,035,028	7.2E-03		
rs8047994	16	61,986,281	7.2E-03	RP11-368L12.1	
rs1350166	12	67,922,581	7.2E-03	CPSF6	
rs11877669	18	44,568,382	7.2E-03	CTIF	

rs10763756	10	30,112,791	7.2E-03		
rs10080213	5	52,805,736	7.2E-03		
rs1001262	5	179,740,232	7.2E-03		
rs9992707	4	186,078,904	7.2E-03	#N/A	
rs11564006	7	27,314,122	7.3E-03		
rs1209438	16	53,138,749	7.3E-03		
rs4868790	5	166,681,168	7.3E-03	ODZ2	2.5E-03
rs2174403	16	77,486,959	7.3E-03	RP11-319G9.3	3.1E-03
rs4245284			7.3E-03		
rs3019626	11	61,564,848	7.3E-03		
rs1209001	7	91,278,295	7.3E-03	CTB-104F4.2	
rs1397988	18	40,276,800	7.3E-03		
rs2700996	7	37,335,714	7.3E-03	ELMO1	5.1E-03
rs495083	9	119,356,717	7.3E-03		
rs2511317	11	90,196,005	7.3E-03	RP11-660M18.2	
rs13088432	3	77,044,375	7.3E-03	ROBO2	
rs1341032	9	74,541,943	7.3E-03	RP11-28P17.3	
rs4664352	2	161,244,689	7.3E-03		
rs11685766	2	28,683,575	7.3E-03	PLB1	
rs7910260	10	60,280,925	7.3E-03		
rs9428757	1	237,118,548	7.3E-03		
rs6451872	5	20,694,307	7.3E-03	RP11-774D14.1	
rs7636173	3	165,938,827	7.3E-03	RP11-71H9.1	
rs1915275	1	237,214,414	7.3E-03		
rs17328231	1	95,791,119	7.3E-03	RP11-286B14.1	
rs11179382	12	71,500,424	7.3E-03		
rs1438650	13	68,379,734	7.3E-03		
rs742146	22	35,250,780	7.3E-03	EIF3D	2.6E-03
rs2018682	22	19,647,432	7.3E-03	XXbac-B135H6.15	
rs6426244	1	245,619,172	7.3E-03		
rs543262	2	169,372,473	7.3E-03	NOSTRIN	
rs2810047	14	96,946,958	7.3E-03		
rs12894942	14	97,402,628	7.3E-03		
rs1553975	3	132,999,266	7.3E-03	CPNE4	1.5E-03
rs1437731	2	240,297,565	7.3E-03		
rs8133357	21	21,439,390	7.3E-03	NCAM2	
rs7041770	9	35,523,348	7.3E-03	RUSC2	
rs931725	2	227,054,278	7.3E-03		
rs7357583	8	19,296,766	7.3E-03	SH2D4A	
rs1936547	13	80,051,349	7.3E-03		
rs12506698	4	137,357,811	7.4E-03	RP11-775H9.2	

rs1676884	11	74,673,280	7.4E-03	ARRB1	
rs1356224	2	13,114,377	7.4E-03		
rs471799	6	12,803,957	7.4E-03		
rs4896067	6	134,873,179	7.4E-03	RP11-557H15.3	
rs2746167			7.4E-03		
rs726739	20	12,142,424	7.4E-03		
rs13029158	2	52,225,047	7.4E-03	AC007682.1	
rs6092192	20	53,855,033	7.4E-03		
rs4075492	8	2,507,431	7.4E-03	RP11-134O21.1	
rs4676435	2	241,096,674	7.4E-03	ANKMY1	6.3E-03
rs6798963	3	169,644,283	7.4E-03	EGFEM1P	
rs7561779			7.4E-03	SLC8A1	
rs9371379	6	155,954,368	7.4E-03		
rs42733	7	28,428,869	7.4E-03	CREB5	2.4E-04
rs1537625	10	7,650,512	7.4E-03	ITIH5	
rs3739593	9	474,336	7.4E-03	RP11-165F24.5	
rs17698657	9	28,109,660	7.4E-03	LINGO2	2.2E-03
rs1867977	10	73,204,962	7.4E-03	CDH23	4.7E-03
rs3912519	16	50,440,889	7.4E-03		
rs1016091	1	34,697,183	7.4E-03		
rs4701131	5	178,915,052	7.4E-03	RUFY1	7.1E-03
rs1037690	5	41,448,858	7.4E-03	PLCXD3	
rs4347211	1	205,044,963	7.4E-03	IL19	
rs966097	9	78,000,164	7.4E-03	PCSK5	9.0E-03
rs1006049	2	71,030,168	7.4E-03	AC007040.7	
rs7733389	5	178,907,603	7.4E-03	RUFY1	
rs1388372	8	127,005,334	7.4E-03	RP11-622O11.2	
rs890228	8	6,647,873	7.4E-03		
rs4744904	9	71,302,087	7.4E-03	RP11-470P21.2	
rs42714	7	28,421,758	7.4E-03	CREB5	2.4E-04
rs966855	5	33,735,534	7.4E-03	ADAMTS12	
rs850511	12	109,724,204	7.4E-03		
rs1469773	9	26,756,179	7.4E-03	RP11-18A15.1	
rs4952981			7.4E-03	THADA	
rs9637407	3	151,181,271	7.5E-03	RP11-651P23.4	
rs10181522	2	50,493,827	7.5E-03	NRXN1	2.3E-04
rs7852392	9	115,479,570	7.5E-03	RP11-18B16.2	
rs2108780	7	7,259,417	7.5E-03	AC005532.5	
rs4843668	16	86,263,115	7.5E-03	JPH3	
rs4234306	3	156,584,525	7.5E-03	PLCH1	
rs2068028	7	4,446,209	7.5E-03		

rs1860312	19	2,524,995	7.5E-03	GNG7	4.6E-03
rs9347879	6	164,935,251	7.5E-03		
rs10192647	2	8,548,532	7.5E-03		
rs10016365	4	114,050,334	7.5E-03	ANK2	4.2E-04
rs9656946	8	124,683,548	7.5E-03		
rs2889090	2	137,708,944	7.5E-03	THSD7B	5.0E-03
rs2659615	11	132,225,458	7.5E-03	OPCML	2.4E-04
rs1735969	21	22,044,472	7.5E-03	AP000475.2	
rs10902221	11	792,379	7.5E-03	SLC25A22	
rs1267070	2	161,696,729	7.5E-03	AC009313.1	
rs2121698	2	46,563,075	7.5E-03	AC018682.6	
rs1434262	9	8,693,733	7.5E-03	RP11-134K1.3	4.7E-03
rs6715733	2	127,477,188	7.5E-03		
rs3091619	20	44,758,167	7.5E-03		
rs11011346			7.5E-03		
rs4354609	10	24,356,140	7.5E-03	KIAA1217	1.4E-04
rs4588237	2	47,796,406	7.5E-03	AC006509.6	
rs9300597			7.5E-03	PCCA	
rs956053	3	10,997,826	7.5E-03		
rs2345962	1	162,008,412	7.5E-03	RP4-640E24.1	
rs10167178	2	129,718,195	7.5E-03	AC079586.1	
rs1993094	7	25,811,535	7.5E-03		
rs12615002	2	40,474,891	7.5E-03	SLC8A1	8.9E-04
rs2921448	10	74,160,029	7.5E-03	MCU	
rs4745960	10	64,387,046	7.5E-03		
rs1378796	3	158,614,482	7.5E-03	VEPH1	
rs4855216	3	165,487,506	7.5E-03		
rs790455	12	91,139,496	7.5E-03		
rs2024585	6	160,255,007	7.5E-03		
rs10492086	12	100,712,072	7.5E-03	GNPTAB	
rs4712580	6	21,173,805	7.6E-03	CDKAL1	3.6E-03
rs6890341	5	27,105,871	7.6E-03	CDH9	
rs4342076	3	147,371,183	7.6E-03		
rs6252	12	28,002,340	7.6E-03	RP11-993B23.3	
rs3816263	17	7,924,882	7.6E-03	ALOX12B	1.3E-03
rs2882444	13	89,800,666	7.6E-03		
rs2381617	9	7,488,487	7.6E-03		
rs1030191	5	166,676,280	7.6E-03	ODZ2	2.5E-03
rs130407	22	30,802,930	7.6E-03	SLC5A1	
rs4867041	5	30,588,718	7.6E-03		
rs2214020	5	9,905,860	7.6E-03	RP11-447B18.1	

rs1901565	9	28,045,900	7.6E-03	LINGO2	2.2E-03
rs4801695	19	61,457,272	7.6E-03	ZSCAN5A	
rs3764465	18	46,825,370	7.6E-03	SMAD4	
rs7513441	1	72,196,705	7.6E-03	NEGR1	
rs11767716	7	3,092,767	7.6E-03	AC024028.1	
rs555267	18	39,246,696	7.6E-03		
rs4055434	6	164,109,891	7.6E-03		
rs7540116	1	169,660,411	7.6E-03		
rs12752933	1	190,897,781	7.6E-03	RGS13	
rs2327221	6	10,143,861	7.6E-03	OFCC1	
rs10199719	2	148,875,899	7.6E-03	MBD5	
rs1475183	13	25,185,826	7.6E-03	ATP8A2	
rs2301677	7	17,292,583	7.6E-03	AC003075.4	
rs4811450			7.6E-03		
rs9328072	6	1,773,164	7.6E-03	GMDS	
rs7556828	2	46,516,676	7.6E-03	AC018682.6	
rs1469863	17	37,220,613	7.6E-03	LEPREL4	
rs4774478	15	61,221,816	7.6E-03	LACTB	
rs10743542	12	8,936,937	7.6E-03		
rs1360382	9	23,369,719	7.6E-03		
rs10512302	9	104,487,695	7.6E-03		
rs4371145	16	80,847,418	7.6E-03		
rs4740969	9	8,912,286	7.6E-03	PTPRD	4.7E-03
rs16920176	8	57,061,690	7.6E-03	LYN	
rs11768582	7	82,668,636	7.6E-03		
rs11750078	5	132,692,272	7.6E-03	FSTL4	1.2E-03
rs965432	2	158,819,527	7.6E-03	CCDC148	3.0E-03
rs17119719	8	14,436,692	7.6E-03	SGCZ	5.9E-04
rs1762529	10	33,008,086	7.6E-03	C10orf68	
rs9318814	13	81,349,619	7.6E-03		
rs11008980	10	32,902,186	7.6E-03	CCDC7	
rs6134919	20	13,510,481	7.6E-03	TASP1	
rs2221511	18	59,530,380	7.7E-03	SERPINB11	
rs1078019	4	38,131,334	7.7E-03	RP11-83C7.2	
rs6782741	3	119,894,154	7.7E-03		
rs11104732	12	87,002,119	7.7E-03	CEP290	
rs4714261	6	39,647,185	7.7E-03	KIF6	
rs2828665	21	24,275,166	7.7E-03		
rs10093667	8	26,760,792	7.7E-03	ADRA1A	
rs4801473	19	62,551,402	7.7E-03	ZNF304	
rs11167068	8	142,618,960	7.7E-03		

rs2001456	6	100,545,730	7.7E-03	RP11-14I4.3	
rs6483140	11	91,053,707	7.7E-03		
rs9814976	3	41,190,800	7.7E-03		
rs8048583	16	31,187,037	7.7E-03	ITGAM	
rs12431159	13	99,873,865	7.7E-03	PCCA	
rs4985702	17	16,977,947	7.7E-03	MPRIP	
rs2683556	10	71,304,127	7.7E-03	COL13A1	8.9E-03
rs525455	10	13,143,291	7.7E-03	RP11-730A19.2	
rs2298629	18	45,572,077	7.7E-03	ACAA2	
rs12084355	1	99,222,557	7.7E-03	LPPR5	
rs9402168	6	130,108,429	7.7E-03	RP11-73O6.4	
rs2738173	8	6,728,348	7.7E-03	GS1-24F4.2	
rs17415614	5	143,121,215	7.7E-03	CTB-57H20.1	
rs1293151	20	52,384,991	7.7E-03		
rs10776644	10	49,660,087	7.7E-03	WDFY4	1.0E-03
rs6590453	11	129,745,971	7.7E-03	RP11-121M22.1	
rs270327	6	153,852,496	7.7E-03		
rs4723037	7	30,966,625	7.7E-03	GHRHR	
rs2821505	9	9,762,724	7.7E-03	PTPRD	4.7E-03
rs1767777	6	11,033,789	7.7E-03	TMEM14B	
rs2792218	9	77,796,917	7.7E-03	PCSK5	9.0E-03
rs1339252	9	77,797,479	7.7E-03	PCSK5	9.0E-03
rs12654791	5	179,744,794	7.7E-03		
rs1351188	11	134,410,991	7.7E-03		
rs4886250			7.7E-03		
rs2022991	6	162,168,159	7.7E-03	PARK2	8.8E-05
rs2569865	6	1,474,786	7.7E-03		
rs181706	21	28,122,934	7.7E-03		
rs9874501	3	167,902,738	7.7E-03		
rs1983666	22	24,745,565	7.7E-03	MYO18B	
rs9635033	13	79,956,028	7.7E-03		
rs1397590	16	47,717,543	7.8E-03		
rs1598828	15	27,582,448	7.8E-03	FAM189A1	
rs2924331	18	51,297,301	7.8E-03	TCF4	6.1E-03
rs7839802	8	14,418,884	7.8E-03	SGCZ	5.9E-04
rs1996483	3	167,607,628	7.8E-03		
rs8088451	18	45,526,032	7.8E-03		
rs10743549	12	8,943,104	7.8E-03		
rs6880335	5	50,788,219	7.8E-03	CTD-2335O3.3	
rs10210385	2	58,851,216	7.8E-03	AC007092.1	
rs169271	20	51,342,873	7.8E-03	TSHZ2	6.7E-04

rs2481031	6	160,676,719	7.8E-03		
rs1969888	13	105,648,715	7.8E-03		
rs719082	7	24,483,720	7.8E-03		
rs408109	8	37,217,210	7.8E-03		
rs10887335	10	86,367,249	7.8E-03		
rs11633343	15	47,911,577	7.8E-03	FGF7	
rs9864901	3	147,005,074	7.8E-03		
rs2149131	13	26,291,325	7.8E-03		
rs881500	15	61,458,525	7.8E-03	CA12	
rs4237861	12	70,953,954	7.8E-03	AC087886.1	1.6E-03
rs9984281	21	34,663,726	7.8E-03	AP000320.6	7.0E-03
rs1224391	9	21,381,698	7.8E-03	RP11-354P17.15	
rs1168338	12	65,045,636	7.8E-03	GRIP1	1.0E-03
rs9295235	6	164,217,031	7.8E-03		
rs9911131	17	55,066,785	7.8E-03	CLTC-IT1	
rs2381800	9	8,425,110	7.8E-03	PTPRD	4.7E-03
rs10175110	2	49,500,618	7.8E-03		
rs10484546	6	29,432,578	7.8E-03	OR5V1	
rs1529764	7	131,729,953	7.8E-03	PLXNA4	6.4E-03
rs1391530	11	80,399,957	7.8E-03		
rs2275496	9	110,681,448	7.8E-03	IKBKAP	
rs4361224	3	39,312,604	7.8E-03		
rs9531108	13	80,218,134	7.8E-03		
rs960962	20	20,301,515	7.8E-03	INSM1	
rs9840567	3	169,708,327	7.8E-03	EGFEM1P	
rs256822	5	155,864,858	7.8E-03	SGCD	
rs13091735	3	169,749,953	7.8E-03	EGFEM1P	
rs588918	11	116,361,852	7.8E-03	SIK3	
rs1351452	11	116,448,564	7.8E-03	SIK3	
rs4076927	3	46,705,753	7.8E-03	ALS2CL	
rs7322446	13	63,756,181	7.8E-03		
rs519813	4	20,130,091	7.8E-03	SLIT2	
rs2147829	14	90,233,622	7.8E-03	RP11-661G16.2	
rs1039596	5	134,441,399	7.8E-03	CTC-203F4.1	
rs10867879	9	71,481,798	7.8E-03	RP11-109D9.4	
rs1958909	14	52,514,477	7.8E-03		
rs4720945	7	11,187,371	7.8E-03		
rs10046283	6	109,525,763	7.8E-03	SESN1	
rs4736935	8	41,144,341	7.8E-03		
rs10151230	14	43,541,226	7.8E-03	RP11-305B6.3	
rs2724178	2	168,904,383	7.8E-03		

rs378322	2	70,616,413	7.8E-03	TGFA	
rs2194505	2	161,671,500	7.9E-03	AC009313.1	
rs1487721	11	45,131,106	7.9E-03	PRDM11	
rs7928370	11	8,681,844	7.9E-03	RPL27A	
rs2075292	11	116,237,722	7.9E-03	SIK3	
rs2757599	6	7,557,267	7.9E-03	SNRNP48	
rs7229783	18	56,434,182	7.9E-03		
rs7081464	10	37,923,943	7.9E-03		
rs4700810	5	178,924,400	7.9E-03	RUFY1	7.1E-03
rs11674865	2	1,846,247	7.9E-03	MYT1L	1.6E-03
rs3768574	1	22,226,697	7.9E-03	LINC00339	
rs12424159	12	127,755,894	7.9E-03	TMEM132C	
rs2027394	9	4,059,657	7.9E-03	RP11-70J12.1	3.3E-04
rs2263000	10	26,066,791	7.9E-03		
rs1635627	8	5,594,564	7.9E-03		
rs2106553	6	67,065,007	7.9E-03		
rs7595911	2	104,621,738	7.9E-03		
rs6749383	2	104,626,334	7.9E-03		
rs268289	10	43,918,152	7.9E-03		
rs9834043	3	146,853,092	7.9E-03		
rs1570896	13	100,386,483	7.9E-03	LINC00411	
rs1538903	14	49,927,228	7.9E-03	CDKL1	
rs11084990	19	2,960,220	7.9E-03	TLE2	
rs7193788	16	81,213,661	7.9E-03	CDH13	
rs4268898	2	24,343,917	7.9E-03	ITSN2	
rs9375796	6	131,382,691	7.9E-03	EPB41L2	
rs4595452	10	55,589,070	7.9E-03	PCDH15	4.8E-03
rs12644632	4	43,608,222	7.9E-03		
rs3925075	16	31,255,249	7.9E-03	ITGAM	
rs611908	11	74,694,735	7.9E-03	ARRB1	
rs1820497	12	72,967,266	7.9E-03	RP11-81H3.2	
rs1424231	16	78,264,252	7.9E-03	RP11-345M22.1	
rs3798221	6	160,918,138	7.9E-03	LPA	
rs6061036	20	29,982,229	7.9E-03	TTLL9	3.5E-04
rs455929	22	21,613,083	7.9E-03		
rs1528847	12	117,690,683	7.9E-03	RP11-357K6.1	
rs11768076	7	30,795,564	7.9E-03	INMT-FAM188B	
rs1757095	9	116,888,215	7.9E-03	TNC	7.3E-03
rs7095717	10	61,718,225	7.9E-03	ANK3	
rs1403724	3	150,500,084	7.9E-03	RP11-206M11.7	
rs7906085	10	19,474,847	7.9E-03		

Table 5. Genome-wide PBAT results. The top 1% most significant results are organized by significance and annotated by gene name if the snp fall within a gene. In addition, for genes that contain significant SNPs, I have also annotated the minimum pvalue observed in our published GWAS for that gene.

					PBAT		PBAT|linkage		Pseudomarker		Count of	Number of	Shared
Gene	Chr	Gene Start	Gene Stop	Min P	count	min p	count	min p	count	min p	Tests	SNPs for Gene	SNP
HDAC4	2	239,969,864	240,323,348	5.9E-05			1	2.2E-04	5	5.9E-05	2	6	
HTR4	5	147,830,595	148,056,798	4.0E-04	2	1.7E-03			1	4.0E-04	2	2	yes
PPARGC1B	5	149,109,861	149,234,585	2.4E-04	1	1.9E-03			1	2.4E-04	2	2	
GRIA1	5	152,869,175	153,193,240	1.4E-08	1	2.8E-03	2	1.4E-08	4	2.3E-04	3	7	
FAM114A2	5	153,369,688	153,418,496	6.9E-05	1	3.1E-03	1	6.9E-05			2	1	yes
SGCD	5	155,297,354	156,194,499	5.3E-05	7	1.1E-03	1	5.3E-05			2	7	yes
MCM3	6	52,128,807	52,149,582	9.3E-06	1	3.7E-03	1	9.3E-06			2	1	yes
TMEM14A	6	52,535,907	52,551,386	1.0E-06	2	7.7E-04	2	1.0E-06			2	2	yes
DST	6	56,322,785	56,819,426	5.6E-06	1	5.9E-03	1	5.6E-06			2	1	yes
KHDRBS2	6	62,390,139	62,996,132	2.0E-05	1	3.4E-03	1	2.0E-05			2	1	yes
EYS	6	64,429,876	66,417,118	2.2E-05	1	4.6E-03	1	2.2E-05			2	1	yes
RIMS1	6	72,596,406	73,112,845	5.9E-07	2	5.1E-04	3	5.9E-07			2	3	yes
KCNQ5	6	73,331,520	73,908,574	2.0E-07	1	3.2E-03	1	2.0E-07	1	3.5E-04	3	2	yes
RP11-73O6.4	6	126,112,111	130,461,627	5.3E-05	3	4.9E-03	2	5.3E-05			2	3	yes
EPB41L2	6	131,160,487	131,384,462	7.8E-06	1	7.9E-03	1	7.8E-06			2	1	yes
VNN1	6	133,002,729	133,035,188	1.4E-05	2	2.3E-03	2	1.4E-05			2	2	yes
AHI1	6	135,604,670	135,830,219	6.1E-05			1	1.8E-04	1	6.1E-05	2	1	yes
IL20RA	6	137,321,108	137,366,298	4.6E-05	1	3.7E-03	1	4.6E-05			2	1	yes
ERI1	8	8,859,657	8,974,256	5.3E-05			1	5.3E-05	1	2.8E-04	2	2	
TNKS	8	9,413,424	9,639,856	2.8E-04	1	1.8E-03			1	2.8E-04	2	2	
MSRA	8	9,911,778	10,286,401	1.0E-07	4	4.5E-04	3	1.0E-07	2	3.6E-05	3	6	yes
XKR6	8	10,753,555	11,058,875	1.8E-04	1	2.6E-03			1	1.8E-04	2	2	
FDFT1	8	11,653,082	11,696,818	1.6E-07	2	1.7E-03	2	1.6E-07	1	4.9E-04	3	3	yes
SGCZ	8	13,947,373	15,095,848	7.7E-05	4	1.3E-03			3	7.7E-05	2	7	
KANK1	9	470,291	746,105	1.6E-07	3	6.2E-05	3	1.6E-07			2	4	yes
GLIS3	9	3,824,127	4,348,392	2.1E-04	2	3.1E-03			1	2.1E-04	2	3	
SEC61A2	10	12,171,636	12,211,960	3.8E-05	3	3.9E-03			2	3.8E-05	2	3	yes
FRMD4A	10	13,685,706	14,504,141	3.7E-05	2	3.7E-05			1	4.2E-04	2	3	
KIAA1217	10	23,983,675	24,836,772	3.3E-04	3	3.0E-03			1	3.3E-04	2	4	
HS3ST4	16	25,703,347	26,149,009	1.5E-04	3	2.0E-03			1	1.5E-04	2	4	
XPO6	16	28,109,300	28,223,241	4.7E-04	1	4.8E-03			1	4.7E-04	2	2	
ITGAM	16	31,271,311	31,344,190	1.1E-04	2	7.7E-03			1	1.1E-04	2	3	
FTO	16	53,737,875	54,155,853	5.1E-04	1	6.3E-03			1	5.1E-04	2	2	
L3MBTL4	18	5,954,705	6,414,910	3.5E-04	2	1.9E-03			1	3.5E-04	2	3	
CTIF	18	46,065,417	46,389,588	9.1E-05	2	6.9E-03	1	9.1E-05			2	2	yes
DCC	18	49,867,158	51,062,269	1.5E-04	1	4.4E-03	5	1.5E-04			2	6	
TCF4	18	52,889,562	53,332,018	2.5E-04	2	4.6E-03	1	2.5E-04			2	2	yes
ATP8B1	18	55,313,658	55,470,327	7.9E-05	1	3.7E-04	1	7.9E-05			2	1	yes
NEDD4L	18	55,711,619	56,068,772	3.1E-04	2	5.5E-04			1	3.1E-04	2	3	

Table 6. Integrated association results. This table summarizes any gene that was implicated in two or more association tests. Shared SNP indicates that the same marker was implicated in at least two tests. No annotation in this column means that different SNPs were identified by different tests.

Chr	Gene Start	Gene Stop	Gene Name	min p value	Source of Evidence	HF (12)	GO Immune Process (3)	GWAS (13)
2	228029281	228179508	COL4A3	4.7E-07	PBAT|Linkage			
2	228336868	228421384	AGFG1	3.9E-05	PBAT|Linkage			
2	239969864	240323348	HDAC4	5.9E-05	Integrated			
5	147830595	148056798	HTR4	4.0E-04	Integrated			
5	149109861	149234585	PPARGC1B	2.4E-04	Integrated			
5	152869175	153193240	GRIA1	1.4E-08	Integrated	yes		1.8E-03
5	153369688	153418496	FAM114A2	6.9E-05	Integrated			
5	155297354	156194499	SGCD	5.3E-05	Integrated	yes		
5	159774758	159797648	C1QTNF2	7.5E-06	PBAT|Linkage			
6	52128807	52149582	MCM3	9.3E-06	Integrated	yes		
6	52535907	52551386	TMEM14A	1.0E-06	Integrated			
6	53794780	54131078	MLIP	3.9E-05	PBAT|Linkage			
6	56322785	56819426	DST	5.6E-06	Integrated	yes		
6	62390139	62996132	KHDRBS2	2.0E-05	Integrated			
6	64429876	66417118	EYS	2.2E-05	Integrated			4.5E-04
6	70576463	70919679	COL19A1	4.4E-05	PBAT|Linkage	yes		8.9E-03
6	72596406	73112845	RIMS1	5.9E-07	Integrated	yes		
6	73331520	73908574	KCNQ5	2.0E-07	Integrated	yes		
6	126112111	130461627	RP11-73O6.4	5.3E-05	Integrated			
6	129897277	130031370	ARHGAP18	3.1E-06	PBAT|Linkage			
6	131160487	131384462	EPB41L2	7.8E-06	Integrated	yes		
6	132891461	132892498	TAAR6	5.1E-06	PBAT|Linkage			
6	133002729	133035188	VNN1	1.4E-05	Integrated		GO:0006979	
6	135604670	135830219	AHI1	6.1E-05	Integrated			8.6E-04

6	137321108	137366298	IL20RA	4.6E-05	Integrated			
8	8859657	8974256	ERI1	5.3E-05	Integrated			
8	9413424	9639856	TNKS	2.8E-04	Integrated			
8	9911778	10286401	MSRA	1.0E-07	Integrated		GO:0006979	8.7E-03
8	10753555	11058875	XKR6	1.8E-04	Integrated			
8	11653082	11696818	FDFT1	1.6E-07	Integrated	yes		
8	13947373	15095848	SGCZ	7.7E-05	Integrated			5.9E-04
9	470291	746105	KANK1	1.6E-07	Integrated			4.4E-04
9	3824127	4348392	GLIS3	2.1E-04	Integrated			3.3E-04
10	12171636	12211960	SEC61A2	3.8E-05	Integrated		GO:0002474	
10	13685706	14504141	FRMD4A	3.7E-05	Integrated	yes		
10	23983675	24836772	KIAA1217	3.3E-04	Integrated			1.4E-04
16	25703347	26149009	HS3ST4	1.5E-04	Integrated			4.3E-03
16	28109300	28223241	XPO6	4.7E-04	Integrated			
16	31271311	31344190	ITGAM	1.1E-04	Integrated			
16	53737875	54155853	FTO	5.1E-04	Integrated			
18	5954705	6414910	L3MBTL4	3.5E-04	Integrated			8.6E-03
18	46065417	46389588	CTIF	9.1E-05	Integrated			
18	49867158	51062269	DCC	1.5E-04	Integrated			7.6E-03
18	52889562	53332018	TCF4	2.5E-04	Integrated	yes		6.1E-03
18	53670844	53858493	AC006305.1	3.0E-05	PBAT|Linkage			
18	55313658	55470327	ATP8B1	7.9E-05	Integrated			
18	55711619	56068772	NEDD4L	3.1E-04	Integrated	yes		

Table 7. Summary of genes implicated in this study. Any gene for which at least one SNP falling within its transcript exceeded the significance threshold for any test conducted in the course of this study is listed. The source of the evidence is additionally annotated, along with

additional evidence, such as expression in the hair follicle (HF), annotation in an immune process in Gene Ontology (GO), and presence in an associated risk haplotype identified in our initial GWAS.

					Risk Allele Frequency				
GWAS Risk Haplotype	Marker	Chr	Position	Risk Allele	Family	Family Affected	Family Unaffected	GWAS cases	GWAS controls
CTLA4_hap1	rs926169	2	204,430,997	A	0.44	0.42	0.46	0.47	0.39
CTLA4_hap2	rs3096851	2	204,472,127	C	0.35	0.36	0.36	0.37	0.31
IL21_hap3	rs7682241	4	123,743,325	A	0.41	0.42	0.42	0.40	0.34
ULBP6_hap4	rs9479482	6	150,399,705	A	0.71	0.76	0.63	0.68	0.57
ULBP3_hap5	rs2009345	6	150,431,441	G	0.50	0.60	0.38	0.50	0.39
STX17_hap6	rs10760706	9	101,763,513	G	0.31	0.29	0.34	0.38	0.31
IL2RA_hap7	rs4147359	10	6,148,445	A	0.37	0.39	0.33	0.39	0.33
IL2RA_hap8	rs3118470	10	6,141,719	G	0.33	0.35	0.31	0.38	0.30
ZNFN1A4_hap10	rs1701704	12	54,698,754	C	0.33	0.35	0.31	0.40	0.33
ERBB3_hap11	rs705708	12	54,775,180	G	0.49	0.48	0.48	0.47	0.53
BTNL2_hap12	rs3129963	6	32,488,186	A	0.88	0.91	0.86	0.93	0.83
BTNL2_hap13	rs1980493	6	32,471,193	A	0.94	0.94	0.94	0.94	0.85
HLA-DQA2_hap14	rs1794282	6	32,774,504	G	0.95	0.96	0.94	0.96	0.90
AGER_hap15	rs2070600	6	32,259,421	A	0.06	0.07	0.06	0.08	0.04
C6orf10_hap16	rs6910071	6	32,390,832	G	0.22	0.22	0.23	0.26	0.18

Table 8. Distribution of GWAS risk alleles in our family cohort. Our GWAS identified 16 independent risk haplotypes. Here I display the frequency of a single proxy SNP for each of 15 haplotypes (one SNP was not typed in this study). For some SNPs, the frequencies within families differ between affected and unaffected family members, which is what would be expected for a cosegregating variant. However, for the majority of SNPs, allele frequencies do not vary between affected and unaffected family members, suggesting that these variants could be necessary but insufficient for disease. These SNPs would not be amenable to detection by linkage.

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Paper 3

Expanded Genome-wide Association Study in Alopecia Areata

Abstract

Alopecia Areata (AA) is one of the most prevalent autoimmune diseases, in which immune destruction is targeted to the hair follicle. Despite the prevalence of AA, there are no evidence-based treatments, which creates an enormous unmet medical need.[1] Prior to our initial genome-wide association study (GWAS), the genetic basis of AA had remained largely unknown, creating barriers to the development of effective therapeutic strategies. That first study implicated eight regions of the genome, seven of which had never previously been studied within the context of AA, and implicated several genes pivotal to immune response. Here, I conduct a follow-up study, by the addition of 800 cases with mild AA to our initial cohort. After stringent quality control filtering, I conducted association analysis of 443,349 SNPs in a cohort of 1801 cases and 3274 controls. The increase in power achieved by this moderate increase in sample size has allowed me to identify an additional region of the genome that harbors risk alleles for AA, on chromosome 16p13.13. This region demonstrated nominal significance in our initial GWAS ($p=1.4x10^{-5}$), and was additionally found to have significant association in a candidate gene study conducted following our GWAS. I next performed a case only analysis to identify markers with allele frequencies that differ between mild (n=1194) and severe (n=604) cases, and identified 6 SNPs with statistically significant association, all of which are located within the HLA class II region. Taken together, this study suggests that increasing sample sizes for GWAS in AA will continue to yield novel associations, as has been seen for other autoimmune diseases. Furthermore, this study provides support to previous studies that found disease severity effects for loci within the HLA region.

Introduction

Alopecia areata (AA) is one of the most prevalent autoimmune diseases, with a lifetime risk of 1.7%.[2] In AA, autoimmunity develops against the hair follicle, resulting in non-scarring

hair loss that may begin as patches, which can coalesce and progress to cover the entire scalp (alopecia totalis, AT) or eventually the entire body (alopecia universalis, AU). The immune attack is focused at the end bulb and spares the stem cell niche, such that hair growth remains possible once the aberrant immune response subsides. The disease waxes and wanes for many patients, leading to bouts of remission between disease relapses. By convention, patients are considered to have severe disease when hair loss affects at least the entire scalp, if not the whole body, for at least one episode of hair loss.

Our group conducted the first genome wide associated study, which identified 139 SNPs that exceeded our threshold for statistical significance ($p \leq 5x10^{-7}$).[3] That study confirmed association of AA with the Human Leukocyte Antigen (HLA) class II region, which had previously been associated with AA through candidate gene studies, and additionally implicated eight additional regions of the genome that had never before been studied within the context of AA. Most of the identified regions contain genes pivotal to immune response that had previously been studied within the context of other autoimmune diseases such as type 1 diabetes (T1D), celiac disease (CeD) and rheumatoid arthritis (RA), including CTLA4, IL-2/IL-21, IL-2RA, PTPN2, and Eos (IKZF4)/ERBB3. One region contains ligands for the NKG2D receptor, an activator of cytotoxic lymphocytes, which had never before been implicated in human disease, ULBP3/ULBP6. Finally two regions contain genes that are expressed in the hair follicle (PRDX5, STX17). All of these associations have subsequently been confirmed in an independent cohort of unrelated AA patients and population matched controls through candidate gene studies.[4-6] The genetic evidence from this study implicates disease mechanisms that are shared with other autoimmune disorders and suggests that therapeutic strategies targeted to these mechanism and efficacious for aligned diseases could be repositioned to treat AA, transforming the therapeutic landscape for this highly prevalent disease.[7]

GWAS in other autoimmune diseases unequivocally demonstrate that increases in sample size will yield novel genetic associations. Currently, nearly 2700 GWAS in the genome.gov database of GWAS have reported sample sizes over 10,000, and four exceed a sample size of 100,000. Among autoimmune diseases, two GWAS have more than 10,000 samples and the largest to date was conducted for inflammatory bowel disease (IBD) with a sample size of more than 75,000. In AA, we are limited in the number of patients available to participate in GWAS, in part because resources have not existed to conduct large-scale international ascertainment. Our first GWAS utilized all the unrelated affected participants of the National Alopecia Areata Registry who self-reported European ancestry and had enrolled up to the time that we conducted our study. Through collaboration with an international colleague, we were able to genotype an additional 800 cases with mild disease (hair loss never exceeded more than 75% of the scalp at any point in their lifetime). I present here association analysis of this expanded GWAS cohort, in addition to a case only analysis that sought to identify disease alleles associated with disease severity.

Materials and Methods

Patient Population

For the initial GWAS, cases were ascertained through the National Alopecia Areata Registry (NAAR), and control data were obtained from publically available data, as previously described.[3] Briefly, there were two sources of control data. First, a dataset was obtained from subjects enrolled in the New York Cancer Project[8] and genotyped as part of previous studies.[9] Second, a dataset was obtained from the CGEMS breast[10] and prostate[11] cancer studies (http://cgems.cancer.gov/data/). The controls were not expanded for this study. The additional 800 patients with mild disease were recruited from outpatient clinics, private dermatology practices and via AA self-support groups in Belgium and Germany. Inclusion criteria followed

published guidelines,[12] and additionally included diagnosis by a trained and experienced clinician. Disease subtype for all patients in this study was determined according to the AA investigation assessment guidelines.[12] All participants provided written informed consent and the study was conducted in accordance with the Declaration of Helsinki Principles. The study was approved by the local IRB committees.

Genotyping

DNA was extracted from peripheral blood leukocytes by salting out with saturated NaCl solution according to standard methods, or by using a Chemagic Magnetic Separation Module I (Chemagen, Baesweiler, Germany) in accordance with the manufacturer's instructions. All cases were genotyped with the Illumina 610K chip. Controls were not genotyped within this study. Data for the controls had been generated in other studies, as described above. These samples had all been genotyped with the Illumina 550K chip, at the center who genotyped our cases, as previously described.[3]

Assessment of Data Quality

Quality control (QC) was performed with Helix Tree software (Golden Helix). Only SNPs that had passed QC thresholds in the initial GWAS were used.[3] Briefly, SNPs that were missing more than 5% data or did not appear to be in Hardy Weinberg Equilibrium in controls ($p<0.01$) had been removed. Once this subset of SNPs was identified in the new set of cases, QC filters were applied and did not identify any additional poor quality SNPs, so analyses were performed on 463,308 SNPs. Poor quality DNA was identified by filtering out samples missing more than 5% data (n=35). Estimates of genome-wide Identity by Descent (IBD) between pairs of samples were calculated to identify related individuals with the cohort. This method identified 2 pairs of duplicate samples and 1 pair of related individuals; one sample from each of these three pairs

was removed. Principal components analysis (PCA) using 3568 ancestry informative markers (AIMs) was performed.[7] This analysis identified 15 samples more than 6 standard deviations units from 5 components, and these were excluded from subsequent analysis. Visual inspection of a plot of the first two eigenvectors following exclusion of identified outliers confirmed comparable distributions between the cases and controls.

Statistical Analysis

Whole genome association tests were performed with Helix Tree software (Golden Helix). Reported association values were obtained with logistic regression assuming an additive genetic model, which assumes additive effects of the risk allele, namely that the risk for homozygotes is twice the risk of heterozygotes, and correcting for residual population stratification with PCA. A threshold for statistical significance of $p<5x10^{-7}$ was used to adjust for multiple testing.[13]

Results

In this study, I expanded our previously reported GWAS cohort by the addition of 800 unrelated cases. After stringent quality control filters to remove questionable samples and markers, my dataset contained 1801 cases, 1054 from the original cohort and 747 from our German colleagues, of which 1194 have mild AA and 604 have severe disease, characterized by total loss of scalp hair. There were 3274 controls.

The first analysis tested 443,349 SNPs for association with AA, comparing allele frequencies of cases with those of controls. A total of eight regions in the genome exceeded my threshold for statistical significance ($p<5x10^{-7}$) (Figure 1). Seven of these regions demonstrated statistically significant association in our initial GWAS, including chromosomes 2q33.2

(CTLA4/ICOS); 4q27 (IL21/IL2); 6p21.32 (HLA), 6q25.1 (ULBP3/ULBP6); 9q31.1 (STX17); 10p15.1 (IL2RA); and 11q13 (PRDX5). A region on chromosome 16p13.13 only achieved nominal significance in our initial GWAS, but surpassed the threshold in this study. A single SNP rs4451969 achieved significance ($p=4.6x10^{-7}$; OR=1.21) (Figure 2). Only one region identified in the initial GWAS failed to pass the threshold for statistical significance here, although it remained nominally significant (chromosome 12q13.2; $minp=1.8x10^{-6}$).

To investigate whether disease alleles can influence severity of disease, I conducted a case-only analysis, comparing allele frequencies among 604 patients with severe disease to those among 1194 patients with mild disease (Figure 3). Only seven SNPs surpassed our threshold for statistical significance and these were all clustered within the HLA class II region (Table 1).

Discussion

The course of genetic discoveries across autoimmune diseases have been similar , such that an initial GWAS with approximately 1000 patients uncovered five to eight risk loci, and as subsequent GWAS and meta-analyses expanded to include up to 5000 patients, the number of bona fide risk loci increased (e.g., to approximately 40 in type 1 diabetes and more than 70 in Crohn´s disease [www.genome.gov/gwastudies]). The most recent meta analysis in Crohn's disease included a cohort of 75,000 samples and identified a total of 163 risk loci.[14] Sample size is thus clearly a determinant of the number of associations that GWAS can reveal for autoimmune diseases. Our initial GWAS in AA contained just over 1000 cases and its findings likely represent just the tip of the iceberg. In this study, we expanded our cohort with the addition of 800 cases and I conducted association analysis, which identified an additional significant locus.

The locus at chromosome 16p13.13 is gene dense, containing at least 13 unique coding transcripts within a 480Kb interval. Several of these genes are most commonly discussed within the context of genetic associations to this region: class II, major histocompatibility complex, transactivator (CIITA), Dexi homolog (DEXI), C-type lectin domain family 16, member A (CLEC16A), suppressor of cytokine signaling 1 (SOCS1), transition protein 2 (TNP2), protamine 1 (PRM1), protamine 2 (PRM2), and protamine 3 (PRM3). The locus has been associated with six different autoimmune diseases through GWAS, including type 1 diabetes, celiac disease, Crohn's disease, multiple sclerosis, ulcerative colitis and primary biliary cirrhosis (www.genome.gov/gwastudies). In our initial GWAS, this locus achieved nominal significance, with a minimum p-value of $1.2x10^{-5}$ for SNP rs8060821.[3] More recently, a candidate gene study in AA identified a statistically significant association at this locus for SNP rs998592 ($p=2.45x10^{-7}$).[4]

Several of the genes at this locus have been implicated in immune functions, including CIITA and SOCS1.[15-19] These genes are both known regulators of type I interferon-gamma mediated signaling via JAK-STAT cascade, a pathway that has been strongly implicated in AA pathology, by gene expression studies (A.M. Christiano and R.Clynes, personal communication). CIITA has also been implicated in Bare Lymphocyte Syndrome, Type II, which is characterized by the abnormal expression of HLA molecules.[20] Despite the extensive literature citing disease associations with SNPs within and near CLEC16A, very little is known about its function. Of interest, a recent study of this locus demonstrated that a number of GWAS–identified risk alleles within an intron of CLEC16A affect the expression of a neighboring gene, DEXI.[21] Gene annotations in Ensembl database indicate that five genes within this locus have demonstrated expression in CD56+ NK cells: CIITA, CLEC16A, PRM1, PRM2, and TNP2 within the GNF Gene Expression Atlas, a project that measured gene expression across 79 different human cell or tissue types.[22] Of all eight genes located at this locus, only CIITA is

observed to be differentially expressed in lesional scalp biopsies (A.M. Christiano, personal communication). While this locus is clearly associated with increased risk for a set of autoimmune diseases, the exact causal mechanism remains unclear and it is possible that several different genes contribute to disease.

It has previously been suggested that mild AA and severe AA may differ in their genetic architecture. .[23,24] In order to address this question, I conducted a case only analysis, in which allele frequencies were compared between mild AA cases and severe AA cases. Only the HLA region exceeded the threshold for statistical significance. Several published studies have found that HLA associations are stronger for patients affected with severe AA than for those with mild AA.[23,24] The lack of additional findings outside of the HLA region could suggest that the underlying genetic architecture is consistent between these two phenotypically dissimilar groups of patients, although it could also be interpreted to reflect a sample size that is insufficient to detect an effect and suggests that if such effects exist, they will be of small magnitude. Revisiting this question in a larger study may help to resolve this ambiguity.

Figures and Legends

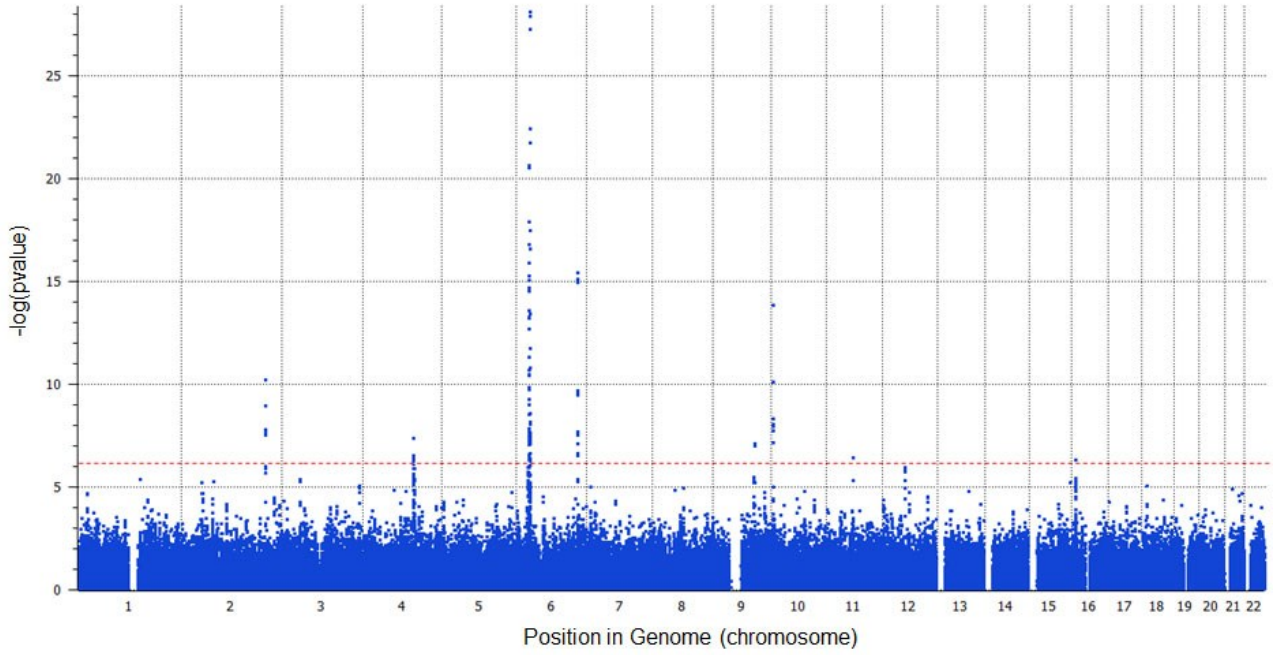

Figure 1. Manhattan plot for genome-wide tests of association. The cohort of unrelated AA patients and controls is expanded to include 1801 cases and 3274 controls. Logistic regression is used to test 443,349 SNPs for association with AA. Eight regions of the genome exceed my threshold for statistical signficance ($p<5x10^{-7}$), indicated by the red line and include regions previously identified in our first GWAS on chromosomes 2, 4, 6, 9, 10, and 11, as well as a new region, on chromosome 16.

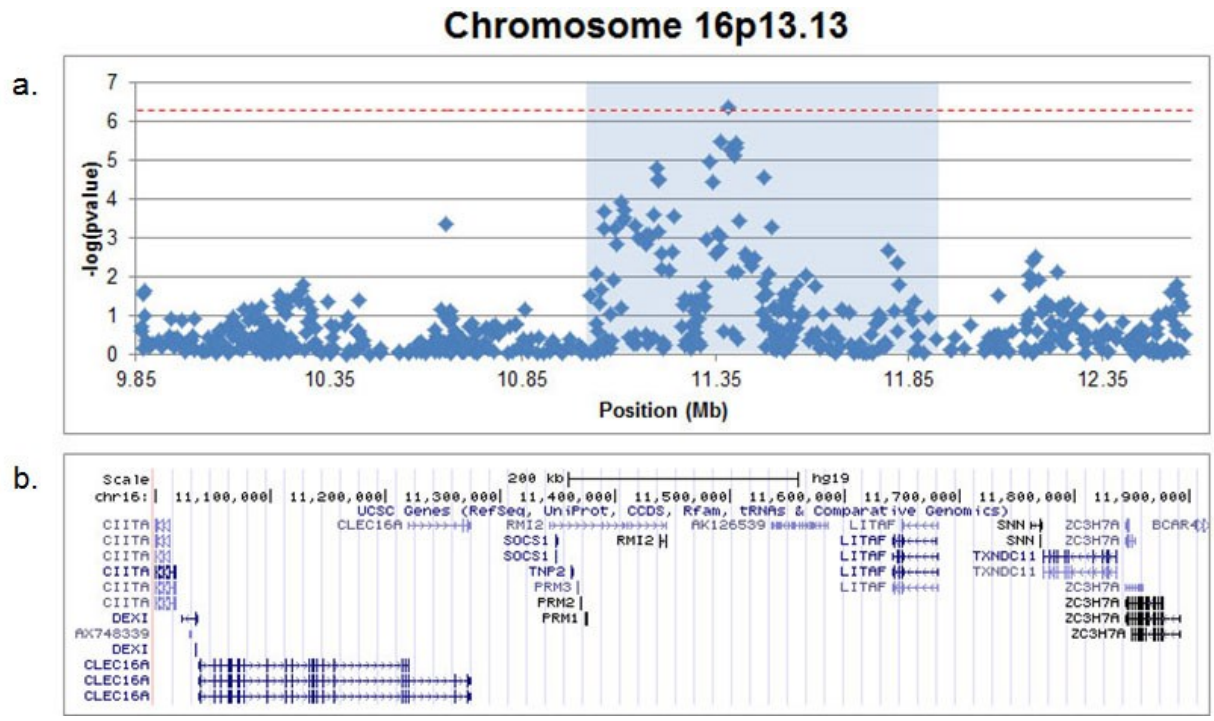

Figure 2. Detailed map of associated SNPs and gene locations for chromosome 16p13.13. (a). A single SNP exceeded my threshold for statistical significance, indicated by the red line. The blue shading indicates the region shown in the transcript map, below. (b). Thirteen genes reside within this region. The SNP with the statistically significant association is indicated by the red asterisk.

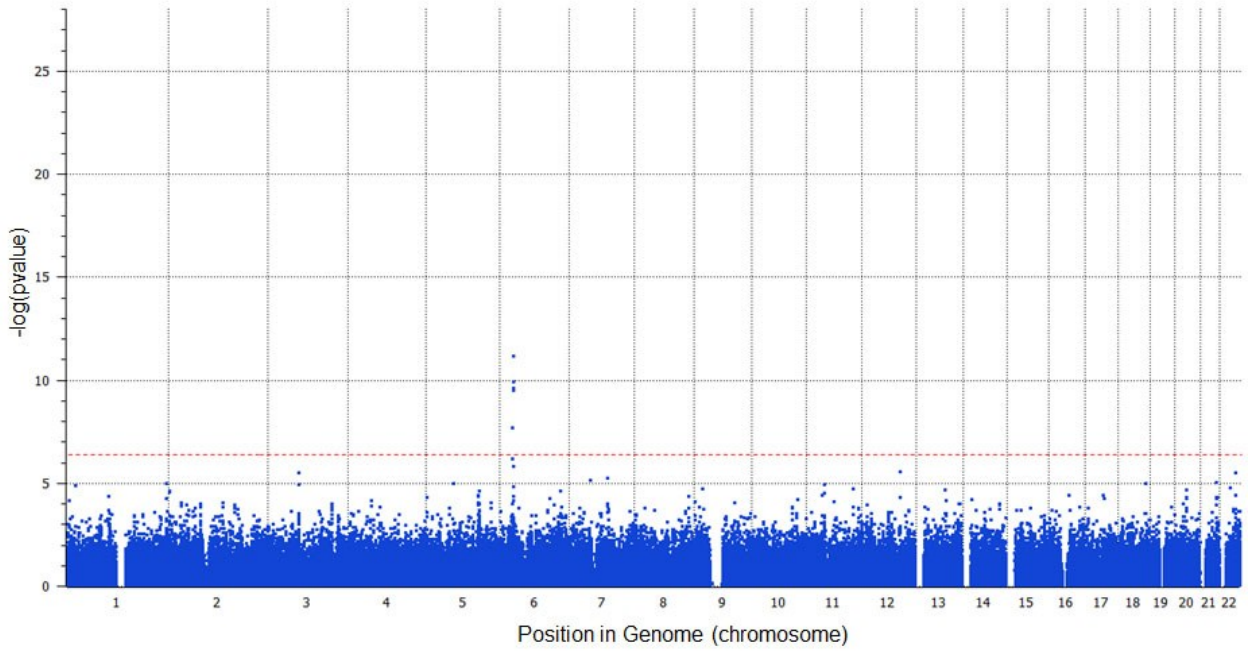

Figure 3. Manhattan plot for a case only genome-wide tests of association. Logistic regression is used to test for differences in allele frequencies for 443,349 SNPs between AA patients with mild disease and AA patients with severe disease. A single genomic region, located on chromosome 6, exceeds my threshold for statistical signficance ($p<5x10^{-7}$), indicated by the red line. The HLA class II cluster of genes reside here.

Tables

SNP	pvalue	Risk Allele	Frequency Severe AA	Frequency Mild AA	Frequency Controls
rs2856725	1.2E-10	A	0.81	0.70	0.61
rs9275572	6.5E-12	G	0.80	0.68	0.59
rs2647012	3.0E-10	G	0.81	0.70	0.61
rs2856717	2.4E-10	C	0.81	0.70	0.62
rs2858305	3.0E-10	A	0.81	0.70	0.62
rs7192	2.1E-08	C	0.79	0.69	0.61

Table 1. Case-only results. Analysis identified six SNPs that exceeded genome-wide significance, all of which cluster in the HLA class II region. SNP ID is presented with pvalue from the association analysis. For all six genetic markers, the frequency of the risk allele is greatest among severe cases of AA, decreased among mild cases of AA, and lowest among controls. Controls were not used in this analysis, frequencies are presented as a comparison.

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Conclusion and Future Directions

Introduction

Alopecia areata (AA) is the most prevalent autoimmune disease in the US.[1,2] With a lifetime risk of 1.7%,[3] it affects both genders with similar frequencies and people of all ages.[4-6] AA affects more individuals than most other autoimmune diseases combined, and yet despite its prevalence, there is an enormous unmet medical need,[7] in part due to the dearth of information about the underlying pathogenesis.

In AA, autoimmunity arises against the hair follicles in the skin, which causes hair loss associated with an aberrant accumulation of immune-response cells around the affected hair follicles. Prior to my study, evidence supporting a genetic basis for AA stemmed from multiple lines of research, including increased risk of disease in first degree relatives,[4,8] twin studies,[9,10] and more recently, from our initial family-based linkage study[11] and GWAS in a cohort of unrelated individuals.[12] Importantly, our initial GWAS identified a set of 16 statistically independent risk haplotypes across 8 loci, implicating specific genes that increase risk of AA, all of which have been validated.[13-15]

Genome wide genetic studies provide a robust strategy to gain critical insight into disease mechanisms, in particular when little is known about the underlying causes of disease. There are currently several methods for gene mapping, including family-based study designs and designs that utilize cohorts of unrelated affected and unaffected people. Each experimental design is subject to limitations that arise from assumptions that are inherent to the method. Therefore, in order to gain a comprehensive understanding of the genetic architecture of AA, I proposed to use a multifaceted approach to gene mapping, employing complementary methods, linkage and GWAS, that leverage our family cohort as well as our collection of unrelated AA cases.

First I proposed to conduct linkage and association tests in a cohort of AA families. The probability that an allele will demonstrate cosegregation with disease in a family, is influenced

by a number of factors, including its frequency in the population and the level of genetic heterogeneity underlying the disease. Furthermore, the variant must be strongly correlated with the phenotype, such that an individual who inherits that allele will most likely develop disease. Variants that have a strong disadvantageous effect on phenotype are likely to be under purifying selection and so we expect them to exist at low frequencies in the population. I proposed to conduct analyses in a family cohort to identify disease genes that harbor rare variants.

I further proposed to conduct genome-wide association tests in a cohort of unrelated AA cases and controls. This method identifies disease alleles that are common in the population. For example, as of December 2012, the median risk allele frequency reported in the NIH database of GWAS findings is 0.35, and more than 99% of risk alleles have a population frequency greater than 1% (www.genome.gov/gwastudies), supporting the notion that GWAS identify disease variants that are common in the population.

Emerging evidence suggests that the genetic architecture of common complex diseases involves both common and rare variants, and the empirical evidence is augmented with sound theoretical arguments.[16-28] For autoimmune diseases in particular, associations with multiple alleles have been documented for a number of loci,[12,29-32] and deep resequencing and fine mapping has identified both rare and common susceptibility variants at loci implicated initially by GWAS.[29,30] Therefore, there is strong rationale for pursuing both methods in my search for AA genes. At the very least, both methods would converge upon a set of genes that harbor rare and common variants. Alternatively, it is possible that linkage methods could identify genes that are under purifying selection, creating a dearth of common variants and therefore remain obscure in GWAS.

Summary of Findings

Family studies conducted here have confirmed the presence of rare disease variants in AA. *Statistic*ally significant evidence for linkage is observed at 2q36.1-q37.3 (LOD=4.17) and nominal evidence is observed at 6p12.2-q15 (LOD=2.31) and 6q22.31-q24.1 (LOD=2.18). An additional 17 regions exceed a LOD score of 1. The cumulative size of all linkage regions in this study with LOD≥1 is 114,440,871 bp. These regions contain 618 protein coding genes, whose transcripts account for 58,556,469 bp, or 51% of the regions. It is estimated that the 20,000 genes in the human genome span about 30Mb of DNA, or account for 1% of the genome. Thus the linkage regions contain a much greater density of genes than expected, which suggests that variation in protein coding genes is driving evidence for linkage.

Of the 618 protein coding genes within the linkage intervals, 14 are located within regions that achieved at least nominal significance ($p \leq 0.001$) in our previously published GWAS, 18 have been annotated as involved in an immune process in the Gene Ontology database, and 161 have been previously identified in a hair follicle gene expression experiment.

In the linkage study, when I examined evidence for association with three analytic methods, I identified 71 SNPs with statistically significant association, 40 of which fell within a protein coding transcript, implicating a total of 26 genes. I next searched for nominal but consistent evidence for association by integrating the top1% most significant SNPs for each of the three methods, I identified 39 genes that are implicated by more than one association statistic, some of which additionally harbor one of the statistically significant SNPs. Therefore, this study identifies a total of 47 genes that contain SNPs with evidence for association within our cohort of AA families.

I next conducted follow-up to study to our initial GWAS, by expanding the size of our cohort with an additional 800 cases, such that the study contained a total of 1801 cases and 3274 controls for which I had 443,349 typed SNPs. While our initial GWAS identified eight

regions of the genome with statistically significant association, only seven remained statistically significant in this study. A region on chromosome 12q13.2 fell below the threshold for significance ($p<5x10-7$). Importantly, the increase in sample size allowed me to detect an additional statistically significant locus at chromosome 16p13.13.

Finally, I investigated whether the genetic architecture for mild AA is different from severe AA, which is characterized by total loss of scalp or scalp and body hair. I conducted a case only analysis and identified six SNPs whose frequencies were increased in severe cases relative to mild cases. All six SNPs reside in the HLA class II region. These results support previous studies that have observed similar findings. [33,34]

Implications of Findings

Six of the genes implicated by association analyses in the AA family cohort are located with linkage disequilibrium blocks that achieved nominal significance in our GWAS ($p<0.001$): AHI1, KN motif and ankyrin repeat domains 1 (KANK1); eyes shut homolog (EYS); GLIS family zinc finger 3 (GLIS3), KIAA1217, and sarcoglycan, zeta (SGCZ). GLIS3 is a particularly interesting candidate gene. Rare mutations in this loci have been implicated in neonatal diabetes,[35] while common variants confer risk to type 1 diabletes.[36] Our GWAS in AA identified several loci that increase risk for both type 1 diabetes and AA.[12,37]

Also of interest, a subset of associated genes maps to pathways that are also implicated by GWAS genes. For example, our GWAS identified a statistically significant association with a SNP in peroxiredoxin 5 (PRDX5), which has a well-established role in response to oxidative stress. Two additional genes that achieved nominal significance in the GWAS are also involved in the same physiological process, MICB and PARK2. Association tests in our family cohort implicate pantetheinase (VNN1) and methionine sulfoxide reductase A isoform a (MSRA), both

of which are annotated as oxidative stress response genes in Gene Ontology (http://www.geneontology.org/).

The GWAS that I conducted in a cohort of unrelated individuals identified an additional associated locus, at 16p13.13, which contains several interesting candidate genes, including CLEC16A, DEXI, and SOCS1, among others. This is the first time that this locus has been implicated for AA in a GWAS. However, a candidate gene study published earlier this year tested a SNP at this locus that was nominally significant in our GWAS locus and found it to be significantly associated in an independent cohort of cases and controls. Furthermore, statistically significant association at this locus has been identified with GWAS for a number of other autoimmune diseases, including type 1 diabetes, celiac disease, Crohn's disease, multiple sclerosis, ulcerative colitis and primary biliary cirrhosis (www.genome.gov/gwastudies).

My investigation into a genetic basis for disease severity only identified six SNPs, all within the HLA region. Given the small size of my sample, which contains 1194 mild cases and 604 severe cases, it is possible both that additional loci contribute to differences in disease severity, but their effects are too small to be detected here.

Future research

The studies conducted here contribute evidence for the involvement of several additional loci that increase risk for AA. My analyses in a family cohort suggest that there are rare variants contributing to disease etiology. Recent studies have shown that whole exome sequencing in families is a powerful emerging technique to identify variants that underlie linkage evidence, both for Mendelian diseases[38] and common chronic diseases.[39] My studies presented here provide a way to prioritize variants identified in a whole exome sequencing study. Therefore, the next logical step would be to conduct such a study in our family cohort. With regard to GWAS, the evidence that has emerged from GWAS in other autoimmune diseases suggests that

increasing the sample size will identify additional risk loci. However, in AA, the major obstacle in leveraging GWAS to the extent that other autoimmune diseases have is the number of cases that have been ascertained for genetic studies. A large international collaboration, modeled after consortia established for other diseases such as rheumatoid arthritis, type 1 diabetes, psoriasis, and inflammatory bowel disease, is urgently needed. Both of these endeavors would substantially increase our understanding of AA etiology and open up novel avenues to explore for therapeutic interventions.

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